

From the department of Women's and Children's Health  
Karolinska Institutet, Stockholm, Sweden

# **INCREASING UPTAKE OF LONG-ACTING REVERSIBLE CONTRACEPTION—LARC**

Niklas Envall



**Karolinska  
Institutet**

Stockholm 2019

All previously published papers were reproduced with permission from the publisher.

Cover illustrated by Benjamin Widén.

Published by Karolinska Institutet.

Printed by Eprint AB 2019

© Niklas Envall, 2019

ISBN 978-91-7831-607-6

# Increasing uptake of long-acting reversible contraception—LARC

## THESIS FOR DOCTORAL DEGREE (Ph.D.)

By

**Niklas Envall**

Public defense: Friday 6<sup>th</sup> of December, 2019, at 9 am, Clarence Craaford (A4:05), NKS Karolinska University Hospital, Solna.

*Principal Supervisor:*

Associate Professor Helena Kopp Kallner  
Karolinska Institutet  
Department of Women's and Children's Health  
Division of Obstetrics and Gynecology  
Department of Clinical Sciences at Danderyd  
Hospital

*Co-supervisor(s):*

Professor Kristina Gemzell Danielsson  
Karolinska Institutet  
Department of Women's and Children's Health  
Division of Obstetrics and Gynecology

*Mentor:*

Ewa Andersson  
Karolinska Institutet  
Department of Women's and Children's Health  
Division of Reproductive Health

*Opponent:*

Associate Professor David K. Turok  
University of Utah School of Medicine  
Department of Obstetrics and Gynecology  
Division of family planning.

*Examination Board:*

Professor emerita Eva Nissen  
Karolinska Institutet  
Department of Women's and Children's Health  
Division of Reproductive Health

Professor emerita Viveca Odling  
Uppsala University

Professor emerita Ellika Andolf  
Karolinska Institutet  
Department of Clinical Science at Danderyd  
Hospital  
Division of Obstetrics and Gynecology



## **PREFACE**

The Swedish model for contraceptive counselling is well developed with easy access from different clinical settings and extensive subsidies for young women. Sweden is a high income country and educational levels among citizens is normally high or at least moderate. Despite this, many Swedish women have an unmet need for contraception or rely on user dependent contraceptive methods resulting in high rates of unintended pregnancies and abortions. What are the underlying reasons to this “failure” from a structural point of view? Can something be done to increase knowledge about contraceptive methods among healthcare providers and women. What adjustments need to be undertaken to better meet the needs of women with regard to contraceptive use? How do we reach women with low levels of education?

The urge to find answers to these questions is the basis for the research in this thesis.

In a world where women need contraception to control for mistimed or unwanted pregnancies for a long period of time, we need to provide evidence-based contraceptive counselling.

There is evidence “out there” that could improve the quality of care and enhance women’s ability to make an informed decision about contraceptive use. In this thesis, the research questions spring from this evidence and aims to evaluate methods to achieve better sexual and reproductive health and respect the fundamental human rights of women.



## ABSTRACT

**BACKGROUND** Unintended pregnancies are an inexhaustible source to life-changing decisions and events for individuals and result in enormous costs for societies having to deal with maternal health services, deliveries, hospital care and abortions. Unmet need of contraception is a contributing factor to unintended pregnancies. Women who rely on user-dependent contraceptive methods experience higher failure rates. Increasing uptake of LARCs has proven to reduce unintended pregnancies and abortions, especially among young women. Several opportunities to counsel women about the most effective contraceptive methods are not accurately seized, such as when in need of emergency contraception, during regular contraceptive counselling and after induced abortion. Swedish women have the highest number of induced abortions among countries with robust statistics, and Sweden has the highest number of teenage abortions among Nordic countries. Improving access to fact-based knowledge during contraceptive counselling, and by finding effective methods for pain management with intrauterine device insertion could increase uptake of the most effective contraceptive methods—long-acting reversible contraception.

**AIM** This thesis includes original research within three subfields that all represent opportunities for provision of effective contraception. The thesis aims to find pathways to increase uptake of LARC by interventions used to improve the quality of care from both a healthcare provider's and a patient's perspective.

**METHODS** **Study I** was an observational cohort study conducted at one reproductive health clinic in Stockholm, Sweden. This study aimed to compare use of an effective contraceptive method following copper-intrauterine device insertion for emergency contraception or use of an emergency contraceptive pill consisting of ulipristal-acetate. **Study II** was a double-blinded, randomized, placebo-controlled trial conducted at one youth clinic and one reproductive health clinic in Stockholm. The aim was to investigate pain reduction with intrauterine device insertion among nulliparous women randomized to intrauterine instillation of either 1% mepivacaine (intervention) or 9% sodium-chloride (placebo/control). **Study III** was a cluster randomized trial conducted at abortion clinics, youth clinics and maternal health clinics (n=28) in Stockholm. The aim was to compare uptake of contraceptive methods, more specifically long-acting reversible contraceptive methods, between women receiving structured contraceptive counselling (intervention) or standard contraceptive counselling (control) (paper III). Satisfaction with the intervention was evaluated from a healthcare

provider's and receiver's perspective (paper IV) to gather information on feasibility and implementability.

**FINDINGS** More women opting for a Copper-intrauterine device for emergency contraception were using effective contraception at follow-up compared to women opting for an emergency contraceptive pill of ulipristal acetate. The IUD group were also less exposed to subsequent unprotected sexual intercourse, and most IUD-users would recommend the method for emergency contraception to a friend (study I). In an intention-to-treat analysis, the reduction of pain with IUD insertion by the use of intrauterine mepivacaine instillation did not reach our anticipated difference compared to placebo. In an additional per-protocol analysis, the difference in pain between intervention- and control groups was statistically significant. Women receiving mepivacaine had a more positive experience of the insertion procedure compared to women receiving placebo. The use of intrauterine instillation for pain management was well accepted by women (study II). Uptake of long-acting reversible contraception was higher among women receiving structured contraceptive counselling compared to women receiving standard contraceptive counselling. The intervention also led to higher initiation rate of long-acting reversible contraception and fewer cases of subsequent pregnancies at 3 months follow-up, compared to control (study III, paper III). The intervention received high satisfaction rates from both healthcare providers and patients. They found it to be supportive in their contraceptive counselling and choice. Healthcare providers estimated the time consumption for using the intervention outside the study to be time-neutral compared to standard contraceptive counselling (study III, paper IV).

**CONCLUSION** At the 6 months follow up, significantly more women opting for a copper-intrauterine device for emergency contraception used an effective contraceptive method. The results of this study support increased promotion and use of copper-intrauterine devices for emergency contraception (study I). Intrauterine instillation of 1% mepivacaine prior to intrauterine device insertion modestly reduces pain; however, the effect size may be clinically significant with fewer women having a "worse than expected" experience (study II). As a stand-alone intervention, structured contraceptive counselling increased uptake of LARCs independent on clinic type and might prevent subsequent unplanned pregnancies (study III, paper III). The intervention had a high provider and receiver satisfaction. The intervention package could be used in several clinical settings to improve quality in contraceptive counselling and to enhance informed decision making regarding contraceptive methods.

## LIST OF SCIENTIFIC PAPERS

- I. Envall N, Groes Kofoed N, Kopp-Kallner H.  
Use of effective contraception 6 months after emergency contraception with a copper intrauterine device or ulipristal acetate - a prospective observational cohort study.  
Acta Obstet Gynecol Scand. 2016 Aug;95(8):887-93
  
- II. Envall N, Lagercrantz HG, Sunesson J, Kopp Kallner H.  
Intrauterine mepivacaine instillation for pain relief during intrauterine device insertion in nulliparous women: a double-blind, randomized, controlled trial.  
Contraception. 2019 Jun;99(6):335-339
  
- III. Emtell Iwarsson K\*, Envall N\*, Bizjak I, Bring J, Kopp Kallner H, Gemzell Danielsson K.  
Increasing uptake of long-acting reversible contraception with structured contraceptive counselling: a cluster randomized trial (under revision).
  
- IV. Envall N, Emtell Iwarsson K, Bizjak I, Kopp Kallner H, Gemzell Danielsson K.  
Improving quality by introducing structure in Contraceptive Counselling – user satisfaction with interventions in a Multicenter Cluster Randomised Trial (under revision).

\*Shared first author

# CONTENTS

Preface.....	1
1 Introduction .....	1
2 Background.....	2
2.1 Review—choice of relevant publications .....	2
2.2 Review of research field.....	3
3 Rationale.....	13
4 Aims and objectives.....	14
4.1 Overarching aim .....	14
4.2 Objectives .....	14
5 Material and methods .....	15
5.1 Tabulated overview of studies .....	15
5.2 Research setting.....	16
5.3 Prospective Observational cohort study. study I, Paper I.....	17
5.4 Double-blind, randomized, controlled trial.....	21
5.5 Cluster randomized trial (paper III & IV).....	26
5.6 Reflection and ethical considerations .....	35
6 Results.....	38
6.1 Tabulated overview of main results.....	38
6.2 Is insertion of Cu-IUDs for emergency contraception an effective way to increase subsequent use of effective contraception? STUDY I, PAPER I.....	38
6.3 Does intrauterine instillation of mepivacaine decrease pain with IUD insertion in nulliparous women? STUDY II, PAPER II .....	40
6.4 Is structured contraceptive counselling with emphasis on method effectiveness an effective way to increase LARC uptake? STUDY III, PAPER III.....	43
6.5 How do healthcare providers and participants experience use of the intervention for structured contraceptive counselling and do they find it to be supportive in their counselling and contraceptive choice? STUDY III, PAPER IV.....	46
7 Discussion.....	50
7.1 Cu-IUDs for emergency contraception .....	50
7.2 Pain management during IUD insertion.....	51
7.3 Structured contraceptive counselling.....	52
7.4 Myths and misconceptions .....	53
7.5 Increasing access to and uptake of LARCs .....	54
7.6 Increasing use of contraceptive implants.....	55
7.7 Provider bias and conscientious objection.....	55
8 Methodological considerations .....	58
8.1 Study I, Paper I.....	58
8.2 Study II, Paper II .....	60
8.3 Study III, Paper III and IV .....	61
9 Conclusion .....	64
10 From pathways to open fields.....	65
10.1 Comprehensive sexuality education.....	65
10.2 Changes are wanted, and needed .....	65
10.3 Future research .....	66
11 Summary.....	67
12 Acknowledgements.....	69
13 References.....	71
14 Appendices .....	78

## LIST OF ABBREVIATIONS

AC	Abortion Clinic
BMI	Body Mass Index
EC	Emergency Contraception
ECP	Emergency Contraceptive Pill
CI	Confidence Interval
COC	Combined Oral Contraception
CSE	Comprehensive Sexuality Education
Cu-IUD	Copper Intrauterine Device
HCP	Healthcare Provider
ICC	Intra-class Correlation
ITT	Intention-to-treat
IUD	Intrauterine Device
IQR	Interquartile Range
LARC	Long-acting Reversible Contraception
LARCs	Long-acting Reversible Contraceptive Methods
LNG	Levonorgestrel
LNG-IUS	Levonorgestrel intrauterine system
MHC	Maternal health clinics
PI	Pearl Index
POP	Progestin Only Pill
PP	Per-protocol
RCT	Randomized Controlled Trial
SARC	Short-acting Reversible Contraception
STIs	Sexually Transmitted Infections
UPA	Ulipristal Acetate
UPSI	Unprotected sexual intercourse
YC	Youth Clinics



# 1 INTRODUCTION

Unintended pregnancies are a significant health problem resulting in human life loss and high costs for societies worldwide. Unintended pregnancies result in many adverse outcomes for women and children such as poor health, bad economy and exposure to social and psychological vulnerability (1-4). In the US, every dollar invested in helping women avoid unintended pregnancies result in a fivefold saving (5). The definition “unintended pregnancies” includes all outcomes of pregnancies of which the most common are unplanned births, miscarriages from unintended pregnancies and induced abortions (6). In a global perspective, women living in developing countries suffer the most with 43% unintended pregnancies (7), out of which approximately 40% end in abortion (6). However, the proportion of unintended pregnancies in more developed countries is estimated to be even higher than in less developed countries, 47% versus 39% (6). (6), and birth is considered unintended if it was not wanted at all or if it occurs sooner than desired (8). Worldwide, an estimated 99.1 million unintended pregnancies occur every year, out of which 56% end in abortion (8). In a global perspective, women living in developing countries suffer the most with 43% unintended pregnancies (7), out of which approximately 40% end in abortion (6). However, the proportion of unintended pregnancies in more developed countries is estimated to be even higher than in less developed countries, 47% versus 39% (6). The figures differ due to use of different mathematical models to estimate proportions of these outcomes, why a process to harmonize the methods to estimate the impact of contraceptive use on reproductive health have been initiated (9).

Unmet need for contraception is part of the explanation behind the high numbers of unintended pregnancies. Access to contraception and knowledge about them is mentioned by the International Planned Parenthood Federation in their sexual rights declaration (10). Unintended pregnancies must be prevented to reach the sustainable development goal number 3 “Good health and well-being”, that covers the reduction of maternal mortality and global access to family planning (11). Unmet need for contraception is highest in the Middle African region at around 26%. The lowest number is found in northern Europe with 7% unmet need(12). If the worldwide unmet need for contraception was fulfilled, it could reduce maternal mortality by nearly one third (13). Uptake of contraceptive methods has an enormous impact on reproductive health (14) and has been shown to lower abortion rates drastically (15). The unmet need for contraception among Swedish women has increased from 8.9% in 2013 (16) to 15.2 % in 2017 (17). This is despite access to contraceptive counselling free of charge from a variety of clinical settings such as youth clinics (YCs) and

maternal health clinics (MHCs). Also, contraceptive counselling should be offered to all women requesting abortion from an abortion clinic (AC) according to national guidelines in Sweden. The counselling is given by healthcare providers (HCPs), mainly midwives with training in contraceptive counselling and medical eligibility criteria (MEC) for contraceptive use. During contraceptive counselling, HCPs inform about available contraceptive methods; thus, the counsellor has a prominent role in the election and use of contraceptive methods.

Efficacy and effectiveness of contraception are described in Pearl Index (PI) presenting the number of pregnancies among 100 women using the method during a year. The PI for typical use (effectiveness), when under the influence of real-life circumstances, including both incorrect and inconsistent use, usually is higher than for perfect use (efficacy).

Effective contraception is commonly defined as having a typical use  $PI \leq 9$  ( $\geq 91\%$  effective), and highly-effective contraception has a typical use  $PI \leq 1$  ( $\geq 99\%$  effective)(18). All methods for long-acting reversible contraception (LARC) such as intrauterine devices (IUDs) and subdermal implants, are highly effective and have the smallest difference between typical and perfect use (14). LARCs have also been shown to be highly effective in reducing numbers of repeat abortion (19-22).

Among countries with robust statistics, Sweden has the highest abortion rate (23). Sweden also has the highest rate of teenage abortions among Nordic countries (24). One explanation could be that a large proportion of Swedish women do not use any contraception at all (17). Another possible explanation could be that Swedish HCPs use less effective counselling methods in their contraceptive counselling because they are not up to date with the latest research and recommendations. Yet, another explanation could be the arrangement of contraceptive counselling which is mainly provided during drop-in services at MHCs, resulting in quick sessions and information narrowed down to methods already known to the user.

## **2 BACKGROUND**

### **2.1 REVIEW—CHOICE OF RELEVANT PUBLICATIONS**

This review is built on the same three topics that represent the foundation of the thesis for doctoral degree; IUDs for emergency contraception (EC), pain management during IUD insertion and contraceptive counselling. Filters were used only to include articles available in English and full text. All publications made before the year 2000 were excluded. Major

parts of this review were used in my half-time report. This text is modified, and new articles have been added to fit the thesis.

The relevant outcome of the articles of interest was separate for each topic, including:

- Provision of different types of EC, pills as well as IUDs, their mechanism of action, effectiveness in preventing unintended pregnancies and subsequent use of contraception
- Methods and interventions for pain management during IUD insertion— pharmacological as well as psychological
- Contraceptive counselling strategies and how they affect uptake and subsequent use of different types of contraception

Studies with primary or secondary outcomes according to these criteria were included. A literature search was done in the Web of Science and Pubmed databases. A search log (appendices I, II and III) for each field was used to gain a clear structure of the recently published research articles and reviews. A combination of Medical Subject Headings (MeSH) in different blocks were used, and relevant articles were identified. Some supporting articles were included as appropriate, as well as relevant references from the bibliographies of articles already included.

## **2.2 REVIEW OF RESEARCH FIELD**

### **2.2.1 IUDs for Emergency Contraception**

Emergency contraception (EC) is used after unprotected sexual intercourse (UPSI) and provides a second chance to avoid unintended pregnancy for those without current contraceptive use or experiencing contraceptive failure. It is also an important method for victims of rape (25) or other kinds of reproductive coercion (26). If used correctly, EC prevents pregnancies that otherwise would have occurred (27), and EC is included on the Essential Medicines List by The World Health Organization (WHO) (28). EC used to be called “the best-kept secret of family planning”, but today bulk of publications on the subject are available, and use is widespread. Several medical regimens and methods have been used and evaluated for EC (29, 30), and the most common are:

- Yuzpe regimen: 12 hours separated intake of combined oral contraceptive pills, for instance, 100 µg ethinyl oestradiol and levonorgestrel (LNG) 0.5 mg. The first dose is taken within 72 hours from UPSI.

- LNG 1,5 mg: Single-dose pill taken as soon as possible, but within 72 hours from UPSI.
- Ulipristal acetate (UPA) 30 mg: Single-dose pill taken as soon as possible, but within 120 hours from UPSI.
- Mifepristone (MFP): Taken as low-dose < 25 mg, mid-dose 25-50 mg or high-dose > 50 mg within 120 hours from UPSI.
- Copper-IUD: Inserted within 120 hours from UPSI.

Effectiveness of EC cannot be calculated in Pearl Index since it is not to be used as an ongoing method for contraception. Different methods vary in how effectively they prevent pregnancy when used for EC. The least effective method is the Yuzpe regimen, followed by the single-dose LNG. UPA and mifepristone are superior to LNG (29, 31), but have not been internally compared in terms of effectiveness within the studies screened for this review. However, although mifepristone is well known as an agent used for inducing abortion, its use for emergency contraception is only registered in five countries, out of which China and Russia are the biggest (32). The most effective method of EC is the Cu-IUD (29).

Emergency contraceptive pills (ECP) are now available over the counter (OTC) in the majority of European countries. In Sweden, both LNG and UPA are found on the open shelves in almost all pharmacies. Although ECPs are easy to access, the assumption that access would lead to decreased numbers of unwanted pregnancies and abortion has not yet been proven (33-36). This can partly be explained by their effectiveness, with LNG preventing about 50%- and UPA about two-thirds of pregnancies that would have occurred without the use of any other contraception (27). Another explanation is that the mechanism of action of the ECPs limits the time window of efficacy. A third explanation is that women not initiating use of effective contraception after emergency contraception remains at high risk of subsequent pregnancies (31). A fourth and probably most important, explanatory factor is an underutilization of ECP. In France for instance, only 11% of women at risk of an unintended pregnancy had used any ECP during one year (37), and women do not use ECP after every episode of UPSI (36). In addition, women's awareness of EC as a contraceptive method is low. In 2017, only 0.9% of Swedish women were aware of the method (17).

LNG is a progestin that works by delaying or inhibiting ovulation. It is only effective when taken in the follicular phase of the menstrual cycle, and before the initiation of increase in luteinizing hormone (LH) (38). LNG is evidently most effective if taken within 72 h from

UPSI (29). UPA, on the other hand, is a progesterone receptor modulator that can be used to inhibit or delay ovulation after the onset of the LH rise until the LH peak. Consequently, it can be used at a later stage of the menstrual cycle and is effective up to 120 hours from UPSI (38, 39). The acceptability for hypothetical new ECPs with a mechanism of action consisting of prevention or disruption of the implantation of an early fertilized egg was high among women seeking different sexual health care settings in the UK (40). This might be a solution to expand the time window for ECP use. A majority of these women were also favourable to a “missed-period pill”, to take on the first few days delay of expected menstruation (40).

In 2011, it was found that high body mass index (BMI >30) of the user could affect the effectiveness of the ECP (41). However, subjects within the study population with a high BMI was few and so were pregnancies among these women. In contrast, the Cu-IUD is independent on the BMI of the treated woman (41). Since UPA is a more effective option than LNG, it has been recommended as the first line EC pill. Lately, a risk of incomplete delay of ovulation by UPA due to interaction with progestin-containing contraceptives has been demonstrated (42). No such interaction is possible for LNG ECP which is a progestin in itself. Therefore, recommendations for ECPs depend on the current or planned use of a hormonal contraceptive method. If a hormonal contraceptive failure occurs, the recommendation is to use an LNG containing ECP (43).

Low use of effective contraception after EC is a well-known risk for unwanted pregnancy, partly since EC-users tend to have repeated UPSIs and, partly because ovulation is delayed and the next fertile window might only be postponed. EC users who have repeated unprotected sex within the same menstrual cycle have a 2–3 folded risk of pregnancy compared to women who abstain from sex (44). Progressive work has been performed to increase the use of contraception after EC. One such project was conducted in the UK, where women buying their LNG ECP from a pharmacy were provided with a box of progestin-only pill (POP) without prescription to enable quick-start. This led to higher subsequent use of contraception compared to standard care that requires women to seek an HCP to receive a prescription (45). This is promising, although the follow up was only 6–8 weeks after EC.

The Cu-IUD has been used as an EC method for more than 40 years (46). Guidelines recommend insertion within five days from UPSI (47, 48) but high effectiveness has been seen for insertions up to 10 days (46) and more recently even up to 14 days (49). The Cu-IUD is highly effective due to a combination of several mechanisms of action, such as

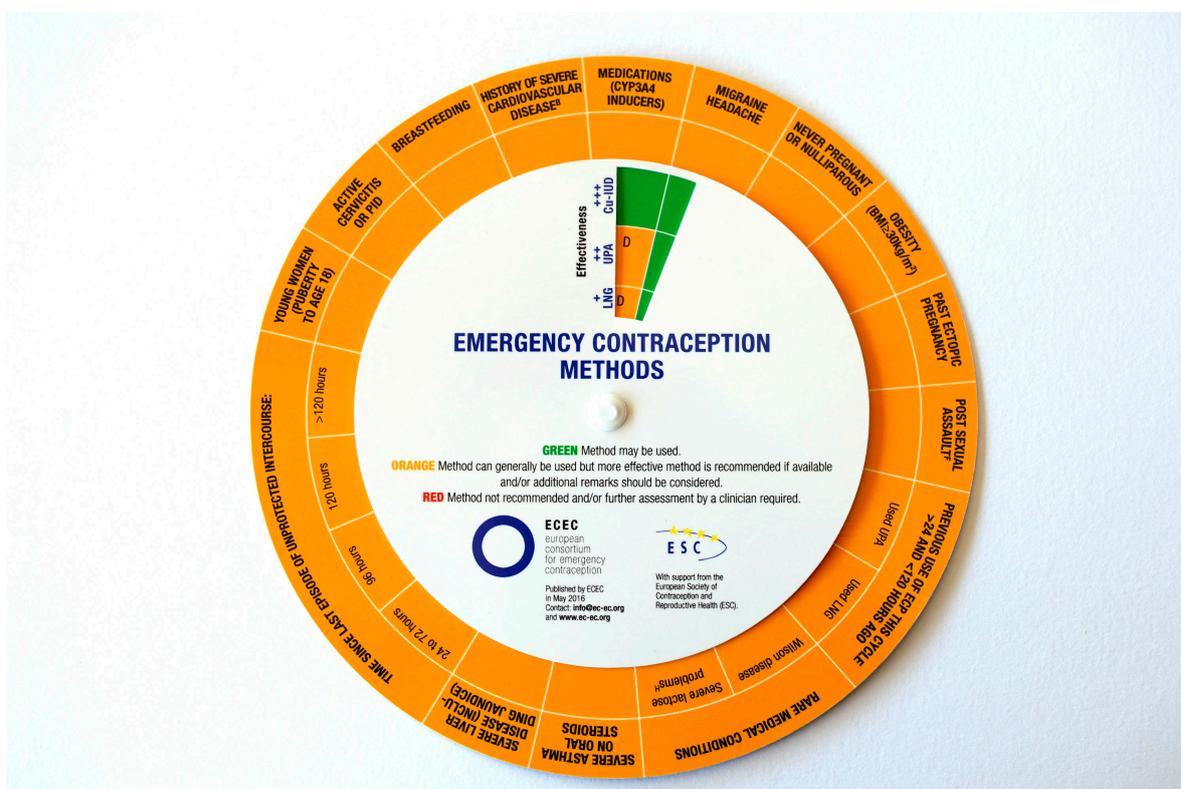
spermicidal effect, oocyte destruction, and an endometrial inflammatory reaction (38). It is superior to all the other EC methods with a failure rate of 0.09% (50, 51). In addition to the EC function, the Cu-IUD provides the user with a LARC for ongoing contraception. The risk of experiencing a pregnancy within one year from Cu-IUD insertion for EC is half compared to if LNG would have been used. To prevent one pregnancy, the number needed to treat is 18 (31).

Introduction of LNG-IUS for EC would widen the market of available methods. The user would also benefit from a LARC that comes with fewer side effects compared to the Cu-IUD. However, provision of LNG-IUS for EC alone would be unsafe since it takes one week after insertion to achieve contraceptive changes in the uterus. These facts are well known and reflected in the recommendations about one-week additional use of condoms and a pregnancy test conducted after three-four weeks if insertion is later than one week from the onset of the last menstruation (52, 53). Thus, the provision of LNG-IUS, together with an LNG ECP seems logical. This had been evaluated in a US trial. The trial concluded that there was no difference between Cu-IUD or LNG-IUS + LNG ECP for EC users in terms of continued use (54). This result contradicts assumptions about higher continued use among those opting for LNG-IUS compared to Cu-IUD for EC. The same study reported three pregnancies in the LNG-IUS + LNG ECP group compared to no pregnancies in the Cu-IUD group, a result that needs to be further evaluated since 43% of study participants reported two or more UPSIs in the last two weeks before IUD insertion (55). One of the reported pregnancies was not detected at the insertion visit, and one was caused by a missed IUD expulsion, ending up in one pregnancy during current IUD use (54). This could have happened to any user since PI for the LNG-IUS is 0.2 (14).

Despite the well-known effectiveness of Cu-IUD for EC, and that they can be safely inserted also in nulliparous women (56, 57), few service providers offer or counsel women about Cu-IUDs for EC (58-62). This is also reflected in deficient awareness of the Cu-IUD for EC among young women who rely on doctors and nurses as their most trusted source of information (63). There might be several types of provider bias (further elaborated in the discussion part of the thesis) that limit access to- and uptake of Cu-IUDs for EC. One study that could be used to exemplify this found that among future healthcare providers in Ghana, the knowledge about when to use Cu-IUDs for EC was poor, with some 55% not being able to pin-point the time-frame for insertion. Almost 40% considered the use of EC in general as morally wrong, and some 55% said EC use promotes promiscuity (64).

To decide what method is best suited for EC, a supportive algorithm can be used (65). Another useful and supportive tool for the choice of EC, produced by the European Consortium for Emergency Contraception (ECEC) is shown in figure 1.

Figure 1. ECEC Wheel



Published with permission (granted 2019-10-30) from Cristina Puig Borràs, coordinator of the European Consortium for Emergency Contraception.

This thesis includes one study exploring use of effective contraception 6 months after the use of either Cu-IUD or ECP for EC (Study I, paper I).

## 2.2.2 Pain management during IUD insertion

One of the most frequently stated reasons for not choosing an IUD is fear of pain during insertion (66-70). This has traditionally limited the use of intrauterine contraception, especially in nulliparous women. Several publications investigate pain management during IUD insertion. However, very few options have proven to be effective (69, 71), and some of the effective methods are painful to receive. Although several studies have shown that nulliparous women tolerate insertion of intrauterine contraception well (72-74), it would be valuable to find a method that is easy for clinics to provide, well accepted by the receiver and effective in reducing pain.

The most feasible type of pain relief would be some kind of pain medication in tablet form—easy to access and easy to administer at home prior to the insertion visit. A frequently recommended prophylactic prior to IUD insertion is nonsteroidal anti-inflammatory drugs, although it has not been proven to improve pain perception (68, 75). No effective reduction in pain perception with IUD insertion was achieved by the prophylactic intake of 800mg ibuprofen (76). A more recent study found oral 150 mg ketoprofen to be effective when used by parous women (77). However, the use of analgesics to ease the pain with IUD insertion might not be as important for parous women as for nulliparous women, since their pain scores are generally low even with no treatment (76).

Most IUDs are inserted by an established routine which includes insertion of specula, placement of a standard single-tooth tenaculum on the ectocervix (portio) followed by sounding the depth of the cavity. Lastly, the IUD is inserted. Pain could be experienced during all these procedures. For instance, the use of a uterine sound could be as or even more painful than the actual insertion (78). A novel method of using “the bioceptive suction cervical retractor” to apply traction on the cervix instead of using the standard one-tooth tenaculum during IUD insertion was evaluated in a pilot study. Use of the new retractor was associated (not significant) with lower pain scores at placement compared to the single-tooth tenaculum, however not significant (79). Another trial suggests that a new simplified routine, without performing bimanual palpation or uterine sounding prior to IUD insertion could affect pain perception positively since the IUD could still be safely and easily inserted even when omitting these procedures (80).

The pain experienced during insertion is often affected by anxiety and anticipated pain (71, 81). To examine whether nursing interventions have proven to be efficient in reducing pain during IUD insertion or not, a literature review of the results from eight publications was conducted (82). This review concludes that different factors, such as no previous vaginal delivery and dysmenorrhea, may predispose for a painful IUD insertion. Anxiety is also one of these factors (70). Hence, an assessment of each patient’s level of anxiety prior to insertion is important, as well as giving comprehensive information and answering questions. Distraction through conversations, presence of an assisting person in the room or by holding a warm water bottle against the stomach during the insertion could also be effective for reducing pain (82). Since there is no best practice advice for these kinds of “verbal anaesthesia” (83), they need to be evaluated further.

The fear of pain during insertion is most often built on stories about other people's experiences (84). The internet has come to be the most important source for collecting information about contraception among adolescents in Sweden (85). Searching the internet for people's experience with IUD insertion results in high numbers of hits, in which many reports high levels of pain during insertion and side effects caused by the IUD. This might lead to higher expectations of pain. Studies have found that anticipated pain is higher compared to experienced pain during insertion (70, 84). This is essential information to be given during pre-insertion counselling.

Many different interventions for application of local anaesthetics have been studied. Topical administration of Lidocaine spray to the surface of the outer part of the cervix (portio) before tenaculum placement has proven to be efficient in reducing the pain of that specific procedure, but it does not decrease pain during insertion (69). A more recent randomized controlled study found it to reduce pain, also with sounding and IUD insertion (86). However, the findings are clearly less valid since the study was not placebo-controlled. Application of 2% lidocaine gel on the portio and intra-cervically does not affect pain during insertion (87).

Intrauterine instillation has also been evaluated. One of those evaluated a new formula of 4% lidocaine gel. The gel was applied on the surface of the portio, inside the cervical canal and into the uterine cavity prior to IUD insertion. It showed significantly lower maximum pain experienced during the first 10 minutes following the insertion compared to placebo (88). However, approximately 36% of those receiving lidocaine and 52% of those receiving placebo reported the procedure to give "strong" or "very strong" discomfort. In comparison, another study evaluating pain during insertion without any pain relief reported moderate or severe pain in 33% of the study subjects (73). Thus, the clinical acceptability of this gel could be questioned. In another study, investigators infused lidocaine 2% 1.2 ml in both nulliparous and parous women using an endometrial aspirator. The difference in pain scores between intervention and placebo was 0.7 cm (3.0 vs 3.7,  $p=0.4$ ) (89). The most recently published trial was a double-blinded placebo-controlled four-arm study, in which the study participants opting for an IUD were randomized to active oral + active instillation, active oral + inactive instillation, inactive oral+active instillation, and inactive oral + inactive instillation prior to insertion. Active drugs were oral Naproxen 375 mg (1 hour prior to insertion) and lidocaine 2% 5 ml naproxen (3 minutes prior to insertion). The instillation was performed with an angiocatheter. There were no differences in VAS pain scores between any of the groups and mean pain scores varied from 3.62-2.87. Notably, women receiving active oral + active

instillation had higher pain scores (mean 3.38) than women receiving just active oral (3.09) or active instillation (2.87) (90).

This thesis includes one study that evaluates a new (at time of study start) non-invasive intervention with intrauterine instillation of mepivacaine by a hydrosonography catheter five minutes prior to insertion.

### **2.2.3 Contraceptive Counselling**

Based on the facts presented in the previous fields, I have chosen to define three main outcomes for successful contraceptive counselling:

- High uptake of highly-effective methods of contraception defined as typical use  $PI < 1$
- High continued use of method started
- High satisfaction with the chosen method

A ground-breaking study about contraceptive counselling, The Contraceptive CHOICE Project, was conducted in the St Louis region in the US and included more than 9000 women. The CHOICE model included a standardized script read to all participants to increase their knowledge about different methods. The model also included prototypes of different contraceptive methods to be used during counselling sessions. In addition to this, HCPs received training in order to increase method-specific knowledge and how to counsel according to the CHOICE protocol (91). All included participants received tiered contraceptive counselling presenting LARCs as the most effective methods. Whilst enrolled, participants were offered their contraception of choice at no cost. Removing the cost-barrier and the promotion of LARC led to a LARC uptake of 75% (92). This proves that LARC forward counselling is effective to achieve high uptake.

This type of standardized counselling is referred to as structured contraceptive counselling. In a follow-up study, to evaluate the use of the CHOICE model in real-life settings, the standardized script to achieve structured contraceptive counselling was used as a single intervention for a first group (enhanced care) of women seeking contraceptive counselling. A second group also received structured counselling, but this time from providers who had undergone contraceptive training and in addition, the costs for contraception was removed (complete choice). Women receiving complete choice had a higher uptake of LARCs and a lower pregnancy rate at 12 months follow up (93). The term structured contraceptive counselling has also been used in other trials. Structured counselling often includes audio-

visual information, presenting evidence-based information, which has been proven effective in increasing use of contraception among sexually active men (94) and continued use of contraceptive injections and pills among women (95). However, structured contraceptive counselling in settings providing all contraceptive methods free of charge does not always result in higher uptake of LARCs, which was the outcome of a study by Langston et al. (96). This used another type of structured counselling called DMT, a double-sided flipchart in a post-abortion setting. This chart includes one side for the patient and one side for the provider, to aid for contraceptive choice and contraceptive counselling (97). In a cluster randomized trial evaluating structured contraceptive counselling no increased use of LARCs could be seen among patients included from abortion clinics (98). It seems like this patient category needs an even more refined method for structured contraceptive counselling than used in those studies.

To remain effective, contraception has to be continued over time. One factor determining continuation is user satisfaction. IUDs, in particular, have a higher continuation and satisfaction rate than any other contraceptive method. The 12 months continuation rate for the Cu-IUD is just slightly lower than for LNG-IUS, 84% versus 88% (99). The Cu-IUD increases menstrual bleeding and menstrual cramping (100), and these side effects constitute the most common reasons for requesting IUD removal (101, 102). However, these side effects have been reported to decrease with time, as do method satisfaction improve (103). In a study evaluating satisfaction among nulliparous women, the statement “very happy or “happy” with their IUD was presented by 83% of the 109 women who participated in the follow-up. No statistical significance was found between LNG-IUS and Cu-IUD users (104). As this study was published, it contributed to fill a knowledge gap about continued use solely among nulliparous women, since the previous publications from CHOICE did not separate nulliparous from parous women in their findings (99). In a later article, the data from CHOICE was stratified by age groups, and the results were presented by the continuation rate for different contraceptives in each age-group. Continued use of LARCs was higher in comparison to non-LARCs in all age groups, and above 75% for all LARCs compared to the highest figure of 51% for non-LARCs (105).

The impact of LARC forward counselling in Sweden is unknown, and study findings report lower method awareness of LARCs compared to SARCs among both contraceptive users and non-users (16). In the year 2013, among women aged 16–29, more than 50% were currently using SARCs and less than 20% were LARC users (16). This is also seen in the statistics for medical prescriptions in Sweden. In 2016, 1 324 518 prescriptions of SARCs

were collected, compared to 113 986 prescriptions of LARCs (106). IUDs are the most cost-effective methods (107) and are also the most eco-friendly in terms of environmental impact (108). These arguments, together with the fact that several studies have shown that LARC promotion leads to a reduction of unintended pregnancies and repeat abortions (22, 109) should appeal to Swedish stakeholders and contraceptive users.

The third study in this thesis evaluates the effects of an intervention of structured contraceptive counselling on LARC uptake. The intervention emphasizes the effectiveness of LARCs over other contraceptive methods, and that they have the highest user satisfaction.

### **3 RATIONALE**

Emergency contraception is an important opportunity to give contraceptive counselling. Few healthcare providers actively counsel women about Cu-IUDs for EC, despite its superior effectiveness compared to ECPs. Knowledge among women and providers are low concerning the use of Cu-IUD for EC. By lowering the thresholds to insertion of Cu-IUDs, we can increase LARC use and by that decrease number of unintended pregnancies.

The barrier of pain toward IUD insertion is well known. Some effective methods exist; however, the urge for a highly effective method that is acceptable to patients and is easy to access for providers is large.

Contraceptive counselling is given to provide women with comprehensive information about available contraceptive methods. Different kinds of interventions introducing structured contraceptive counselling have been evaluated, most of them resulting in higher uptake of LARCs and lower pregnancy rates. However, within abortion clinics, interventions have failed to affect LARC uptake. The effects of structured contraceptive counselling in a high-income setting with existing contraceptive subsidies need to be evaluated, as well as satisfaction with the interventions used from an HCP's and receiver's perspective.

Increasing the use of LARCs is to date without a doubt the most effective way of reducing unintended pregnancies and hence decreasing the numbers of abortions, much likely also in a Swedish setting.

## **4 AIMS AND OBJECTIVES**

### **4.1 OVERARCHING AIM**

This thesis includes original research within three subfields that all represent opportunities for provision of effective contraception. The overall aim is to find pathways to increase uptake of LARC by interventions used to improve quality of care from both a HCP's a patient's perspective.

### **4.2 OBJECTIVES**

- To compare use of an effective method of contraception 6 months following insertion of a copper intrauterine device or intake of ulipristal acetate for emergency contraception.  
(Paper I)
- To evaluate whether intrauterine mepivacaine instillation before intrauterine device insertion decreases pain compared to placebo.  
(Paper II)
- To evaluate the effect of structured contraceptive counselling on LARC uptake and pregnancy rates in abortion clinics, maternal health clinics and youth clinics.  
(Paper III)
- To evaluate user satisfaction of healthcare providers and participants with an intervention used in a cluster randomized trial and to characterize which providers and patients found the intervention most helpful.  
(Paper IV)

## 5 MATERIAL AND METHODS

### 5.1 TABULATED OVERVIEW OF STUDIES

Table 1. Overview of study design, participants and methods

	<b>Research question</b>	<b>Design and participants</b>	<b>Data collection and outcomes</b>	<b>Data analysis</b>
<b>Study I, Paper I</b>	Is insertion of Cu-IUDs for emergency contraception an effective way to increase subsequent use of effective contraception?	Prospective observational cohort study. Patients presenting with need of emergency contraception (n=79).	Primary outcome <i>use of effective contraception</i> measured at 6 months follow up. Secondary outcomes measured at 3 and 6 months follow up.	Descriptive statistics and multivariable logistic regression. Intention to treat analysis.
<b>Study II, Paper II</b>	Does intrauterine instillation of mepivacaine decrease pain with IUD insertion in nulliparous women?	Double-blind, randomized, controlled trial. Nulliparous patients opting for an IUD (n=86).	Primary outcome <i>VAS pain scores at insertion procedure steps</i> measured immediately after each step. Secondary outcomes measured at 7–10 days, 3 months, and 6 months follow-up.	Descriptive statistics and two group comparisons. Intention to treat and per-protocol analyses.
<b>Study III, Paper III</b>	Is structured contraceptive counselling with emphasis on method specific effectivity an effective way to increase LARC uptake?	Multicenter cluster randomized trial. Clinics providing contraceptive counselling (n=28). Patients $\geq 18$ years, sexually active without a wish to conceive (n=1338).	Primary outcome <i>Choice/prescription of LARC</i> measured at first visit. Secondary outcomes measured at 3 months follow-up.	Descriptive statistics of clinics and participants. Logistic mixed models with random intercept for clinic type.
<b>Study III, Paper IV</b>	How do healthcare providers and patients experience use of the intervention for structured contraceptive counselling and do they find it to be supportive in their counselling and contraceptive choice?	Multicenter cluster randomized trial. Healthcare providers (n=62) and participants at intervention clinics (n=658).	Secondary outcome <i>User satisfaction with intervention</i> measured immediately after first visit (participants) and after completed enrolment of study participants (healthcare providers).	Descriptive statistics and two group comparisons.

## 5.2 RESEARCH SETTING

In Sweden, contraceptive counselling can be accessed in a variety of settings. Midwives provide most counselling and prescriptions in YCs and in MHCs. Gynaecologists also issue prescriptions, but that is more common in cases of discovered contraindications or health issues that need to be considered by a physician. All women requesting an abortion are by routine receiving contraceptive counselling.

A YC is a clinic for adolescents and young people between 12 and 25 years of age. They are staffed with midwives, social counsellors and are supported by consultant gynaecologists and paediatricians. The youths do not have to suffer from a medical condition or mental health issues to seek care from a YC. The YCs are open on a year-round basis with no exception for school holidays. Examples of services provided by the YCs are sexual- and reproductive health counselling including contraception, EC, pregnancy testing, STI testing and other health issues such as stress, anxiety, depression and eating disorders. Most contraceptive counselling is provided during scheduled appointments, but drop-in services are also available. The YCs are operating on behalf of the municipality or the region (former county council).

MHCs are staffed with midwives with the assignment to monitor pregnancy and taking care of pregnant women's health. The assignment also includes screening for cervical cancer and contraceptive counselling. The services include scheduled appointments for contraceptive counselling but most clinics, at least in Stockholm region, meet most of their patients during drop-in services. These services are, unfortunately, often limited by time and midwives are meeting with vast numbers of patients during each drop-in session. The MHCs in Stockholm is operating on behalf of the region.

Midwives at Swedish YCs and MHCs play an essential role in providing effective contraception and are most often skilled inserters of IUDs and contraceptive implants. In Sweden, abortion is conducted upon the request of the woman up to gestational week 18. Between week 18-22 a permission has to be granted from the National Board of Health and Welfare (Socialstyrelsen). The ACs are staffed with midwives, medical doctors and nurses. Some clinics are run independently by midwives with special training. Abortions are generally made early in pregnancy, with 57% performed before week 7 and 84% before week 9. In 2018, 93% of abortions were medical. Contraceptive counselling is included in the abortion care, with midwives providing most of the counselling.

**Study I and II** were conducted at a sexual health clinic in Stockholm, the RFSU Clinic run by the Swedish Association for Sexuality Education on behalf of the region. Annually the clinics meet with 12 000 patients during 19 000 healthcare meetings. The most common reason for visiting the clinic is STI testing, but a large number of patients also seek the clinic to receive contraceptive counselling. The clinic is open for patients with a lower age limit of 18. No underaged patients are rejected care, but they are advised to seek care from a YC if in need of future reproductive health services. The clinic is located in the city centre of Stockholm, and visitors come from all over the country, but most commonly they are residents living in the Stockholm region. This results in a variation of visitors with regard to migrant and educational status. The clinic offers both drop-in services and scheduled appointments.

**Study II** was also conducted at a YC in Upplands Väsby. This YC is located in the centre of Upplands Väsby incorporated in a shopping mall. The location is suitable for youths since there is no apparent reason for visiting a shopping mall. Annually, midwives within the YC see approximately 1200-1500 patients. This clinic serves a mixed group of patient with regard to migrant status. Most contraceptive counselling is provided during scheduled appointments.

**Study III** was conducted at ACs, YCs and MHCs in the Stockholm region. Recruitment processes are explained in the following section of the thesis.

## **5.3 PROSPECTIVE OBSERVATIONAL COHORT STUDY. STUDY I, PAPER I**

### **5.3.1 Study design and hypothesis**

**Study I** was a prospective observational cohort study. The hypothesis was that patients opting for a Cu-IUD would use effective contraception at 6 months to a higher extent compared to patients opting for UPA (primary outcome). In addition, we hypothesized that participants in the Cu-IUD group would have had less unprotected sexual intercourses and fewer pregnancies.

### 5.3.2 Population, groups and outcomes

Table 2. Summary of study population, groups and outcomes

<b>Population</b>	Patients presenting with need of emergency contraception
<b>Group 1</b>	Cu-IUD for emergency contraception
<b>Group 2</b>	UPA for emergency contraception
<b>Primary outcome</b>	Use of an effective contraceptive method at 6 months follow up
<b>Secondary outcomes</b>	Adverse events, use of an effective contraceptive method at 3 months follow up, method acceptability, reason for choosing either Cu-IUD or UPA for EC, subsequent unprotected sexual intercourse, pregnancies

### 5.3.3 Details on primary and secondary outcomes

The primary outcome *use of effective contraception* was selected a priori and was defined as methods having a typical use PI of less than nine. We included IUDs (hormone-releasing and copper), implant, COC, vaginal ring, patch, POP and injections in our definition of effective contraception according to the most used report from contraceptive failure in the United States (14). Use of effective contraception at 6 months follow-up was set as the primary outcome since we hypothesized that the low effectiveness of ECP was due to the fact that few women initiate effective contraception after the use of ECP. In addition, we hypothesized that most IUD users would remain with their device for at least 3 months to give themselves a chance to evaluate the method fully. Use at 3 months as a secondary outcome was an important endpoint since the loss to follow-up usually increases the longer the time to follow-up.

*Adverse events* during IUD insertions and use of ECPs are rare. Vasovagal reactions or syncope might happen during IUD insertion, as well as IUD dislocation, uterine perforation and insertion failure (110, 111). We measured vasovagal reactions and/or syncope and insertion failures at first visit. During follow-up, other complications related to the IUD were reported, such as heavy bleeding and excessive pain. Any adverse events were recorded in the patient's medical record and managed by the provider according to clinical practice. Any other side effects related to the method used for EC, such as tender breasts, nausea, irregular bleeding and headache, were also reported.

We measured the *acceptability* of Cu-IUD for EC at first visit by asking two questions; would you choose Cu-IUD if you were to use EC again and would you recommend Cu-IUD for EC to a friend? Another measure of acceptability was insertion experience described as easier than expected, as expected or worse than expected. At follow-up participants opting for Cu-IUDs were asked whether they would opt for another IUD taking the experience of

the first period of use into account, and if they would recommend and already had recommended IUD insertion to a friend. *Continued use of Cu-IUD* and *reasons for IUD removals* were recorded at the follow-up to get a broader idea of user satisfaction with the chosen method and why patients chose not to remain with their IUD.

*Reasons for choosing either Cu-IUD or UPA for EC* was recorded at the first visit, for instance, “fear of pain with IUD insertion”, and grouped after similarity to calculate proportions. *Subsequent unprotected sexual intercourse* and *Pregnancies* were self-reported and measured at both 3 and 6 months follow-up.

#### **5.3.4 Eligibility criteria**

All patients were screened for the need of EC by using standardized questions asked to all clinic visitors; do you use any contraception, and when did you last have unprotected sex? All patients who reported unprotected sexual intercourse within the last 5 days were assessed for eligibility. Patients  $\geq 18$  years and with an ability to use both UPA and the Cu-IUD were included. We excluded patients with a known uterine anomaly, cervical stenosis, previous conization, signs of ongoing genital infection, and known bleeding disorder.

#### **5.3.5 Enrolment and obtaining informed consent**

Eligible patients received verbal and written study information, including study purpose and could ask questions prior to inclusion. Women who chose not to participate received method according to choice as per clinical practice. Study information was available in Swedish. All patients opting for a Cu-IUD received a gynaecological exam to screen for ongoing genital infection (e.g. abnormal vaginal discharge or pronounced inflammatory reaction). If the provider found an ongoing infection, the patient would have been excluded and replaced with another study participant. However, no such cases were reported. All patients accepting participation signed informed consent.

All participants received structured counselling about EC with emphasis on the effectiveness of Cu-IUD over UPA. Group allocation was according to method preference.

Patients opting for UPA were given a single dose 30mg oral UPA (ellaOne®) free of charge, to be taken immediately. They were informed about known side effects and that another pill was recommended if vomiting occurred within three hours from intake. The importance of initiating an effective method of contraception after the back-up period was highlighted (42), and they received contraceptive counselling and prescription of any selected contraceptive method.

Prior to insertion, patients opting for a Cu-IUD received information about insertion procedure, known risks and side effects and about the importance to seek care if experiencing heavy bleeding, excessive pain and/or signs of infection. Patients were also informed to keep their Cu-IUD at least until their next menstrual period. They were offered oral pain medication (1g paracetamol and 400 mg ibuprofen) according to clinical practice and had the device (Nova-T 380<sup>®</sup>) inserted at the first visit according to protocol. Patients were free to leave the facility once they felt ready.

### **5.3.6 Clinical assessments**

#### **First visit**

- Reproductive and gynecological history including last menstrual period, ongoing bleeding, gravidity, parity, and previous medical and/or surgical abortions
- Pregnancy test
- Standard protocol for IUD insertions including bimanual palpation, gynecological exam and measurement of uterine size (no ultrasound).
- Vasovagal reactions or syncope

#### **Follow-up**

- Complications and side effects of chosen method

In accordance with the study site protocol for EC, all participants were offered a follow-up visit after three weeks to rule out pregnancy and to allow for participants to ask questions and receive further contraceptive counselling if needed. No data collection for the study outcomes were collected at this visit, nor were any IUD removals or prescription of other contraceptive methods recorded.

### **5.3.7 Follow up and measurement of outcomes**

Follow up data were collected through telephone interviews. The primary outcome was measured at 6 months follow-up. Secondary outcomes were measured at the first visit and 3 and 6 months follow-up. Follow-up data were mainly collected by a research team member who had not been involved in any previous study-related activities in a strive to reduce social-desirability bias caused by the patient-provider relationship (112). To collect data within the given time frame for follow-up and to decrease loss to follow-up, some participants were contacted by one of the investigator midwives who had provided the EC.

### **5.3.8 Sample size**

We hypothesized a difference in the use of effective contraception 6 months after use of emergency contraception, with higher proportions among participants opting for a Cu-IUD than participants opting for UPA. We expected the use to be 90% in the Cu-IUD group and 30% in the UPA group. The sample size was calculated to show the 30% anticipated difference between groups with a power of 80% and an alpha of 0.05, resulting in 32 participants in each study arm. To allow for 20% loss to follow up, we aimed at recruiting a total of 39–40 in each group.

### **5.3.9 Data management**

All participants received a study-id. This number was stored together with the participant's full name, personal identity number (i.e. social security number) on a specific separated list that served as a code key. All data from first visit and follow-ups were collected on paper CRFs and manually transferred into a computer-based spreadsheet prior to analyses.

### **5.3.10 Analyses**

Participants in both groups received their preferred method for EC at the first visit. We did not collect any data on repeated use of EC due to vomiting within three hours, and no such cases were reported at follow-up. Hence analysis was made according to intention-to-treat (ITT). A two-sided p-value of  $<0.05$  was considered statistically significant.

Descriptive statistics with chi-square tests and Fisher's exact tests were used to compare baseline characteristics and categorical outcomes between groups. Mann-Whitney U-tests were used for comparison of non-normally distributed variables such as age and parity. Variables that might affect primary and secondary outcomes were analyzed in a binary logistic regression. We included and dichotomized age ( $\geq 25$  or  $< 25$  years), gravidity (yes/no), parity (yes/no) and current use of contraception (yes/no). All data analyses were performed in SPSS version 23.

## **5.4 DOUBLE-BLIND, RANDOMIZED, CONTROLLED TRIAL**

### **5.4.1 Study design and hypothesis**

Study II was a double-blind, randomized, controlled trial. We hypothesized that intrauterine mepivacaine instillation would numb the uterine and cervical lining and reduce pain with IUD insertion. We also hypothesized that mepivacaine would provide a more effective pain relief than saline solution (NaCl).

## 5.4.2 Population, intervention, control and outcomes

Table 3. Summary of study population, intervention, control and outcomes

Population	Nulliparous patients opting for an intrauterine device
Intervention	Intrauterine instillation of mepivacaine 5 minutes prior to insertion
Control/Placebo	Intrauterine instillation of NaCl 5 minutes prior to insertion
Primary outcome	Difference in VAS score with IUD insertion between intervention and placebo
Secondary outcomes	Adverse events, VAS with intrauterine instillation, all insertion procedure steps and VAS when leaving the clinic, method acceptability, continued use of IUD

## 5.4.3 Details on primary and secondary outcomes

Primary outcome *VAS score with IUD-insertion* was measured using a paper-printed 10-cm visual analogue scale, marked with no pain at the 0-cm anchor point and worst pain imaginable at the 10-cm anchor point. The same procedure was used for measuring the VAS scores of the secondary outcomes. Patients generally left the clinic within 10 minutes after insertion, but no exact time-frame from insertion to this VAS measurement was calculated.

*Adverse events* and any other complications and/or side effects were measured and recorded in the same manner as presented in the previous study. One important difference was that patients with any such experience were encouraged to seek the healthcare facility that performed the IUD insertion since the follow up was also blinded to the interviewer.

*Method acceptability* was measured with four questions on intrauterine instillation and IUD insertion: I would opt for another IUD if I knew it would be like this (yes/no); I would recommend others to use IUD after this IUD insertion (yes/no); I would recommend this method for pain relief to others (yes/no); In comparison to my expectations, this IUD insertion was (easier than expected/as expected/worse than expected).

To get a broader idea of user satisfaction, *Continued use of Cu-IUD*, as well as *reasons for IUD removals*, were measured at follow-up. In addition, patients were asked if they were pleased with their IUD (yes/no/somewhat pleased).

## 5.4.4 Eligibility criteria

All patients opting for an IUD for pregnancy prevention were screened for eligibility. Eligible patients were 18 years or older and nulliparous. Exclusion criteria were previous conization,

known cervical stenosis, signs of ongoing genital infection, known uterine abnormality, bleeding disorder or any local anesthetic contraindication.

#### **5.4.5 Randomization and masking**

A study coordinator not involved in any other participant-related work prepared opaque, sealed and numbered envelopes. A computer-generated randomization list with random permuted blocks of 6 to 10 from [www.randomization.com](http://www.randomization.com) was used. Eligible patients were randomly assigned to intervention (mepivacaine 1% 10 ml) or control group (NaCl 0.9% 10 ml) in a 1:1 allocation ratio by consecutive opening of envelopes containing the allocation code unique to each study site. The randomization and preparation of study drug were performed without the presence of the study investigator or the participant, hence double-blinded. Blinded research personnel outside the clinics performed the follow-up.

#### **5.4.6 Enrolment and obtaining informed consent**

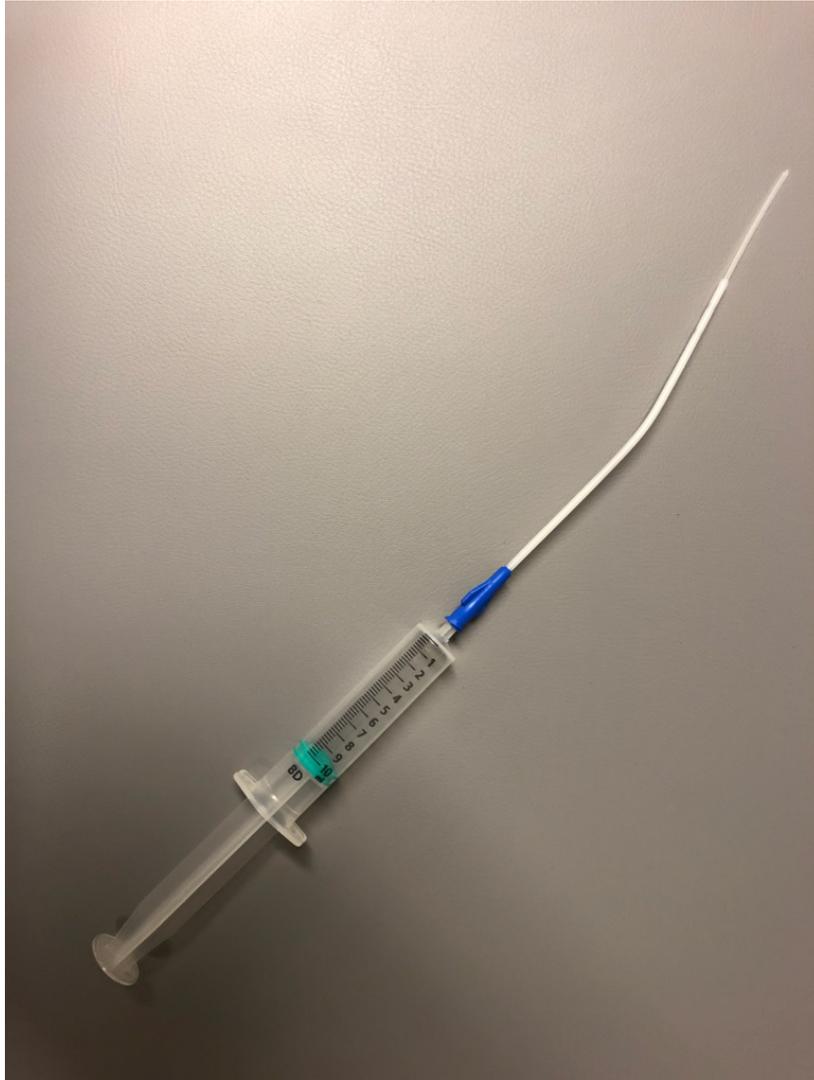
Eligible patients received verbal and written study information, including study purpose, IUD type according to preference (not free of charge) and alternatives to participation (no intrauterine instillation). All patients could ask questions prior to inclusion. Study information was available in Swedish. All patients received a gynecological exam to screen for ongoing genital infection (e.g. abnormal vaginal discharge or pronounced inflammatory reaction). If the provider found an ongoing infection, the patient would have been excluded and replaced with another study participant. However, no such cases were reported. All patients accepting participation signed informed consent.

#### **5.4.7 Details on intervention and control**

Participants were informed about the study procedure, known risks and side effects and about the importance to seek care if experiencing heavy bleeding, excessive pain and/or signs of infection prior to intrauterine instillation and IUD insertion. Participants received an intrauterine instillation of the assigned study treatment (mepivacaine or NaCl) with a sterile hydrosonography catheter (figure 1). This catheter is thin (1.6 mm) and flexible without a balloon tip. After instillation, participants remained in lithotomy position for 5 min to allow for the fluid to act on the uterine and cervical lining. Then the IUD insertion was performed according to a standardized protocol to remove any disparities in insertion technique.

Patients were free to leave the facility once they felt ready.

Figure 1. Hydrosonography catheter used for intrauterine instillation



#### 5.4.8 Clinical assessments

##### First visit

- Reproductive history including gravidity, parity, and previous medical and/or surgical abortions
- Gynecological history including last menstrual period, ongoing bleeding, numbers of days with “fresh blood” during normal period, pain score on a 10 point VAS for normal period cramping, intake of pain medications during normal period
- Pregnancy test
- Standard protocol for IUD-insertions including bimanual palpation, insertion of speculum, gynecological exam, tenaculum placement and measurement of uterine size (no ultrasound) followed by IUD placement
- Vasovagal reactions or syncope

### **Follow-up**

- Current pain related to IUD or period on a 10 point numerical scale.
- Ongoing bleeding
- Complications and side effects of chosen method

#### **5.4.9 Follow up and measurement of outcomes**

Follow up data were collected through telephone interviews. Primary outcome was measured at first visit. Follow-ups to collect secondary outcomes were performed at 7-10 days, 3 and 6 months after the insertion. Follow-up data were collected by a research team member who had not been involved in any previous study related activities and the participant's study allocation was blinded.

#### **5.4.10 Sample size**

In a previous study assessing IUD insertion pain after pretreatment with misoprostol, the mean pain score in the control group was  $6.5 \pm 1.8$  on a 10-cm VAS (113). We hypothesized a 20% decrease in VAS pain score in our intervention group, equivalent to an absolute decrease of 1.3 cm, consistent with previous studies on clinically relevant reduction of VAS for acute pain (114, 115). To demonstrate this difference with a power of 90% at an alpha of 0.05, each study arm needed 38 participants. To account for an expected loss to follow-up of 10% to 15%, we aimed to enrol 86 participants.

#### **5.4.11 Data management**

All participants received a study-id. This number was stored together with the participant's full name, personal identity number (i.e. social security number) on a specific separated list that served as a code key. All data from first visit and follow-ups were collected on paper CRFs, and manually transferred into a computer based spreadsheet prior to analyses.

#### **5.4.12 Analyses**

Participants' study allocation remained blinded until data analysis. Type of IUD was according to participants' preference, and IUD types inserted in the study were two levonorgestrel (LNG) intrauterine system (IUS) products containing 52 mg (Mirena<sup>®</sup>) or 13.5 mg (Jaydess<sup>®</sup>) and one copper IUD (Nova-T 380<sup>®</sup>).

To perform an adequate instillation, the hydrosonography catheter had to be inserted at least 4 cm to reach the internal cervical os. One of the study investigators excluded one participant in

each study arm from further participation (no data collection) since this depth was not reached (both received their IUDs). After consulting the principle investigator, this management was changed, and all other instillations were performed as intended, and participants were included in an ITT analysis. An additional per-protocol (PP) analysis for the primary outcome was performed in which three inadvertently enrolled underaged women were excluded. A two-sided p-value of  $<0.05$  was considered statistically significant.

Inferential statistics with independent sample t-test was used to compare baseline characteristics between groups. Mann-Whitney U-tests were used for comparison of non-normally distributed variables such as age and period cramping as well as VAS scores. Variables that might affect primary outcomes were analyzed in a multivariable linear regression that showed no differences and thus omitted from the article (paper II). Chi-square tests and Fisher's exact tests were used as appropriate for categorical variables. All data analyses were performed in SPSS version 24.0.

## **5.5 CLUSTER RANDOMIZED TRIAL (PAPER III & IV)**

### **5.5.1 Study design and hypotheses**

Study III was a cluster randomized trial conducted in abortion clinics (AC), youth clinics (YC) and maternal health clinics (MHC) in the Stockholm region. We hypothesized that more participants receiving contraceptive counselling according to a specific structure (intervention) would choose/receive prescriptions of LARCs compared to participants receiving standard contraceptive counselling (control). We also hypothesized that more participants in the intervention arm would have initiated LARC use and would have a lower pregnancy rate at follow-up than participants in the control arm (paper III). To evaluate user satisfaction with the intervention, participants from intervention clinics were asked specific questions and healthcare providers from intervention clinics were invited to complete a questionnaire (paper IV).

## 5.5.2 Population, intervention, control and outcomes

Table 4. Summary of study population, intervention, control and outcomes

Population	Patients receiving contraceptive counselling (paper III & IV) Healthcare providers giving structured contraceptive counselling (paper IV)
Intervention	Structured contraceptive counselling comprising: <ul style="list-style-type: none"> <li>- Educational video</li> <li>- 4 key-questions</li> <li>- Effectiveness chart of available contraceptive methods</li> <li>- Box of contraceptive models</li> </ul>
Control	Standard contraceptive counselling
<b>Primary outcome</b>	LARC uptake (paper III).
Secondary outcomes	LARC initiation, pregnancies (paper III). User satisfaction with intervention (paper IV).

## 5.5.3 Details on primary and secondary outcomes

The primary outcome was the proportion of participants with uptake of LARCs. Uptake included choice and prescriptions where applicable. The outcome selection was made a priori to measure the intervention effect on the patients' intention to use LARCs at the first visit. This information was collected from questionnaires completed by the healthcare provider.

*LARC initiation* was defined as having had an IUD or contraceptive implant inserted within the follow-up period. Data were self-reported, and no imputation was used to account for missing data due to loss to follow-up or withdrawal.

*Pregnancy* data (yes/no) and how the participant chose to deal with the pregnancy (preparing to give birth/planning an abortion/had an abortion/had a miscarriage/any other outcome/undecided) was also self-reported. However, for participants with missing data due to loss to follow-up, electronic records were scrutinized for any visits to obstetrics and gynaecology units or maternal health clinics in order to rule out current pregnancy or abortion. This outcome was selected to assess if the intervention affected contraceptive uptake and resulted in fewer pregnancies. *User satisfaction with the intervention* was collected from participants at the first visit.

Healthcare providers received and completed a questionnaire after study enrolment had stopped. Participants and providers evaluated the educational video, the effectiveness chart and the box of contraceptive models. Also, providers evaluated the use of key-questions and rated their satisfaction with the intervention as a whole. Ratings of the different intervention parts was: very good, good, no opinion, poor, very poor. Participants and providers were asked if they found the intervention parts to be *supporting their*

*contraceptive choice/counselling* (yes/no). Providers also assessed *time consumption* to perform their counselling according to the intervention. This was measured on a 30-minute VAS marked with -15 minutes at the left anchor point and +15 minutes at the right anchor point. Providers were also asked if they considered the intervention to affect the patients' contraceptive choice and whether they would like to use the intervention in their routine counselling after completion of the study.

#### **5.5.4 Eligibility criteria**

There were no specific inclusion or exclusion criteria for clinics, such as number of visitors per year, migrants within the catchment area or baseline prescription of LARC. All abortion clinics, youth clinics and maternal health clinics providing contraceptive counselling within the Stockholm region were eligible. The only exclusion criteria was ongoing competing study participation.

Eligible patients were  $\geq 18$  years, sexually active or planning to be sexually active within 6 months and had pregnancy prevention as primary purpose of their contraception. Patients were excluded if they had undergone sterilization or had a sterilized partner.

#### **5.5.5 Randomization and masking**

Randomization was stratified by clinic type. For youth- and maternal health clinics randomization was also stratified by proportion of migrants within their catchment area. Randomisation was performed by an independent statistician using the statistical software R (version 3.4.0). Clinics were allocated to intervention or control at a ratio of 1:1 within each clinic type. Randomization masking of clinic allocation was not possible since healthcare providers at intervention clinics received study specific training.

#### **5.5.6 Training of healthcare providers**

Before study initiation, in addition to a start-up meeting at all study sites, HCPs at intervention clinics were invited to participate in a 3-hour training session. Participating HCPs received updates from previous research within the field of contraception and contraceptive counselling with emphasis on method-specific effectiveness and effectiveness. HCPs were also introduced to the study procedure, the four different parts of the intervention, and how they were meant to be used in the study-specific structured contraceptive counselling. The research team also offered training in LARC insertion skills. However, there was no interest in LARC insertion training among HCPs thus, no such training sessions took place.

### **5.5.7 Enrolment and obtaining informed consent**

An open invitation was sent to abortion clinics, youth clinics and maternal health clinics in the Stockholm region. Clinics were informed about the study design and that an intervention of structured contraceptive counselling was to be evaluated with regards to participants' uptake of contraceptive methods (paper III) as well as user satisfaction from both an HCP's and patient's perspective (paper IV). Clinics were offered a meeting with a member of the research team to receive more details about the trial and to be able to assess what participation would mean to the healthcare providers who would include patients in the study. No further details of the intervention or study outcomes were discussed in order to minimize spillover to clinics which would eventually be randomized to control, except the fact that clinics randomized to intervention would receive study-specific training. A total of 33 clinics accepted participation.

Patients receiving contraceptive counselling from participating clinics were informed about the study. They were either addressed by a clinic assistant, the healthcare provider or a member of the research team. Prior to receiving full study information, patients were screened for eligibility. Written information was available in Swedish and English. In case of insufficient language skills, study information was translated by a professional interpreter, and these participants were informed to complete the follow-up questionnaires together with someone who could translate the questions. The information included study design, the purpose of the study presented as intervention effect on uptake and continued use of contraceptive methods, the period for follow-up and clinic group allocation (intervention or control). Furthermore, they were informed about alternatives to participation (contraceptive counselling according to clinical routine). All patients accepting participation signed informed consent.

HCPs from intervention clinics received an email with an invitation to evaluate the intervention after enrolment of study participants had stopped (paper IV). An electronic survey was linked to the email, and the providers were informed that completing the survey meant that they accepted study participation and gave their consent for the research team to collect and store information of them as study subjects.

### **5.5.8 Details on intervention and control**

The intervention consisted of four different parts:

1. A seven minute long educational video with members of the research team presenting available contraceptive methods with emphasis on effectiveness, mechanism of

- action, administration and added health benefits of the different contraceptive methods. The video was to be seen by the participant prior to meeting with their HCP.
2. 4 key-questions to be asked by the healthcare provider. Questions were formulated to make the participant reflect on how to deal with a pregnancy if it was to occur at that moment, for how long contraception was needed and to describe menstrual period cramping and bleeding.
  3. A modified tiered effectiveness chart (116) of available contraceptive methods. Our effectiveness chart presented typical use failure rate of available methods in percent (%) on the left side and in modified Pearl Index with numbers of pregnancies among 10 000 users on the right side (figure 2).
  4. A box of contraceptive models. The prototypes were shown to participants for them to see actual method size and to easier explain administration and insertion of methods (figure 3).

Participants at intervention clinics received the study-specific structured contraceptive counselling. Participants at control clinics received standard contraceptive counselling. Standard contraceptive counselling follows no specific structure. All contraceptive counselling was given by midwives or medical doctors. These HCP categories are as such trained in contraceptive counselling and medical eligibility criteria (MEC).

Figure 2. Tiered effectiveness chart

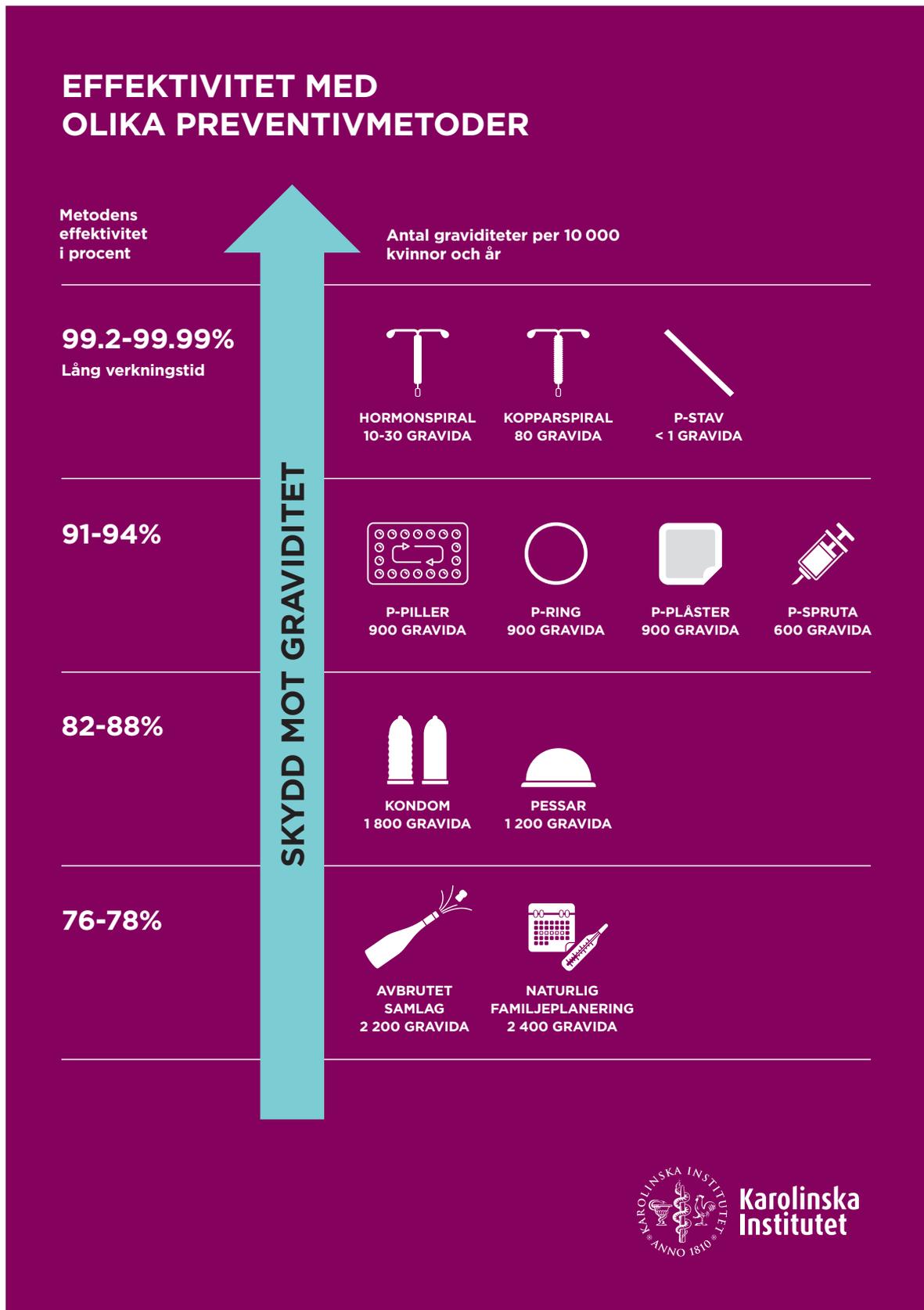


Figure 3. Box of contraceptive models



### **5.5.9 Clinical assessments**

#### **First visit**

- Intended method for contraceptive use (prior to counselling)
- Reproductive and contraceptive history including gravidity, parity, previous medical and/or surgical abortions, previous and current use of contraceptive methods
- Contraindications for contraceptive use

#### **Follow-up**

- Contraceptive initiation and reasons for non-initiation or termination
- Change in contraceptive use and underlying reason
- Complications and side effects of chosen method
- Unprotected sexual intercourse
- Pregnancies and how these were handled

### **5.5.10 Follow-up and measurement of outcomes**

Follow-up data were collected through electronic questionnaires sent by email. Participants who did not finish their surveys were contacted by SMS or telephone. The primary outcome was assessed at the first visit. Follow-ups to collect data on secondary outcomes were performed at 3 months and are currently planned for 6 and 12 months with results finalized in May 2020. Most telephone interviews to collect follow-up data were performed by research team members who had not been involved in any previous participant related study activities. None of the follow-ups was performed by HCPs who provided the counselling. To minimize numbers of participants lost to follow up, a team member who administered almost all enrolment at maternal health clinics also conducted telephone interviews.

### **5.5.11 Sample size**

Because of the cluster design, an intraclass correlation (ICC) factor affects the sample size, making the number of participants needed larger compared to non-cluster trials. The sample size was calculated to show a difference in proportions of participants choosing LARCs in a two-group comparison between intervention and control groups. An assumed ICC of 0.05 was used, equivalent to the ICC observed in a previous study (98). We expected the mean age of patients seeking contraceptive counselling to be approximately 25 years. At the time of study start, current use of LARCs among Swedish women aged 18–29 was 15% (16). We expected that 30% of participants in the intervention arm would choose LARCs. To show the anticipated 15% difference in LARC choice with a 90% power at an  $\alpha=0.05$  the aim was to include 24 clinics, contributing with an average of 50 participants. This would result in 600

participants in each group, yielding a total sample size of 1200. To allow for a lower mean of 30 participants per clinic, 28 clinics were included. The sample size calculations were performed by using the package CRTSize in R version 3.4.0. No power calculation was performed for secondary outcomes.

#### **5.5.12 Data management**

All HCPs received a provider-id. This number was stored together with the name of the provider on a separated list and served as a code key. Providers recorded their id in the electronic questionnaires that was administered for each study participant that received contraceptive counselling (paper III). The list was used to collect email addresses to which the invitation to evaluate the intervention was sent. Data was collected in an electronic survey and exported to a computer-based spreadsheet prior to analysis (paper IV).

All participants received a study-id. This number was stored together with the participant's full name, personal identity number (i.e. social security number) and email address (used for follow up) on a specific separated list that served as a code key. All data from the first visit and follow-up were collected in electronic questionnaires and was exported into a computer-based spreadsheet. Copies of first visit questionnaires were printed by the HCP to serve as a back-up to secure primary outcome measures. Data management plans (DMP) for first visit and follow-up were produced. Data cleaning was securely performed by members of the research team together with independent statisticians from a statistical agency (the same agency that performed sample size calculation and randomization).

#### **5.5.13 Analyses**

The intervention effect was estimated by using logistic mixed effects models (including covariates known to affect contraceptive choice) with random intercept for clinic to account for clustering. To measure intervention differences by clinic type, we assessed the treatment effect for each clinic type separately. ICC estimates and their 95% confident intervals were calculated using the random intercept logistic model ICC from Wu, Crespi & Wong (117). A two-sided p-value of less than 0.05 was considered statistically significant. Secondary outcomes were analysed with logistic mixed models, including clinic as random effects and intervention and clinic type as fixed effects. Data analyses were performed in SPSS version 25 and R version 3.6.0. For more details, please see the appended manuscript (paper III).

Chi-square tests and Fisher's exact tests were used to analyse proportions of user satisfaction. A one-sample Kolmogorov-Smirnov test was used to analyse the HCPs' estimation on time consumption.

## **5.6 REFLECTION AND ETHICAL CONSIDERATIONS**

All studies in this thesis received ethical approval by the regional ethical review board in Stockholm, Sweden:

**Study I** – Dnr 2013/2069-31/1, amendment (increased number of participants to account for loss to follow-up) 2014/1805-32.

**Study II** – Dnr 2013/1514-31/4, amendment 2016/543-32.

**Study III** – Dnr 2017/525-31/4, amendment 2018/940-32 and 2019-00931. Approval for conducting the study at clinics within SLSO was also obtained (SLSO-1545).

All subjects were given verbal and written information about the studies before signing their informed consent for study participation. Furthermore, all patients were informed that participation was voluntary and that withdrawal was to be accepted at any time without affecting the current or future treatment and healthcare. They were also informed that declining participation would mean that they received standard care according to today's clinical routine.

In research ethics, a principle of equity of study participants is constant. All studies in this thesis evaluate treatment and interventions that are assumed to be beneficial for participants in one of the two groups. However, the other subjects receive standard care or treatment with placebo, which constitutes very little discomfort. Hence, study participation is of no harm to any subjects. In the broader perspective, the overall aim to increase use of LARCs should be considered positive for the individual user and the society at large as LARCs lead to reduced numbers of unintended pregnancies and abortions.

For study I, some participants were found eligible for study participation by a screening of their most recent sexual history during visits for sexually transmitted infection testing. They were then informed about their risk of unintended pregnancy if they reported unprotected sexual intercourse. Women received structured counselling about EC regardless of the reason for the visits. Before the start of the study, this was considered a risk of increased levels of anxiety among those that were unaware of their risk. However, to give EC counselling to women in need is considered best practise, especially since previous study

findings have shown low use of EC among women seeking abortion care services. All study participants received the same structured counselling and were offered or prescribed EC according to preference. Eligible participants were counselled by all midwives employed at the clinic during the study period. These midwives also performed the IUD insertions and data collection at first visit. This methodology may increase the risk of biased information due to a wish to please the provider because of a provider-patient relationship (112).

For study II, the intrauterine instillation required an additional waiting time of five minutes between administration and insertion of the IUD. Since this waiting time had to be spent in the lithotomy position, it could be experienced as unnecessary and unpleasant. Risk of adverse events related to the intervention was assessed as minimal since no sharp objects were to be used and that the study drug was to be administered inside the uterine cavity and not injected in any tissue. The use of mepivacaine did not require any specific actions to prepare treatment of any adverse events since the risk of allergic reactions was assessed as minimal. Participants randomized to intervention could benefit from less pain during insertion if mepivacaine proved to be effective. Finding a non-invasive and effective method for pain management during IUD insertion could lead to increased uptake of IUDs since the fear of pain barrier could be removed.

For study III, patients were informed about the study either in a private room or in the reception area/waiting room. Due to the interior design of some participating clinics, study information could not be given in an entirely private area which could be found stressful by the patient. In addition, most MHCs provide contraceptive counselling as a drop-in service, and the waiting room was often crowded with other patients resulting in a cramped and noisy space. To receive study information and to fully comprehend the meaning of study participation, under those circumstances, could be difficult. However, the experience from HCPs and study staff recruiting participants in those clinics was that patients were more likely to decline rather than accepting participation under those circumstances. Participants recruited from clinics randomized to intervention received structured contraceptive counselling with an emphasis on the effectiveness of LARCs. They were asked questions about how they would react to an unintended pregnancy, for how long they needed their contraception, and how much pain and bleeding they experience during menstruation. These questions could be found intrusive if your initial intention for a visit was a prescription renewal.

Risk of higher rates of contraceptive drop out among users that have not been fully involved in the choice of method has been discussed. However, study findings can be

interpreted as the method started is the only predictor for high continued use, all in favour of LARCs above other methods (19-21). In this study, the intervention could be considered beneficial over standard care since it means that participants in the intervention arm most likely will receive a more comprehensive contraceptive counselling. However, to include standard care in clinical trials is not unusual, and this was not considered an ethical obstacle as participants from clinics randomized to control received standard care.

For study III, paper IV, no other ethical considerations concerning study participants, apart from those raised above, were taken into account. To evaluate user satisfaction with the received intervention, especially without the presence of the provider, could not be seen as intrusive or to come with a risk of biased information. However, this study also analyses user satisfaction from the HCP's perspective. Invitations were sent to providers that had delivered the intervention. To receive a questionnaire to your work or private email address could come with a feeling of being "controlled". On the other hand, to not evaluate the intervention from a provider's perspective could also be considered unethical. The providers invested work into delivering the intervention and could be considered to have the right to raise their opinion about feasibility if the intervention were to be implemented as part of their future clinical praxis.

There were no financial incentives for any study participants in the thesis, and costs for any contraception had to be paid for by the participant unless covered by existing subsidies. Clinics participating in study III received a small compensation of €2 for each recruited participant, but no individual reimbursement was given to HCPs for contributing to participant recruitment (paper III) or completing their evaluation of the intervention (paper IV).

## 6 RESULTS

### 6.1 TABULATED OVERVIEW OF MAIN RESULTS

This table contains the main results of the different studies within this thesis. A summary of the findings related to each study specific research questions are presented under the following subheadings. More details are found in the appended reprints of Papers I–IV.

Table 5. Overview of study objectives and finding

	<b>Objectives</b>	<b>Main results</b>
<b>Study I, Paper I</b>	To compare use of an effective method of contraception 6 months following insertion of a copper intrauterine device or intake of ulipristal acetate for emergency contraception.	Participants opting for a Cu-IUD for EC were using effective contraception at 6 months follow-up to a higher extend than participants opting for UPA.
<b>Study II, Paper II</b>	To evaluate whether intrauterine mepivacaine instillation before intrauterine device insertion decreases pain compared to placebo.	In the ITT-analysis, intrauterine mepivacaine instillation did not decrease pain scores with IUD insertion compared to placebo.  The PP-analysis showed a decrease in pain scores with IUD insertion.  More participants receiving mepivacaine experienced insertion as easier than expected or as expected compared to placebo
<b>Study III, Paper III</b>	To evaluate the effect of structured contraceptive counselling on LARC uptake, LARC initiation and pregnancy rates in abortion clinics, maternal health clinics and youth clinics.	More participants receiving structured contraceptive counselling chose/received a prescription of LARCs compared to standard contraceptive counselling.  Structured contraceptive counselling was associated with higher LARC initiation at three months follow-up compared to standard contraceptive counselling.
<b>Study IV, Paper IV</b>	To evaluate user satisfaction of healthcare providers and participants with an intervention used in a cluster randomized trial and to characterize which providers and receivers found the intervention most helpful.	Both HCPs and participants reported high satisfaction with the intervention used in the trial.  HCPs reported use of the study intervention to be time neutral compared to standard contraceptive counselling.  No certain identifiers of satisfaction could be determined among HCPs  More migrant and 2 <sup>nd</sup> generation migrants than non-migrants found the educational video to be supporting contraceptive choice comped to

### 6.2 IS INSERTION OF CU-IUDS FOR EMERGENCY CONTRACEPTION AN EFFECTIVE WAY TO INCREASE SUBSEQUENT USE OF EFFECTIVE CONTRACEPTION? STUDY I, PAPER I

Participants were recruited from February 2014 to January 2015. Out of 101 women who were invited to participate, 22 declined. The majority of these women chose UPA for EC. A total of 39 women were recruited in the UPA group, and 40 women were recruited in the

Cu-IUD group. Four women were lost to three months follow up in the Cu-IUD group whereas seven and eight were lost to three months and six months follow-up in the UPA group, respectively. Analyses for the secondary outcomes (3 months follow-up) and the primary outcome (6 months follow-up) included 68 and 67 women, respectively. The flow chart is available in the appended reprint of paper I.

No insertion failures nor any expulsions were reported during the study period. Mean age differed between groups with women being significantly older in the Cu-IUD group ( $p=0.004$ ). Baseline characteristics are presented in table 6.

More women in the Cu-IUD group were using an effective contraceptive method at three and six months follow-up (table 7). LARC use at six months follow-up was higher in the Cu-IUD group compared to the UPA group ( $p<0.001$ ). A figure presenting all contraceptive methods used by participants at first visit, at 3 months and at 6 months follow-up is available in the appended reprint of paper I.

In the Cu-IUD group, one participant had her IUD removed due to suspected infection, and one was accidentally dislodged during cervical cytology testing. Continued use of Cu-IUD after three and six months was 35/37 (94.6%) and 28/36 (77.8%), respectively. Method acceptability was high, with most women rating the insertion procedure as easier than expected or as expected (24/35, 68.6%). In addition, 31/36 (86.1%) stated that they would recommend the Cu-IUD for EC to a friend.

Numbers of women reporting subsequent UPSI within the follow-up period were 4/36 (11.1%) in the Cu-IUD group compared to 14/31 (45.2%) in the UPA group ( $p=0.02$ ). The patient who had her IUD removed due to infection started COC, which failed and was pregnant at three months follow up. There were four pregnancies in the UPA group, out of which three were terminated, and one continued.

The most pronounced reason for not choosing the Cu-IUD for EC was fear of pain during insertion (30.3%, 10/33).

No adverse events during IUD insertion were reported.

Table 6. Baseline characteristics by study group

	<b>Cu-IUD</b>	<b>UPA</b>	<b>p-value<sup>a</sup></b>
Age	27 (20–40)	24 (18–38)	0.004
Parity	0 (0–3)	0 (0–1)	0.405
Previous abortion	0 (0–1)	0 (0–1)	0.948

Data are median (range).

<sup>a</sup>Mann-Whitney U-test

Cu-IUD, copper intrauterine device; UPA, ulipristal acetate

Table 7. Use of effective contraception at 3 and 6 months after Cu-IUD or UPA for emergency contraception.

	<b>Effective method</b>	<b>No effective method</b>	<b>Missing</b>	<b>p-value</b>
<b>3 months</b>				
Cu-IUD	35/36 (97.2%)	1/36 (2.8%)	4	<0.001
UPA	19/32 (59.4%)	13/32 (40.6%)	7	
<b>6 months</b>				
Cu-IUD	30/36 (83.3%)	6/36 (16.7%)	4	0.03
UPA	18/31 (58.1%)	13/31 (41.9%)	8	

<sup>a</sup>Fisher's exact test.

Cu-IUD, copper intrauterine device; UPA, ulipristal acetate

### **6.3 DOES INTRAUTERINE INSTILLATION OF MEPIVACAINE DECREASE PAIN WITH IUD INSERTION IN NULLIPAROUS WOMEN? STUDY II, PAPER II**

Participants were enrolled from November 2013 to May 2017, with the last follow-up contact in November 2017. Out of 105 patients assessed for eligibility, 19 were excluded, and 86 (82%) were randomized. A total of 81 and 78 women were included in the ITT and PP analysis, respectively. The flow chart of participants is available in the appended reprint of paper II.

Baseline characteristics and type of IUD inserted for the 41 women in the intervention group, and the 40 in the placebo group are detailed in table 8. In the ITT analysis, pain scores with IUD insertion was 1.1 cm less in the intervention group compared to the placebo group (4.8 vs 5.9). Among pain scores for all procedure steps, the difference with sounding reached 1.5 cm between the groups ( $p=0.048$ ). More women receiving the intervention reported the IUD insertion to be easier than expected or as expected compared to women receiving placebo, and fewer women reported it as worse than expected. Exact figures on the primary and secondary outcomes measured at the first visit are presented in table 9.

In the PP analysis, the median pain score with IUD insertion was 4.8 (IQR 3.1–5.5) in the mepivacaine group compared to 6.0 (IQR 3.4–7.6) in the placebo group ( $p=0.033$ ).

No significant differences between groups were found with regards to acceptability of method for pain relief, continued use of IUD, opting for another IUD in the future and recommendation of IUD to a friend. Overall, 75 (92.6%) study participants reported that they would recommend the intrauterine instillation for pain relief to a friend.

For more details and figures, please see the appended reprint of paper II.

Table 8. The baseline characteristics and type of IUD of study participants by analgesia used before IUD insertion.

	<b>Mepivacaine (n=41)</b>		<b>Placebo (n=40)</b>		<i>P</i> *
	Median	IQR	Median	IQR	
Age (years)	22	19.5–25.5	22	20–25.8	0.835
Usual period cramping (VAS)	4	2.4–6.1	3.2	2–6.5	0.674
Previous Medical Abortion	6 (14.6)		5 (12.5)		1
Previous Surgical Abortion	1 (2.4)		3 (7.5)		0.36
Previous IUD insertion	7 (17.1)		6 (15)		1
<b>Type of inserted IUD</b>					
LNG-IUS 52 mg	20 (48.8)		18 (45)		0.82
Copper-IUD	12 (29.3)		11 (27.5)		0.29
LNG-IUS 13.5 mg	3 (7.3)		14 (35)		0.62
LNG-IUS 19.5 mg	1 (2.4)		0 (0)		1

All data are presented as median, interquartile range and n (%).

IQR, interquartile range; VAS, visual analog scale; IUD, intrauterine device; LNG-IUS, levonorgestrel releasing intrauterine system.

Table 9. The primary and secondary outcomes during and after IUD insertion by analgesia used before the procedure

	<b>Mepivacaine (n=41)</b>		<b>Placebo (n=40)</b>		<i>p</i> <sup>a</sup>
	Median	IQR	Median	IQR	
<b>VAS</b>					
Baseline pain	0	0–0.2	0	0–0.1	0.734
Instillation of study drug or placebo	1.4	0.8–2.9	2.2	0.3–3.5	0.319
Tenaculum	2.2	0.9–3.4	2.4	0.3–4.5	0.487
Sounding	3.4	1.7–5.9	4.9	2.6–6.6	0.048
IUD insertion	4.8	3.1–5.8	5.9	3.3–7.5	0.062
Before leaving the clinic	1.3	0.5–2.5	1.3	0.6–3.7	0.545
<b>Overall experience of IUD insertion</b>					
Easier than expected	26 (63.4)		15 (37.5)		0.006 <sup>b</sup>
As expected	12 (29.3)		11 (27.5)		
Worse than expected	3 (7.3)		14 (35)		

\*Two group comparison using independent sample t-test and Mann-Whitney U-test where appropriate

All data are presented as median, interquartile range and n (%).

IQR, interquartile range; VAS, visual analog scale; IUD, intrauterine device.

<sup>a</sup>Two group comparison using Mann-Whitney U-test.

<sup>b</sup>Chi-square test, 2x3 contingency table.

#### **6.4 IS STRUCTURED CONTRACEPTIVE COUNSELLING WITH EMPHASIS ON METHOD EFFECTIVENESS AN EFFECTIVE WAY TO INCREASE LARC UPTAKE? STUDY III, PAPER III**

A total of 28 clinics were randomized and included in the analysis. Mean cluster size was 47 with a variation from 11–60 recruited participants. Baseline characteristics of clinics are presented in table 10.

From Sept 2017 to May 2019, a total of 1359 patients were enrolled. The analysis of the primary outcome included 1338 participants. The loss to follow-up, including withdrawals was 19.6% (129/658) in the intervention group and 21.9% (149/680) in the control group, leaving 1058 (79.1%) to be included in the analyses of the secondary outcomes. The study flow of clinics and participants is available in the appended paper III.

Groups differed with a lower proportion of participants in the intervention group who had experienced a vaginal birth or with current or most recent use of LARC. Baseline characteristics of participants are presented in Table 11.

More participants in the intervention group chose/received prescriptions of LARCs after counselling compared to the control group. Table 12 presents the result of the mixed model analysis on the intervention effect in total and for each clinic type as subgroups. The estimated intraclass correlation was 0.01 (95% CI, 0.00–0.05).

Intended LARC use prior to counselling did not differ between intervention and control groups. For participants without intended LARC use, the post-counselling proportion of participants choosing LARCs was higher in the intervention group (145/523, 27.7%) compared to the control group (66/513, 12.9%, OR 3.02, 95% CI 2.14–4.28).

LARC initiation at the three months follow-up was higher among participants in the intervention group (213/528, 40.3%) than in the control group (153/531, 28.8%, OR 1.74, 95% CI 1.22–2.49). Within the 3 months follow-up period 6/527 (1.1%) and 16/531 (3%) participants had experienced a pregnancy in the intervention and control group, respectively (OR 0.38, 95% CI 0.08–1.68).

For more details, please see the appended reprint of paper III.

Table 10. Baseline characteristics of clinics

	<b>Intervention (n=14)</b>	<b>Control (n=14)</b>
<b>Clinic type</b>		
<b>Abortion clinic</b>	2 (50.0%)	2 (50.0%)
Participants	111 (49.1%)	115 (50.9%)
Average cluster size*	55.5	57.5
<b>Youth clinic</b>	6 (46.2%)	7 (53.8%)
Participants	283 (48.6%)	299 (51.4%)
Average cluster size*	47.2	42.7
<b>Maternal health clinic</b>	6 (54.5%)	5 (45.5%)
Participants	264 (49.8%)	266 (50.2%)
Average cluster size*	44.0	53.2

\*Number of participants recruited per clinic

Table 11. Baseline characteristics of participants

	Intervention (n=658)	Control (n=680)
<b>Sociodemographic characteristics</b>		
<b>Age (years) (n=1338)</b>		
Median (IQR)	24 (20–29)	24 (20–30)
<b>Current relationship (n=1295)</b>		
Single	181 (28.3%)	167 (25.5%)
Partner – living together	260 (40.7%)	276 (42.1%)
Partner – living apart	187 (29.3%)	201 (30.6%)
Other	11 (1.7%)	12 (1.8%)
<b>Highest completed education (n=1295)</b>		
Primary school	70 (11.0%)	77 (11.7%)
Secondary school	329 (51.5%)	365 (55.6%)
College/University	239 (37.4%)	214 (32.6%)
Unknown	1 (0.2%)	0 (0%)
<b>Reproductive and contraceptive history</b>		
Current or previous pregnancy (n=1335)	223 (34.0%)	257 (37.8%)
Nulliparous (n=1332)	538 (82.3%)	531 (78.3%)
Medical abortion (n=1333)	137 (20.9%)	152 (22.4%)
Surgical abortion (n=1332)	44 (6.7%)	48 (7.1%)
Vaginal birth (n=1333)	98 (15.0%)	133 (19.6%)
Caesarean sectio (n=1333)	29 (4.4%)	40 (5.9%)
<b>Most recent or current contraception (n= 1289)</b>		
LARC*	77 (12.1%)	111 (17.0%)
SARC†	357 (56.1%)	358 (54.8%)
Other‡	134 (21.1%)	122 (18.7%)
None	68 (10.7%)	62 (9.5%)

LARC = long-acting reversible contraceptive \*intrauterine device or subdermal implant.

SARC = short-acting reversible contraceptive †combined pill, progestin only pill, contraceptive injection, transdermal patch or vaginal ring.

‡Condom, Diaphragm, Smartphone application, Fertility awareness methods.

Table 12. Primary outcome by clinic type

	LARC* choice/prescription		Intervention effect		P-value
	Intervention (n = 658)	Control (n = 680)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Adj. OR
<b>Total</b> (n = 1338)	267 (40.6%)	206 (30.3%)	1.70 (1.19–2.35)	2.77 (1.99–3.86)	<0.001
<b>Abortion clinic</b> (n=226) <sup>†</sup>	83 (74.8%)	64 (55.7%)	2.36 (1.34–4.15)	3.37 (1.76–6.47)	<0.001
<b>Youth clinic</b> (n=582)	123 (43.5%)	76 (25.4%)	2.31 (1.48–3.62)	3.31 (2.01–5.46)	<0.001
<b>Maternal health clinic</b> (n = 530)	61 (23.1%)	66 (24.8%)	0.99 (0.53–1.83)	1.92 (1.03–3.57)	0.039

Models were adjusted for age, highest completed education, previous pregnancy with and without previous abortion, intended use of LARCs, and clinic type.

LARC, long-acting reversible contraceptive; OR, odds ratio

\*Intrauterine contraception or subdermal implant.

<sup>†</sup>The model for the abortion clinics was estimated without the random intercept for clinic. All models were adjusted for intended LARC use and pregnancy/abortion.

## 6.5 HOW DO HEALTHCARE PROVIDERS AND PARTICIPANTS EXPERIENCE USE OF THE INTERVENTION FOR STRUCTURED CONTRACEPTIVE COUNSELLING AND DO THEY FIND IT TO BE SUPPORTIVE IN THEIR COUNSELLING AND CONTRACEPTIVE CHOICE? STUDY III, PAPER IV

Fourteen clinics were randomized to provide the study intervention in contraceptive counselling. In the intervention clinics, 1085 eligible patients were invited to participate out of which 658 enrolled. Participants were recruited from Sept 2017 to May 2019. The flowchart of clinics and participants is available in the appended reprint of paper IV. Among HCPs providing contraceptive counselling, 55/62 (88%) completed the electronic survey and 639/658 (97.1%) participants had data on satisfaction rates. Baseline characteristics of HCPs and participants are presented in table 13 and 14.

Receiver and provider satisfaction with the educational video, the effectiveness chart, and the box of contraceptive models are presented in table 15. More migrant and 2nd generation migrant participants found the effectiveness chart to be supportive in their contraceptive choice compared to non-migrant participants (64.4% and 70.2% vs 54.5%,  $p=0.028$ ).

HCPs satisfaction with the key-questions and overall satisfaction with the intervention are presented in table 16. Most HCPs would like to use the intervention package in their routine counselling (please see the figure in the appended reprint of paper IV). More HCPs working at maternal health care clinics were less satisfied with the intervention as a whole compared to HCPs working at youth- or abortion clinics ( $p=0.025$ ).

A discrepancy between the proportion of HCPs reporting full intervention adherence (96.5%, 632/655) and the proportion of participants reporting having received all parts of the

intervention was present, with 10.3% (66/638) not shown the effectiveness chart and 19.1% (122/639) not shown the box of contraceptive

HCPs assessed the use of the intervention outside the study to be time-neutral compared to routine counselling (median 0, IQR -5 to 5). HCPs believed that that the intervention affected the patients' contraceptive choice to a large extent (70.9%, 39/55) or some extent (18.2%, 10/55).

For more details, please see the appended reprint of paper IV.

Table 13. Baseline characteristics of healthcare providers.

<b>Age group (years), n=55</b>	
20–29	2 (3.6)
30–39	10 (18.2)
40–49	21 (38.2)
50–59	10 (18.2)
≥60	12 (21.8)
<b>Clinic type</b>	
Abortion clinic	11 (20.0)
Youth clinic	19 (34.5)
Maternal health service	25 (45.5)
<b>Occupation</b>	
Medical doctor	4 (7.3)
Midwife	51 (92.7)
<b>Work experience within occupation (years)</b>	
1–2	5 (9.1)
3–4	1 (1.8)
5–9	15 (27.3)
10–14	9 (16.4)
15–19	5 (9.1)
≥20	20 (36.4)
<b>Work experience of contraceptive counselling (years)</b>	
0–2	10 (18.2)
3–4	7 (12.7)
5–9	11 (20.0)
10–14	10 (18.2)
15–19	9 (16.4)
≥20	8 (14.5)

Data are n (%)

Table 14. Baseline Characteristics of participants.

<b>Age, median (IQR) , n=658</b>	<b>24 (20-29)</b>
<b>Highest completed education, n=639</b>	
Elementary school	70 (11.0)
High school	329 (51.5)
College/University	239 (37.4)
Unknown	1 (0.2)
<b>Foreign background, n=638</b>	
Non migrant	490 (76.8)
Migrant	90 (14.1)
2 <sup>nd</sup> generation migrant	58 (9.1)
<b>Reproductive and contraceptive history</b>	
Ever pregnant, n=656	223 (34.0)
Nulliparous, n=654	538 (82.2)
Abortion, n=655	166 (25.3)
<b>Most recent or current contraception, n=636</b>	
LARC <sup>a</sup>	77 (12.1)
SARC <sup>b</sup>	357 (56.1)
Other <sup>c</sup>	134 (21.1)
None	68 (10.7)
<b>Clinic type, n=658</b>	
Abortion clinic	111 (16.9)
Youth clinic	283 (43.0)
Maternal health clinic	264 (40.1)

Data are n (%) unless stated otherwise. IQR, Interquartile range; LARC, long-acting reversible contraception; SARC=short-acting reversible contraception. <sup>a</sup>intrauterine device or subdermal implant. <sup>b</sup>combined pill, progestin only pill, contraceptive injection, transdermal patch. <sup>c</sup>condom, diaphragm, smartphone application, fertility awareness methods

Table 15. User satisfaction with intervention parts by healthcare providers and participants.

	<b>Healthcare provider n=55</b>	<b>Participant n=658</b>	<b>Participant missing</b>	<b>P-value</b>
<b>Educational video</b>				
Very good	25 (45.5)	378 (57.4)	19 (2.9)	0.09
Good	27 (49.1)	230 (35.0)		0.04
No opinion	3 (5.5)	28 (4.3)		0.5
Poor	0 (0)	3 (0.5)		1
Very poor	0 (0)	0 (0)		
Video was supportive in contraceptive counselling/choice	41(74.5)	431 (65.5)	19 (2.9)	0.19
<b>Effectiveness chart</b>				
Very good	32 (58.2)	318 (48.3)	20 (3.0)	0.16
Good	20 (36.4)	221 (33.6)		0.77
No opinion	2 (3.6)	33 (5.0)		1
Poor	1 (1.8)	0 (0)		
Very poor	0 (0)	0 (0)		
Effectiveness chart was supportive in contraceptive counselling/choice	52 (94.5)	355 (54.0)	37 (5.6)	<0.001
<b>Box of contraceptive models</b>				
Very good	31 (56.4)	292 (44.4)	19 (2.9)	0.09
Good	17 (30.1)	177 (26.9)		0.53
No opinion	7 (12.7)	48 (7.3)		0.18
Poor	0 (0)	0 (0)		
Very poor	0 (0)	0 (0)		
Models were supportive in contraceptive counselling/choice	50 (90.1)	326 (49.5)	39 (5.9)	<0.001

Data are n (%). Significance calculated with Chi-Square and Fisher's exact test where appropriate.

Table 16. User satisfaction with intervention parts rated only by healthcare providers

<b>Key-questions</b>	
Very good	17 (30.1)
Good	23 (41.8)
No opinion	11 (20.0)
Poor	4 (7.3)
Very poor	0 (0)
Questions were supportive in contraceptive counselling	41 (74.5)
<b>Overall satisfaction with intervention</b>	
Very good	21 (38.2)
Good	29 (52.7)
No opinion	4 (7.3)
Poor	1 (1.8)
Very poor	0 (0)

Data are n (%).

## 7 DISCUSSION

This thesis aims to find pathways to increasing uptake of LARC by the use of clinical interventions for improved quality of care from both an HCP's and a patient's perspective. The results show that uptake of LARC can be achieved by emphasizing the effectiveness of LARC methods and making provision more acceptable. The findings show that provision of Cu-IUDs for EC is an effective clinical routine that increases use of effective contraception, and a high proportion of Cu-IUD users would recommend this method of EC to a friend. Thereby the use of the Cu-IUD for emergency contraception can be increased, and regular use of LARCs for contraception can be achieved in a diverse clinic setting. Women's most frequent reason for not choosing the Cu-IUD was fear of pain during IUD insertion, a finding serving as a connecting thread to the second trial in the thesis. Intrauterine mepivacaine prior to IUD insertion did not prove to be as effective in reducing pain as anticipated but positively affected the experience of the insertion procedure. The results show that a highly acceptable method for pain relief resulted in significantly fewer women experiencing the IUD insertion as worse than expected, and such a method for pain relief could increase the use of IUDs for contraception.

Furthermore, the findings demonstrate that structured contraceptive counselling consisting of different counselling tools increases uptake of LARCs, hence contributing to a lower risk of subsequent unintended pregnancies. Finally, our findings prove that structured contraceptive counselling has high acceptability both among patients receiving it and among HCPs providing it. The different studies all contribute to increasing access and uptake of LARC.

### 7.1 CU-IUDS FOR EMERGENCY CONTRACEPTION

Most clinicians know that the Cu-IUD is the most effective method for EC and that IUDs can be promoted to nulliparous women. Despite this, few service providers offer IUDs as EC for women (58-60). Hence, our study of Cu-IUD compared to UPA for EC according to the users' preference is important for the provision of arguments to increase access to- and uptake of LARCs for women who need EC. It is the first study of its kind in a Swedish setting. The results are of great value since they fill the knowledge gap about reasons for not choosing the most effective method even though it is clearly recommended by the HCP, and offered free of charge. The results also strengthen previous findings of fear of pain as a barrier to uptake of IUDs (118, 119). At follow up 3 women in the UPA group had initiated LARC use—2 Cu-IUDs and 1 LNG-IUS. This could be by chance, but it is also likely that

the counselling about IUDs as the most effective method contributed to the decision to have one inserted in a later stage. The only pregnancy in the Cu-IUD group occurred after IUD removal and subsequent failure with oral contraception. All three women who experienced a pregnancy had an abortion within the follow-up period. This finding support previous findings that the method for contraception is the most important factor influencing future risk experiencing an unintended pregnancy (19-22).

## **7.2 PAIN MANAGEMENT DURING IUD INSERTION**

A common misconception is that young women and those without previous experience of vaginal delivery are not good candidates for IUDs. With regard to the relative effectiveness of LARCs to other less user-friendly methods, especially among young women (14), nulliparous women are excellent candidates for IUDs. IUDs are currently recommended as first-line contraception for young women (120-122). Nulliparity is, however, one factor that increases the risk of painful insertion (68, 83), and finding an effective and well-accepted method for pain relief in this patient group has previously failed. Although it has been shown that young and nulliparous women accept IUD insertion well, reporting mild to moderate pain experience with the procedure (74, 123), there is an urge to find a truly effective method since the fear of pain during insertion still limits the uptake of IUDs (66-70). Sounding is included as a standard routine in the insertion procedure and is well known to cause discomfort and pain (78). In our study population, the pain experienced during sounding differed significantly between intervention and placebo. All insertion procedures could add up and affect the total experience of the insertion. Thus, this finding is relevant. However, IUDs can be safely inserted in most women without sounding (80), making this secondary outcome less relevant than insertion pain score. The findings in this thesis show that nulliparous women treated with intrauterine mepivacaine prior to insertion had rather low pain scores (median 4.8), but also that the treatment was associated with a better total experience of the insertion. No clinically significant pain reduction cutoff has yet been established. Problems with using VAS for measuring pain perception is further elaborated in the following section of methodological considerations. As explored in the review part of the thesis, some effective methods are painful to receive or cause discomfort to the receiver (88, 124). It could be argued that a method for effective pain relief has to be somewhat pain-free to receive to be acceptable. Participants in our study reported low pain scores with intrauterine installation—1.4 and 2.2 in the intervention and placebo groups respectively—and most women (92.6%) would recommend this method for pain relief to a friend. These findings suggest that this method for pain relief is highly acceptable to patients.

Future studies of intrauterine mepivacaine are of interest and planned, and if found effective, it could be an important method used to address women with fear of pain and hence increasing uptake of IUDs.

### **7.3 STRUCTURED CONTRACEPTIVE COUNSELLING**

Despite easy access to contraception, Swedish women have a low uptake of effective contraception in comparison to other high-income countries (12). One possible explanation is that Swedish women are afraid to use hormonal contraception resulting in use of less effective methods for contraception such as safe periods, condoms and withdrawals/interrupted intercourse (16, 17). This has led to high rates of unwanted pregnancies and abortions, and it could be argued that the Swedish model needs improvement.

Our intervention package for structured contraceptive counselling included an educational video with information about contraceptive methods with an emphasis on method effectiveness. The use of educational videos as intervention parts has been evaluated by other researches, finding it to increase method-specific knowledge (125, 126) and affect contraceptive choice toward use of more effective contraceptive methods (98, 125). Our findings support the use of video as a supporting media prior to contraceptive counselling since it increases uptake of the most effective methods and has high acceptability both among HCPs and patients.

The use of contraceptive models in counselling makes women more aware of their actual size and route of administration, which might lead to finding them smaller and less frightening than imagined (119). A vast majority (80%) of HCPs found the box of contraceptive models to be very supportive in their contraceptive counselling. Approximately 50% of the participants found the box of models to be supportive in their contraceptive choice. However, 10% were never shown the models, and another 5% did not evaluate this part of the intervention. Altogether, these findings support the use of models during counselling to improve uptake of LARCs.

The use of tiered charts to communicate contraceptive effectiveness has proven to increase method-specific knowledge and to increase uptake of LARCs (116, 127, 128). The effectiveness chart used in our intervention was modified to present differences between contraceptive methods both in pregnancies per year among 10 000 users and effectiveness in per cent. This dual presentation was chosen to reach women who find it easier to overlook the differences presented in either numbers or proportions. Different designs were

piloted among HCPs and lay-people before the final version was set. This approach was evidently effective since the effectiveness chart received high satisfaction rates from both HCPs and participants, and was found to be supportive in contraceptive counselling (94.5%) and choice of contraceptive method (54.0%). This was the part of the intervention that most HCPs wanted to continue to use in their future routine counselling (90.9%).

Our intervention included key-questions. They were intended as counselling catalysts, to make women reflect about how to deal with pregnancy, for how long contraception was needed, but also to catch information about menstrual bleeding and cramping. The use of One Key Question<sup>®</sup> has been proven to increase the proportion of women receiving contraceptive counselling within primary care settings (129). The key-questions used in our intervention received high satisfaction rates, and they were also found to be supportive in contraceptive counselling by 74.5% of the HCPs. The HCPs in our trial are as such trained in contraceptive counselling, and more than 80% of the HCPs had 3 or more years work experience of providing contraceptive counselling. These findings demonstrate that our intervention could also be used in other clinical settings that generally do not actively provide contraceptive counselling. From a cost perspective, this could save societies money by task-sharing between specially trained contraceptive counsellors and other clinicians, for instance, general practitioners, and by such means increase women's access to facts-based information and contraceptive counselling.

Findings from this thesis demonstrate that women without intended LARC use prior to counselling have a higher uptake of LARCs if they receive structured contraceptive counselling. The intervention, with evidence-based information about health benefits with all contraceptive methods and key-question to address specific health issues that might be helped by the use of a certain method, might, of course, result in choice and initiation of another method than a LARC method. Inevitably, some women who intended to use LARCs would not be suitable for these methods. Although the counselling was intended to increase LARC use, this was only the intention in women where LARC use was suitable.

#### **7.4 MYTHS AND MISCONCEPTIONS**

LARC methods are surrounded by myths and misconceptions. During contraceptive counselling, it is common to meet patients who believe that IUDs cause abortion, pelvic inflammatory disease and infertility. Some also believe that LARCs cause ectopic pregnancies as well as weight gain and acne. Common myths and misconceptions among HCPs include that adolescents prefer to use condoms or pills, that parental consent is required

prior to LARC provision and that threads of IUDs must be checked regularly. All these myths and misconceptions are conclusively proven false in a review by Russo et al. (130). The findings from this thesis show that LARCs are highly acceptable methods with high continuation rate and proportions of participants recommending LARC use to a friend. Effective clinical interventions to increase the uptake of long-acting reversible contraception. The video prior to the counselling addressed all myths and misconceptions about contraceptive methods which may have affected contraceptive choice. However, addressing these myths and misconception among women who are not using contraception remains a challenge.

## **7.5 INCREASING ACCESS TO AND UPTAKE OF LARCS**

Studies in Sweden show contraceptive use among young women has increased thanks to the subsidy system. However, the cost is not an important factor affecting women's contraceptive choices (131) and that few women would change their method of contraception if they were all available free of charge (16). However, LARCs have a higher upfront cost than other contraceptive methods, and removing the cost-barriers has proven to increase the use of LARCs in low resource settings resulting in a reduction of unintended pregnancies (132, 133). Sweden has adopted a subsidy system allowing almost all contraceptive methods free of charge to women below 21 years, and a low cost (approximately €10/year) for women up to the age of 26. This might be reflected in the responses of costs not being a factor influencing contraceptive choice. Although the recent trend is upwards regarding LARC use in Sweden, use of LARCs are still low and, in addition, the trend is pointing in a negative direction regarding the use of other contraceptive methods. In 2017 as compared to 2013, more women had an unmet need for contraception (17). The most recent national statistics show a decrease in abortion rates among teenagers and young women up to 29 years of age (134). This could be explained by the increased use of LARCs within these age groups (17). However, this positive trend might be changing in the nearest future since more women today rely on no method at all compared to 2013 figures (16, 17). Women in the older age groups, 30-39 years, where the most pronounced decrease in use of contraception is seen, are also having increasing numbers of abortions (134).

Apparently, we need to move forward and increase contraceptive use overall in addition to using more effective methods. The findings from this thesis will serve as successful examples of what can be achieved with evidence-based information and provision of structured contraceptive counselling and focus on the most effective contraceptive methods. The next step in Sweden, apart from changing counselling routines within clinics, would be to

implement same-day, also known as streamlined provision of IUDs and contraceptive implants, which is not the case in most clinics today. Studies have found that multiple visits to receive IUDs or implants are a barrier to LARC uptake (135-137). Another follow-up study using the Contraceptive CHOICE model for contraceptive counselling, including same-day insertion, led to higher uptake of LARCs (138). Same-day insertion of LARC is considered best practice (139). Efforts have to be made in reducing barriers to streamlining insertion, such as rapid pregnancy tests, more time for each patient, insertion prior to receiving results from STI tests and increasing method-specific knowledge and insertion skills, as these have been shown to often limit the access (62, 98, 128).

## **7.6 INCREASING USE OF CONTRACEPTIVE IMPLANTS**

The contraceptive implant is the most effective contraception available, with a PI of 0.05 (140). Worldwide use is a mere 0.7% compared to the use of IUDs that constitute 14%. Thereby both the implant and IUDs are considered underutilized methods (12). It is often stated that the negative side effects of the implant, such as prolonged or irregular bleeding are unacceptable to the user. This statement is not justified, since the 12-month continuation rate of the implant is 84%, equivalent to the continuation rate of IUDs (105). In addition to its high effectiveness and high continuation rate, the implant is effective in reducing dysmenorrhea caused by endometriosis (141). Based on these findings, it becomes clear that the implant is a neglected option for many women and should be promoted to a greater extent. Women have been shown to have preprocedural anxiety regarding implant insertion (142), something that needs to be addressed during contraceptive counselling. However, a counselling argument to make more women consider implants for contraception could actually be that the implant insertion comes with less pain than the insertion of an IUD (142) a factor that might influence the likelihood to opt for another device in the future. Also, candidates should be informed that there is effective pain relief at hands for the inserter.

## **7.7 PROVIDER BIAS AND CONSCIENTIOUS OBJECTION**

In the online LEXICO English dictionary, bias is defined as “Inclination or prejudice for or against one person or group, especially in a way considered to be unfair”(143). The definition of provider bias varies in the literature. A review of provider bias in family planning concludes that it includes denying access to contraceptive methods due to prejudice, discouraging use of specific methods due to incorrect medical rationale, inadequate technical skills or personal beliefs of the provider (144). Provider bias is considered an important type of medical barrier since it might include scientifically unjustified medical rationales. It affects

the way providers present and recommends contraceptive methods (145). Since trained HCPs give contraceptive counselling, the information must not be affected by their personal beliefs and/or lack of method-specific knowledge. As method use is vigorously affected by provider bias (145), our intervention for the provision of evidence-based structured contraceptive counselling targets this risk by reducing differences in the information provided during contraceptive counselling. It also targets the risk of women being exposed to incorrect medical rationales or unfair prejudice by HCPs. Removing provider bias enables informed choice about contraceptive use, in many family planning programs used as a guiding principle (144).

Access to EC is not only affected by factors such as over the counter availability of ECPs in pharmacies and access to skilled IUD inserters for obtaining Cu-IUDs for EC. The providers' definition of when the pregnancy actually occurs might also affect the counselling and methods for EC that women can access, as well as the sociopolitical context in which the provider works. Although the most adopted definition of pregnancy is implantation of a fertilized egg in the uterus, some providers interpret the biological process of pregnancy to occur at the moment of the sperm fertilizing the egg. In the US, a significant interaction between providers definition of the start of a pregnancy to be when the sperm fertilizes the egg and practising in areas with high republican vote shares was shown. These providers were less likely to provide EC (146). This is a form of provider bias that has to be eliminated for women to access high-quality care and a full range of contraceptive methods.

In Sweden, a case of conscientious objection to providing IUD insertion, EC and abortion care has been taken to the industrial court, where the case of a midwife's right to conscientious objection was disliked. The Swedish abortion law does not include the right to conscientious objection. This is based on the right of the woman seeking abortion care not having to meet these healthcare providers (147). The same kind of arguments has been raised in terms of the right to conscientiously deny IUD insertions based on the assumption that it will prevent an already fertilized egg from implanting. This type of case was recently processed in the higher supreme court in Norway, in which the provider was awarded damages from the employer for unjustified reasons for dismissal (148). Norway and Sweden are neighbouring countries, and there is a risk that these processes might influence Swedish stakeholders. These types of arguments are dangerous to women seeking reproductive health care since women with unmet need for contraception are at high risk of unintended pregnancies (16, 17, 131) that will affect their social and psychological well-being and

economic situation (1-4). Internationally, reproductive healthcare is the only medical field that allows HCPs to limit legally regulated access to care by conscientious objection (149).

To deny reproductive healthcare, such as abortion and contraception, based on arguments of “conscientious freedom” is more aptly called “dishonourable disobedience”, since it violates the woman’s right to lawful healthcare, and passes all the consequences onto the woman herself (150). Sweden, Finland and Iceland, as opposed to Denmark and Norway, do not allow conscientious objection (149). Sweden has for long been regarded as a country ahead of many other countries in terms of gender equity, which is probably reflected in the decision not to allow conscientious objection. For the sake of women’s and children’s health, I argue, that is a line we should defend and keep promoting in our advocacy work.

## 8 METHODOLOGICAL CONSIDERATIONS

This thesis is based on research with different study methodologies approaching the aim from different perspectives, including prospective observational analyses from cohorts as well as individual and cluster randomized trial analyses. Including opinions from both HCPs and patients gives us a broader picture of the feasibility of the clinical routines and interventions. Different study designs contribute to elucidating the clinical problems at hand from different angles. These methodologies have their inherent strengths and limitations which need to be taken into account. When evaluating study findings, it is important to assess the risk of biased study results. Bias is defined as “Any process at any stage of inference which tends to produce results or conclusions that differ systematically from the truth” (151).

### 8.1 STUDY I, PAPER I

#### 8.1.1 Design

Observational prospective cohort studies do not include randomization, and the researcher does not predefine the exposure status. Instead, the study subjects are observed both regarding exposure and outcome. The level of evidence is lower than for an adequately powered RCT (152), which could have been another appropriate design for this study to improve the external validity (generalizability). However, the results of prospective design can be used to assess internal validity (proves causality between exposure and outcome), and the results are often reliable (able to be replicated in other studies) (153, 154). A significant limitation of this study design is that it requires large sample sizes to detect rare events (155). In this study, the sample size was not powered to detect differences in pregnancies, which was selected as a secondary, yet important outcome. Another limitation is that it is time and money consuming. Two important forms of biases with this study design is selection bias and attrition bias (loss to follow-up). Both groups must be selected from the same source of population (156). Women loss to follow-up result in missing data and subjects loss to follow-up may differ from those who are followed for the whole period. Any such differences should, if possible, be examined (152). We did not specifically analyze differences between women loss to follow up and women who were included in the analysis of primary outcome introducing a risk of attrition bias. However, the baseline characteristics did not differ between study groups, apart from women opting for Cu-IUD was slightly older (27 vs 24 years)—a factor introduced in a logistic regression analysis showing no interaction to choice of method for EC.

### **8.1.2 Finding eligible participants and recruitment**

The research setting in study I was the RFSU Clinic which provides STI testing in addition to contraceptive counselling. During clinic visits, women were screened for UPSI by the use of standardized forms for obtaining sexual history. Some women did not have contraceptive counselling in mind when first deciding to attend the clinic, and were addressed with the risk of unintended pregnancy in case of having had a recent UPSI. They were actively counselled about their need for EC, and some women accepted study participation. This way of finding eligible patients was successful in terms of rapid enrolment. However, the main reason for visiting the clinic was never recorded. In hindsight, that would have been an important factor to control for in the analysis of study outcomes since it could have affected the choice of method for EC as well as the use of- or continued use of effective contraception. It could also have added to the study results if found that women unaware of their risk of unintended pregnancy were more likely to choose the less effective method.

Study information was given from the same contraceptive counsellor who also obtained the consent from study participants and provided the method of choice. This methodology adds to the feasibility of the study. Both methods were available on-site for immediate provision.

We had a rather low proportion, 21.8%, of women declining participation. This reduces selection bias. However, most women not accepting participation did so based on an unwillingness to take extra time to participate in any trials, and most of these women choose UPA for EC. These factors might introduce selection bias. The fact that women were not randomized might also introduce selection bias, since women opting for a Cu-IUD may have been more motivated to initiate effective contraception.

### **8.1.3 Follow up**

Follow-up data were mainly collected by a member of the research team who had not been involved in any previous patient-related procedures. This approach is suitable to eliminate biased information due to social desirability. The data was collected through telephone interviews, which proved to be an exhausting and time-consuming process. Getting hold of participants from a phone with an unknown or hidden number was difficult, and most patients returned the call only after having ensured themselves that the caller was not a salesperson.

## **8.2 STUDY II, PAPER II**

### **8.2.1 Design**

Mepivacaine has not been used in previous research on pain relief with IUD insertion, has a low toxicity, and the hydrososonography catheter is easy to access. Hence, the results from this study would be of great interest if found effective in reducing pain with IUD insertion.

The main strength of the study was the use of a double-blinded randomized placebo controlled design. Double-blinded RCTs are considered the “Gold standard” for intervention trials. The randomization process can eliminate the influence of confounders that might affect the outcome, out of which some could be unknown or immeasurable and therefore not controlled for in a prospective observational trial. The blinding process eliminates the risk of co-variation due to patient’s or HCP’s expectations. The placebo control is important to remove the risk of effects on outcomes achieved by the placebo effect and study participation as such (154). For randomization, study sites were given blocks of 6-10 numbered envelopes containing the study allocation. One clinic started from number zero, and one started at number 86. In this way, each clinic inserted the same number of IUDs in the intervention- as in the placebo group. Both mepivacaine and placebo (NaCl) are odourless and clear, minimizing the risk of unblinding during intrauterine instillation.

### **8.2.2 Follow-up**

In this study, the person who collected the follow-up data was blinded to the study allocation of the participant. This also reduces the risk of experimenter bias. Also in this study follow-up was conducted through telephone interviews. To reduce the risk of high loss to follow-up, several attempts to reach the participants were made. When finally getting hold of the patient, the responses might be affected by a feeling of being chased or just “get it over with”. In addition, some participants might have been ashamed for not answering the phone or returning the calls.

### **8.2.3 Insertion procedure**

All IUDs were inserted following a standardized protocol to limit the risk of differences in pain due to differences in insertion procedures. In addition, only one HCPs at the study sites performed all the insertions to reduce risk of inter-provider variability.

### **8.2.4 Pain assessments**

We did not reach our anticipated difference in VAS pain scores between active treatment and placebo. Although validated for measuring procedural pain and widely used in trials, VAS

could be biased by factors such as a difference in scales used (horizontal, vertical) and presentation (description of zero- and top anchor points)(157). During completion of the mepivacaine manuscript, we came across different approaches in the use of VAS, for instance, used to measure worst pain experienced during a 10-minute period from the actual procedure (88) and a 9 point VAS-scale (89). We used the most simple, and commonly used, 100 mm horizontal VAS and collected our VAS measures immediately after the procedure to eliminate the risk of recall bias. However, to compare study outcomes from different studies to one another is obviously difficult due to methodology disparities.

VAS-scales are also more sensitive to small changes as compared to other descriptive ordinal scales (157). In our case, the VAS-scores— analyzed with a non-parametric Mann-Whitney u-test due to normality violation (158)—had an IQR of 3.1–5.8 cm in the intervention group and an IQR of 3.3–7.5 in the control group. The ITT analysis yielded a p-value of 0.062. Outliers affected the IQR in a way so that the between-groups difference was 1.1 cm. When performing the PP analysis, removing 3 inadvertently included underaged women—which happened to include two outliers—and their VAS scores yielded an IQR of 3.1–5.5 in the intervention group and 3.4–7.6 in the control group and a between-groups difference of 1.2 cm. This difference was statistically significant, with a p-value of 0.033. The p-value in the PP analysis rejects the null hypothesis that there is no difference in pain reduction between mepivacaine and placebo (159).

However, such small differences might not always be considered clinically significant. In our study, we measured total insertion experience with a simpler ordinal scale, including “easier than expected, as expected” or “worse than expected”. Testing for differences between our intervention and placebo groups, we found that women receiving mepivacaine were less likely to have a “worse than expected” experience ( $p=0.006$ ), which we considered to be a more clinically relevant result. Based on this, we argue that the total experience could be of higher value than pain scores in VAS when assessing clinical significance in future trials of pain with IUD insertion.

## **8.3 STUDY III, PAPER III AND IV**

### **8.3.1 Design**

Cluster randomized trials are different from individually randomized trials. The cluster design allows for evaluating intervention effects on a group level and makes more extensive studies more feasible with regard to time consumption. In this study, clinics were randomly assigned to intervention or control. In addition, to enable testing of our intervention on a large study

population, this approach was chosen to eliminate the risk of spillover effects among providers working in the same clinics. However, Stockholm is a quite small region, and although staff from participating clinics were told not to speak about the study to other midwives in the region, this could have happened, resulting in spillover effects.

### **8.3.2 Recruitment**

Recruitment of study participants is sometimes hard, especially when there are no obvious positive effects that might come from participating. Clinics were informed about the target number of patients (50) to recruit at each clinic (cluster size), and that the recruitment period was estimated to be 6 months. Clinics that reached the target quickly were encouraged to enroll 10 additional patients to adjust for other clinics that did not reach the preferred number of participants. This explains the variation in cluster size. At ACs and YCs, most participants were recruited by HCPs working at the clinic during scheduled visits, whereas in MHCs, a research staff member (mostly myself) had to be present and facilitate recruitment. Letting a research team member, not working at the actual clinic, handle the recruitment could lead to higher numbers of patients declining participation, which is from one point of view a limitation that introduces selection bias. From another point of view, it might be easier for women to decline participation since everyone was informed that participation was voluntary, and the fact that there was no treater-patient relationship present might reduce social desirability bias.

### **8.3.3 Randomization and blinding**

Clinics were randomized by a statistician. An attempt to collect baseline prescription of different contraceptive methods from participating clinics was performed, but not all clinics provided these numbers. However, in addition to clinic type and proportion of migrants within the clinic's catchment area, the numbers we did receive was used to stratify the randomization. This was an attempt to make sure that clinics with an already high LARC prescription would be evenly distributed between intervention and control arms of the study, increasing the external validity of the results.

Clinics allocation to either intervention or control was blinded up until study start. Then HCPs from intervention clinics received study-specific training and therefore blinding past this point was no longer possible.

### **8.3.4 Intervention adherence**

There was a discrepancy between HCP-reported intervention adherence (96.5%) and participants reporting to have received all parts of the intervention. Participants reported that they were not shown the effectiveness chart or the box of contraceptive models in 10.3% and 19.1% of cases, respectively. This discrepancy might be explained by the fact that women were not informed about what parts constituted the intervention. Also, some HCPs reported that some women had already decided upon what method to use and therefore were no longer open to further counselling as a reason for not showing all intervention parts. Women were not asked about adherence to the 4 key-questions as we perceived that they would not be able to distinguish these questions from the regular counselling routine. Since the study had an intention to treat approach and aimed to catch the true intervention effect in a real-life setting, no women were excluded from analysis due to lack of intervention adherence.

### **8.3.5 Follow-up**

Prior to enrolment, patients were informed about the follow-up period of 12 months, and that they would receive an email with a link to an electronic questionnaire at 3 (paper III), 6 and 12 months after the first visit. During recruitment, the use of email for follow up applied to most participants, however, some would rather receive a telephone call or did not have an email address. During follow-up, we noticed that the response rate was not to our satisfaction, and the routine was changed to collect both email addresses and telephone numbers to be able to call and remind participants to complete the questionnaires or even collect the answers over the phone. This increased the response rate, and the final loss to follow-up for paper III was 20.9%. In addition to the email approach, in which participants could postpone and subsequently forget to complete the follow-up, the large proportion of participants from ACs and YCs is seen as explanatory factors since these patient groups usually have a higher loss to follow-up rate.

### **8.3.6 Analyses and results**

The analyses of data for paper III were performed with help from a statistician. The cluster design comes with difficulties in the analysis process due to ICC, a factor that affects p-values negatively. Our findings are important to share since they might have an impact on the Swedish model for contraceptive counselling as well as in other high-income countries. Including this kind of study design and such a large trial increases the power of the findings of the thesis, and in hindsight overcoming all the obstacles by the help of others shows the importance of team efforts in advanced research.

## 9 CONCLUSION

Use of effective contraception after emergency contraception is higher among women who are actively counselled about and offered insertion of a Copper-IUD compared to emergency contraceptive pills. Based on the effectiveness, high continuation rate and acceptability, providers should promote the Copper-IUD for emergency contraception (study I).

Intrauterine mepivacaine instillation reduced VAS pain scores with IUD insertion by 1.1 cm in the intention-to-treat population and 1.2 cm in the per-protocol population compared to placebo, just below the anticipated difference of 1.3 cm selected for clinical significance a priori. Fewer intervention receivers had a “worse than expected” experience of the insertion procedure than placebo receivers. A future larger sample size study, with a higher potency 2% mepivacaine and the total experience selected as the primary outcome could be of interest (study II).

Structured contraceptive counselling with a focus on effectiveness of contraceptive methods results in a higher uptake of LARCs among the participants. The study intervention had a highly pronounced effect also in abortion clinics, which has previously been difficult to achieve. The vast majority of HCPs and participant were satisfied with the intervention and considered it to be supportive in their contraceptive counselling and contraceptive choice. The findings imply that structured counselling is an important and effective tool which could be easily introduced into several clinical settings. Structured contraceptive counselling can affect the uptake of contraception from user-dependent less effective methods to LARCs by enhanced informed decision-making, and by such means improve the quality of care.

## **10 FROM PATHWAYS TO OPEN FIELDS**

### **10.1 COMPREHENSIVE SEXUALITY EDUCATION**

As a midwife in one of Sweden's largest clinics for sexual health, the RFSU Clinic, providing services for STI testing and contraceptive counselling as well as psychotherapy, I got to meet with a large number of patients who are lacking knowledge about their body, their risks of acquiring sexually transmitted infections (STIs) and how to prevent unintended pregnancies. RFSU is an important non-governmental organization fighting for sexual and reproductive health and rights both in Sweden and internationally. The right to receive facts-based information and to choose from a full range of contraception has been the foundation of RFSU since it was founded in 1933. In Sweden, all students are entitled to receive sexuality education in school. However, from the study findings and clinical experience from the RFSU Clinic, it is evident that the quality of this education is highly variable and frequently poor—especially with regards to contraception and prevention of STIs. RFSU will keep fighting to make Swedish and international politician respect the fundamental rights to comprehensive sexuality education and a full range of contraception, including LARCs.

### **10.2 CHANGES ARE WANTED, AND NEEDED**

When providing contraceptive counselling for several years at the RFSU Clinic, I experienced the lack of time with each patient to limit the possibility to provide comprehensive contraceptive counselling. This was even more clear during our drop-in clinics. At an early stage, by information gathered from research in the field, I started to use a more structured form of counselling. I based it on motivational interviewing and started by presenting the most effective methods. Many women expressed that they had never been counselled about LARCs before, although some of them had used contraception for many years. Most women receive their contraceptive counselling from midwives at MHCs, and most counselling is provided during drop-in hours. Although reimbursement from the country regions for providing contraceptive counselling is adjusted to allow for approximately 20-minute sessions, MHCs are often pushed to provide their services within 10 minutes—sometimes even shorter—to be able to serve all the patients that visit the clinics.

The waiting rooms are small, and most often so full of patients that there are not enough seats for everyone. To see the waiting area cramped with patients causes much stress, and the quality in the services provided becomes poor. Strategies to deal with this situation makes midwives take shortcuts in their counselling, for instance, by just asking what contraceptive method the woman use and if she is pleased with it. If the answer is positive, a quick blood-

pressure is taken, and a prescription renewal is administered. This type of counselling comes with risks of missing essential contraindications. In addition, women are not informed about other methods that might be even more suitable. This has traditionally led to high use of less effective methods, resulting in numerous of unintended pregnancies and abortions. Women want comprehensive information. Women have the right to comprehensive information. And more importantly, women need comprehensive information to enhance informed decisions about contraceptive use. Introducing structure, with emphasis on method effectiveness in contraceptive counselling, improves quality of care. It might also save time. Effectiveness is the most important factor expressed when deciding upon contraceptive use, and when presented with the most effective methods first, women tend to choose them over less effective methods. Thus, much time is saved during this type of counselling since information about less effective methods is experienced as redundant by the patient. Another time- and money-saving factor is built into the name of LARCs—they can be used for a long time. LARCs have high continuation rates, and women using LARCs do not have to pay annual visits to clinics for prescription renewals. The thesis findings support the introduction of structured contraceptive counselling and provision of Cu-IUDs for EC to increase uptake of LARC—and by such means protecting women from unintended pregnancies and subsequent abortions.

### **10.3 FUTURE RESEARCH**

Based on the study findings, implications for future research has been revealed.

1. We need to conduct qualitative studies on HCPs experiences with using structured contraceptive counselling to make adjustments to the intervention to increase quality even more
2. We need to do qualitative research with women receiving contraceptive counselling, to gain a better understanding about the decision-making process when it comes to use of contraception
3. We need to do research about internet as a source of information about contraception
4. We need to keep doing research about pain management during IUD insertion, to be able to provide women in need with effective pain relief.
5. We need to conduct implementation research of methods to promote systemic uptake of the study findings into routine practice.

The list could be made longer, but research is time consuming and requires a lot of resources. This will be a good start.

## 11 SUMMARY

Unintended pregnancies are an inexhaustible source to life-changing decisions and events for individuals and result in enormous costs for societies having to deal with maternal health services, deliveries, hospital care and abortions. Unintended pregnancies could be prevented by the use of effective contraception and LARC methods, including IUDs and implants, have the highest effectiveness, the highest user satisfaction and the highest rates of continued use. By increasing uptake of LARC, women would be less exposed to mistimed and unwanted pregnancies that are known to affect their social- and psychological well-being as well as their economic situation. In addition, societies could save huge amounts of money since LARCs are the most cost-effective methods. All money invested in preventing unintended pregnancies pays back fivefold.

Women value the effectiveness higher than any other factor when deciding upon contraceptive use, and women want more comprehensive contraceptive counselling than HCPs think they do. Comprehensive counselling, especially when given in a structured form, result in higher uptake of LARCs, which—in addition to being very effective—also are known to decrease other health-related issues such as heavy menstrual bleeding and dysmenorrhea. By increasing LARC use, improvements in women's reproductive health are achieved.

This thesis aims to find pathways to increase uptake of LARC by interventions used to improve the quality of care from both an HCP's and a patient's perspective. The thesis builds on one observational cohort study, one double-blinded randomized, controlled trial and one cluster randomized trial. All studies were conducted in clinics providing contraceptive services in the region of Stockholm, Sweden.

Study I aimed to compare use of an effective method of contraception 6 months following insertion of a copper intrauterine device or intake of ulipristal acetate for emergency contraception. The hypothesis was that patients opting for a Cu-IUD would use effective contraception at 6 months to a higher extent compared to patients opting for UPA (primary outcome). In addition, we hypothesized that participants in the Cu-IUD group would have had less unprotected sexual intercourses and fewer pregnancies. The results show that participants opting for a Cu-IUD for EC use effective contraception at 6 months follow-up to a greater extent than participants opting for UPA. The proportion of women with subsequent unprotected sexual intercourse during the follow-up period was lower in the Cu-IUD group compared to the UPA group. The differences pregnancies, 1 in the Cu-IUD group and 3 in the UPA group, did not reach statistical significance.

Study II aimed to evaluate whether intrauterine mepivacaine instillation before IUD insertion decreases pain compared to placebo. The hypothesis was that intrauterine mepivacaine instillation would numb the uterine and cervical lining and reduce pain with IUD insertion. We also hypothesized that mepivacaine would provide a more effective pain relief than saline solution (NaCl). In the ITT-analysis, intrauterine mepivacaine instillation

did not decrease pain scores with IUD insertion compared to placebo. The PP-analysis showed a decrease in pain scores with IUD insertion. More participants receiving mepivacaine experienced insertion as easier than expected or as expected compared to placebo.

Study III aimed to evaluate the effect of structured contraceptive counselling on LARC choice, LARC initiation and pregnancy rates in abortion clinics, maternal health clinics and youth clinics (paper III). It also aimed to evaluate user satisfaction of healthcare providers and patients with the intervention used and to characterize which providers and patients found the intervention most helpful (paper IV). The results show that more participants receiving structured contraceptive counselling chose LARCs compared to women receiving standard contraceptive counselling and that LARC initiation at 3 months follow-up was higher among women receiving structured contraceptive counselling. Both HCPs and participants reported high satisfaction with the intervention used in the trial. HCPs reported the use of the study intervention to be time neutral compared to standard contraceptive counselling. No individual identifiers of satisfaction could be determined among HCPs. More migrant and 2nd generation migrants than non-migrants found the educational video to be supportive in making their contraceptive choice.

The study findings show that evidence-based contraceptive counselling focusing on method effectiveness is successful in increasing uptake of LARC, both when in need of EC and during regular contraceptive counselling. The findings suggest that women could have better experiences with IUD insertions if treated with intrauterine mepivacaine, which is important since the fear of pain during IUD insertion limits uptake of LARC.

## 12 ACKNOWLEDGEMENTS

Starting by thanking someone other than my lovely wife would be a crime deserving harsh punishment. Jessica – you have been there for me during this whole process, taking care of our other family members and serving all our fundamental needs. Thank you for everything!

Secondly, my supervisors deserve all the gratitude I can elicit. To Helena Kopp Kallner, for believing in me and boosting my self-esteem during this process. And for pushing me when losing my speed or track. You are a true “master mind” with no limits when it comes to exploring new research topics and areas of improvement within the field of women’s health. Nothing seems impossible in your presence. I have learnt so much from you, and I am so glad to continue the journey towards evidence-based reproductive healthcare with you. To Kristina Gemzell Danielsson, for being the professor everyone need by their side. No one is as accurate in their supervision as you. Although you might seem occupied with workloads considered lethal to any mentally sane and normally functioning person, you always seem to find time to direct and help out your doctoral students and co-workers. And last but not least, always happy!

Also I wish to thank Karin Emtell Iwarsson for great mind-wrecking discussions and structure. Without you, I don’t think I would have been able to pull the great LOWE study around. And Isabella “Bella” Bizjak, without your positivism and your efforts our team work would have been so much harder.

Ewa Andersson, thank you so much for mentoring me in the beginning. You made me feel welcome in the research family of the department of Reproductive Health at KI. Most importantly you believed in me as a researcher and pushed me into becoming a doctoral student.

There are others I need to mention. First I would like to thank Amanda Cleeve, for being such an inspiration and for providing me with the best thesis ever. We have both experienced true life changing events during our study period and if you could make it, so could I. Annette D, Ulrika F, Helen F and Annelie W, you have also helped me through this process. Thank you!

To my family, thank you for supporting me and helping me through hard times during this period.

To all my colleagues at Dalarna University for supporting me and making my first period easy and cozy.

Finally, to all my colleagues at RFSU. Thank you for helping me produce research of great value. Eva Marie Sundberg, thank you for believing in me and supporting me in the decision to start my career as a researcher. Without you and your open mind to new projects I would not be where I am today.

## 13 REFERENCES

1. Gipson JD, Koenig MA, Hindin MJ. The effects of unintended pregnancy on infant, child, and parental health: a review of the literature. *Stud Fam Plann.* 2008;39(1):18-38.
2. Hardee K, Eggleston E, Wong EL, Irwanto, Hull TH. Unintended pregnancy and women's psychological well-being in Indonesia. *Journal of biosocial science.* 2004;36(5):617-26.
3. Tsui AO, McDonald-Mosley R, Burke AE. Family planning and the burden of unintended pregnancies. *Epidemiologic reviews.* 2010;32:152-74.
4. Logan C, Holcombe E, Manlove J, Ryan S. The consequences of unintended childbearing: A white paper. Washington, DC: Child Trends. 2007.
5. Sonfield A, Hasstedt K, Gold RB. Moving forward: Family planning in the era of health reform. 2014.
6. Sedgh G, Singh S, Hussain R. Intended and unintended pregnancies worldwide in 2012 and recent trends. *Stud Fam Plann.* 2014;45(3):301-14.
7. Darroch J, Audam S, Biddlecom A, Kopplin G, Riley T, Singh S, et al. Adding it up: investing in contraception and maternal and newborn health, 2017. Fact sheet New York: Guttmacher Institute. 2017.
8. Bearak J, Popinchalk A, Alkema L, Sedgh G. Global, regional, and subregional trends in unintended pregnancy and its outcomes from 1990 to 2014: estimates from a Bayesian hierarchical model. *The Lancet Global health.* 2018;6(4):e380-e9.
9. Askew I, Weinberger M, Dasgupta A, Darroch J, Smith E, Stover J, et al. Harmonizing Methods for Estimating the Impact of Contraceptive Use on Unintended Pregnancy, Abortion, and Maternal Health. *Global health, science and practice.* 2017;5(4):658-67.
10. Federation IPP. Sexual rights: an IPPF declaration. London: IPPF. 2008.
11. UN General Assembly. Transforming our world: the 2030 Agenda for Sustainable Development [internet]. United Nations; 2015 [cited November 2<sup>nd</sup>, 2019]. Available from: <https://www.refworld.org/docid/57b6e3e44.html>
12. United Nations. Department of Economic and Social Affairs, Population Division. Trends in Contraceptive Use Worldwide 2015. 2015.
13. Ahmed S, Li Q, Liu L, Tsui AO. Maternal deaths averted by contraceptive use: an analysis of 172 countries. *Lancet.* 2012;380(9837):111-25.
14. Trussell J. Contraceptive failure in the United States. *Contraception.* 2011;83(5):397-404.
15. Sedgh G, Henshaw SK, Singh S, Bankole A, Drescher J. Legal abortion worldwide: incidence and recent trends. *Int Fam Plan Perspect.* 2007;33(3):106-16.
16. Kopp Kallner H, Thunell L, Brynhildsen J, Lindeberg M, Gemzell Danielsson K. Use of Contraception and Attitudes towards Contraceptive Use in Swedish Women - A Nationwide Survey. *PLoS One.* 2015;10(5):e0125990.
17. Hellstrom A, Gemzell Danielsson K, Kopp Kallner H. Trends in use and attitudes towards contraception in Sweden: results of a nationwide survey. *Eur J Contracept Reprod Health Care.* 2019;24(2):154-60.
18. Stewart J, Breslin WJ, Beyer BK, Chadwick K, De Schaepdrijver L, Desai M, et al. Birth Control in Clinical Trials: Industry Survey of Current Use Practices, Governance, and Monitoring. *Therapeutic innovation & regulatory science.* 2016;50(2):155-68.
19. Rose SB, Lawton BA. Impact of long-acting reversible contraception on return for repeat abortion. *American journal of obstetrics and gynecology.* 2012;206(1):37 e1-6.
20. Heikinheimo O, Gissler M, Suhonen S. Age, parity, history of abortion and contraceptive choices affect the risk of repeat abortion. *Contraception.* 2008;78(2):149-54.
21. Cameron ST, Glasier A, Chen ZE, Johnstone A, Dunlop C, Heller R. Effect of contraception provided at termination of pregnancy and incidence of subsequent termination of pregnancy. *Bjog.* 2012;119(9):1074-80.
22. Winner B, Peipert JF, Zhao Q, Buckel C, Madden T, Allsworth JE, et al. Effectiveness of long-acting reversible contraception. *The New England journal of medicine.* 2012;366(21):1998-2007.
23. Singh S, Remes L, Sedgh G, Kwok L, Onda T. Abortion Worldwide 2017: Uneven Progress and Unequal Access. New York, Guttmacher institute. 2018.
24. Institutionen för hälsa och välfärd. Aborter i Norden 2017 [internet]. THL; 2017 [cited November 2<sup>nd</sup>, 2019]. Available from: <https://thl.fi/sv/web/thlfi-sv/statistik/statistik-efter-amne/sexuell-och-reproduktiv-halsa/aborter/aborter-i-norden>
25. Consensus statement on emergency contraception. *Contraception.* 1995;52(4):211-3.
26. Haeger KO, Lamme J, Cleland K. State of emergency contraception in the U.S., 2018. *Contraception and reproductive medicine.* 2018;3:20.

27. Glasier A. Emergency contraception: clinical outcomes. *Contraception*. 2013;87(3):309-13.
28. WHO. The 19th WHO model list of essential medicines. Geneva: World Health Organization; 2015.
29. Shen J, Che Y, Showell E, Chen K, Cheng L. Interventions for emergency contraception. *Cochrane Database Syst Rev*. 2017;8:CD001324.
30. Shen J, Che Y, Showell E, Chen K, Cheng LA. Interventions for emergency contraception. *Cochrane Database Syst Rev*. 2019(1):333.
31. Turok DK, Jacobson JC, Dermish AI, Simonsen SE, Gurtcheff S, McFadden M, et al. Emergency contraception with a copper IUD or oral levonorgestrel: an observational study of 1-year pregnancy rates. *Contraception*. 2014;89(3):222-8.
32. Benagiano G, Bastianelli C, Farris M, Brosens I. Selective progesterone receptor modulators: an update. *Expert opinion on pharmacotherapy*. 2014;15(10):1403-15.
33. Polis CB, Schaffer K, Blanchard K, Glasier A, Harper CC, Grimes DA. Advance provision of emergency contraception for pregnancy prevention (full review). *Cochrane Database Syst Rev*. 2007(2):CD005497.
34. Mulligan K. Access to Emergency Contraception and its Impact on Fertility and Sexual Behavior. *Health Econ*. 2015.
35. Group EC. Emergency contraception. Widely available and effective but disappointing as a public health intervention: a review. *Hum Reprod*. 2015;30(4):751-60.
36. Michie L, Cameron ST. Emergency contraception and impact on abortion rates. *Best practice & research Clinical obstetrics & gynaecology*. 2019.
37. Goulard H, Moreau C, Gilbert F, Job-Spira N, Bajos N. Contraceptive failures and determinants of emergency contraception use. *Contraception*. 2006;74(3):208-13.
38. Gemzell-Danielsson K, Berger C, P GLL. Emergency contraception - mechanisms of action. *Contraception*. 2012.
39. Berger C, Boggavarapu NR, Menezes J, Lalitkumar PG, Gemzell-Danielsson K. Effects of ulipristal acetate on human embryo attachment and endometrial cell gene expression in an in vitro co-culture system. *Hum Reprod*. 2015;30(4):800-11.
40. Willetts SJ, MacDougall M, Cameron ST. A survey regarding acceptability of oral emergency contraception according to the posited mechanism of action. *Contraception*. 2017;96(2):81-8.
41. Glasier A, Cameron ST, Blithe D, Scherrer B, Mathe H, Levy D, et al. Can we identify women at risk of pregnancy despite using emergency contraception? Data from randomized trials of ulipristal acetate and levonorgestrel. *Contraception*. 2011;84(4):363-7.
42. Cameron ST, Berger C, Michie L, Klipping C, Gemzell-Danielsson K. The effects on ovarian activity of ulipristal acetate when 'quickstarting' a combined oral contraceptive pill: a prospective, randomized, double-blind parallel-arm, placebo-controlled study. *Hum Reprod*. 2015;30(7):1566-72.
43. Unit FoSaRHFCE. FSRH Guideline: Emergency Contraception March 2017 (Amended December 2017). [Internet]. Faculty of Sexual & Reproductive Health [cited October 20<sup>th</sup>, 2019]. Available from: <https://www.fsrh.org/documents/ceu-clinical-guidance-emergency-contraception-march-2017/>.
44. Cheng L, Che Y, Gulmezoglu AM. Interventions for emergency contraception. *Cochrane Database Syst Rev*. 2012(8):Cd001324.
45. Michie L, Cameron ST, Glasier A, Larke N, Muir A, Lorimer A. Pharmacy-based interventions for initiating effective contraception following the use of emergency contraception: a pilot study. *Contraception*. 2014;90(4):447-53.
46. Cleland K, Zhu H, Goldstuck N, Cheng L, Trussell J. The efficacy of intrauterine devices for emergency contraception: a systematic review of 35 years of experience. *Hum Reprod*. 2012;27(7):1994-2000.
47. American College of O, Gynecologists. ACOG Practice Bulletin No. 112: Emergency contraception. *Obstet Gynecol*. 2010;115(5):1100-9.
48. World Health Organization, Emergency Contraception, Fact Sheet 244. 2012.
49. Thompson I, Sanders JN, Schwarz EB, Boraas C, Turok DK. Copper intrauterine device placement 6-14 days after unprotected sex. *Contraception*. 2019;100(3):219-21.
50. Cheng L, Che Y, Gulmezoglu AM. Interventions for emergency contraception. *Cochrane Database Syst Rev*. 2012;8:CD001324.
51. Goldstuck ND, Cheung TS. The efficacy of intrauterine devices for emergency contraception and beyond: a systematic review update. *Int J Womens Health*. 2019;11:471-9.
52. Attia AM, Ibrahim MM, Abou-Setta AM. Role of the levonorgestrel intrauterine system in effective contraception. Patient preference and adherence. 2013;7:777-85.

53. Antikonception – behandlingsrekommendation. Information från Läkemedelsverket 2014;25(2):14–28.
54. Sanders JN, Turok DK, Royer PA, Thompson IS, Gawron LM, Storck KE. One-year continuation of copper or levonorgestrel intrauterine devices initiated at the time of emergency contraception. *Contraception*. 2017;96(2):99-105.
55. Sanders JN, Howell L, Saltzman HM, Schwarz EB, Thompson IS, Turok DK. Unprotected intercourse in the 2 weeks prior to requesting emergency intrauterine contraception. *American journal of obstetrics and gynecology*. 2016;215(5):592.e1-.e5.
56. Curtis KM, Tepper NK, Jatlaoui TC, Berry-Bibee E, Horton LG, Zapata LB, et al. U.S. Medical Eligibility Criteria for Contraceptive Use, 2016. *MMWR Recommendations and reports : Morbidity and mortality weekly report Recommendations and reports*. 2016;65(3):1-103.
57. Foran T, Butcher BE, Kovacs G, Bateson D, O'Connor V. Safety of insertion of the copper IUD and LNG-IUS in nulliparous women: a systematic review. *Eur J Contracept Reprod Health Care*. 2018;23(5):379-86.
58. Ekelund M, Melander M, Gemzell-Danielsson K. Intrauterine contraception: attitudes, practice, and knowledge among Swedish health care providers. *Contraception*. 2014;89(5):407-12.
59. Luchowski AT, Anderson BL, Power ML, Raglan GB, Espey E, Schulkin J. Obstetrician-gynecologists and contraception: practice and opinions about the use of IUDs in nulliparous women, adolescents and other patient populations. *Contraception*. 2014;89(6):572-7.
60. Harper CC, Speidel JJ, Drey EA, Trussell J, Blum M, Darney PD. Copper intrauterine device for emergency contraception: clinical practice among contraceptive providers. *Obstet Gynecol*. 2012;119(2 Pt 1):220-6.
61. French VA, Rangel AV, Mattingly TL. Access to emergency contraception in Kansas City clinics. *Contraception*. 2018;98(6):482-5.
62. Biggs MA, Kaller S, Harper CC, Freedman L, Mays AR. "Birth Control can Easily Take a Back Seat": Challenges Providing IUDs in Community Health Care Settings. *Journal of health care for the poor and underserved*. 2018;29(1):228-44.
63. Goodman SR, El Ayadi AM, Rocca CH, Kohn JE, Benedict CE, Dieseldorff JR, et al. The intrauterine device as emergency contraception: how much do young women know? *Contraception*. 2018.
64. Mohammed S, Abdulai AM, Iddrisu OA. Pre-service knowledge, perception, and use of emergency contraception among future healthcare providers in northern Ghana. *Contraception and reproductive medicine*. 2019;4:1.
65. Stone R, Rafie S, El-Ibiary SY, Vernon V, Lodise NM. Emergency Contraception Algorithm and Guide for Clinicians. *Nurs Womens Health*. 2017;21(4):297-305.
66. Asker C, Stokes-Lampard H, Beavan J, Wilson S. What is it about intrauterine devices that women find unacceptable? Factors that make women non-users: a qualitative study. *J Fam Plann Reprod Health Care*. 2006;32(2):89-94.
67. Envall N, Groes Kofoed N, Kopp-Kallner H. Use of effective contraception 6 months after emergency contraception with a copper intrauterine device or ulipristal acetate - a prospective observational cohort study. *Acta Obstet Gynecol Scand*. 2016;95(8):887-93.
68. Hubacher D, Reyes V, Lillo S, Zepeda A, Chen PL, Croxatto H. Pain from copper intrauterine device insertion: randomized trial of prophylactic ibuprofen. *American journal of obstetrics and gynecology*. 2006;195(5):1272-7.
69. Lopez LM, Bernholc A, Zeng YW, Allen RH, Bartz D, O'Brien PA, et al. Interventions for pain with intrauterine device insertion. *Cochrane Database Syst Rev*. 2015(7):126.
70. Murty J. Use and effectiveness of oral analgesia when fitting an intrauterine device. *J Fam Plann Reprod Health Care*. 2003;29(3):150-1.
71. Gemzell-Danielsson K, Jensen JT, Monteiro I, Peers T, Rodriguez M, Di Spiezio Sardo A, et al. Interventions for the prevention of pain associated with the placement of intrauterine contraceptives: An updated review. *Acta Obstet Gynecol Scand*. 2019.
72. Suhonen S, Haukkamaa M, Jakobsson T, Rauramo I. Clinical performance of a levonorgestrel-releasing intrauterine system and oral contraceptives in young nulliparous women: a comparative study. *Contraception*. 2004;69(5):407-12.
73. Gemzell-Danielsson K, Schellschmidt I, Apter D. A randomized, phase II study describing the efficacy, bleeding profile, and safety of two low-dose levonorgestrel-releasing intrauterine contraceptive systems and Mirena. *Fertil Steril*. 2012;97(3):616-22.e1-3.
74. Marions L, Lovkvist L, Taube A, Johansson M, Dalvik H, Overlie I. Use of the levonorgestrel releasing-intrauterine system in nulliparous women--a non-interventional study in Sweden. *Eur J Contracept Reprod Health Care*. 2011;16(2):126-34.

75. Allen RH, Bartz D, Grimes DA, Hubacher D, O'Brien P. Interventions for pain with intrauterine device insertion. *Cochrane Database Syst Rev.* 2009(3):Cd007373.
76. Bednarek PH, Creinin MD, Reeves MF, Cwiak C, Espey E, Jensen JT. Prophylactic ibuprofen does not improve pain with IUD insertion: a randomized trial. *Contraception.* 2015;91(3):193-7.
77. Abbas AM, Ali SS, Salem MN, Sabry M. Effect of oral ketoprofen on pain perception during copper IUD insertion among parous women: A randomized double-blind controlled trial. *Middle East Fertil Soc J.* 2018;23(4):491-5.
78. Maguire K, Davis A, Rosario Tejeda L, Westhoff C. Intracervical lidocaine gel for intrauterine device insertion: a randomized controlled trial. *Contraception.* 2012;86(3):214-9.
79. Turok DK, Simmons RG, Cappiello B, Gawron LM, Saviers-Steiger J, Sanders JN. Use of a novel suction cervical retractor for intrauterine device insertion: a pilot feasibility trial. *BMJ sexual & reproductive health.* 2019;45(1):47-53.
80. Christenson K, Lerma K, Shaw KA, Blumenthal PD. Assessment of a simplified insertion technique for intrauterine devices. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics.* 2016;134(1):29-32.
81. Akdemir Y, Karadeniz M. The relationship between pain at IUD insertion and negative perceptions, anxiety and previous mode of delivery. *European Journal of Contraception and Reproductive Health Care.* 2019;24(3):240-5.
82. McCarthy C. Intrauterine contraception insertion pain: nursing interventions to improve patient experience. *Journal of clinical nursing.* 2017.
83. Bahamondes L, Mansour D, Fiala C, Kaunitz AM, Gemzell-Danielsson K. Practical advice for avoidance of pain associated with insertion of intrauterine contraceptives. *J Fam Plan Reprod Health Care.* 2014;40(1):54-60.
84. Brima N, Akintomide H, Iguyovwe V, Mann S. A comparison of the expected and actual pain experienced by women during insertion of an intrauterine contraceptive device. *Open Access J Contracept.* 2015;6:21-6.
85. Folkhälsomyndigheten. Sexuality and health among young people in Sweden. 2017:1-146.
86. Hajiesmaello M, Mohammadi E, Farrokh-Eslamlou H. Evaluation of the effect of 10% lidocaine spray on reducing the pain of intrauterine device insertion: A randomised controlled trial. *SAJOG-S Afr J Obstete Gynaecol.* 2019;25(1):25-9.
87. McNicholas CP, Madden T, Zhao Q, Secura G, Allsworth JE, Peipert JF. Cervical lidocaine for IUD insertional pain: a randomized controlled trial. *American journal of obstetrics and gynecology.* 2012;207(5):384 e1-6.
88. Tornblom-Paulander S, Tingaker BK, Werner A, Liliacreutz C, Conner P, Wessel H, et al. Novel topical formulation of lidocaine provides significant pain relief for intrauterine device insertion: pharmacokinetic evaluation and randomized placebo-controlled trial. *Fertil Steril.* 2015;103(2):422-7.
89. Nelson AL, Fong JK. Intrauterine infusion of lidocaine does not reduce pain scores during IUD insertion. *Contraception.* 2013.
90. Miles SM, Shvartsman K, Dunlow S. Intrauterine lidocaine and naproxen for analgesia during intrauterine device insertion: randomized controlled trial. *Contraception and reproductive medicine.* 2019;4:13.
91. Madden T, Mullersman JL, Omvig KJ, Secura GM, Peipert JF. Structured contraceptive counseling provided by the Contraceptive CHOICE Project. *Contraception.* 2013;88(2):243-9.
92. Peipert JF, Madden T, Allsworth JE, Secura GM. Preventing unintended pregnancies by providing no-cost contraception. *Obstet Gynecol.* 2012;120(6):1291-7.
93. Madden T, Paul R, Maddipati R, Buckel C, Goodman M, Peipert JF. Comparison of unintended pregnancy at 12 months between two contraceptive care programs; a controlled time-trend design. *Contraception.* 2019;100(3):196-201.
94. Danielson R, Marcy S, Plunkett A, Wiest W, Greenlick MR. Reproductive health counseling for young men: what does it do? *Family planning perspectives.* 1990;22(3):115-21.
95. Canto De Cetina TE, Canto P, Ordonez Luna M. Effect of counseling to improve compliance in Mexican women receiving depot-medroxyprogesterone acetate. *Contraception.* 2001;63(3):143-6.
96. Langston AM, Rosario L, Westhoff CL. Structured contraceptive counseling--a randomized controlled trial. *Patient education and counseling.* 2010;81(3):362-7.
97. Project WHOatI. Decision-making tool for family planning clients and providers. Baltimore and Geneva: Bloomberg School of Public Health and WHO; 2005.
98. Harper CC, Rocca CH, Thompson KM, Morfesis J, Goodman S, Darney PD, et al. Reductions in pregnancy rates in the USA with long-acting reversible contraception: a cluster randomised trial. *Lancet.* 2015;386(9993):562-8.

99. Peipert JF, Zhao Q, Allsworth JE, Petrosky E, Madden T, Eisenberg D, et al. Continuation and satisfaction of reversible contraception. *Obstet Gynecol.* 2011;117(5):1105-13.
100. Sanders JN, Higgins JA, Adkins DE, Stoddard GJ, Gawron LM, Turok DK. The Impact of Sexual Satisfaction, Functioning, and Perceived Contraceptive Effects on Sex Life on IUD and Implant Continuation at 1 Year. *Women's health issues : official publication of the Jacobs Institute of Women's Health.* 2018;28(5):401-7.
101. Grunloh DS, Casner T, Secura GM, Peipert JF, Madden T. Characteristics associated with discontinuation of long-acting reversible contraception within the first 6 months of use. *Obstet Gynecol.* 2013;122(6):1214-21.
102. Hubacher D, Chen PL, Park S. Side effects from the copper IUD: do they decrease over time? *Contraception.* 2009;79(5):356-62.
103. Sanders JN, Adkins DE, Kaur S, Storck K, Gawron LM, Turok DK. Bleeding, cramping, and satisfaction among new copper IUD users: A prospective study. *PLoS One.* 2018;13(11):e0199724.
104. Hall AM, Kutler BA. Intrauterine contraception in nulliparous women: a prospective survey. *The Journal of Family Planning and Reproductive Health Care.* 2016;42(1):36-42.
105. Rosenstock JR, Peipert JF, Madden T, Zhao Q, Secura GM. Continuation of reversible contraception in teenagers and young women. *Obstet Gynecol.* 2012;120(6):1298-305.
106. Socialstyrelsen. Statistik om läkemedel 2016. [Internet]. Socialstyrelsen; 2017. [cited January 20<sup>th</sup>, 2018]. Available from: <http://www.socialstyrelsen.se/publikationer2017/2017-3-33>
107. Mavranzouli I. The cost-effectiveness of long-acting reversible contraceptive methods in the UK: analysis based on a decision-analytic model developed for a National Institute for Health and Clinical Excellence (NICE) clinical practice guideline. *Hum Reprod.* 2008;23(6):1338-45.
108. Blithe DL. Pipeline for contraceptive development. *Fertil Steril.* 2016.
109. Gibbs SE, Rocca CH, Bednarek P, Thompson KM, Darney PD, Harper CC. Long-Acting Reversible Contraception Counseling and Use for Older Adolescents and Nulliparous Women. *The Journal of adolescent health : official publication of the Society for Adolescent Medicine.* 2016.
110. Johnson BA. Insertion and removal of intrauterine devices. *Am Fam Physician.* 2005;71(1):95-102.
111. Farmer M, Webb A. Intrauterine device insertion-related complications: can they be predicted? *J Fam Plann Reprod Health Care.* 2003;29(4):227-31.
112. Nederhof AJ. Methods of coping with social desirability bias: A review. *European journal of social psychology.* 1985;15(3):263-80.
113. Saav I, Aronsson A, Marions L, Stephansson O, Gemzell-Danielsson K. Cervical priming with sublingual misoprostol prior to insertion of an intrauterine device in nulliparous women: a randomized controlled trial. *Hum Reprod.* 2007;22(10):2647-52.
114. Todd KH, Funk KG, Funk JP, Bonacci R. Clinical significance of reported changes in pain severity. *Annals of emergency medicine.* 1996;27(4):485-9.
115. Gallagher EJ, Liebman M, Bijur PE. Prospective validation of clinically important changes in pain severity measured on a visual analog scale. *Annals of emergency medicine.* 2001;38(6):633-8.
116. Steiner MJ, Trussell J, Johnson S. Communicating contraceptive effectiveness: an updated counseling chart. *American journal of obstetrics and gynecology.* 2007;197(1):118.
117. Wu S, Crespi CM, Wong WK. Comparison of methods for estimating the intraclass correlation coefficient for binary responses in cancer prevention cluster randomized trials. *Contemporary clinical trials.* 2012;33(5):869-80.
118. Bharadwaj P, Akintomide H, Brima N, Copas A, D'Souza R. Determinants of long-acting reversible contraceptive (LARC) use by adolescent girls and young women. *Eur J Contracept Reprod Health Care.* 2012;17(4):298-306.
119. Bharadwaj P, Saxton JC, Mann SN, Jungmann EM, Stephenson JM. What influences young women to choose between the emergency contraceptive pill and an intrauterine device? A qualitative study. *Eur J Contracept Reprod Health Care.* 2011;16(3):201-9.
120. Burke PJ, Coles MS, Di Meglio G, Gibson EJ, Handschin SM, Lau M, et al. Sexual and reproductive health care: a position paper of the Society for Adolescent Health and Medicine. *The Journal of adolescent health : official publication of the Society for Adolescent Medicine.* 2014;54(4):491-6.
121. Ott MA, Sucato GS. Contraception for adolescents. *Pediatrics.* 2014;134(4):e1257-81.
122. Francis JKR, Gold MA. Long-Acting Reversible Contraception for Adolescents: A Review. *JAMA pediatrics.* 2017;171(7):694-701.
123. Brockmeyer A, Kishen M, Webb A. Experience of IUD/IUS insertions and clinical performance in nulliparous women--a pilot study. *Eur J Contracept Reprod Health Care.* 2008;13(3):248-54.

124. Mody SK, Kiley J, Rademaker A, Gawron L, Stika C, Hammond C. Pain control for intrauterine device insertion: a randomized trial of 1% lidocaine paracervical block. *Contraception*. 2012;86(6):704-9.
125. Sanders JN, Moran LA, Mullholand M, Torres E, Turok DK. Video counseling about emergency contraception: an observational study. *Contraception*. 2019;100(1):54-64.
126. Dineley B, Patel T, Black M, Koziarski R, Lamarche L, Costescu D. Video Media in Clinic Waiting Areas Increases Interest in Most Effective Contraceptive Methods. *Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC*. 2018;40(10):1302-8.
127. Lopez LM, Steiner M, Grimes DA, Hilgenberg D, Schulz KF. Strategies for communicating contraceptive effectiveness. *Cochrane Database Syst Rev*. 2013(4):Cd006964.
128. Thompson KMJ, Rocca CH, Stern L, Morfesis J, Goodman S, Steinauer J, et al. Training contraceptive providers to offer intrauterine devices and implants in contraceptive care: a cluster randomized trial. *American journal of obstetrics and gynecology*. 2018;218(6):597.e1-e7.
129. Stulberg DB, Dahlquist IH, Disterhoft J, Bello JK, Hunter MS. Increase in Contraceptive Counseling by Primary Care Clinicians After Implementation of One Key Question(R) at an Urban Community Health Center. *Matern Child Health J*. 2019;23(8):996-1002.
130. Russo JA, Miller E, Gold MA. Myths and misconceptions about long-acting reversible contraception (LARC). *The Journal of adolescent health : official publication of the Society for Adolescent Medicine*. 2013;52(4 Suppl):S14-21.
131. Emtell Iwarsson K, Larsson EC, Gemzell-Danielsson K, Essen B, Klingberg-Allvin M. Contraceptive use among migrant, second-generation migrant and non-migrant women seeking abortion care: a descriptive cross-sectional study conducted in Sweden. *BMJ sexual & reproductive health*. 2019.
132. Peipert JF, Madden T, Allsworth JE, Secura GM. Preventing Unintended Pregnancies by Providing No-Cost Contraception. *Obstetrics and Gynecology*. 2012;120(6):1291-7.
133. Gyllenberg F, Juselius M, Gissler M, Heikinheimo O. Long-Acting Reversible Contraception Free of Charge, Method Initiation, and Abortion Rates in Finland. *Am J Public Health*. 2018;108(4):538-43.
134. Socialstyrelsen. Statistik om aborter 2018. [Internet]. Socialstyrelsen:2019. [Cited November 2<sup>nd</sup>, 2019]. Available from: <https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/statistik/2019-5-18.pdf>
135. Stanek AM, Bednarek PH, Nichols MD, Jensen JT, Edelman AB. Barriers associated with the failure to return for intrauterine device insertion following first-trimester abortion. *Contraception*. 2009;79(3):216-20.
136. Bergin A, Tristan S, Terplan M, Gilliam ML, Whitaker AK. A missed opportunity for care: two-visit IUD insertion protocols inhibit placement. *Contraception*. 2012;86(6):694-7.
137. Baron MM, Potter B, Schrage S. A Review of Long-Acting Reversible Contraception Methods and Barriers to Their Use. *WMJ : official publication of the State Medical Society of Wisconsin*. 2018;117(4):156-9.
138. Buckel C, Maddipati R, Goodman M, Peipert JF, Madden T. Effect of staff training and cost support on provision of long-acting reversible contraception in community health centers. *Contraception*. 2019;99(4):222-7.
139. Obstetricians ACo, Gynecologists. Increasing access to contraceptive implants and intrauterine devices to reduce unintended pregnancy. *Committee Opinion*. 2015;642.
140. Strauss JF, Barbieri RL, Yen SSC. Yen & Jaffe's reproductive endocrinology : physiology, pathophysiology, and clinical management. 2019.
141. Carvalho N, Margatho D, Cursino K, Benetti-Pinto CL, Bahamondes L. Control of endometriosis-associated pain with etonogestrel-releasing contraceptive implant and 52-mg levonorgestrel-releasing intrauterine system: randomized clinical trial. *Fertil Steril*. 2018;110(6):1129-36.
142. Callahan DG, Garabedian LF, Harney KF, DiVasta AD. Will it Hurt? The Intrauterine Device Insertion Experience and Long-Term Acceptability Among Adolescents and Young Women. *Journal of pediatric and adolescent gynecology*. 2019.
143. Oxford Dictionaries. Definition of Bias by Lexico. [Internet] Oxford; 2019. [cited October 29<sup>th</sup>, 2019]. Available from: <https://www.lexico.com/en/definition/bias>.
144. Solo J, Festin M. Provider Bias in Family Planning Services: A Review of Its Meaning and Manifestations. *Global health, science and practice*. 2019;7(3):371-85.
145. Shelton JD, Angle MA, Jacobstein RA. Medical barriers to access to family planning. *Lancet*. 1992;340(8831):1334-5.
146. Wagner BG, Cleland K, Batur P, Wu J, Rothberg MB. Emergency contraception: Links between providers' counseling choices, prescribing behaviors, and sociopolitical context. *Social science & medicine (1982)*. 2019;242:112588.
147. Riksdag S. Abortlag (1974:595).

148. International A. Doctor's freedom protected: Norwegian Supreme Court affirms conscience rights of medical staff. 2018 2018-10-11.
149. Fiala C, Gemzell Danielsson K, Heikinheimo O, Guethmundsson JA, Arthur J. Yes we can! Successful examples of disallowing 'conscientious objection' in reproductive health care. *Eur J Contracept Reprod Health Care*. 2016;21(3):201-6.
150. Fiala C, Arthur JH. "Dishonourable disobedience"—Why refusal to treat in reproductive healthcare is not conscientious objection. *Woman-psychosomatic gynaecology and obstetrics*. 2014;1:12-23.
151. Sackett DL. Bias in analytic research. *The Case-Control Study Consensus and Controversy*: Elsevier; 1979. p. 51-63.
152. Song JW, Chung KC. Observational studies: cohort and case-control studies. *Plastic and reconstructive surgery*. 2010;126(6):2234.
153. L. G. *Epidemiology*. Elsevier; 2013. p. 155-76.
154. Misra S. Randomized double blind placebo control studies, the "Gold Standard" in intervention based studies. *Indian journal of sexually transmitted diseases and AIDS*. 2012;33(2):131.
155. Manolio TA, Bailey-Wilson JE, Collins FS. Genes, environment and the value of prospective cohort studies. *Nature Reviews Genetics*. 2006;7(10):812.
156. Elwood M. *Critical Appraisal of Epidemiological Studies and Clinical Trials*. 3rd Ed. ed. Oxford: Oxford University Press; 2007.
157. Paul-Dauphin A, Guillemin F, Virion JM, Briancon S. Bias and precision in visual analogue scales: a randomized controlled trial. *American journal of epidemiology*. 1999;150(10):1117-27.
158. Page P. Beyond statistical significance: clinical interpretation of rehabilitation research literature. *International journal of sports physical therapy*. 2014;9(5):726-36.
159. Batterham AM, Hopkins WG. Making meaningful inferences about magnitudes. *International journal of sports physiology and performance*. 2006;1(1):50-7.

## **14 APPENDICES**

Appendix I: Search log – IUD for EC

Appendix II: Search log – Pain management during IUD insertion

Appendix III: Search log – Contraceptive counselling