Contraception and unplanned pregnancies

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Cover illustration: Quote by Elise Ottesen-Jensen, Swedish-Norwegian pioneer in sexual and reproductive health rights and the founder of RFSU (the Swedish Association for Sexuality Education).

To Henrik, Ragnar, Elvira and Klara

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Abstract

Aims: The overall aim of this thesis was to describe the relationship between contraceptive use, abortion, birth and fertility rates among women in different age groups in Sweden and the other Nordic countries.

Material and methods: Data on contraception, fertility, birth, and abortion from 1975-2015 was collected from national databases in the five Nordic countries Denmark, Finland, Iceland, Norway and Sweden (Paper I-III). In Paper IV data on reproductive health and socio-economic status (SES) was collected mainly from questionnaires sent to four cohorts of 19-year-old women resident in Gothenburg between 1981 and 2011. Paper V was a multicentre randomised controlled equivalence study where the impact of immediate versus delayed insertion of an etonogestrel releasing contraceptive implant on complete abortion rates after a medical abortion was evaluated.

Results: The user rates of hormonal contraceptives and a copper intrauterine device among all women aged 15-49 years in the Nordic countries varied between 31% and 44%. The highest use was in Denmark and the lowest in Iceland. Combined hormonal contraceptives (CHC) were the most common methods. A small increase of long-acting reversible contraception (LARC) was seen. The user rates of hormonal contraceptives among 18-19 years old teenagers varied between 54% and 63%. CHC were the most common methods, but LARC increased more than in the group of women aged 15-49 years. The overall abortion rates in the Nordic countries fell during the study period. The average fertility and birth rates in the Nordic countries remained stable. Teenage birth and abortion rates declined continuously 1975-2015. There was no clear correlation between higher overall hormonal contraception prevalence and lower abortion rate. Instead other factors have to be considered, such as differences in the proportions of different types of hormonal contraceptives and prevalence in specific age groups. Lower contraceptive use in low SES areas compared to middle and high SES areas was detected in the most recent assessment of 19 years-old women. Equivalence was established for the two insertion modes of a contraceptive implant.

Conclusions: On a global scale the Nordic countries have a high prevalence of contraceptive use, low abortions rates and a stable fertility rate, except for teenagers where a steady decline in both births and abortions was found. An association between low SES and low contraceptive use among 19-year-olds in the most recent assessment was found which might imply widening inequalities. A contraceptive implant can be inserted on the same day as administration of mifepristone for early medical abortion without hampering the abortion. It has the potential to increase the number of women who can receive the most effective methods of contraception at the time of abortion.

Keywords: contraception, abortion, births, socioeconomic status, postabortion contraception

Sammanfattning på svenska

Tillgång till preventivmedel och abort är en viktig del i sexuell och reproduktiv hälsa som ger möjlighet att själv bestämma när och hur många barn man vill ha. Hög preventivmedelsanvändning i ett land går ofta hand i hand med lågt antal oplanerade graviditeter och aborter, men alla tre parametrarna kan också påverkas av många andra faktorer. Det övergripande syftet med avhandlingen var att beskriva och analysera förhållandet mellan preventivmedelsanvändning, aborter, födslar och fertilitetsnivå hos kvinnor i olika åldersgrupper i Sverige och dom andra nordiska länderna.

I studie I-II användes data, som samlats in från nationella databaser i alla dom nordiska länderna, gällande uttagna recept på preventivmedel, sålda kopparspiraler, antal aborter, födslar och fertilitetsgrad för samtliga kvinnor i åldern 15-49 år. I studie III användes data, som samlats in på samma vis, gällande uttagna recept på preventivmedel, antal aborter och födslar för tonåringar, 13-19 år. Studie IV baserades i huvudsak på svar från enkäter gällande reproduktiv hälsa, som skickats till fyra grupper med slumpmässigt utvalda 19-åriga kvinnor i Göteborgsområdet med 10 års intervall under åren 1981-2011. Studie V var en randomiserad kontrollerad ekvivalensstudie där insättning av en p-stav i direkt anslutning till att en abort startades eller vid ett återbesök jämfördes avseende eventuella effekter på aborten.

I studie I-II fann man att andelen kvinnor i åldern 15-49 år i dom nordiska länderna som använde ett hormonellt preventivmedel eller kopparspiral varierade mellan 31 och 44% åren 2008-2013. Danmark hade högst användartal o Island lägst. Kombinerade metoder (p-piller, p-ring, p-plåster) var dom vanligaste metoderna, men en liten ökning av långverkande reversibla metoder (p-stav och spiraler) kunde ses. Andelen födslar och fertilitetsgrad låg stabilt under åren 1975-2013 för alla länder utom Island där man såg en nedgång. Andelen aborter minskade i Danmark och Finland, låg stabilt i Sverige och Norge samt ökade på Island under åren 1975-2013.

I studie III såg man att andelen 18-19-åringar i Danmark, Norge och Sverige som använde hormonella preventivmedel varierade mellan 54% och 63% under åren 2008-2015. Kombinerade metoder var vanligast, men man fann en större ökning av långverkande reversibla metoder jämfört med hela gruppen kvinnor i åldern 15-49 år i studie I-II. Både abort- och födslofrekvensen gick kontinuerligt ner bland tonåringarna i dom nordiska länderna under åren 1975-2015.

Det fanns ingen tydlig korrelation mellan högre preventivmedelstal och lägre aborttal i dom nordiska länderna. Andra faktorer som skulle kunna påverka dessa parametrar noterades. Olika typer av hormonella preventivmedel har olika hög säkerhet och följsamhet och fördelningen av olika hormonella preventivmedelsmetoder skilde sig något åt mellan länderna. Även andelen preventivmedelsanvändare skilde sig åt i olika åldersgrupper.

I studie IV noterades år 2011 en lägre preventivmedelsanvändning bland 19-åringar i Göteborg i områden med lägst socioekonomisk status jämfört med övriga områden. Detta kunde inte ses 1981, 1991 och 2001.

Studie V visade att det är lika säkert, avseende om en medicinsk abort blir genomförd utan komplikationer, att sätta in en p-stav i direkt anslutning till besöket på abortmottagningen som ifall den sätts in vid ett återbesök efter 2-4 veckor. I studien såg man också att en större andel kvinnor i den tidiga gruppen fick sin p-stav insatt än i den sena gruppen, en större nöjdhet med att få ett preventivmedel insatt direkt istället för vid ytterligare ett besök samt en lägre andel graviditeter inom ett halvår efter aborten.

Sammanfattningsvis har dom nordiska länderna, jämfört med resten av världen, en hög preventivmedelsanvändning, låga aborttal och stabil fertilitetsgrad förutom hos tonåringar där både andelen aborter o födslar minskar. En nytillkommen association mellan låg socioekonomisk status och låg preventivmedelsanvändning hos 19-åringar noterades. Insättning av en p-stav i direkt anslutning till en medicinsk abort är en säker metod och ökar möjligheten för kvinnor att få ett preventivmedel med mycket hög säkerhet.

List of publications

I. Contraceptive use in the Nordic countries.
Lindh I, Skjeldestad FE, Gemzell-Danielsson K, Heikinheimo O, Hognert H, Milsom I, Lidegaard Ø. Acta Obstet Gynecol Scand. 2017 Jan;96(1):19-28.

II: High birth rates despite easy access to contraception and abortion: a cross-sectional study.
Hognert H, Skjeldestad FE, Gemzell-Danielsson K, Heikinheimo O, Milsom I, Lidegaard Ø, Lindh I. Acta Obstet Gynecol Scand. 2017 Dec;96(12):1414-1422.

III. Reduction in teenage pregnancies – a cross-sectional multinational study.
Hognert H, Skjeldestad FE, Gemzell-Danielsson, K, Heikinheimo O, Milsom I, Lidegaard Ø, Lindh, I (Submitted 2018).

IV. The changing pattern of contraceptive use and pregnancies in four generations of young women.
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V. Immediate versus delayed insertion of an etonogestrel releasing implant at medical abortion –a randomized controlled equivalence trial.
Hognert H, Kopp Kallner H, Cameron S, Nyrelli C, Jawad I, Heller R, Aronsson A, Lindh I, Benson L, Gemzell-Danielsson K. Hum Reprod. 2016 Nov;31(11):2484-2490.

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List of abbreviations

BMI: Body Mass Index

CHC: Combined Hormonal Contraceptives

COC: Combined Oral Contraceptive

Cu-IUD: Copper Intrauterine Device

EC: Emergency Contraception

EMA: European Medicines Agency

FR: Fertility Rate

hCG: human Chorionic Gonadotropin

ITT: Intention To Treat

IUD: Intrauterine Device

LAC: Latin America and Caribbean

LAM: Lactational Amenorrhea Method

LARC: Long Acting Reversible Contraception

LMIC: Low and Middle Income Countries

LNG-IUS: Levonorgestrel-Releasing Intrauterine System

POP: Progestogen-Only Pill

PP: Per Protocol

SAC: South America and the Caribbean

SDG: Sustainable Development Goals

SES: Socioeconomic Status

SRHR: Sexual and Reproductive Health Rights

STI Sexually Transmitted Infection

TFR: Total Fertility Rate

UN: United Nations

VTE: Venous Thromboembolism

Contents

Introduction

Easy access to contraception and abortion is an essential part of sexual and reproductive health rights (SRHR) since it enables individuals and couples to decide when and how many children they want to have. Access to family planning methods is also a cornerstone in the fight to reduce poverty, maternal and infant mortality and to increase educational level, especially for girls and women. The United Nations (UN) has taken several big steps to increase access to family planning services. The first was the Programme of Action at the International Conference on Population and Development in 1994 in Cairo with the goal to provide access to a full range of safe and reliable family-planning methods by 2015.[1] Although improvements have been seen the mission was not accomplished and therefore another important step was taken when the UN General Assembly adopted the Sustainable Development Goals (SDG) in 2015 where Goal nr 3 includes:

"By 2030, ensure universal access to sexual and reproductive health-care services, including for family planning, information and education, and the integration of reproductive health into national strategies and programmes." Family planning indicators include "Contraceptive prevalence rate" and "Unmet need for family planning".[2]

Contraception from a global and regional perspective

Global, regional and country-specific levels of contraceptive prevalence rates are presented regularly by the Department of Economic and Social Affairs, Population Division at the UN.[3] Until recently the reports from the UN has consisted of contraceptive prevalence among women who are married or in-union since this is how the majority of countries in the world have presented their data. In the future the aim is to include all women of reproductive age irrespective of their marital or in-union-status.[4] This is a welcome change

since individuals who are not currently in union might also have a need for contraceptives. It will also make comparisons between Europe and other parts of the world easier to perform since European surveys of contraceptive prevalence more often include all women of reproductive age. This is also the case in the studies included in this thesis.

In the UN report from 2015 contraceptive prevalence among women married or in-union in the world was 64% with the lowest prevalence in Chad (6%) and the highest in China (83%). 57% of the contraceptives used were considered modern methods and included IUDs, sterilisation, condoms, diaphragms, all kinds of contraceptive pills, injectables, rings and patches, while the rest consisted of traditional methods such as coitus interruptus/withdrawal and safe periods. Regionally, Middle and Western Africa had the lowest prevalence (23% and 17% respectively) and Eastern Asia the highest (81%) (Figure 1).
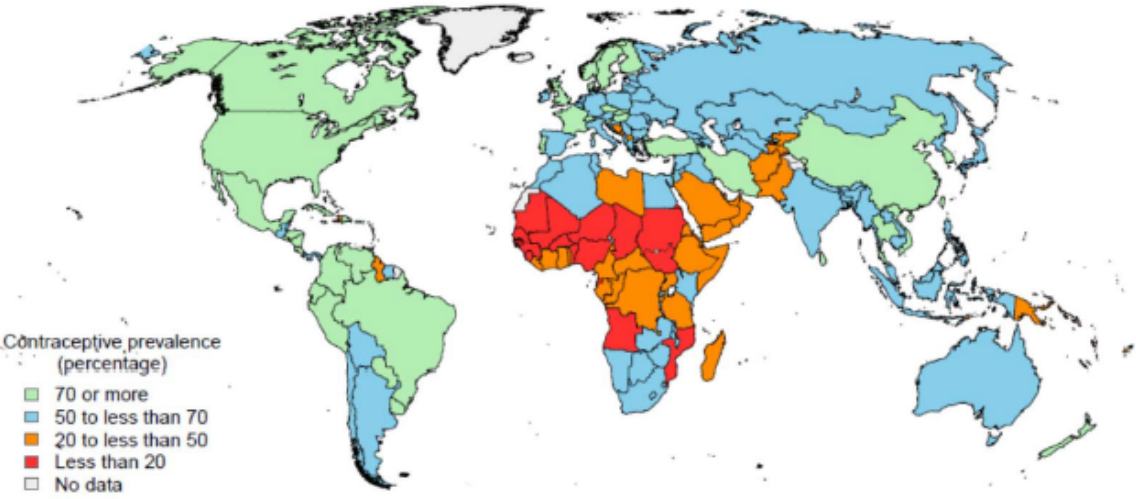

Figure 1. Percentage of women using any method of contraception among those aged 15 to 49 who are married or in-union 2015. Source: Trends in Contraceptive Use Worldwide 2015. United Nations, Department of Economic and Social Affairs, Population Division (2015).

Contraceptive use has increased over time worldwide until approximately the year 2000 when the rate started to stabilise in all parts of the world except for Africa where it is still increasing, although from a lower level (Figure 2).
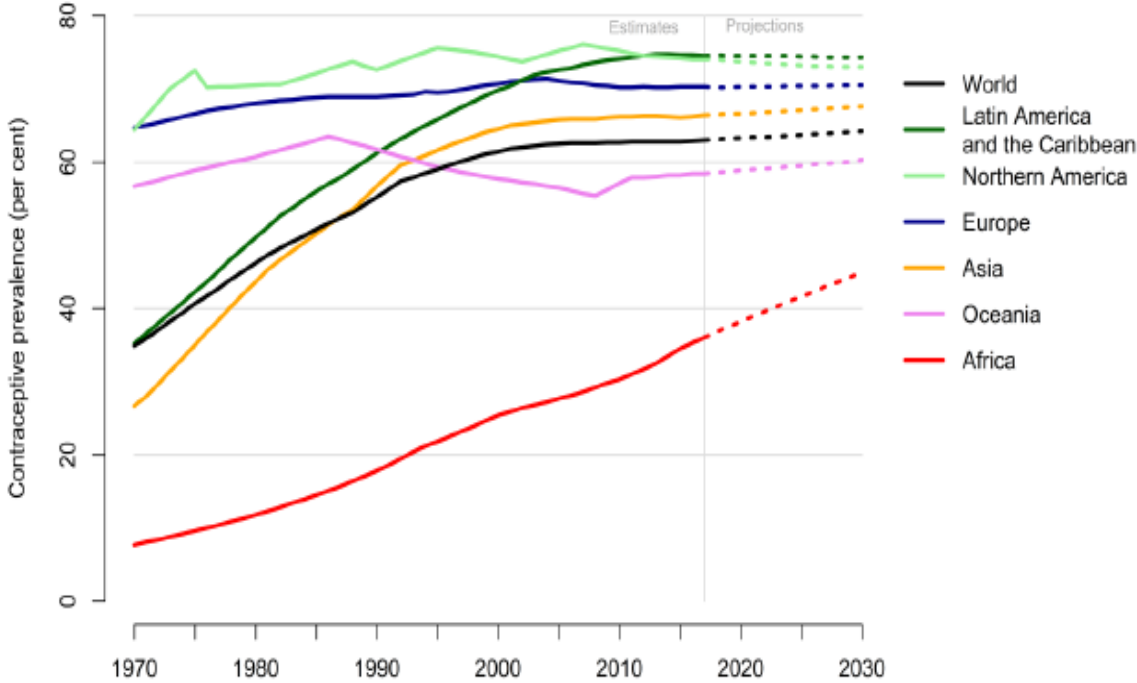
Figure 2. Contraceptive prevalence (any method) among married or in-union women, by regions, from 1970 to 2030. Source: World Family Planning 2017 – Highlights. United Nations, Department of Economic and Social Affairs, Population Division (2017).

Method-specific contraceptive prevalence varies to a great extent across the world. In 2015 female sterilisation was the most common method in Asia (24%) and Latin America and the Caribbean (26%) among married or in-union women while the pill was the most common method in Europe (22%) and Oceania (22%). IUDs had their highest prevalence in Asia (17%, especially in China where it was 38%) and the male condom in Europe (17%) (Figure 3).[5]
European surveys confirm the results of the UN publications indicating a high prevalence of contraceptive pill use in Europe. However within Europe there is a great variation. In a cross-sectional study from 2008[6], which included women 15-49 years of age (irrespective of marital status) from 14 countries in different parts of Europe, 49% of the French and 38% of the German, but only 16% of the
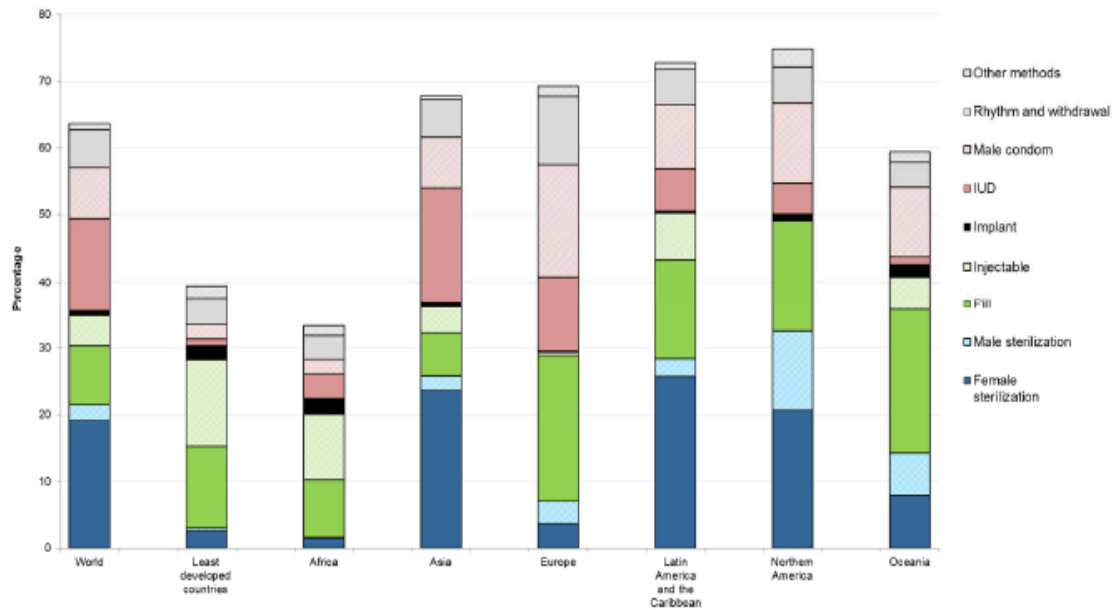
Figure 3. Contraceptive prevalence among married or in-union women aged 15 to 49 by method and region, 2015. Source: Trends in Contraceptive Use Worldwide 2015. United Nations, Department of Economic and Social Affairs, Population Division (2015).

Baltic women relied on contraceptive pills. Condom use was more common in Southern Europe, with the highest prevalence in Italy (39%). In Scandinavia, which included Denmark, Norway and Sweden, 29% of the women relied on contraceptive pills, 15% on any kind of IUD/IUS and 11% on the male condom.[6] In another large cross-sectional European survey from 2011 women 18-49 years of age from France, Germany, Rumania, Sweden and the UK were included. The results confirm the findings from the study from 2008, but with slightly higher user rates, which might reflect the different age group; 18-49 instead of 15-49. The pill was used by 54% in Germany, 51% in France, 35% in Sweden, 24% in the UK and 22% in Romania. Male condom was the second most common method in all countries.[7]

Neither the UN reports nor the European surveys discriminate between different kinds of oral contraceptive pills. Also copper-intrauterine devices (Cu-IUD) and levonorgestrel-releasing intrauterine systems (LNG-IUS) are included in the same group in the above-mentioned reports except for the study by Cibula et al.[6]

Although the prevalence of contraceptives is high in the Nordic countries including Denmark, Finland, Iceland, Norway and Sweden there is still a small proportion of unmet need for contraceptives. According to the UN report the unmet need varied between 6 and 10% in the Nordic countries among married or in-union women. This was confirmed by a cross-sectional study in Sweden in 2015 where women 16-49 years of age were included and reported an unmet need of 9%.[8]

Contraceptive methods

Before the introduction of the pill in 1960[9] women and men had to rely on different kinds of condoms, cervical caps, IUDs and fertility awareness methods with highly varying efficacy and safety as birth control. The development of vulcanisation of rubber by Hancock and Goodyear led not only to the production of tyres, but also of cheap and functional rubber condoms in the 1850s which replaced the expensive and less efficient condoms made of e.g. animal intestines and silk.[10] One of the first intrauterine devices was introduced by Gräfenberg in Europe in the 1920s but the IUDs did not start to gain acceptance until the 1950s.[11]

After the introduction of the first combined oral contraceptive pill in the USA a number of other hormonal methods have been developed relying on the same pharmacologic mechanism as the first pill. But at the same time as the first pill was introduced also a new view on sexuality and contraception evolved, which made way for further development and refinement of other already existing contraceptive methods such as the IUD and condoms.

The efficacy of a contraceptive method is measured according to the Pearl Index (PI), which is defined as the number of women who get pregnant during the first year of use among 100 women using a given method. The lower the PI the more effective the method. Today the following contraceptive methods are available:

- Combined hormonal contraceptives (CHC): Combined oral contraception (COC), vaginal rings, patches and injections
- Progestogen-only methods: Progestogen-only pill (POP), implants, injections and LNG-IUSs
- Cu-IUDs
- Emergency contraception
- Barrier methods –condoms, diaphragms
- Male and female surgical sterilisation
- Fertility awareness methods
- Lactational amenorrhea method (LAM)
- Withdrawal/coitus interruptus

CHC

This is the method of the first original "pill". CHC consists of both an estrogen and a progestogen component where the progestogen has the main contraceptive effect, by preventing fertilisation, mainly by inhibiting ovulation and thickening cervical mucous.

Estrogen mainly contributes to stabilising the bleeding pattern.[12] The most common form is the COC, while patches and vaginal rings are less used. In some parts of the world, but not the Nordic countries, also a combined injection is available.[13] The CHC has many health advantages such as decreased dysmenorrhea and menorrhagia and lower risk of ovarian, endometrial and colon cancer apart from its contraceptive effect. The main disadvantage of CHC is the risk of venous tromboembolism (VTE).[12] In Europe COC is one of the most common contraceptives used.[5]

Progestogen-only methods

In contrast to CHC progestogen-only methods contain only a progestogen, which is still the main contraceptive agent. The bleeding pattern is more unpredictable compared to CHC, but the risk of VTE is considered to be

eliminated with the majority of the progestogen-only methods. The LNG-IUS is a safe method with a fairly predictable bleeding pattern, while the POP is more unpredictable. The subcutaneous implant is considered the safest contraceptive method available, but can also cause irregular bleeding. The injection offers a high rate of amenorrhea but can cause osteoporosis when used for more than two years.[14]

Cu-IUD

The Cu-IUD consists of a plastic frame with copper attached to it and is inserted into the uterus where its main contraceptive action is interference with the sperms ability to move in the uterine cavity and hence not reach the egg. Cu-IUD offers a hormone-free alternative to women with conditions where hormones are contraindicated. The disadvantages is the risk for dysmenorrhea and menorrhagia.[12]

Emergency contraception

There are three types of emergency contraception –Cu-IUD, levonorgestrel (LNG) pills and ullipristal acetate (UPA) pills. LNG and UPA primarily prevent or postpone ovulation. LNG can be administered up to 72h and UPA until 120h after unprotected intercourse. In a randomised trial LNG prevented 69% and UPA 85% of the pregnancies that could be expected and therefore UPA is recommended as the first choice of oral emergency contraception.[15]

IUDs can be inserted up to five days after intercourse and prevent about 99% of pregnancies after an episode of unprotected sex. This makes the IUD the most effective form of emergency contraceptive.[16]

Barrier methods

These methods work by physically preventing sperm from entering the uterus. They include male condoms, female condoms, cervical caps,

diaphragms and contraceptive sponges impregnated with spermicide. Since they are highly user-dependent the PI varies extensively between perfect and typical use. Condoms are the only method that also protect against Sexual Transmitted Infections (STI).[12]

Male and female surgical sterilisation

Surgical sterilisation is available in the form of tubal ligation for women and vasectomy for men. Female sterilisation has been one of the most common methods in parts of the world but has now started to give way for IUDs instead. With tubal ligation, complications occur in 1 to 2 percent of procedures with serious complications usually due to the anesthesia. The methods are highly efficient with a PI of 0,5 for female sterilisation and 0,15 for male sterilisation and should be considered irreversible.[17 18]

Fertility awareness methods

The aim of fertility awareness methods is to determine the most fertile days of the menstrual cycle and indicate what days to avoid unprotected sexual intercourse. This could include monitoring basal body temperature, cervical secretion or simply the day of the cycle. The latest contribution in this group of methods is applications for mobile phones, which help to predict safe and unsafe periods. The methods are highly user-dependent and therefore the PI varies extensively between perfect and typical use. [14]

Lactational amenorrhea method (LAM)

The LAM is used correctly if the woman has post-partum amenorrhea, if breastfeeding is the infant´s only source of food and no more than 6 months has passed since childbirth. If all the three criteria of LAM are met the failure rate is between 0.45 and 2.45% according to a Cochrane review.[19]

Withdrawal/coitus interruptus

Withdrawal means ending intercourse before ejaculation. The main risk of the withdrawal method is that the man may not perform the manouver correctly or in time. Since it is very user-dependent there is a great difference between perfect and typical use. In 2015 the prevalence in the world was 3% among married or in-union women, but in Southeast Europe and Western Asia a larger amount of couples rely on this method.[14]

Efficacy of different contraceptive methods

The efficacy of different types of contraception varies extensively. Pregnancy rates during perfect use shows how effective a method can be when the directions for use are followed completely correct. Pregnancy rates during typical use shows how effective a method is during actual use including inconsistent or incorrect use. Many methods are considered very safe when used perfectly, but the more user-dependent a method is the bigger the risk for inconsistent or incorrect use. Trussell et al reviewed the evidence of perfect and typical use of the contraceptive methods available (Table 1).[18] In the table it is notable that for the almost non-user-dependent methods, consisting of sterilisation and the long-acting reversible contraceptives (LARC) LNG-IUS, Cu-IUD and implants, perfect and typical use are almost identical. The other methods, which have to be taken or used at a certain time, show a greater variance between typical and perfect use, especially the non-hormonal methods. Studies among women seeking abortion have identified inconsistent or incorrect use of user-dependent and short-acting contraceptives and/or recent change to another method as possible causes for an unintended pregnancy.[20 21] In the CHOICE study it was shown that LARC decreased the risk of repeated abortions and teen pregnancies to a larger extent compared to short-acting methods.[22]

*Table 1. Pear index (PI) during perfect and typical use. Source: Trussell J. Contraceptive failure in the United States. Contraception 2011;**83**(5):397-404 and Antikonception – behandlingsrekommendation. Information från Läkemedelsverket 2014;25(2):14–28.*

Percentage of women experiencing an unintended pregnancy within the first year of use (PI)		
Method	**Perfect use**	**Typical use**
No method	85	85
Male sterilisation	0,10	0,15
Female sterilisation	0,5	0,5
LNG-IUS (Mirena)	0,2	0,2
Cu-IUD (> 300 mm2)	0,6	0,8
COC and POP	0,3	9
Patch	0,3	9
Vaginal ring	0,3	9
Injection (Depo-Provera)	0,2	6
Implant (Implanon)	0,05	0,05
Diaphragm with spermicides	6	12
Spermicides	18	28
Male condom	2	18
Female condom	5	21
Withdrawal	4	22
Fertility awareness methods	0,4–5	24

Induced abortion from a global and regional perspective

Sedgh et al. have collected and evaluated global data on abortion rates on a regular basis and the latest report published in 2016 covers abortion rates from 1990-2014.[23] Abortion rates on global, regional or country level are often defined as number of abortions/1000 women 15-44 years of age in one year. Marital status or other age groups can be included in the definition of sub groups. From 1990-1994 to 2010-2014 the overall global abortion rate did not change significantly (40 to 35/1000 women) but in the developed countries it fell from 46 to 27/1000 women compared to developing countries were there was no significant difference (39 to 37/1000 women). On a regional level the Caribbean and South America displayed the highest rates (59 and 48/1000 women respectively) while the lowest rates were in Northern America at 17 and

Western and Northern Europe at 16 and 18/1000 women respectively. Eastern Europe showed the largest decline from 88 to 42/1000 women (Figure 4).[23] Abortion rates in the Nordic countries have been monitored closely since the liberalisation of the abortion laws in the 1970s. On a global scale the abortion rate for the Nordic countries is low at around 15/1000 women 15-44 years of age in 2015 and the abortion rate in the region has fallen from 1975 and onwards.[24]
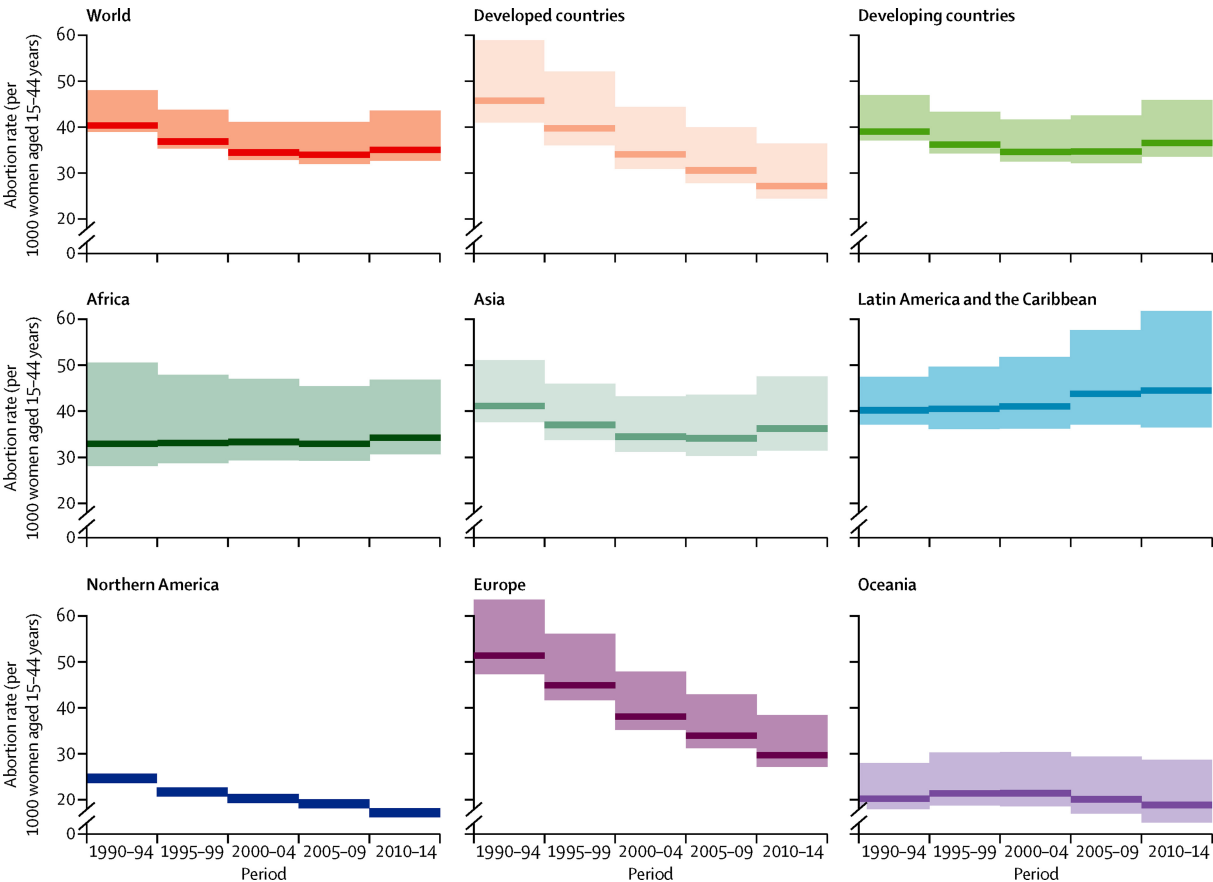
Figure 4. Global and regional incidence rate estimates (per 1000 women aged 15-44 years), 1990-94 to 2010-14. Source: Abortion incidence between 1990 and 2014:global, regional and subregional levels and trends. Sedgh, G et al. Lancet 2016 July; 388(10041)

According to a study by WHO and the Guttmacher Institute[25] only 55% of all abortions were safe in 2010-2014, which means that 25 million abortions a year were performed in an unsafe manner. An abortion is classified as safe if it is

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performed by a trained health worker using a method recommended by the WHO. 14% of all abortions 2010-2014 were classified as "least safe", indicating they were performed by an untrained person using a non-recommended and often dangerous method. 31% were classified as "less safe" abortions and were either performed by trained personnel but with out-dated methods or without a trained health worker but with a recommended method. The highest mortality and morbidity levels were seen where least safe abortions were performed, as was the case in Eastern, Middle and Western Africa. In Latin America 60% of all abortions were classified as less safe, but the fatality case rates were much lower than in areas with least safe abortions.[25] This probably reflects the increasing self-administration of medical abortion with recommended drugs and doses despite restrictive abortion laws, but also health care systems that are able to manage complications.[26]

The overall abortion rate is higher in countries with very restrictive abortion laws than countries with liberal laws, which often reflects poor family planning resources, including access to contraceptives, in general.[25]

The relationship between contraception and abortion prevalence

Increasing contraception prevalence often leads to decreasing abortion rates, but is not observed at every point of time. During the 20th century and especially after the 1950s many countries have gone through a period of fertility transition with dramatic falls in Fertility Rates (FR) (Figure 5).

The desire for a lower FR or fewer children has been driven by women's empowerment and the increasing well-being and status of children. This has been achieved due to e.g. better health care services,, demands for education of women, technological and economic changes and changing norms. Family planning facilities have been a means to reach the desired FR. [27] Even in countries where contraceptive use has increased the increase has not always

been enough to achieve the desired FR and then abortion rates have increased simultaneously. When the country has reached the desired FR, abortion rates
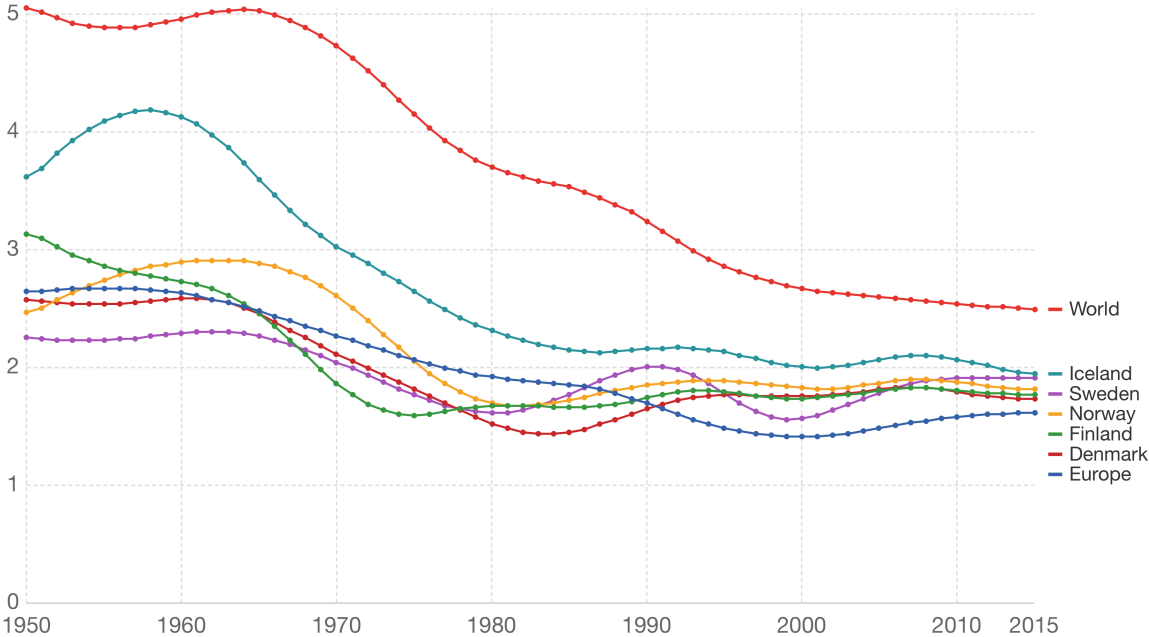

Figure 5. Total fertility rates 1950-2015.
Source: OurWorldInData.org/fertility-rate. UN Population Division (2017 revision)

have often started to fall while the contraceptive use remains stable or continues to increase. The abortions that still occur then are mainly due to contraceptive failure and to a lesser extent due to an unmet need for contraception.[28-30] In other countries an increase in contraception prevalence has been accompanied by an immediate fall in the abortion rate. This has been the case in e.g. the former republics of the Soviet Union, where abortion was available but modern contraceptive methods were almost entirely absent during the Soviet era. Following the dissolution of the Soviet Union in 1991 there has been an inflow of contraceptives and the need for abortion has declined.[30]

When reviewing the latest updates of contraceptive prevalence and abortion rates in different regions of the world there are some discrepancies. For instance Latin America and Caribbean (LAC) has a high rate of modern contraceptive methods and a high rate of abortions, even though the region has reached a low FR.[27] According to Sedgh et al. 29% of all abortions are performed by women

not married or in-union[23], but when contraception prevalence is described only women who are married or in-union are included. Hence the contraception prevalence might be much lower among sexually active women who are not married or in union. Also LAC has a high prevalence of modern contraceptives, but the greatest proportion consists of female sterilisation. This is a very safe method usually used when a woman has decided not to have any more children, but before that she might have many years of an unmet need for contraception and being at a high risk of unintended pregnancies and abortions.

Abortion methods

There are written testimonies about abortions that took place e.g. among the ancient Greeks, in the Roman empire and later on, but it is very difficult to estimate any rates. Many of the older abortion methods have proved to be either useless or dangerous to the woman and it was not until the 20th century safe methods started to evolve. Medical abortions were performed with intra-amniotic injections of hypertonic saline, hyperosmololar urea or extraamniotic injection of the antiseptic ethacridine lactate. The latter was a fairly safe method, but with a long induction-abortion interval.[31] The introduction of prostaglandin analogues in the 70s and the progesterone inhibitor mifepristone in the 80s for medical abortion changed abortion practice dramatically and now provides a safe regimen also in areas where healthcare services are scarce.[32-35]

Medical abortion

The most common medical procedure is the administration of the progesterone inhibitor mifepristone followed by the prostaglandin analogue misoprostol 24-48 hours later. Misoprostol has a high affinity to the uterus and causes contractions and expulsion of the pregnancy. With misoprostol alone high and

repeated doses are required which can cause side effects such as nausea and other gastrointestinal symptoms.

Mifepristone was developed in France in the 80s and was shown to cause cervical ripening and contractility of the uterus which ended with a successful abortion in 60-80 per cent of all cases. It was a Swedish research team who discovered that apart from the effect of mifepristone itself on the uterus and cervix it also increases the sensitivity to misoprostol and hence shortens the time to expulsion and makes it possible to lower the doses of misoprostol.[36] The combined treatment with mifepristone and misoprostol is recommended by WHO as the first line of treatment, but in areas where mifepristone is prohibited or not available the WHO has given recommendation on how misoprostol can be used alone.[37]

The proportion of medical abortions is increasing and has reach very high levels in the Nordic countries. In 2015 medical abortions were the method of choice in 96% of the cases in Finland, 90% in Sweden, 70% in Denmark and 87% in Norway. [24] The increase has been more modest in other European countries with a prevalence of 58% in France in 2012 and 20% in Germany in 2013.[38]

Surgical abortion

Surgical abortion can be performed either in local or under general anesthesia while the uterine cavity is being emptied. Dilatation and Evacuation (D&E) or curettage was the predominant method until the vacuum exeres (VA) was discovered already in the beginning of the 20th century. The method was refined during the 1960s and 70s when a plastic cannula was introduced and reduced the risks of the procedure. The method is considered very safe and is the surgical method of choice up to gestational week 14.[39] In the Nordic countries this is practically the only surgical method available since abortions in later pregnancy weeks are medical. In other parts of the world D&E is used in later pregnancy weeks.[31]

Post-abortion contraception

In Europe and globally a significant proportion of women having an abortion have had one or more previous abortions. In Europe a variation between 21 and 60% has been reported. In the Nordic countries the prevalence is around 40%.[40-44] LARC has been shown to be highly effective in preventing unintended pregnancy and repeat abortions.[22 45-48] Studies show that most women (83%) ovulate in the first cycle after a medical abortion.[49] Other studies have shown that 15% of women resume sexual intercourse within one week of a medical abortion[50] and 51% within two weeks.[51] Immediate start of any contraceptive is therefore desirable and since LARC has been shown to prevent repeat abortions to a larger extent than other methods LARC is preferable. However, the start of any method is better than no method at all in preventing a repeat abortion.[45]

CHC, POP and progestogen-injections can be started the same day as misoprostol is given or a surgical abortion is performed.[13] LARC can be inserted immediately after a surgical abortion, with well documented effectiveness, compliance and safety.[52] After a medical abortion, the practice has been to provide LARC at a follow up visit several weeks after treatment. Since many women prefer performing a home-follow-up with a pregnancy test there is no need for a follow up visit at the health care centre. Also, many women who have been scheduled for follow-ups do not turn up.[53] This applies in particular to settings where women have to travel long distances for abortion care or where services are poor or expensive. Unfortunately many women then miss the opportunity to receive a LARC method. Therefore it would be an advantage if LARC could also be started immediately after medical abortions. Smaller studies have been performed where IUDs have been fitted within a week after the abortion without any adverse effects compared to the standard insertion weeks later.[50 54 55] Concerning implants the WHO advises

immediate implant insertion[13] but this practice has not been widely implemented due to the theoretical concerns about interaction between the progestogen-inhibitor mifepristone and the progestogen-containing implant which could affect the efficacy of the medical abortion negatively. Three pilot studies have reported slightly diverging results concerning success rates of abortion when an etonogestrel-containing implant was inserted at the time of treatment with mifepristone.[56-58] There is also one randomised controlled trial that investigated the efficacy rates of medical abortion when an implant was either inserted in close connection to the treatment with mifepristone or at a standard follow up visit, but the study misses information on how soon after the intake of mifepristone the implant was inserted.[59]

Socioeconomic status (SES)

SES has been shown to influence contraceptive use and rates of unintended pregnancies. In high-income countries, such as Canada, France, the United Kingdom and the United States several studies have shown that low SES is a risk factor for low contraceptive use, no contraception at first intercourse and a high rate of unintended pregnancies and abortions. [60-64] In studies in the Nordic countries SES has been identified as an influencing factor, but mainly in specific groups, such as women having a second or more induced abortion or immigrant women, rather than the general population.[65-67]

Also in low and middle income countries (LMIC) low SES is associated with less use of contraceptives[68] but in contrast to high income countries, high instead of low SES is associated with a high rate of abortions. This could be explained by the fact that women with high SES in LMIC have a greater knowledge about abortion facilities than women with low SES and hence easier to compensate for an unmet need for contraception, which is more often the case in LMIC than in countries with high income.[69]

Several studies have focused exclusively on the impact of SES on adolescent pregnancy and motherhood. Socioeconomic deprivation is considered to be both an effect of and a risk factor for teenage births.[70-73]

Aims

The overall aim of this thesis was to describe and explore the relationship between contraceptive use, abortion and birth rates among women in Sweden and the other Nordic countries.

The specific aims were:

- To describe and compare contraceptive availability and use in the Nordic countries and compare usage by age in the three countries, Denmark, Norway and Sweden. A secondary aim was to assess prescribing patterns in relation to the recommendations from the European Medicines Agency (Paper I)

- To describe and compare contraceptive use, fertility, birth and abortion rates in different age groups in the Nordic countries (Paper II)

- To describe and compare hormonal contraceptive use, birth and abortion rates among teenagers in the Nordic countries (Paper III)

- To describe contraceptive use and pregnancies in four generations of 19-year old women. A secondary aim was to relate contraceptive use and pregnancies to SES (Paper IV)

- To compare the effect of immediate versus delayed insertion of an etonogestrel releasing contraceptive implant on complete abortion rates of a medical abortion. Secondary aims were to compare complication rates, insertion rates, acceptability of the timing of insertion and pregnancy rate within 6 months after the abortion. (Paper V)

Methods

Three different types of research methodology are used in this thesis. Three of the studies are longitudinal and cross-sectional register-based studies, one is a cross-sectional questionnaire-based study and the fifth study is a randomised controlled equivalence trial.

Observational studies

Conditions in the Nordic countries are favourable for epidemiological studies. There are population registers with a personal identification number system containing information on the total population of each country providing the ability to obtain random samples of the total population. In addition to the population registers there are national databases on a large number of health related topics such as medical prescriptions, births and abortions.

Paper I, II and III

Data for Paper I, II and III was collected from national databases in the five Nordic countries; Denmark, Finland, Iceland, Norway and Sweden. The following databases were utilised: National Health Registries[74], the Tigrab Database[75]and the Danish National Registry of Medicinal Product Statistics, [76] in Denmark, the National Institute for Health and Welfare[24] and the Finnish Medicines Agency[77] in Finland, the Directorate of Health[78] and the Icelandic Medicines Agency[79] in Iceland, the Norwegian Institute of Public Health[80] and the Norwegian Prescription Database[81] in Norway and the National Board of Health and Welfare in Sweden[82]. Birth and abortion rates were according to international praxis defined as the number of births or abortions per 1000 women aged 15-44 during one year.[23]

To estimate contraceptive use data on redeemed prescriptions of hormonal contraceptives was retrieved from the national databases and sales figures for

the Nova-T intrauterine device (IUD) from the main manufacturer (Bayer AG, Berlin, Germany). The data was presented as Defined Daily Doses (DDD). In these studies contraceptive use is defined as DDD/100 women and day, i.e. percentage of women using contraceptives. In accordance with international practice women 15-49 years of age were included. [83].

Use of methods such as fertility awareness methods, condoms and diaphragms was not estimated since they are not registered. Women who were infertile, not heterosexually active, pregnant or had the wish to get pregnant were included in the study population since all variables were collected on a group level from anonymous data concerning women of reproductive age (15-49).

Demographic data was collected from Facts about the Nordic Region[84] and information about policies, guidelines and legislation concerning contraceptives and abortions was collected from each Nordic country by members of the research group.

In paper III total fertility rates (TFR) for all Nordic countries were collected from Eurostat[85]. TFR was defined as the average number of live births a woman would ever deliver if she were to experience the fertility rate of a given period and survive through her reproductive period of life.

Paper IV

Paper IV is based on data retrieved from postal questionnaires sent out to a random sample of 19-year-old women resident in Gothenburg. In 1981 a prospective longitudinal population study of women living in the city of Gothenburg was initiated[86]. The women were born 1962 and were 19 years of age. This age was chosen in order to be able to collect the information from the women themselves without parental consent. A random sample of every fourth woman was obtained (n = 656) from the population register.

In 1991, a new group of 19 year-old women (born in 1972), also residing in Gothenburg, was invited to participate in the study. A one in three sample (n = 780) was obtained from the population register.

A similar postal questionnaire was sent out ten years later in 2001 to a third cohort of 19-year old women (born 1982). A one in three sample (n = 666) was obtained at random from the population register.

In 2011 the last cohort was recruited among women born 1992. Due to declining response rates all 19-year-old women in the Gothenburg region were invited to participate. Apart from postal questionnaires also electronic reminders and questionnaires translated into English were used in the assessment in 2011.

The questionnaire consisted of approximately 40 questions about contraception, pregnancies, reproductive history and factors such as height, weight and smoking. The questionnaire has undergone only minor changes during the course of this study as it was considered of importance that the same questions were asked on each assessment. The only changes that were made consisted of new questions about contraceptive methods that were not available when the study started in 1981, e.g. implants and the levonorgestrel-releasing intrauterine system.

The Swedish population register contains information regarding civil status, nationality, home address, income and level of education linked to the individual's personal identification number. Each district in the city of Gothenburg has been classified according to a three-point socio-economic index (low, medium and high SES) based on the mean level of education, income and profession/social group for all the inhabitants in each district.[87 88] Using this index, it was possible to group the study participants into three levels of SES.

Randomised controlled study -Paper V

Paper V was performed as a randomised controlled equivalence trial. An equivalence design, instead of superior design, was chosen since the method we

aimed to study had advantages for women, such as fewer visits to the clinic, when compared to the standard method.

Women with pregnancies below 64 days gestation and opting for the etonogestrel releasing subdermal implant (Nexplanon®) as post abortion contraception, were asked to participate. Participants were recruited at outpatient family planning clinics from five Swedish sites and one Scottish site. Participants were randomised to either immediate insertion of the implant one hour after swallowing mifepristone (Mifegyne®) or to insertion at the follow up visit 2-4 weeks later (standard method). The study was unblinded for ethical and practical reasons.

All women received mifepristone 200 mg in the clinic and 24-48 later vaginal misoprostol 800 mcg hours was administered. Follow up was either in the clinic or via telephone using a self-performed low sensitivity urinary hCG-test two to four weeks later[53 89]. At the follow up women completed a questionnaire with questions regarding: duration and quantity of bleeding; the worst pain they had experienced during the abortion on a visual analogue scale (1-10); if they had had unscheduled visits to the abortion service; if they had received any extra treatment for a complication related to the abortion; and if they would prefer immediate or delayed insertion if they were ever to have a medical abortion again. All centres in the study had access to patient records for the entire region in which the abortion took place.

The primary aim was to determine if immediate insertion is equivalent to delayed insertion (standard treatment) for a successful completion of the abortion without the need for vacuum aspiration. Assuming 97% success in both groups, and a two sided margin of equivalence (-5% - 5%) 252 patients per group would be required to establish equivalence with an alpha of 0.05 and a power of 90%. The primary outcome was assessed at follow up at two to four weeks, and/or by patient records.

Secondary outcomes were serious adverse events and adverse events of special interest, rates of insertion of the implant and preferred allocated time of insertion. Furthermore satisfaction with the implant, continued implant use and pregnancies and repeat abortions where reported by the patients at telephone follow up three and six months after the abortion.

Statistical analysis

Paper IV

Fisher's exact test and ANOVA with Tukey's Studentized Range (HSD) test for post hoc comparisons were used in the analysis of possible differences in basic characteristics, contraceptive use and pregnancy outcome between the four cohorts (SAS 9.1; SAS Institute Inc., Cary, NC, USA).

Paper V

The primary outcome was analysed with a generalised estimating equation model using a binomial distribution and an identity link and presented as a risk difference with a 95% confidence interval. The intention to treat (ITT) population was defined as all women randomised except women who withdrew consent before abortion or insertion of the contraceptive implant, or did not receive medical abortion (Figure 7). The per protocol (PP) population was defined as all women in the ITT analysis except those who changed their mind about method of contraception before insertion of the implant or had implant insertion at the wrong delayed timing. The primary analysis was performed on the PP population corroborated by the ITT population. This is in accordance with the CONSORT statement since the usually smaller differences in the ITT analysis makes it easier to establish equivalency/noninferiority and is considered anticonservative as opposed to when it is used in superior studies. In addition a

sensitivity analysis was performed excluding all women in the PP population who did not come for follow up. All other analyses were presented for the ITT population. Fisher´s exact test was used to evaluate the differences between the groups regarding categorical data. Continuous variables are presented as medians and range and compared between groups using Mann-Whitney U-test. Differences were considered statistically significant if the two sided p-value was less than 0.05.

Ethical approval

Paper I-III

In Norway, the board of the Norwegian Prescription Database reviewed the study protocol and gave permission for use of the data. Studies using anonymous data from nationwide registers are by Norwegian legislation exempted from the need of institutional regulatory board approvals and written informed consent from the patients. In Denmark, permissions were achieved from Datatilsynet (journal no 2010-41-4778). In Finland, Iceland and Sweden no ethical approval was required as these anonymous data are publicly available from the national bodies of these countries. Patients were not directly involved in the study since only aggregated data on group-level was used.

Paper IV

The study was approved by the Ethics Committee in Gothenburg, Sweden (e.g. 1981: 023; 2006: 330; 2011: 778). The National Data Inspection Board approved the study design and informed consent was obtained from each participant.

Paper V

The institutional review board of Karolinska Institutet, Stockholm, Sweden, granted ethical approval for all Swedish sites (permit no 2013/907-31/4). The ethical committee approval number for the Edinburgh site was IRAS 141042 ref 14/SS/011.

Methodological considerations

Paper I-III

The fact that abortions and births rates traditionally are described as the number/1000 women aged 15-44 years while contraceptive use is described as the percentage of women aged 15-49 years using contraception, constituted a challenge when we merged the data into one set. Other options, .e.g to present both births, abortions and contraceptive use either as number/1000 women or as the percentage of women, were discussed in the research group, but in order to be able to compare our results with other studies we chose the standard way of presenting the data.

Many studies, including European surveys, describe contraceptive use prevalence as percentage of all women 15-49 years of age. However, as discussed in the Introduction, studies on a global level often describe contraceptive use only among women who are married or in-union. This has to be taken into consideration when comparing the results in this thesis with those studies[3].

Since the study population includes all women in a certain age group and not only a sample of observations all measures were highly significant. To illustrate the accuracy of this statement the chi square p-value for two randomly chosen differentials in the data set were calculated (Table 2).

Table 2.

Data from Paper II, year 2013	Denmark	Finland	Norway	p-value
Total hormonal contraceptive user rate	39,9%	39,7%		0.0015
CHC user rate	26,3%		17,9%	<0.00001

Even for such a small difference as 0,2% the p-value was 0.0015 and it was not detectable for the comparison of CHC user rates in Denmark and Norway.

Paper IV

In order to validate the reliability of the questionnaire it was tested by letting 30 women answer the questionnaire twice with a 3-week-interval. The agreement of the answers to five specific questions was checked (agreement ranged between 90-100%). Furthermore ten questions were selected and understanding of the questions was checked in a group of 10 women. The level of understanding ranged from 89-100%, which was considered satisfactory.

Paper V

Altogether 12 women were excluded from the study after randomisation but before the treatment had actually started. If the randomisation had been done even closer to the start of the abortion this loss of research persons might have been reduced. Since 8 out of 12 withdrew their consent one has to consider if the information about the study had not been sufficient before the randomisation procedure.

Results

Paper I

In this paper contraceptive use in the Nordic countries from 2010 to 2013 was explored with an emphasis on LARC, adherence to recommendations from European Medicines Agency (EMA) and emergency contraception (EC). The study population consisted of 5 814 064 women aged 15-49 years in 2013.

In all countries there was a slight increase in hormonal contraceptive use from 2010 to 2013. Finland and Denmark had the highest rate of overall hormonal contraceptive use, increasing from 38 to 40%; Iceland had the lowest use (30–31%).

LARC

The use of LARC increased successively over time in all countries except in Norway. In 2013 Sweden had the highest rate of LARC with 20% followed by Finland 18%, Denmark 16%, Norway 11% and Iceland 10%. The percentage use of LNG-IUS and Cu-IUD was 11%/3% in Denmark, 8%/2% in Iceland, 8%/1% in Norway, 15%/1% in Finland and 11%/7% in Sweden.

Use of COC recommended as first line treatment

Comparisons were made between the use of COC recommended as first line treatment by the EMA versus other forms of CHC products. In Denmark the proportion of EMA-recommended products increased markedly from 13% to 50% between 2010 and 2013. Finland remained almost exclusively on non-recommended products throughout the study period, while in Iceland and Norway the proportions of recommended products increased to some extent.

Sweden started off at a high level of recommended products with a slight decrease during the study period.

Emergency contraceptive pill

Norway had the highest sales figures for emergency contraceptive pills with 12.6 sold packages/100 women in 2013 and Denmark the lowest with 8.2 sold packages/100 women. All countries had a slight decrease in the use of emergency pills during the period 2010 - 2013.

Paper II

In this paper contraceptive user rates and fertility, birth and abortion rates in the Nordic countries were explored. When possible data were also stratified according to age groups with a 5-year-interval. The study population consisted of 5 814 064 women aged 15-49 years in 2013.

Fertility, birth and abortion rates among women of reproductive age

FR remained stable around 1.8 in all countries except for Iceland where the rate declined from 2.7 to around 1.9. In 2013 the fertility rate was 1.7 in Denmark, 1.8 in Finland and Norway and 1.9 in Sweden and Iceland.

Birth rates displayed similar patterns as the overall FR in all countries.

Abortion rates declined in Denmark and Finland, increased in Iceland and remained stable in Norway and Sweden. The changes in abortion rates took place mainly between 1975 and 1995 whereas from 1997 and onwards a relatively stable pattern was seen in all countries.

Contraceptive use among women of reproductive age

The overall use of hormonal contraceptives and Cu-IUD among women aged 15-49 years during 2008-2013 was higher in Denmark (39-44%), Sweden (40-42%) and Finland (40-41%) compared to Norway (33-34%) and Iceland (31-33%). The levels of hormonal contraceptive use in each country were fairly stable during 2008-2013, with the exception of Denmark where a small increase was noted mainly due to an increasing use of the LNG-IUS. In 2013, the estimated use of Cu-IUD´s and POP was highest in Sweden (7% for each methods) whereas Finland had the highest use of the LNG-IUS (15%).

Hormonal contraceptive use, birth and abortion rates in different age groups

Hormonal contraceptive use, birth and abortion rates for Denmark, Norway and Sweden during the period 2008-2013 were also stratified according to age. The age group 15-19 years is described in the section on Paper III.

In summary CHC was the most common method in the age groups ranging from 15-29 years of age for all three countries. In the age groups 34-44 CHC decreased gradually whereas the use of LNG-IUS increased to become the dominant contraceptive method. This changing scenario was seen in older age groups in Denmark than in Norway and Sweden.

In all three countries, births reached a peak among 30-34 year old women and abortion rates were highest among women of 20-24 years of age. Sweden had the highest abortion rates and lowest rate of contraceptive use in the age group 20-24 years.

Paper III

In this paper trends in contraceptive use, abortion and birth rates among all teenagers in the Nordic countries were explored. For Denmark, Norway and

Sweden the study population was also stratified into the subgroups of 13-14, 15-17 and 18-19 years old women. The study population consisted of all 749 709 15-19 years old women in all Nordic countries and all 815 044 13-19 years old women in Denmark, Norway and Sweden respectively in 2015.

Overall birth and abortion rates among teenagers 15-19 years, 1975-2015

There has been a steady decline in teenage pregnancies during the study period attributed to a decline in both abortions and births (Figure 6). Abortion rates varied to some extent until 1999 but have thereafter declined continuously in all the Nordic countries and reached their lowest levels ever in 2015.
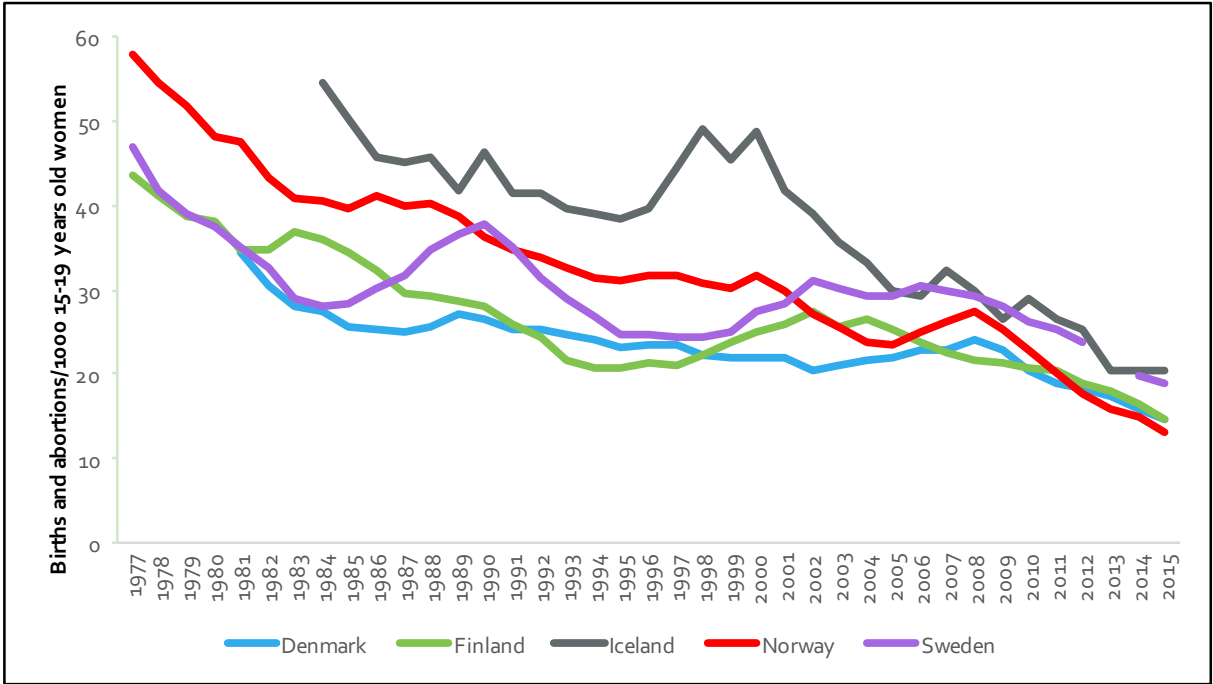

Figure 6. Pregnancies, including births and abortions, among teenagers 1975-2015 in the Nordic countries.

Age-stratified use of hormonal contraceptives, births and abortions in Denmark, Norway and Sweden, 2008-2015

Both rates of contraceptive use, births and abortions were very low among 13-14 years old women. Denmark had a higher use of hormonal contraceptives among 15-17-year-olds (from 40 to 34%) compared to Norway (from 25 to 27%) and Sweden (from 29 to 30%). Among 18-19 year-old women user rates went from 63 to 61% in Denmark, 56 to 61% in Norway and 54 to 56% in Sweden. A more marked decrease in birth rates was seen among 18-19-year-old in Norway (from 20 to 10 per 1000 teenagers) compared to the other two countries where Norway started off on a higher level in 2008 (Fig. 3c).

CHC were the most popular contraceptive methods in all age groups, especially among the Danish teenagers. There was an increase in LARC among 15-17-year-olds, but this was more marked among the 18-19-year-olds with levels increasing from 2 to 6% in Denmark, 2 to 9% in Norway and 7 to 17% in Sweden. This was mainly due to increasing levels of LNG-IUS in Denmark and Sweden and of implants in Norway.

Paper IV

In this paper a number of reproductive health issues and their relationship to SES in four generations of young Swedish women was investigated.

Current contraceptive use was higher in 2001 (78%) ($p < 0.01$) and 2011 (69%) ($p < 0.05$) compared with 1981 (60%) and 1991 (62%). CHC was the most common form of contraception in all cohorts ($p < 0.0001$) but there was a modest increase of LARC in the later cohorts.

The proportion of teenage mothers decreased from 4.4% (1981) to 1.6% (2011) ($p < 0.01$). BMI was significantly higher in the last cohort compared to the two

first cohorts ($p < 0.001$). The proportion of smokers decreased successively between the four cohorts from 41% in 1981 to 19% in 2011 ($p < 0.001$).

The percentage of young women who had ever been pregnant at ≤19 years of age was lower in the assessment from 2001 (7.4%) ($p < 0.05$) than in 1991 (12.9%) and 2011 (12.2%) which corresponds to the pregnancy rate described in Paper III. In 2001 there had been a decline in pregnancies during the five years before the questionnaire was sent out and vice versa in 1991 and 2011 (Figure 1b, Paper III).

Association between SES and contraception, pregnancy, smoking and BMI

There was no significant difference in the prevalence of current or ever use of contraception according to SES area in 1981, 1991 and 2001, but in 2011 there was a lower prevalence of contraceptive use in low SES areas compared to both of the other SES groups. More women had been pregnant in the low SES areas than in the higher SES areas ($p < 0.05$) in 1981, 1991 and 2011.

There were more smokers in low ($p < 0.05$) SES areas compared to high SES areas in 1981 and 1991, but no correlation between SES and smoking in 2001 and 2011. BMI was higher in the low SES groups ($p < 0.05$) in 2001 and 2011.

Paper V

This study investigated if immediate insertion (1 hour after the intake of mifepristone) of a subdermal contraceptive implant affected the efficacy of medical abortion compared to the standard treatment with delayed insertion at the follow up visit, in a randomised controlled equivalence trial.

The study population was enrolled between October 2013 and October 2015 and in the ITT population 261 women were scheduled for delayed insertion (standard treatment) and 277 to immediate insertion. The flow of patients is described in Figure 7.
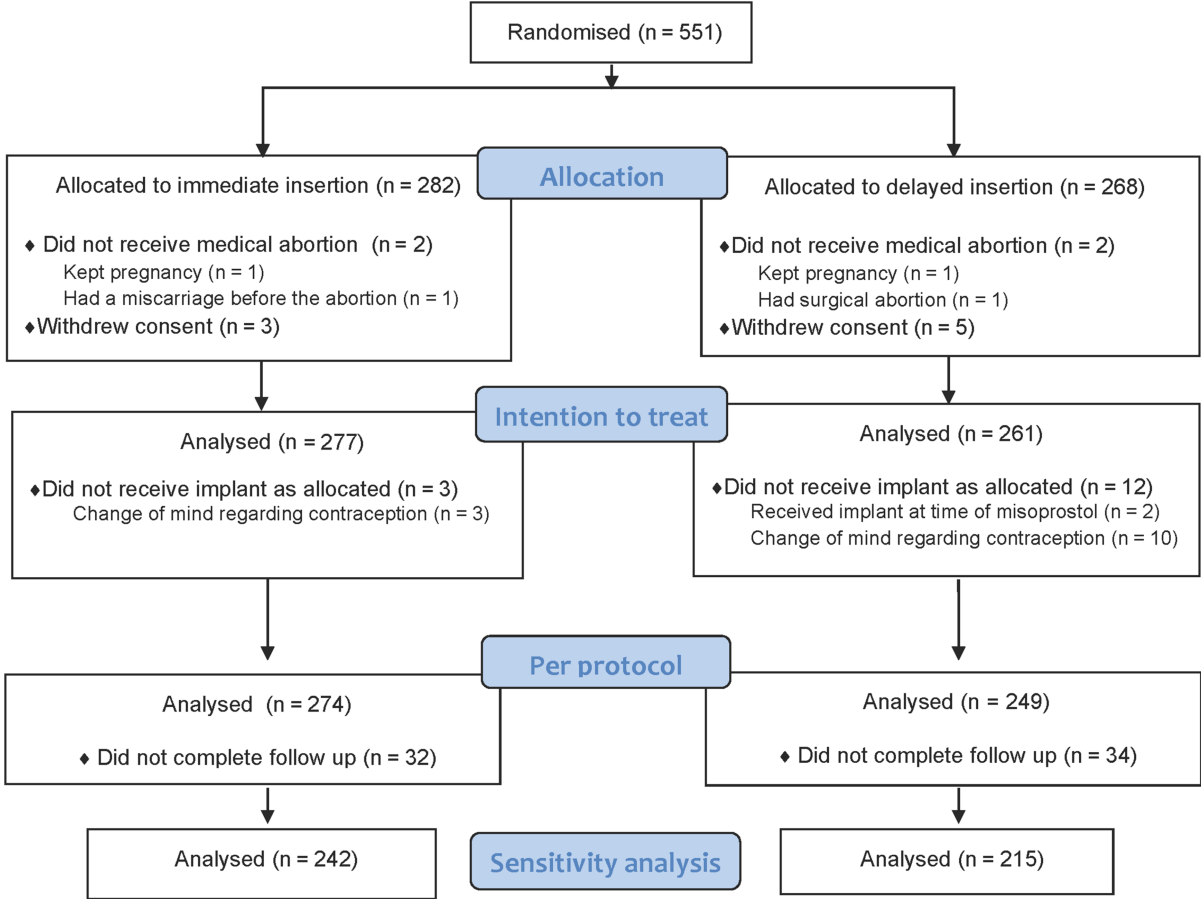

Figure 7. Trial flow-chart. Source Paper 5.

The main outcome was successful completion of the abortion without the need of a surgical intervention. In the PP analysis 16/274 (5.8%) of women in the immediate insertion group and 10/249 (4%) in the delayed insertion group had a surgical intervention resulting in a risk difference of 1.8% (95% CI −0.4% to 4.1%). Since this was within the pre-specified margin of ±5% equivalence between the two groups could be established. The results were similar for the ITT population with a risk difference of 1.3% (95% CI −0.9% to 4.1%). Insertion rate and acceptability of time of insertion was statistically higher in the

group of immediate insertion and there were fewer pregnancies in the group of immediate insertion than delayed. Table 3.

Table 3. Primary and secondary outcomes.

	Immediate insertion	**Delayed insertion**	
Surgical intervention	16/274 (5,8%)	10/249 (4%)	Risk difference 1,8%*
Insertion rate	274/277 (99,2%)	187/261 (71,6%)	P<0.001
Pregnancy within 6 months	2/274 (0,7%)	10/261 (3,8%)	P=0.018
Acceptability of time of insertion	180/277 (64,9%)	51/261 (19,5%)	P<0.001

*Risk difference 1,8% (95% CI -0,4-4%) Equivalence within +5% established

Discussion

Fertility rate

While a large part of the world outside Europe is still in the middle of the fertility transition with a strong wish among its inhabitants to lower their TFR, Europe's concern is instead a declining or stable low TFR well below replacement level which is illustrated in Figure 8.[85] All the Nordic countries have kept a higher TFR than the rest of Europe since 1990 and onwards.
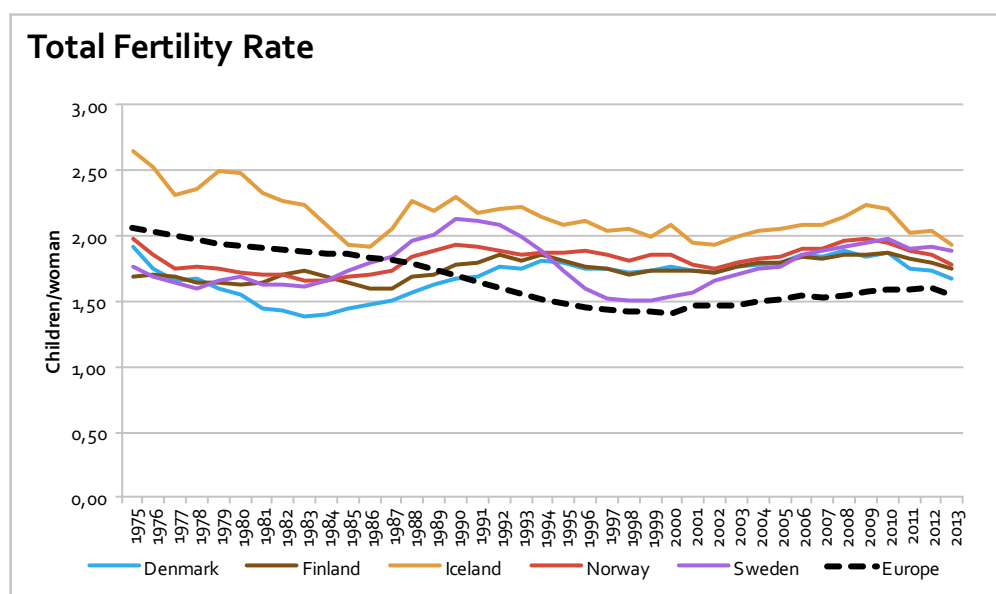

Figure 8. Total fertility rate in the Nordic countries and Europe. Source: Paper II and Eurostat (the broken line).

Studies show that governmental support for combining family with a working career is the key to keeping a high birth rate and TFR.[90 91] The means for this might differ from country to country. In the Nordic countries parental leave for both women and men and accessible and affordable child-care is offered. Also in France there is a strong support for combining work and family life and France has a TFR similar to the Nordic countries. The Nordic countries and France are both good examples of that it is possible to combine high birth rates with good access to family planning methods including safe abortion on women's request.[90 91]

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Increasing use of LARC

There is robust scientific evidence of the high efficacy of LARC methods [18 46]. During the last 10-15 years the promotion of LARC as the most effective form of contraception has increased. Still only a very small increase of LARC was noticed between 2008 and 2013 in Paper I and II. The positive trend towards increasing use of LARC is much more obvious among the oldest teenagers in Paper III, which also covers the years 2014-2015. The finding is supported by Paper IV where an increase of LARC among teenagers in a longer perspective is seen. There was a shift towards recommending LARC already in the Swedish guidelines for contraception in 2005 which was updated in 2014. Norway has done similar recent updates. The evidence for LARC being suitable also for teenagers is still growing. In a review, including 12 studies and 4886 women, on the use of LARC among adolescents an overall continuation rate of 84% after 12 months of use was found. The majority of the adolescents in this review were using an IUD.[92] Another review focusing specifically on LNG-IUS confirmed the high continuation rate, but also examined the effect on treatment of dysmenorrhea, endometriosis and menorrhagia. A high acceptability and reduction in symptoms was found.[93] The continuation rates described in these studies are very high compared to continuation rates of non-LARC methods such as COC, the patch, the ring and DMPA-injections. In a sub-analysis of the CHOICE project 81% of women aged 14-19 years continued with LARC but only 44% with non-LARC. There was also a lower continuation rates of non-LARC methods when compared with older women in the same study. [94] Even lower 1-year-continuation- rates for non-LARC were observed in a study by Raine et al where only 32,7% continued with COC.[95]

The results from Paper V where it was shown that one of the LARC methods, an implant, can be offered at the same day as a woman is having an abortion and therefore only needs one visit to the abortion clinic is an important contribution to the spreading of this highly effective LARC.

The relationship between contraception and abortion prevalence

In Paper II and III there was no clear correlation between high overall contraceptive user rates and low abortion rates and vice versa when the Nordic countries were compared. For instance Iceland with the lowest contraception prevalence also had the second lowest abortion rate while Sweden with the second highest contraception prevalence had the highest abortion rate. Among the teenagers in Paper III births and abortions declined in all countries to its lowest levels ever at the same time as LARC increased, but still the correlation between highest contraceptive use and lowest abortion rate was absent. A number of possible reasons for this have been discussed in Paper I and II:

- a lower contraceptive user rate in the highly fertile and sexually active age group of 20-24-year old women in Sweden compared to the same age groups in Denmark and Norway. This is the age group with the highest abortion rate.
- we were not able to estimate the proportion of women using no method at all or methods such as condoms, diaphragms, fertility awareness methods or coitus interruptus. The proportion of non-users and users of the mentioned methods, which are highly user-dependent, might differ between the countries and affect unintended pregnancy rates.
- the proportions of different hormonal methods vary between the countries. Sweden had a higher user rate of POP than the others and the continuation rate for POP is lower than for other oral methods.[96]

Other approaches might also be considered. In 2010-2014 the global abortion rate was 35/1000 women 15-44 years of age and in the developed world 27/1000. In a global context all the Nordic countries have low abortion rates, including Sweden. This in turn means it is not as easy to detect a certain factor

to further lower these rates, compared to countries with huge unmet need for contraception where any increase in any contraception method probably will have an effect. As discussed in the Introduction a country may have increasing contraceptive prevalence and increasing abortion levels at the same time since both might be needed for a limited period of time to reach the fertility rate and number of children one wishes for. With time abortion rates usually stop increasing when the contraception prevalence is high enough to cover the main need for contraception and the fertility rate is stable. The abortions that still occur then are mainly due to contraceptive failure or non-use. Other parameters might change though which increase the unmet need for contraception again. As for many other countries the average age for having a first child has increased from 24 in 1970 to 29 in 2010 in Sweden and since the years between 24 and 29 is a period of high fertility the time with a need for highly effective contraceptives is extended. This has been illustrated in the French paper Effectiveness of family planning policies: The abortion paradox. Also in France the average age for having a first child has increased during the last 40 years with a concomitant increasing need for effective contraceptives.

As shown in Figure 9 the authors reported an increasing contraceptive prevalence among women 18-29 years of age but an almost unchanged abortion rate. An extended need for effective contraceptives has been met and an increasing number of unwanted pregnancies has been avoided but very little has happened to the abortion rate.[97] This might be the case also in Sweden and Norway where the abortion rates has remain stable since 1975. There is support for an increasing contraception prevalence from 1981 to 2011 in Sweden in Paper IV.
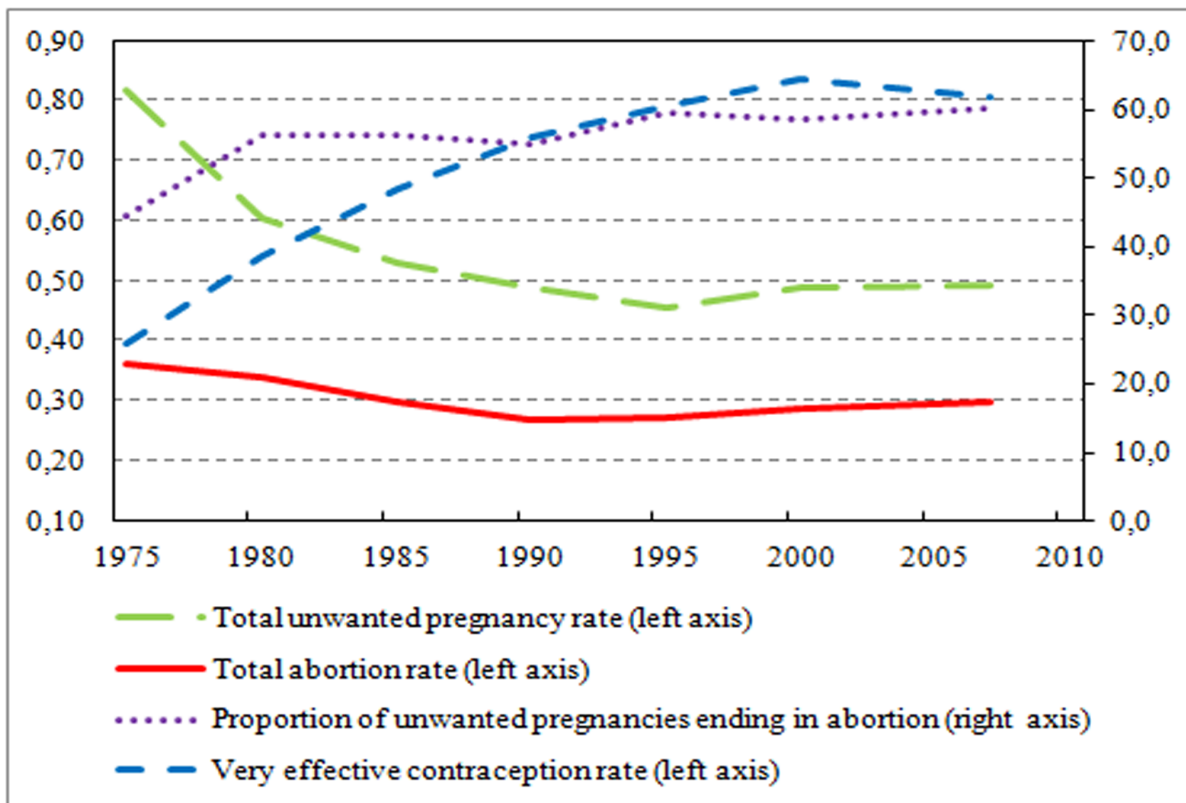
Figure 9. Trends in unwanted pregnancies, probability of ending them, abortion rates and very effective contraception rate for women 18–29. Left axis: rate per woman. Right axis: Percentage. Source: Effectiveness of family planning policies: the abortion paradox. Bajos, N et al. PLoS one, 2014, 9(3)

Adherence to EMA recommendations

From 2009 epidemiological studies have shown a differential risk of venous thrombosis according to type of progestogen in COC [98] and the EMA has updated its recommendations on first line COC to be those containing levonorgestrel, norgestimate or norethisterone, which have the lowest risk of venous thrombosis.[99] During the study period 2010-2013 in Paper I the adherence to this recommendation varied substantially between the Nordic countries with the highest level in Denmark (50% in 2013) and the lowest in Finland (1% in 2013). This might imply that the time has come for mutual guidelines on contraception for all Nordic countries.

Discontinuation due to mental effects

In Paper IV mental side effects, such as depression and reduced libido, as reasons for discontinuation of CHC use increased substantially over time across the four cohorts from 15 to 55% (p < 0.001). This is in accordance with other epidemiological studies, but other explanations than the use of CHC itself has been sought for, such as important life events or depression already before the start of the CHC. In a review article it was found that 15% experienced a decreasing libido during the use of CHC [100], but the study designs varied. Two Swedish randomised placebo-controlled trials have recently been conducted in order to evaluate side effects of COC. In one study COC use was associated with small but significant mood side effects in the intermenstrual phase. The findings were driven by a subgroup of women who clearly suffered from COC-induced side effects.[101] In the other study, where effects on libido were investigated, no significant reduction in overall sexual function was found in the COC group compared to the control group, but there was a significant impairment in three out of seven sub-domains: sexual desire, arousal and pleasure.[102] Although small, these findings should be taken into consideration in the contraceptive counselling.

The impact of socioeconomic status (SES)

The association of low SES and lower contraceptive use and higher teenage pregnancy rate in Paper IV is consistent with the findings in other studies from high income countries.[60-64] It is also in accordance with the result of studies from other parts of the health care sector. For instance, Hakeberg and Wide Boman have reported about poorer oral and general health in low SES areas in a study also conducted in the Gothenburg area.[103] Bergstrom et al have shown that the outcome after an acute myocardial infarction is worse for residents from low SES areas in Sweden.[104]

What is notable in the results in Paper IV though, is that there was no detectable difference in contraceptive use between the three SES groups in the three early cohorts of women, but in the assessment from 2011 a difference was shown. This implies a widening inequality in more recent years. It also suggests that there is a greater need for information and sexual education in low SES areas in order to reverse this trend.

Also a proportionally higher BMI was recorded in low SES compared to high SES areas in the later cohorts from 2001 and 2011 compared to the analyses from 1981 and 1991. This might have implication on the contraceptive prevalence since an increasing BMI limits contraceptive choices.

Response rate

Response rates in epidemiological studies have declined steadily for many years [105]. In a review on response rate of surveys performed during 1970-2003 the steepest decline was seen after 1990. The overall decline varied between ≈0,5-2%/year and was dependent on the study design. Cohort and cross-sectional studies, which applies best to Paper IV, had a decline of 0,54%/year. It corresponds well with the response rates in Paper IV where the response rate was 91% in 1981, 82% in 1991, 77% in 2001 and 53% in the last cohort of women included in 2011. Due to the knowledge of declining response rates the sampled population in 2011 was increased to 100% of the total population of 19-year-old women. It has been suggested that web-based surveys might increase the response rate but the results from earlier studies have been divergent. In more recent studies web-based surveys seems to have the same response rates as postal surveys though. [106 107] In a Cochrane review from 2009 a number of factors were found to increase response rates, such as pre-notification, follow-up contact, shorter questionnaires, providing a second copy of the questionnaire at follow up, mentioning an obligation to respond, university sponsorship, incentives and an assurance of confidentiality. The odds of response were

reduced when the questionnaire included questions of a sensitive nature. [108] For future studies or follow-up of the present cohorts in Paper IV these factors along with a web-based survey option should be considered.

Strengths and limitations

The strength of Paper I-III was the use of national register data, where all women of reproductive age in the Nordic countries are included. All the registries are considered reliable.

Data on redeemed prescriptions have been extracted from the databases. When assessing contraceptive use, pharmacy claims have been shown to be more reliable than self-reported use.[109]

Online purchases of pharmaceutical drugs without a registered prescription are not included in the study. Since prescribed hormonal contraceptives are available and affordable to most women of reproductive age in the Nordic countries, the proportion of online purchases without a prescription is not considered to be significant.

A limitation in Paper I-III was the lack of age specific data on contraceptive use from Finland and Iceland. This would have been of special interest since Finland has the lowest abortion rate. Another limitation in Paper I-III was the lack of age specific data on Cu-IUDs and the lack of data on all other non-hormonal methods.

The main strength of Paper IV was the design that allowed a comparison of contraception, pregnancies and other health factors in random samples of women of the same age from the same urban area during a period of 30 years. Another strength was the possibility to connect this information to the SES of the area of residence and hence assess the possible influence of socioeconomic factors.

A limitation in Paper IV was that the response rate to the questionnaire successively decreased during the course of this 30- year study. The lower response rates in the most recent cohorts compared to the earlier cohorts is in agreement with the successive reduction in response rates to questionnaires reported in the literature.

The strength of Paper V was the randomised equivalence trial design and the fact that it was a multi-center study, which ensures that the results are independent of the study centre. The limitation was the loss to follow-up, but the proportion of women who did not complete follow-up did not differ between groups and the results of the sensitivity analysis did not differ from the ITT or PP analysis.

Conclusions

- The user rates of hormonal contraceptives and Cu-IUD among all women of reproductive age in the Nordic countries varied between 31% and 44% in 2008-2013. The highest use was in Denmark and the lowest in Iceland. CHC followed by the LNG-IUS were the most common methods. A small increase of LARC was detectable during the study period (Paper I and II).

- The overall abortion rates of the Nordic countries fell during the study period with declining rates in Denmark and Finland, increasing rate in Iceland and stable rates in Norway and Sweden. The changes in abortion rates took place mainly between 1975 and 1995 whereas from 1996 and onwards a relatively stable pattern was seen in all countries (Paper II).

- In contrast to the declining average fertility and birth rates in Europe, rates in the Nordic countries remained stable from 1975 and onwards and close to the replacement level (Paper II).

- The user rates of hormonal contraceptives among teenagers 18-19 years of age were rather similar in Denmark, Norway and Sweden and varied between 54% and 63%. CHC were the most common method, but a more pronounced increase of LARC, compared to the group of all women of reproductive age, was seen in all the countries (Paper III).

- Teenage birth and abortion rates declined continuously since 1975 and reached an all-time-low in 2015 in all the Nordic countries (Paper III).

- There was no clear correlation between higher overall hormonal contraception prevalence and lower abortion rate. Instead other factors have to be considered, such as: differences in the proportions of different types of hormonal contraceptives and in prevalence in specific age groups; the increased need for contraceptives due to delayed childbirth; and the lack of data concerning non-users and users of non-hormonal contraceptives (Paper II and III).

- Lower contraceptive use in low SES areas compared to middle and high SES areas was detected in the most recent assessment of 19 years-old women in the Gothenburg area. This was not seen in the earlier assessments and may imply a widening inequality in more recent years (Paper IV).

- A contraceptive implant can be inserted on the same day as administration of mifepristone for early medical abortion. It has the potential to increase both satisfaction with the abortion procedure for women and the number of women who receive the most effective methods of contraception at the time of abortion (Paper V).

Future perspectives

During the work with this thesis the difference between the Swedish abortion registry and the registries in the other Nordic countries has been made apparent. Since all abortion patients have been anonymised already before being reported to the National Board of Health and Welfare in Sweden it is impossible to follow e.g. complication rates or connect the registry to the prescription database, which would make it possible to identify what contraceptive prescriptions women who have had an abortion have received. From the 1st of February 2017 abortions should be reported to the patient registry though, which will hopefully improve the possibility to secure the quality of the abortion care and also make research on abortion-related issues easier.

While the new reporting procedures of abortions in Sweden might improve research nationally many of the challenges in research on abortions internationally will not be solved with the help from registries. On the contrary, after the introduction of medical abortion many abortions are now being handled completely by the woman herself. This takes place in countries were abortion is illegal and/or health care facilities do not offer abortion care. The drugs are purchased on the internet, in pharmacies or from private persons. Kapp et al have summarised the research gap concerning self-induced medical abortion, its methodological challenges as well as important research question about safety, needs of education and support and safe distribution of high quality medical abortion drugs.[110] Important research has already been done on home-abortion[111] and self-test for follow up[53] in high-income and liberal settings which have made way for self-use in poorer or more restrictive settings. This is an interesting field of research.

Not only abortions but also contraceptive user patterns might be increasingly challenging to follow by registries, also in the Nordic countries. Although contraceptives are easily accessible and affordable for many women and men, many find it comfortable to purchase goods on the internet and this might also

be the case for contraceptives in the future. Regulations might support registration of the purchases, but not necessarily. Surveys, in the form of questionnaires or interviews, will probably be needed also in the future when studying contraceptive use, unintended/intended pregnancies, abortions and other reproductive health issues.

The findings in Paper IV which may imply increasing inequality concerning contraception prevalence in low and high SES areas calls for research on how to reach and empower the most vulnerable women in the society.

LARC has many advantages, the high effectiveness being the most important, but it has one disadvantage: it has to be inserted by a trained person. A long-acting method that the woman could apply herself sounds like the ultimate method, also suitable in settings where there are no health care facilities. In fact, The Population Council has developed a one-year combined hormonal contraceptive vaginal ring, which is fitted by the woman herself, and is now awaiting permission from the FDA to distribute the ring.[112] Just like the self-administered medical abortions, this is also in line with increasing self-use and self-monitoring instead of in-facility-care. As long as research guarantee that the methods are safe and efficient the development towards a well-informed self-management of reproductive health issues should be welcomed since it empowers women and gives them control over their own lives.

Acknowledgements

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