Happy with the method? Sexual function changes in young women using contraception
Happy with the method?
Sexual function changes in young women using contraception

by

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Dedication

This thesis is dedicated to my Grandmother, Moldován Erzsébet, who was a teacher of physics and, as far back as I can remember, proclaimed the praise of science and the joy of learning.
Acknowledgements

I would like to thank all of you that in different ways made this thesis possible. Without the help of others, I could not have reached my goal!

Professor emeritus Mats Hammar, my main supervisor. How lucky I am! I have enjoyed your patience, warmth, humour, and never-ending interest in whatever was on my mind. You have supported me in many ways. Your trust in me and my work has made me grow and has kept me going on with research at times when I preferred to give it up. I am grateful for the time I spent with you. Observing how you act has taught me invaluable skills concerning research, clinics, and being a colleague. You are also a role model for multi-tasking and how to balance it with a rich private life.

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List of scientific papers

I. Hormonal contraception and sexual desire: A questionnaire-based study of young Swedish women
Agota Malmborg, Elin Persson, Jan Brynhildsen, and Mats Hammar
The European Journal of Contraception & Reproductive Health Care. 2015 Sept; 25:1-10

II. A survey of young women’s perceptions of the influence of the Levonorgestrel-Intrauterine System or copper-intrauterine device on sexual desire
Agota Malmborg, Jan Brynhildsen and Mats Hammar

III. Sexual function and combined oral contraceptives: a randomised, placebo-controlled trial
Cecilia Lundi*, Agota Malmborg*, Julia Slezak, Kristina Gemzell, Danielesson, Marie Bixo, Hanna Bengtsdotter, Lena Marions, Ingela Lindh, Elvar Theodorsson, Mats Hammar and Inger Sundström-Poromaa
*Equal contribution
Endocrine Connections. 2018 July, 7: 1208-1216

IV. Women’s experiences of sexual function related to use of contraception, a qualitative study
Agota Malmborg, Louise Brynte, Gabriella Falk, Jan Brynhildsen, Mats Hammar and Carina Berterö
Submitted manuscript

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Vad är temat för denna avhandling?
Denna avhandling, som baserar sig på fyra vetenskapliga publikationer, studerar förändringar av sexuell funktion, som kan upplevas av en del kvinnor i samband med användning av hormonella preventivmetoder.

Varför är ämnet viktigt?
En kategori av patienter som ofta dyker upp på preventivmedelsmottagningar eller gynekologiska mottagningar, är kvinnor som uppger att de upplever eller har upplevt nedsatt lust och/eller påverkan på sitt psykiska mående i samband med användning av hormonella preventivmedel. Dessa kvinnor kan ha stora svårigheter att finna en preventivmetod som de känner sig nöjda med. Många alternativa metoder till hormonella metoder har nackdelar, tex låg tillförlitlighet eller ökade besvär med blödningar och smärta, som kan göra dem olämpliga för den specifika kvinnan. Detta kan resultera i att kvinnan kanske väljer en mindre säker metod, eller att inte använda någon metod alls, som i sin tur kan leda till fler oönskade graviditeter.

Varför är detta ämne svårt att studera?
Vad ville vi ta reda på?
Hur vanligt förekommande är lustbiverkan bland unga kvinnor som använder någon form av preventivmetod? Är det vanligare bland dem som har en hormonell metod jämfört med dem som använder hormonfria metoder? Påverkar denna eventuella biverkan viljan att avsluta eller byta metod? (Studie I)
Finns det ett direkt och statistiskt säkerställt samband mellan användningen av ett p-piller och påverkan på sexuell funktion? Kan det vara sänkningen av testosteronhalten som vi vet uppstår vid användning av p-piller som åtminstone delvis kan förklara ett eventuellt samband? (Studie II)
Vad kan vi lära oss av kvinnor som i samband med preventivmedelsanvändning upplever en påverkan på sexuell funktion? Hur märker de det och vad menar de när de uppger sådana biverkningar? Vad blir följderna för fortsatt metodval? (Studie III)

Hur gjorde vi?
Vi skickade en enkät till alla 22, 25 och 28 åriga kvinnor i Linköpings kommun med frågor om nuvarande och tidigare preventivmedelsanvändning och upplevda positiva och negativa biverkningar. En del av enkätan berörde frågor kring sexuell funktion. Totalt analyserades 1850 svar. (Studie I, vars resultat är publicerat i artikel I och II)
I studie nummer två deltog 200 kvinnor som lottades till att använda ett p-piller eller ett sockerpiller. Alla var tvungna att också använda ett hormonfritt graviditetsskydd såsom kondom eller kopparspiral. Under studiens gång på tre månader jämförde vi förändring i sexuell funktionsnivå genom ett formulär de fick fylla i före och i slutet av studien. De fick också lämna blodprover och härprover för testosteronanalyser.(Studie II och artikel III)
Slutligen intervjuade vi 24 av kvinnorna som i enkätstudien, (dvs studie I) uppgivet en påverkan vid hormonell preventivmedelsanvändning. Intervjuerna spelas in och skrevs ut som text för att därefter analyseras enligt en strukturerad kvalitativ metod. (Studie III och artikel IV)

Vilken kunskap har vi tillfört?
Vi fann att de som använde hormonella metoder mer än dubbelt så ofta upplevde en negativ biverkan på sin lust (27%) jämfört med de som använder hormonfria metoder (12%). Denna skillnad gällde oavsett vilken sorts hormonell metod man använde. Minskad lust ensamt, eller i kombination med försämrat psykiskt mående var den vanligaste orsaken till att man övervägde att avbryta eller byta metod. (Artikel I och II)
I jämförelsen mellan ett p-piller och sockerpiller (placebo) fann vi ingen skillnad i sexuell funktion som helhet men en liten skillnad av lusten. Kvinnorna som hade lottats till p-pillret hade, jämfört med kvinnor som lottats till sockerpiller en statistiskt säkerställd större
minskning av poängen som angav sexlusten. Denna minskning var dock så pass liten att det är osäkert om det i praktiken är av någon betydelse. Testosteronhalten i blodet minskade som förväntat men den mängd som lagrades i håret förblev densamma. Någon tydlig koppling mellan minskning av testosteronhalt och minskning av sexlusten fann vi inte.

(Artikel III)

Kvinnorna vi intervjuade beskrev sina upplevelser olika men ett gemensamt tema var att det ofta tar tid och kräver erfarenheter av både användning av hormoner men också den egna menscyklens variationer för att förstå samband. Ökad förståelse gav insikt i kopplingen mellan hormoner och egen sexuell funktion samt för vissa även psykiskt mående. Negativa upplevelser var främst en känsla av avstängdhet, att kroppen inte reagerade på sexuella stimuli, dvs torrhet och minskad lust. Huruvida man sedan valde ett hormonfritt alternativ eller fortsatte med hormonell metod efter en sådan insikt, berodde på graden av påverkan och omständigheterna för övrigt i livet. Gemensamt dock var att om man hade upplevt dåligt psykiskt mående i samband med hormonell metod var det en mer avgörande faktor än påverkan på sexuell funktion. (Artikel IV)

Sammanfattningsvis har vi lärt oss att sexuella biverkningar i form av minskad lust som sätts i samband med användning av hormonella preventivmedel kan upplevas av ca en fjärdedel av unga användare. Det påverkar hur dessa kvinnor väljer metod. Upplevelsen kan vara stark eller mindre betydelsefull men om kvinnan söker för det bör det tas på allvar. Hon bör bekräftas och inte ifrågasättas och med bland annat våra studieresultat som bakgrund stöttas till att prova sig fram tills hon finner en metod hon kan vara nöjd med. Det direkta, så kallade kausala sambandet, kan finnas mellan hormoner och sexlust men är sannolikt inte märkbar för de flesta och behöver studeras ytterligare för att säkerställas. Vi behöver också lära oss mer om vad det är som gör att vissa drabbar men inte andra.
Abstract

**Background:** Sexuality and contraception are closely linked topics. In theory, hormonal contraception use might affect female sexual function in both positive and negative directions. Some women experience and report adverse sexual function changes while they use hormonal contraception while others report no or positive changes. Questions of causality, the potential mechanisms of action, and how to counsel women reporting adverse changes have been a matter of debate but scientific consensus is lacking on the answers. Increased knowledge of women’s experiences of sexual function effects related to hormonal contraceptive use, could enhance contraceptive counselling and in a wider perspective contribute to tailored recommendations for contraceptives, increased compliance, and thereby reduced numbers of unwanted pregnancies and abortions.

**Material and Methods:** The first study was a cross-sectional study with 1851 women, aged 22, 25 and 28 years, who answered a questionnaire regarding contraception use, positive and negative side effects, contraceptive counselling, and aspects of sexual function. The second study was a randomised double-blind placebo-controlled multicentre clinical trial. In this study we compared 102 women who used a combined oral contraceptive with 100 women who took placebo, regarding sexual function scores evaluated with the McCoy Female Sexuality Questionnaire. We measured testosterone level changes in serum and hair as a secondary outcome. The third study was a qualitative study in which we explored women’s experiences of the negative effects of hormonal contraceptive use on sexual function. We interviewed 24 selected women who had reported previous experiences of adverse sexual function changes while using a hormonal contraceptive method.

**Results and Conclusions:** Young Swedish women who used hormonal contraception, reported a negative change in sexual desire more than twice as often
as women who used hormone-free contraceptive methods. A similar difference was seen between users of the levonorgestrel-intrauterine system compared with users of the copper-intrauterine device.

The experience of an adverse sexual desire effect, which the women thought was due to contraceptive use, was a strong predictive factor for reconsideration of the contraceptive method.

We found no change in the total score of sexual function during the use of a combined oral contraceptive compared with placebo. Sexual interest and lubrication which were two aspects of the total sexual function, were found to be negatively associated with the use of the tested combined oral contraceptive. Changes were small however, and the clinical relevance of these findings is therefore unclear. Furthermore, lubrication change did not persist following adjustment for change in self-rated depression scores.

The biologically active fraction of testosterone embedded in hair did not decrease during combined oral contraceptive treatment and no reliable associations were found between the induced serum testosterone level decrease and sexual desire changes.

Women reporting negative sexual function effects while using hormonal contraception, described lubrication difficulties and decreased sexual desire associated with both contraceptive use and parts of the menstrual cycle. Associations became obvious with time and experience and consequently contraceptive choice became easier with age, experience, and better understanding, all of which we concluded could be facilitated by a responsive contraceptive counsellor.

Our findings indicate the need for further evaluation of sexual function changes in the selected group of women who seem to be susceptible to the use of hormonal contraceptives.
**Abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>BMI</td>
<td>body mass index</td>
</tr>
<tr>
<td>CHC</td>
<td>combined hormonal contraception</td>
</tr>
<tr>
<td>COC</td>
<td>combined oral contraception</td>
</tr>
<tr>
<td>Cu-IUD</td>
<td>copper intrauterine device</td>
</tr>
<tr>
<td>DRSP</td>
<td>Daily Record of Severity of Problem</td>
</tr>
<tr>
<td>FAI</td>
<td>free androgen index</td>
</tr>
<tr>
<td>FSFI</td>
<td>Female Sexual Function Index</td>
</tr>
<tr>
<td>HC</td>
<td>hormonal contraception</td>
</tr>
<tr>
<td>IUC</td>
<td>intrauterine contraception</td>
</tr>
<tr>
<td>LARC</td>
<td>long acting reversible contraception</td>
</tr>
<tr>
<td>Lng-IUS</td>
<td>levonorgestrel intrauterine system</td>
</tr>
<tr>
<td>MADRS</td>
<td>Montgomery-Åsberg Depression Rating Scale</td>
</tr>
<tr>
<td>MFSQ</td>
<td>McCoy Female Sexuality Questionnaire</td>
</tr>
<tr>
<td>PMS</td>
<td>premenstrual symptoms</td>
</tr>
<tr>
<td>POP</td>
<td>progestin only pill</td>
</tr>
<tr>
<td>SD</td>
<td>standard deviation</td>
</tr>
<tr>
<td>SHBG</td>
<td>serum hormone binding globulin</td>
</tr>
<tr>
<td>T</td>
<td>total testosterone</td>
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</table>
In my everyday gynaecological practice, I meet women with sexual function concerns. Irrespective of age or the reason for the appointment, sexual function inevitably arises as a matter of discussion. When women discuss their sexuality, it is a sign of having established a good physician-patient relationship. Unfortunately, I repeatedly fail to give answers or clear advice regarding the loss of libido often claimed by users of hormonal contraceptives. The frustration of being a limited clinician was the starting point of a project that later grew into this thesis. Since then, seven years have passed and still there are no certain answers but on the road to accomplishing PhD studies, I learned how to deal with uncertainty. And that is not so bad.

Preface
Background

The need for contraception and contraceptive method development might be as old as sexuality itself. In many countries, an extensive range of effective contraceptive choices are available and easily accessible, however the number of unwanted pregnancies and abortions is still high. Around 2% of women aged 15-44 years in Sweden, underwent abortion during 2018.(1) The unmet need of contraceptive use in Sweden was estimated to be 8.9% in 2013.(2)

One reason to discontinue safe and effective contraception is experiences of adverse effects on mood and sexual function.(3-5)

Hormonal contraception use in Sweden and worldwide

Combined oral contraception (COC) seems to be the most popular form of reversible contraception in Europe and the United States. It is also the most widespread contraceptive method geographically in the world.(6, 7) In Sweden as well as the other Nordic countries, hormonal contraception (HC) is used by around 40% of women aged 15-49 years.(8) In Sweden, in contrast to many other European countries, most contraceptive prescriptions are issued by nurse midwives who are also the medical personnel mostly responsible for contraceptive counselling. A smaller proportion of the contraceptive prescriptions are issued by gynaecologists and by general practitioners.(9)

Hormonal contraception

The first oral contraceptive pill was introduced in 1961.(10) Since then many different pharmacological formulations and ways of administration have stepwise been developed. Figure 1 shows the different groups and administration routes of HC available in Sweden.

All types of HC exert their contraceptive effect through the action of a progestin compound, which is a synthetic progestogen. The progestogens are a class of steroid hormones including the different kinds of progestins used in contraceptives as well as progesterone produced during the luteal phase of the menstrual cycle.(11)

Combined hormonal contraception (CHC) refers to a group of contraceptives that includes not only a progestin but an oestrogen as well. The purpose of adding an oestrogen is to mimic the natural cycle and to prevent unscheduled bleedings.(11)
Figure 1. The different groups of hormonal contraception available in Sweden.

Oestrogens used in CHC are ethinyloestradiol, oestradiol valerate, and oestradiol, in order of how common they are. Ethinyloestradiol is synthetic and is by far the most common oestrogen in COC. Its pharmacological effects of suppressing and inhibiting ovulation are similar to those of the biological oestradiols whereas its effects on the hepatic synthesis of serum binding globulin (SHBG) and hemostatic factors are more marked.(12) The dose of ethinyloestradiol in CHC has historically been decreased in order to reduce the risk of venous thromboembolism related to CHC use.(13) After intake, oestradiol valerate is converted to oestradiol which is the most potent oestrogen produced during the ovulatory cycle. Oestradiol containing COC is the most recently developed type of CHC.

Step by step new types of progestins have been developed and are often referred to as different generations of progestins. This development is driven by the wish to
decrease the amount of the oestrogen compound and to minimise the androgen side effects of progestins.(12)

Table 1 shows some of the currently available progestins in Sweden and their androgenic properties.(14, 15) It should be pointed out though that all COC could be defined as antiandrogenic due to the decreased levels of circulating free testosterone they induce, although some formulations depending on the specific progestin, are more anti-androgenic than others.(15, 16)

<table>
<thead>
<tr>
<th>Progestin generation</th>
<th>Example of progestin</th>
<th>Androgenic</th>
<th>Antiandrogenic</th>
</tr>
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<tbody>
<tr>
<td>First</td>
<td>Norethisterone acetate (NET)</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>Second</td>
<td>Levonorgestrel (LNG)</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>Third</td>
<td>Desogestrel (DSG)</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Fourth</td>
<td>Drospirenone (DRSP)</td>
<td>0</td>
<td>++</td>
</tr>
<tr>
<td>Biological progestin</td>
<td>Nomegestrol acetate*(NOMAC)</td>
<td>0</td>
<td>(+)</td>
</tr>
<tr>
<td></td>
<td>Progesterone (P4)</td>
<td>0</td>
<td>+</td>
</tr>
</tbody>
</table>

Table 1. Androgenic properties of progestins.

* Nomegestrol-acetate is the progestin compound in the COC used in study II.

**Sexual function**

Normal female sexual function is not clearly defined in the literature. It is more often defined by the absence of sexual dysfunction.(17) Physiology is though the cornerstone of normal sexual functioning including anatomical, neurobiological, and psychological mechanisms.(18) The understanding of female sexual function has developed from the simplified four stages model of Masters and Johnson(19), through the circular model of Basson(20)(fig 2), into a wider biopsychosocial paradigm, which considers aspects such as differentiation of the
brain, brain functioning, and psychophysiology as well. (18)

Fig. 2 (Basson, JAMC 10 MAI 2005; 172 (10))
Sex response cycle, showing responsive desire experienced during the sexual experience as well as variable initial (spontaneous) desire.

Still, current clinical definitions as well as assessment methods are based on diagnostic criteria of sexual dysfunction. (21) To make this situation more complicated, currently there are two international diagnostic classifications, the DSM-5 (Diagnostic and Statistical Manual of Mental Disorders) (22) and the ICD-10 (International Statistical Classification of Diseases and Related Health Problems - Tenth Revision) (23). The ICD-10 is focused on the definition of medical conditions, and the DSM-5 primarily defines psychiatric conditions. Based on a recent international consensus of sexual dysfunctions, female sexual function can be divided into the following aspects: sexual desire, sexual arousal, orgasm, sexual pleasure, and absence or presence of genital-pelvic pain. The aspect of sexual arousal
is often referred to as ‘lubrication’ including both swelling and lubrication. ‘Sexual satisfaction’ is sometimes considered synonymous to ‘sexual pleasure’. (24)

The two most widely used assessment tools of female sexual function for scientific use, are the Female Sexual Function Index (FSFI)(25) and the McCoy Female Sexuality Questionnaire (MFSQ)(26). The FSFI is a tool for assessing aspects of sexual function in women. It has 19 items, scoring 0 to 5 or 6 with a scoring system for six domains of female sexuality: desire, arousal, lubrication, orgasm, satisfaction, and pain. (25) It has been developed and has shown good reliability and validity for women with various sexual dysfunctions and is validated for translations into more than 20 languages. (27, 28) The Swedish translation was made by a pharmaceutical company and was later validated by Ryding et al. (29) The MFSQ in its current form was first used in the 1990s to evaluate the relationship between use of oral contraceptives and sexuality in university women in California. (30) There is no validation of the Swedish translation but the MSFQ has extensively been used in French, Italian and Scandinavian studies assessing sexual function related to hormonal fluctuations due to both hormonal treatment and natural changes such as those that occur in the menopausal transition. (31, 32) The MFSQ is further described in the method section and the Swedish version is shown in the Appendix.

Positive effects of HC
The use of COCs and other HC offers several health benefits. HC, if used as prescribed, is not only a high efficacy protection against unplanned pregnancies but also offers treatment for women suffering from heavy menstrual bleeding, dysmenorrhoea, endometriosis, premenstrual symptoms and acne. COC use is also associated with a decrease in the risk of ovarian cancer, endometrial cancer and colorectal cancer. (33) The health benefits of contraceptive use can indirectly increase sexual function. HC use can also eliminate the fear of pregnancy and thereby potentially provide a more relaxed and enjoyable sexual experience. (34)
Sexual function over the menstrual cycle
Current literature suggests that female sexual function is to some extent influenced by hormonal changes over the menstrual cycle. Several studies report increased sexual activity and desire around mid-cycle. However, a few other studies, report no associations. Sexual activity initiated by women has been suggested to be most frequent some days prior to, and during ovulation after which it declines during the luteal phase of the cycle. Neuroimaging has shown brain activity changes indicating that hormonal fluctuations during the menstrual cycle influence sexual interest/desire and arousal along with mood, cognition, and memory.

A lingering and common idea is that androgens are the primary regulators of libido in women just as in men. Fluctuating levels of total testosterone have been measured during the menstrual cycle with peak levels at the time of ovulation. Oestradiol, however, exhibits a much more pronounced, mid-cycle peak than testosterone. More data suggest that the within-cycle variations in desire are mediated by fluctuating levels of progesterone and oestradiol; increased progesterone as an inhibitory signal and increased oestradiol as a stimulatory signal.

The effects of steroid hormones are mediated by steroid receptors both in the central nervous system and in peripheral tissue. In biopsies, the progesterone receptor in the vulvar vestibule has been shown to have lower concentrations during the luteal phase compared to the follicular phase. This indicates a non-linear correlation of circulating steroid hormone levels and peripheral tissue reactions and makes conclusions regarding hormone levels and their effects complicated.

Altogether, considering that endogenous sex hormone fluctuations and the intricately tuned menstrual cycle can influence women’s sexual function, it is plausible to assume that exogenous hormonal treatment such as HC, could affect sexual function as well, in both positive and negative directions.

Progestogens and sexual function
The primary contraceptive mechanisms of action of progestogens are a dose-dependent suppression of ovulation and an effect on the cervical mucus causing it to remain thick and viscous, inhibiting sperm penetration. Many variables affect the potency and possible side effects of the different progestogens. Dosage, bioavailability, protein binding, receptor binding affinity, different metabolites and multiple receptors and signalling pathways, and differing
inter-individual variability make the available research results difficult to extrapolate into clinically relevant information for progestogens in general. (49)

Some studies have shown that the biologically active progestogen, progesterone, has a negative effect on sexual desire and sex drive. (38, 50) However, the progesterone level fluctuates over the menstrual cycle whereas all HC use implies a more continuous level of progestogen over time.

The progestin-related potential negative effects on female sexual function could also be secondarily mediated by suppression of ovarian function and the subsequent decrease of endogenous oestrogen production. (48)

Another potential mechanism of progestins affecting sexuality could be related to the direct binding of progesterone to oxytocin receptors inhibiting oxytocin receptor functioning. Oxytocin has several functions in pair-bonding and sexual function. (51) On the other hand, some studies report no adverse sexual function effects or even an increased sexual satisfaction and increased intercourse frequencies with progestin use, especially with third and fourth generation COCs and low systemic dose methods such as the levonorgestrel-intrauterine system (Lng-IUS). (52)

It is likely that different progestins and preparations have different potential to influence female sexual function. (53)

**Oestrogens and sexual function**

Studies of the menopausal transition have found that declining sexual functioning is most closely related to declining oestrogen levels. (54, 55) Loss of desire, decreased sexual responsiveness and genital sensation, difficulty achieving orgasm, and painful intercourse might be symptoms of low circulating oestradiol and testosterone levels but altogether the available data do not support systemic oestrogen therapy for the treatment of female sexual dysfunction in menopause. Instead, topical vaginal oestrogen is considered as the first-line treatment. This counteracts vulvovaginal atrophy and thereby improves sexual function. (56)

The importance of the role of oestrogens in women of fertile age and their sexual function is confirmed by the finding that levels of salivary oestradiol positively predicted women’s sexual desire during the normal menstrual cycle and oestrogen levels peaked just prior to ovulation. (45)

HC induces a suppression of gonadotrophins, which leads to reduced ovarian stimulation and thereby reduced production of oestradiol, but also of progesterone, androstenedione, and testosterone. (57) The fact that no certain difference between contraceptive methods with or without oestrogens has been demonstrated regarding
female sexual function, implies that the oestrogen compound in CHC is probably of secondary importance. (56) Comparisons of biological or bioidentical oestrogens and ethinylestradiol regarding receptor activity and sexual function are lacking. (58) Therefore, no conclusions can be drawn about whether the exogenous oestrogen substitute in CHC could modulate sexual function differently to the endogenous oestrogens. However, the more recently developed COCs that contain bioidentical oestrogens could in theory offer a more favourable profile of side effects.

**Testosterone and sexual function**

The literature regarding female sexual function and the role of testosterone is contradictory. In women who experience sexual dysfunction following oophorectomy, testosterone treatment has been shown to be beneficial. (59) On the other hand, postmenopausal low serum testosterone levels were not associated with low scores of sexual function evaluation. (60) Likewise, some studies on pre-menopausal women indicate that measures of general sexual desire are not related to testosterone levels. (38, 45, 50)

Androgens in women are produced in the adrenal glands in a constant manner and in fluctuating amounts in the ovaries. Some researchers claim a linear correlation between sexual activity and hormonal testosterone profile that peaks during the periovulatory phase. (37, 61)

The largest fraction of circulating androgens is bound to serum proteins, most considerably to the serum binding globulin (SHBG) and albumin, leaving approximately 1-2% of the total level unbound, called the biological active fraction. (62) Only the unbound fraction can bind to the androgen receptors and exert its actions on brain and peripheral tissue. Measurement of the biological active fraction of testosterone in serum samples is costly and time-consuming and is therefore seldom carried out. It is most often calculated mathematically as the free androgen index (FAI) from total testosterone (T) and SHBG; in which the FAI = (100 T/SHBG). (63) Testosterone levels in saliva and hair represent the biologically active concentrations of testosterone. Methods to measure testosterone in saliva and hair have been developed. (64-67)

During use of COC, circulating levels of total testosterone decrease due to negative feed-back leading to reduced production of testosterone from the ovarian theca cells. Furthermore, bioavailable free testosterone also decreases with use of COC due to
increased production of SHBG in the liver. The oestrogen dose and progestin type of the COC influence the increase of SHBG and in turn the decrease of bioavailable testosterone. (11) On a theoretical basis the change of androgen levels in the specific woman could induce a change of sexual function. (68) Also, given that androgens are required for the synthesis of the glycoproteins needed for mucous formation, this may explain the decreased lubrication noted by some women. (69)

In summary, the clinical implication of HC related suppressed but still within a normal range androgen levels, is unclear. (68)

<table>
<thead>
<tr>
<th>HC and endogenous steroid hormones</th>
</tr>
</thead>
<tbody>
<tr>
<td>HC use induces to various degrees a decrease of the mean circulating oestradiol, progesterone and testosterone levels. However, steroid hormone levels remain within a normal range and the effects of the changes on sexual function are unclear.</td>
</tr>
</tbody>
</table>

In summary, existing evidence for an association between sexual function and contraception is inconsistent, and additional research is needed. Nevertheless, there are theoretically several potential ways that HC directly or indirectly might interfere with women’s sexual function. Considering the large number of women using HC, the complaint of adverse sexual function effects is an issue that deserves attention from the researchers even if the prevalence of sexual side effects is presumed to be low. Increased knowledge of women’s experiences, especially those who report adverse sexual function effects related to HC use, could enhance contraceptive counselling, and in a wider perspective contribute to tailored recommendations for contraceptives, increased compliance, and thereby a decreased numbers of unwanted pregnancies and induced abortions.
Hypotheses

❖ Sexual desire negatively affected by contraceptive use is a more common experience reported by young Swedish women using hormonal contraception than women using hormone-free contraception and it is a predictive factor for discontinuation of the method. *(Study I, Paper I)*

❖ The reported prevalence of adverse sexual function effects differs among hormonal contraceptive users depending on the type of method. *(Study I, Paper II)*

❖ Aspects of sexual function are influenced by the use of a combined oral contraceptive. *(Study II, Paper III)*

❖ Study III *(Paper IV)* is a qualitative study and therefore has no hypothesis. Please see aims instead on the next page.
Aims of this thesis

General aim
❖ To explore and describe sexual function in young Swedish women using hormonal and hormone-free contraception, and to contribute new knowledge that could improve contraceptive counselling for women who experience such adverse effects.

Specific aims
❖ To determine whether a decrease in sexual desire is more prevalent among women using hormonal contraception than among women using hormone-free contraception. (Study I, Paper I and II)
❖ To explore whether the adverse sexual function effects reported by intrauterine contraception (IUC) users differ among Lng-IUS users compared with copper intrauterine device (Cu-IUD) users. (Study I, Paper II)
❖ To explore whether the experience of decreased sexual desire is a predictive factor for discontinuation or change of contraceptive method. (Study I, Paper I)
❖ To compare changes in aspects of sexual function between women treated with a combined oral contraceptive or placebo. (Study II, Paper III)
❖ To investigate associations between sexual function and testosterone levels in serum and hair. (Study II, Paper III)
❖ To explore the experiences of effects of hormonal contraceptive use on sexual function in a selected group of women who have previously reported negative sexual function changes while using hormonal contraception. (Study III, Paper IV)
### Material and methods

A summary of the methods used in the three studies and four papers is presented in Table 2.

<table>
<thead>
<tr>
<th>Study Presented in Paper</th>
<th>I and II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of study</strong></td>
<td>Observational</td>
<td>Experimental and interventional</td>
<td>Qualitative</td>
</tr>
<tr>
<td><strong>Design</strong></td>
<td>Cross-sectional study</td>
<td>Randomised double-blind placebo-controlled multicentre clinical trial</td>
<td>Interview study</td>
</tr>
<tr>
<td><strong>Source of data</strong></td>
<td>Self-constructed, validated questionnaire&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1. McCoy Female Sexuality Questionnaire&lt;sup&gt;b&lt;/sup&gt; 2. Testosterone in serum and hair</td>
<td>Open structured Interviews</td>
</tr>
<tr>
<td><strong>Subjects</strong></td>
<td>1851 women, ages 22, 25, and 28 years</td>
<td>202 women (102 COC&lt;sup&gt;b&lt;/sup&gt; and 100 placebo)</td>
<td>24 women, ages 27, 30, and 33 years</td>
</tr>
<tr>
<td><strong>Statistics and method of analyses</strong></td>
<td>Descriptive statistics, Chi-square test, multiple logistic regression</td>
<td>Student’s t-test, Chi-square test, Mann-Whitney U test, Spearman’s rank correlation test</td>
<td>Thematic analysis</td>
</tr>
</tbody>
</table>

Table 2. Summary of the three studies and four papers included in the thesis.

<sup>a</sup>Questionnaires shown in appendices

<sup>b</sup>Combined oral contraceptive (1.5 mg oestradiol and 2.5 mg nomegestrol acetate)
Study I – The Questionnaire study (Papers I and II)

Study population and setting
All women turning 22, 25, and 28 years and living in Linköping 2013 according to the population register (N3870), were included in the survey. The three age groups were arbitrarily chosen but with the aim of getting a sufficiently large sample and having different age-groups represented among young women’s age groups. No other inclusion or exclusion criteria were applied. Linköping is a university city, with around 150,000 inhabitants at the time of the study. The population is mainly urban and contains an above-average number of university students.

The questionnaire
The questionnaire was developed by the research team to match the study questions and the chosen study population. It was divided into three parts. Part I contained questions about demographic background. Part II concerned current and previous contraceptive use and included questions about positive and negative side effects and whether contraceptive counselling had been sought and given. The prototype for Parts I and II was a Swedish epidemiologic questionnaire previously used by colleagues in Gothenburg.(70) Part III aimed to evaluate sexual function and was a compiled version of two pre-existing and validated instruments, the McCoy Female Sexuality Questionnaire (MFSQ)(26) and the Female Sexual Function Index (FSFI)(25). In total, the questionnaire had 30 questions. The variables were, except for height and weight, nominal, and pre-formulated with between two and 16 response alternatives. Additional space for personal comments followed the questions about side effects.

The questions of most importance for our main outcomes are listed below and the complete questionnaire in Swedish is shown in the Appendix.

Sexual desire
- ‘Do you find that your current contraceptive method affects your sexual desire?’ The response alternatives were: (1) no; (2) yes, for the worse; (3) yes for the better; (4) I use no contraceptives
- ’How often during the last four weeks have you felt sexual desire or sexual interest?’: (1) Daily; (2) Once or a couple of times/week; (3) Never or almost never
• ‘How often have you engaged in any sexual activity during the last four weeks?’: (1) Daily; (2) Some or a couple of times/week; (3) Occasionally; (4) Never
• ‘In the last four weeks, how often did you attain orgasm during any kind of sexual activity?’: (1) Every time or almost every time; (2) More than half of the times; (3) Occasionally; (4) Never
• ‘During the last four weeks, how satisfied have you been with your sex life?’: (1) Very satisfied; (2) Rather satisfied; (3) Rather unsatisfied; (4) Very unsatisfied
• ‘Are you satisfied with your sexual desire level?’: (1) Yes; (2) No, I wish it was less; (3) No, I wish it was higher

Current contraceptive use
• The question about current contraceptive method had 14 response alternatives to cover all known contraceptive methods. For the purpose of analysis, these were merged into the following groups of interest: (1) COC, patch and ring; (2) Progestogens [progestogen only pill (POP), rod or injection]; (3) Lng-IUS; (4) Cu-IUD; (5) Condom and other barrier methods; (6) Other [all other hormone-free methods]

Adverse effects
• Two questions in the questionnaire concerned whether the woman had considered giving up or changing her current contraceptive method or whether she had considered doing so with a previous HC. If ‘Yes’, she could as a cause tick one or several of the side effects listed in the questionnaire or add a personal comment.

The questionnaire was content validated with two methods. First, a comprehension test was carried out on three women of the similar age as the selected population of the study. These women filled out the questionnaire and then they were interviewed about possible difficulties of understanding the questions and the response alternatives. Second, test-retest stability with a two-week interval was performed with eight 25-year-old volunteers. The two occasions rendered different answer alternatives in 11 of the 30 questions. The difference in the number of alternative steps of these 11 questions had a median of zero and a mean value of 0.12-0.5. Minor clarifications to some of the questions were made in accordance with the results from
the two validating methods. The final questionnaire (in Swedish) is presented in the Appendix.

**Data collection**

The questionnaires were posted to the participants through the traditional mailing system in March 2013. Two reminders were sent out two and four months later to those who had not replied. In total 1851 women returned completed questionnaires. The process is shown in Table 3 bellow.

Data collection was ended in November 2013. We used optic reading of the questionnaires and the information was converted into electronic data for analysis. Not until absolute accordance between optic and manual reading was ensured in three complete questionnaires, the automatic optical reading was started. Responses with personal comments were scanned. Questionnaires that were unreadable optically were read and added to the data file manually instead. Responses that were unreadable even manually, were included in the response rate calculation and as missing answers in the analyses.

<table>
<thead>
<tr>
<th>Birth year (age)</th>
<th>Eligible according to population register</th>
<th>Women not reached*</th>
<th>Probably received questionnaires</th>
<th>Returned completed questionnaires</th>
<th>Response rate %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1991 (22)</td>
<td>1471</td>
<td>36</td>
<td>1435</td>
<td>685</td>
<td>47.7</td>
</tr>
<tr>
<td>1988 (25)</td>
<td>1321</td>
<td>53</td>
<td>1268</td>
<td>644</td>
<td>50.8</td>
</tr>
<tr>
<td>1985 (27)</td>
<td>1074</td>
<td>41</td>
<td>1037</td>
<td>522</td>
<td>50.3</td>
</tr>
<tr>
<td>Total</td>
<td>3870</td>
<td>130</td>
<td>3740</td>
<td>1851</td>
<td>49.5</td>
</tr>
</tbody>
</table>

Table 3. Data collection and response rate.

*Envelopes returned unopened, invalid address.

**Outcomes**

The main outcome measures were:

- Self-reported sexual desire changes related to all contraceptive methods. *(Paper I)*
- The Lng-IUS and Cu-IUD users were additionally compared regarding aspects of sexual functioning: sexual desire level, sexual activity, orgasm frequency, satisfaction with sex life and satisfaction of desire level. *(Paper II)*
- Considering whether to quit or to change contraceptive method related to the experience of adverse effect on sexual desire *(Paper I)*
Study II – The randomised clinical trial (Paper III)
This study was initiated at Uppsala University and was designed to investigate both mood and sexual function side effects. In paper III we reported the results regarding sexual function. Additional publications describing effects on mood are not included in this thesis. (71, 72)

Participants and setting
Women aged 18-35 years, healthy according to self-report and who agreed to use barrier contraception during the study or had a copper IUD or had been sterilised, were eligible for the study. The standard exclusion criteria for COC use in clinical routines were applied in the study. No additional exclusion criteria were used. Seven Swedish centres were involved in the study, Uppsala, Stockholm (two hospitals), Linköping, Örebro, Umeå, and Gothenburg. The participants were recruited by advertisements in newspapers, on local notice boards and on student-websites.

Outcomes
The main outcome measures were the daily assessment of mood symptoms with the assessment tool Daily Record of Severity of Problem (DRSP) (73), reported elsewhere (71), and aspects of sexual function scores measured with the McCoy Female Sexuality Questionnaire (MFSQ) (74).
A secondary outcome was testosterone level in serum and hair. The self-rated depression score assessed using the Montgomery-Åsberg Depression Rating Scale (MADRS) was also a secondary outcome used in both the evaluation of sexual function and evaluation of mood symptoms. The MADRS scores reflect depressive symptoms during the past three days on a scale ranging from 0 to 54. (75) Additional outcomes were set to investigate risk factors for mood side-effects. These were previous psychiatric history, personality traits, baseline mood, and genetic factors. None of these outcomes were included or reported in paper III or this thesis.

The MFSQ
This questionnaire has been validated in several different languages and is used to evaluate female sexual function and dysfunction (26). It is shown in the Appendix. The MFSQ assesses sexual function during the last four weeks and consists of 19 questions. Eighteen of these use a seven-point Likert scale and one question asks about intercourse frequency. (The Likert scale is a rating scale used to measure...
attitudes or opinions. With this scale, respondents are asked to rate items on a level of agreement. (76) The questionnaire is categorised into six domains, as shown in Table 4. The higher the total scores the better the sexual function. Arbitrarily, we defined a clinically significant deterioration as a 30% decrease in the score from baseline to the last visit.

<table>
<thead>
<tr>
<th>Domains</th>
<th>Questions (question number)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Sexual interest/(desire) Enjoyment of sexual activity (1)</td>
</tr>
<tr>
<td></td>
<td>Level of sexual interest (5)</td>
</tr>
<tr>
<td></td>
<td>Frequency of sexual thoughts and fantasies (3)</td>
</tr>
<tr>
<td></td>
<td>Excitement/arousal during sexual activity (4)</td>
</tr>
<tr>
<td>II</td>
<td>Satisfaction with frequency of sexual activity Satisfaction with frequency of sexual activity (2)</td>
</tr>
<tr>
<td></td>
<td>Decreased satisfaction due to partner´s disinterest (9)</td>
</tr>
<tr>
<td>III</td>
<td>Vaginal lubrication Vaginal lubrication (6)</td>
</tr>
<tr>
<td></td>
<td>Insufficient lubrication (17)</td>
</tr>
<tr>
<td></td>
<td>Painful sexual intercourse (18)</td>
</tr>
<tr>
<td>IV</td>
<td>Orgasm Additional stimulation to reach orgasm (16)</td>
</tr>
<tr>
<td></td>
<td>Frequency of orgasm (14)</td>
</tr>
<tr>
<td></td>
<td>Pleasure of orgasm (15)</td>
</tr>
<tr>
<td></td>
<td>Enjoyment of sexual intercourse (13)</td>
</tr>
<tr>
<td>V</td>
<td>Partner Erectile problems, partner (19)</td>
</tr>
<tr>
<td></td>
<td>Satisfaction with partner as friend (11)</td>
</tr>
<tr>
<td></td>
<td>Satisfaction with partner as lover (10)</td>
</tr>
<tr>
<td>VI</td>
<td>Attractiveness How sexually attractive have you considered yourself? (7)</td>
</tr>
<tr>
<td></td>
<td>How sexually attractive towards your partner have you considered yourself? (8)</td>
</tr>
<tr>
<td>(VII)</td>
<td>Intercourse frequency Intercourse/week or month (12)</td>
</tr>
</tbody>
</table>

Table 4. The domains and belonging questions in the MFSQ. Numbers in brackets refer to the question number in the MFSQ. 
*Sexual interest* is the denomination used in the MFSQ, elsewhere in this thesis referred to as ‘sexual desire’.

**Testosterone in hair and serum**

Hair cells have androgen receptors which bind free testosterone from the circulation. Scalp hair grows approximately one cm per month, which enables a retrospective evaluation of the long-term biologically active plasma concentration during the period of growth. (63) Hormone analysis in hair has the additional advantage of circumventing difficulties in determination of the biologically active fraction, and the samples are stable at room temperature facilitating storage and transport. (77)
Blood and hair samples for testosterone measurements were collected either at inclusion or at randomisation visits (depending on whether the woman had used HC or not prior to the study inclusion), and at the last visit at the end of the third treatment cycle. Blood samples were separated to yield serum samples. Separation into serum was achieved by centrifugation after 30 minutes of sedimentation time. The serum samples were stored at -70 degrees Celsius on site until sent to the laboratory in Uppsala.

Serum levels of testosterone and SHBG were determined by using an electrochemiluminescence immunoassay (78) at an accredited laboratory at Uppsala University hospital. FAI (63) was calculated as (testosterone/SHBG) x 100.

Hair samples were cut as close as possible to the scalp, with the proximal end marked, and the samples were stored in envelopes in room temperature. In the laboratory, a 1 cm hair segment from inclusion visit samples and a 3 cm hair segment from third cycle samples, were finely cut with scissors and samples of about 10 mg hair were prepared before chemical homogenisation. Measurements of long-term bioavailable testosterone levels in hair is a recently developed method, and uses a competitive radioimmunoassay in speed-vaced methanol extracts of homogenised hair (65). This analysis was performed at the department of Clinical Chemistry at Linköping University Hospital.

**Trial design**

The trial design is shown in Figure 3 below. During the study, the study patients had four visits with the midwife or the physician. The first visit was the inclusion visit when the study patients met with the physician. Oral and written information was given before consent and the inclusion and exclusion criteria were checked. A medical history was taken, background information was noted, weight was measured, and the assessment formulas were recorded. During the first cycle no hormonal treatment was allowed. Women who planned to switch from another HC, had this first month as a ‘washout’ month following inclusion. The MFSQ was filled out and blood and hair samples were taken either at inclusion (women with no HC) or at the next visit, at randomisation after washout (women with another HC at inclusion).

The second visit was performed after completion of the hormone-free cycle and the women were randomised to either COC or placebo. The third visit took place at the end of the first treatment cycle. The fourth and last visit was at the end of the third
treatment cycle for evaluation, to fill out the MFSQ, and to provide blood and hair samples. At inclusion and before each treatment cycle, urine pregnancy tests were analysed.

**Figure 3. Design of Study III.** Only main outcome measures shown.

DRSP: Daily Record of Severity of Problem, MFSQ: McCoy Female Sexuality Questionnaire

**Randomisation and double blinding**
The capsules containing COC (1.5 mg oestradiol and 2.5 mg nomegestrol acetate) and the identical placebo pills were prepared by the National Corporation of Swedish Pharmacies (Apoteket AB). They performed packaging and computerised randomisation in blocks of four. Randomisation codes were kept at the Uppsala University Hospital Pharmacy until the study was completed, thus ensuring a double-blind procedure was followed.

**Study III – The interview study (Paper IV)**
This was a qualitative study.
Questions raised and that remained unanswered during the analyses of studies I and II inspired the planning of study III. These were:
What do women really mean when stating they experience impaired sexual function? How do these experiences affect relationship and contraceptive method choice? How are these matters discussed with the contraceptive counsellor?

**Epistemology**

In this study, we consider the researcher to be part of what she is studying and the data she collects. Hence, we assume that knowledge is situated, it is constructed, and is interpreted in the specific setting. We believe that the new knowledge is created by the researcher and the informant together, and consequently our experiences and preconceived ideas are part of the results.

**Participants**

The selection of participants was purposive. The last question in the questionnaire described under Study I was: ‘Are you interested in taking part in an interview regarding contraception and sexual desire?’ The ones responding ‘yes’ were asked to provide contact details for future contact. Women who, according to the questionnaire, also reported adverse sexual function related to HC, were regarded as eligible for the interview study. Figure 5 shows the selection process. The sample size was calculated according to Fugard and Potts(79) and is shown in figure 4.

![Figure 4. Sample size calculation according to Fugard and Potts(79)](image-url)
Figure 5. Selection process of informants. The random selection was performed manually, and to yield three similar sized age-groups. Women were contacted in order of appearance on a list created in 2013. The women were listed by age and the time for returned questionnaires.

**Data collection**

The interviews followed an interview guide that is shown in the Appendix. The interview guide allowed the interviewers to iteratively add, change and reorder the questions to maintain a free and relaxed interview situation.

Each interview was conducted by either Dr Malmborg or a registrar colleague, Dr Brynte. In 11 interviews out of 24 the other researcher was present making notes. In those cases, the second researcher was involved in the small talk prior to the interview, actively listened during the interview, and at the end of the interview she
added further clarifying questions. When just one interviewer was present the field notes were written directly after the interview. Interview details are presented in Table 5.

<table>
<thead>
<tr>
<th>ID</th>
<th>Age</th>
<th>Duration (min)</th>
<th>Location</th>
<th>Interviewer</th>
<th>Transcriber</th>
<th>Written pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>W1</td>
<td>30</td>
<td>35</td>
<td>University group-room</td>
<td>AM (LB)</td>
<td>AM</td>
<td>10</td>
</tr>
<tr>
<td>W2</td>
<td>27</td>
<td>46</td>
<td>University group-room</td>
<td>AM (LB)</td>
<td>Secretary</td>
<td>11</td>
</tr>
<tr>
<td>W3</td>
<td>33</td>
<td>55</td>
<td>Informant’s home</td>
<td>LB (AM)</td>
<td>Secretary</td>
<td>12</td>
</tr>
<tr>
<td>W4</td>
<td>30</td>
<td>32</td>
<td>Hospital group-room</td>
<td>LB (AM)</td>
<td>Secretary</td>
<td>8</td>
</tr>
<tr>
<td>W5</td>
<td>27</td>
<td>53</td>
<td>Hospital group-room</td>
<td>LB (AM)</td>
<td>Secretary</td>
<td>12</td>
</tr>
<tr>
<td>W6</td>
<td>30</td>
<td>74</td>
<td>University group-room</td>
<td>LB (AM)</td>
<td>Secretary</td>
<td>13</td>
</tr>
<tr>
<td>W7</td>
<td>33</td>
<td>81</td>
<td>Hospital group-room</td>
<td>LB</td>
<td>Secretary</td>
<td>17</td>
</tr>
<tr>
<td>W8</td>
<td>30</td>
<td>65</td>
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<td>LB</td>
<td>Secretary</td>
<td>14</td>
</tr>
<tr>
<td>W9</td>
<td>33</td>
<td>58</td>
<td>Informant’s home</td>
<td>LB</td>
<td>Secretary</td>
<td>13</td>
</tr>
<tr>
<td>W10</td>
<td>30</td>
<td>61</td>
<td>Informant’s work</td>
<td>AM (LB)</td>
<td>Secretary</td>
<td>12</td>
</tr>
<tr>
<td>W11</td>
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<td>73</td>
<td>Informant’s work</td>
<td>LB (AM)</td>
<td>Secretary</td>
<td>19</td>
</tr>
<tr>
<td>W12</td>
<td>30</td>
<td>55</td>
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<td>LB (AM)</td>
<td>Secretary</td>
<td>16</td>
</tr>
<tr>
<td>W13</td>
<td>33</td>
<td>46</td>
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<td>AM (LB)</td>
<td>LB</td>
<td>14</td>
</tr>
<tr>
<td>W14</td>
<td>33</td>
<td>102</td>
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<td>LB (AM)</td>
<td>Secretary</td>
<td>26</td>
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<tr>
<td>W15</td>
<td>33</td>
<td>64</td>
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<td>AM</td>
<td>Secretary</td>
<td>13</td>
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<tr>
<td>W16</td>
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<td>44</td>
<td>Hospital group-room</td>
<td>AM</td>
<td>AM</td>
<td>12</td>
</tr>
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<td>W17</td>
<td>30</td>
<td>64</td>
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<td>Secretary</td>
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<tr>
<td>W18</td>
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<td>AM</td>
<td>Secretary</td>
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<td>W19</td>
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<td>AM</td>
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<td>13</td>
</tr>
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<td>33</td>
<td>69</td>
<td>Hospital group-room</td>
<td>AM</td>
<td>LB</td>
<td>18</td>
</tr>
<tr>
<td>W22</td>
<td>30</td>
<td>70</td>
<td>Informant’s work</td>
<td>AM</td>
<td>Secretary</td>
<td>15</td>
</tr>
<tr>
<td>W23</td>
<td>30</td>
<td>69</td>
<td>Informant’s work</td>
<td>AM</td>
<td>Secretary</td>
<td>13</td>
</tr>
<tr>
<td>W24</td>
<td>33</td>
<td>59</td>
<td>Hospital group-room</td>
<td>AM</td>
<td>Secretary</td>
<td>13</td>
</tr>
</tbody>
</table>

Table 5. Interview details. a The women in order of inclusion named as W1-W24; b Duration of interviews without the preceding ‘small talk’; c AM= Agota Malmborg, LB=Louise Brynte. In parentheses, the second interviewer, when present. d All the transcribers followed the same transcription key

The interviews were audio-recorded and transcribed verbatim. The median interview duration time was 60 minutes.

**Data analysis**

Our approach was inductive, and thus prioritised participant voices and experiences. Thematic analysis(80) was used based on a constructionist perspective focusing on latent themes. Coding was conducted on a theoretical basis looking for the content
answering our study questions, but we kept an open mind and included non-expected aspects for further analysis. The six steps of thematic analysis are shown in Table 6.

<table>
<thead>
<tr>
<th>Phase</th>
<th>Example/Description</th>
<th>Researchers involved</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Data were transcribed or listened to. Transcriptions were read and re-read to get data set familiarity. Notes on each data item were made.</td>
<td>All</td>
</tr>
<tr>
<td>2</td>
<td>Initial coding was performed with collated data. In this phase triangulation was used. Excerpt from W4: 'And then I just felt like stopping using it. And it was when I noticed a great desire difference, and it wasn’t that I noticed it was decreased before, but afterwards...you just felt “wow, okay, okay”'(giggling)’. Initial code: discovered increased sexual desire after stopping HC use. Coding: AM</td>
<td>AM, LB and GF</td>
</tr>
<tr>
<td>3a</td>
<td>Initial themes were generated as a map for each data item. Example: The initial code shown above was included in the initial theme called 'positive discoveries after discontinuation’.</td>
<td>AM, CB</td>
</tr>
<tr>
<td>3b</td>
<td>Initial themes were merged into preliminary themes for each data item with collated codes. Example of the preliminary themes for W19 is shown in the appendix.</td>
<td>AM, GF, CB</td>
</tr>
<tr>
<td>4</td>
<td>The themes were checked with the coded extracts and data and used to generate a thematic map for the entire data set. The thematic map is thus a compilation of the preliminary theme maps from step 3b. Shown as a complement in the appendix.</td>
<td>AM, GF, LB, CB</td>
</tr>
<tr>
<td>5</td>
<td>The themes were again processed redefined and clarified into a few distinct themes and the final denominations and meanings of the story told by the themes. Once again, the themes were compared with collated interview extracts. Then the whole research team had to agree upon the final denominations. The final themes are shown and explained in the results section as a scale model and are shown in more detail in paper IV.</td>
<td>AM, CB, GF, MH, JB</td>
</tr>
<tr>
<td>6</td>
<td>Last, literature analysis was conducted along with report writing with the themes presented as a coherent pattern strengthened by quotes. The result of this step is paper IV.</td>
<td>AM mainly All researchers involved</td>
</tr>
</tbody>
</table>

Table 6: Thematic analysis in six steps.

AM: Agota Malmborg, PhD student, consultant in obstetrics and gynaecology
LB: Louise Brynte, registrar obstetrics and gynaecology
GF: Gabriella Falk, PhD, senior consultant obstetrics and gynaecology
CB: Carina Berterö, professor, qualitative researcher and subject representative of nursing in acute and critical care
JB: Jan Brynhildsen, professor, senior consultant obstetrics and gynaecology
MH: Mats Hammar, professor emeritus in obstetrics and gynaecology
The Nvivo 12 Pro software program was used for allocation of the text for initial coding and for keeping track of the citations used. Thematic maps were created using the Power-Point software program. All the analyses were manually performed.

Statistics and calculations applied in studies I and II (papers I-III)
For papers I-III the demographic data comparisons between groups were performed using chi-square tests and Student’s t-test. For all statistical analyses, we used the SPSS statistical package software program and p values less than 0.05 were considered statistically significant.

Papers I and II
Reports of adverse sexual desire effects related to contraceptive use, were compared between groups of different contraception methods by chi square test. When the expected count was less than five, Fischer’s exact test was used.
A binary multiple logistic regression model was used to adjust the findings for possible confounders asked for in the questionnaire. For this purpose we dichotomised the answer to several questions in the questionnaire presented in Table 7 shown in the end of this section, page 39.

Paper III
Sample size
Sample size was primarily calculated for the outcome of mood changes and was 150+150 patients. A separate calculation undertaken according to changes in aspects of sexual function led to a need of a smaller sample size. Hence, the initial sample size was not changed. The sample size calculation is further discussed in the ‘Methodological considerations and limitations’-section on page 55-56.

Test statistics
The scores for each domain of MFSQ were summarised. Differences between base line scores and after three treatment cycles scores were defined as Δ-scores with negative values indicating a worsening, and positive values indicating an improvement.
Changes in total MFSQ scores and of each sexual function domain separately were compared between the treatment groups using Mann-Whitney U test.
The sexual function domains with a statistically significant change at the end of the third treatment cycle were adjusted for the change in self-related depression scores (MADRS) by ordinal regression analyses. Correlations between serum testosterone, hair testosterone, FAI and MFSQ were tested with Spearman’s rank correlation.
<table>
<thead>
<tr>
<th>Original question</th>
<th>Original answer alternatives in the questionnaire</th>
<th>Regrouped answers</th>
<th>Numeric value in the regression analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you find that your current contraceptive method affects your sexual desire?</td>
<td>No, Yes for the better, Yes for the worse</td>
<td>No, Yes for the better</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes for the worse</td>
<td>1</td>
</tr>
<tr>
<td>How often during the last 4-weeks have you felt sexual desire or sexual interest?</td>
<td>Daily, Once or a couple of times/week, Never or almost never</td>
<td>Daily, Once or a couple of times/week</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Never or almost never</td>
<td>1</td>
</tr>
<tr>
<td>How often have you been engaged in any sexual activity during the last 4-weeks?</td>
<td>Daily, Some or a couple of times/week, Occasionally, Never</td>
<td>Daily, Some or a couple of times/week</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Occasionally, Never</td>
<td>1</td>
</tr>
<tr>
<td>In the last 4-weeks, how often did you attain orgasm during any kind of sexual activity?</td>
<td>Every time or almost every time, More than half of the times, Occasionally, Never</td>
<td>Every time or almost every time, More than half of the times</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Occasionally, Never</td>
<td>1</td>
</tr>
<tr>
<td>During the last 4 weeks, how satisfied have you been with your sex life?</td>
<td>Very satisfied, Rather satisfied, Rather unsatisfied, Very unsatisfied</td>
<td>Very satisfied, Rather satisfied, Rather unsatisfied</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rather unsatisfied, Very unsatisfied</td>
<td>1</td>
</tr>
<tr>
<td>Are you satisfied with your sexual desire level?</td>
<td>Yes, No, I wish it was less, No, I wish it was higher</td>
<td>Yes, No, I wish it was less, No, I wish it was higher</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No, I wish it was higher</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 7. Showing the key questions as in the questionnaire and the operationalised versions used in the multiple regression analyses in paper I and II.
Ethical considerations

General considerations and approvals
The effort and time consumed by the work on this thesis, which to some degree prevented the researchers from engaging in clinical practice, can be justified by the generation of new and clinically relevant scientific knowledge for the benefit of individual patients. Through having a thorough research plan and implementing revisions of the plan we were able to ensure a reasonable likelihood that this project would generate the knowledge that was sought. Ethical approvals were obtained for all the included studies, thereby ensuring a favourable balance of potential benefits over risks to the participants.

We took measures to protect the privacy and confidentiality of the study subjects throughout the whole project, for example by handling the study material with respect for the local guidelines and regulations of the university and other authorities. The participants in studies II and III gave their written informed consent to participate. In study I the act of responding and returning the questionnaire was regarded as providing consent to participate. An information letter sent alongside with the questionnaire explained the confidentiality measures and that participation was voluntary.

Studies I and III were approved by the regional Ethical Review Board in Linköping, Dnr 2013/257-31. Study II was approved by the regional Ethical Review Board in Uppsala, Dnr 2013/161.

Study specific ethical considerations

Study I
The questionnaire included questions about contraceptive use and sexuality which can potentially violate personal integrity. If the women receiving the questionnaire felt any discomfort, they could simply refrain from answering.

At the end of the questionnaire, a question asked about interest in participation in a future interview-based study. All women that expressed interest in further participation were sent a confirmation email and were informed that due to the large number of interested women, we were not able to pursue interviews with all. The
The purpose of this email was to decrease the risk of disappointment for those who expected to be interviewed.

**Study II**

The study procedures were in accordance with the international ethical standards for human experimentation and followed Good Clinical Practice. The women for this study were recruited by advertisements and therefore we can assume their engagement was on a voluntary base. Nonetheless, there was a potential risk that some of the women participated just to have the benefit of contraceptive counselling that was given within the frame of the study, and consequently they would have been in a dependent situation to the caregiver. To minimise this risk, it was clearly pointed out in both the written and oral information that consent could be withdrawn at any time throughout the study without consequences for current or future treatment or counselling.

There was also a risk that women with previous complaints of adverse mood or sexual function effects while using HC would again develop such adverse effects if randomised for active treatment. Indeed, we noted a higher discontinuation rate among women allocated to the active treatment; therefore, we can conclude that women who might have experienced adverse effects felt free to drop out.

Since the study was blinded, there was an increased risk of unintended pregnancies if the women did not use an additional barrier method as agreed at inclusion. To decrease the risk of unintended pregnancies, the information was repeated at each visit and the participants were given a urinary pregnancy test at the end of each treatment cycle. One case of pregnancy was detected in the placebo group. This woman chose to perform an early medical abortion without complications.

Upon completion of the study, the women were paid, 1000 SEK as a small/symbolic compensation for loss of income during the study visits.

**Study III**

Due to time limitations and other practical reasons, five years passed after the questionnaire study until we had the possibility to pursue the interview study. Women who were eligible according to the purposeful sampling used, were again contacted using a standardised email reminding them of their former interest in participating. Communication with these women was only resumed if they confirmed that they were still interested in participation.
The interview itself could potentially evoke discomfort or anxiety and all participants were informed that they could interrupt the interview or refrain from answering any question they disliked. They were also assured that they could contact the researcher if at any stage after the interview they wanted to withdraw their consent. Two of the interviews revealed health and psychological problems, for which professional help was offered at the clinic.
Results and discussion

A summary of the results from the four papers is presented in Table 8 below.

| Paper | Study | Results | Hypotheses*
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>I</td>
<td>Decrease in sexual desire was reported by 27% of HC users compared with 12% of non-hormonal method users. Experiencing adverse sexual effects during HC use was alone or along with other adverse effects the most common reason for reconsidering contraceptive method choice.</td>
<td>Confirmed</td>
</tr>
<tr>
<td>II</td>
<td>I</td>
<td>The difference between hormonal and hormone-free contraception was found in the sub-group of intrauterine contraceptive users as well. The Lng-IUS users reported more often negative sexual desire effects of their contraception and an overall lower sexual desire level compared with the Cu-IUD users.</td>
<td>Rejected</td>
</tr>
<tr>
<td>III</td>
<td>II</td>
<td>Compared to placebo, use of an oestradiol and nomegestrol acetate containing, COC influenced sexual function by association with a small reduction of sexual interest.</td>
<td>Confirmed</td>
</tr>
<tr>
<td>IV</td>
<td>III</td>
<td>A selected group of women with previously reported adverse sexual effects while using HC, described lubrication difficulties and decreased sexual desire associated with both contraceptive use and the menstrual cycle. Subsequent choice between hormonal or non-hormonal contraceptive methods depended primarily on experienced adverse effects on mood, and secondarily on sexual function, weighed against the disadvantages experienced during the person’s own menstrual cycle.</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

Table 8. Summary of the results of the three studies and four papers included in the thesis.
* See list of hypotheses on page 23

Contraceptive use and reported adverse sexual function effects

The most common contraceptive method in the studied age groups (22-, 25- and 28-year-old) was the COC (Paper I) which is in line with other studies both in Sweden and the rest of the Western European countries and the United States. (81-83)
Adverse effect on sexual desire was reported among 27-28% of women using any kind of HC and 9-12% of women using hormone-free contraception. The difference between hormone-free and hormonal contraceptive methods was statistically significant after adjustment for the identified confounders that were included in the questionnaire; age, education level, depression, BMI, parity and the type of relationship. (Paper I).

Although the HC users reported adverse effects on sexual desire more than twice as often as users of non-hormonal contraceptives, the actual sexual desire level as well as sexual activity level, and satisfaction with sex life did not differ between hormonal and non-hormonal method users. (See Table 9 on the next page.)
Variables of sexual function*  | Factors found to influenceb  
--- | ---  
Low sexual desire level | BMI >30 (OR 2.0; 1.2-3.2), occasional or no partner (1.5; 1.6-2.1), depression (OR 2.2; 1.4-3.3), having children (OR 1.9-1.3-2.8)  
Low sexual activity level | Older age groups – 25 years (OR 1.5;1.1-1.9) and 28 years (OR 1.8; 1.3-2.3), occasional or no partner (OR 9.3; 6.8-12.6), depression (OR 1.7; 1.1-2.6), having children (OR 1.7; 1.1-2.3)  
Low orgasm frequency | Youngest age group (OR 1.5; 1.1-2.0), HC use (OR 1.3; 1.1-1.7)  
Low sex life satisfaction | Oldest age group (OR 1.5; 1.1-2.0), occasional or no partner (OR 3.5; 2.8-4.5), depression (OR 2.1; 1.4-3.1),  
Low satisfaction with sexual desire | Oldest age group (OR 1.5; 1.2-2.0), steady partner (OR 2.4; 1.9-3.0), depression (OR 2.1; 1.5-3.2) HC use (OR 1.5;1.2-1.9)  
To find sexual desire negatively affected by contraception use | Steady partner (OR 2.4; 1.7-3.4), HC use (OR 2.4; 1.7-3.4)  

Table 9. (Study I) Results of logistic regression calculations for each of the sexual function variables in the questionnaire.

*Definitions and dichotomisation are shown in table 7.

*Only statistically significant factors shown.

As shown in Table 9, having a steady partner was just as important as HC use for the OR of reporting the contraceptive method to negatively affect sexual desire. This finding emphasises the importance of the context in which sexual function is evaluated. According to Basson’s model of female sexual function (Figure 2) (20), sexual desire is largely driven by responsiveness to different stimuli and to a lesser extent by spontaneous or innate desire. Changes to a responsive type of sexual desire are probably more likely to become evident for women living with a partner than for women not in a steady sexual relationship. On the other hand, in a Swedish epidemiological study, low sexual desire was reported by 29% and insufficient lubrication by 11% of the women. (84) With such a high prevalence of low sexual desire, we might just have found the normal prevalence in our questionnaire as well. The HC users could then have been prone to thinking that the change of sexual desire was due to their contraceptive method whereas the hormone-free contraceptive users had other explanatory theories that we did not ask for in the questionnaire. However, the women in the interview study (paper IV), were aware of the multidimensional nature of sexual function and many reasoned around both the quality of their partnership as well as other causes for sexual function changes. Only after repeated trials of different HC use and periods of being without HC, did they express certainty.
about the associations between HC and sexual desire changes or/and lubrication difficulties.

The Lng-IUS involves low systemic hormone release, so we expected to find a smaller proportion of women reporting adverse sexual desire effects in this group compared to groups of women using other HC methods. At the time of the study it was also routine in clinical practice to suggest the Lng-IUS as an alternative for women with mood or sexual desire complaints with COC or POP. Therefore, we compared the subgroups using intrauterine contraception. After adjusting for confounding factors, we found a fivefold risk of Lng-IUS users reporting sexual desire decrease compared with Cu-IUD users. (Paper II) One explanation could be that the IUC users were a selected group with previous experience of adverse effects of other contraceptive methods. Ninety-four percent of the Lng-IUS users and 91% of the Cu-IUD users had previously used an HC. Some women might be more vulnerable to hormonal exposure and may repeatedly experience negative side effects irrespective of the hormonal method used. (85) In a large Swedish survey of contraceptive use, the use of less effective contraceptive methods as well as the number of women with fear of HC-related side effects increased with age. (82)

The specific adverse sexual effects related to HC described by women in the interview study need to be seen in the light of the favourable effects they described regarding the natural menstrual cycle. Most women found increased readiness and sex drive in addition to well lubricated and easily responding vulva around the ovulation period. In relation to this, hormonal treatment was described as causing desensitisation, feelings of dullness, and non-responsiveness to sexual stimuli. Vaginal and vulvar dryness with subsequent pain or decreased sensitivity were also commonly mentioned.

'Yes, all those things that happen when you get aroused (... I noticed a great change with that. Most of all the degree of lubrication, it made a great difference. Because, in beforehand I was thinking that if I stop using the pill and I have to use the condom it would be a problem. That I would feel it chafe. But it was not a problem at all...’ (W4)
Women with irregular or heavy bleeding, pain, or disturbing premenstrual symptoms, described increased sexual desire and wellbeing around the mid-cycle, similar to what was also reported by women with no cycle-related problems. Nevertheless, the drawbacks of a problematic cycle were repeatedly described as, overall, a worsening element of sex life.

**Hormonal contraception and causality of sexual function changes**

Since female sexuality is complex and HC is a heterogenous group involving different types of oestrogens and progestins, overall causality is difficult to investigate. In study II, we compared the influence of a modern COC (1.5 mg oestradiol and 2.5 mg nomegestrol acetate) with placebo regarding female sexual function. We found no difference of overall sexual function level changes between the treatment groups.

<table>
<thead>
<tr>
<th>Domains of sexual function</th>
<th>Combined oral contraceptive</th>
<th>Placebo</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sexual interest /desire</td>
<td>81 -2.0 (-5.0-0.5)</td>
<td>90 -1.0 (-3.0-2.0)</td>
<td>0.019</td>
</tr>
<tr>
<td>Satisfaction sexual activity</td>
<td>80 0.0 (-2.0-0.0)</td>
<td>89 0.0 (-1.0-1.0)</td>
<td>0.060</td>
</tr>
<tr>
<td>Vaginal lubrication*</td>
<td>57 -2.0 (-3.0-1.0)</td>
<td>58 0.0 (-1.0-2.0)</td>
<td>0.005</td>
</tr>
<tr>
<td>Orgasm*</td>
<td>57 -1.0 (-4.0-1.0)</td>
<td>58 0.0 (-2.3-2.0)</td>
<td>0.147</td>
</tr>
<tr>
<td>Partner</td>
<td>67 0.0 (-2.0-0.0)</td>
<td>66 0.0 (-2.0-1.3)</td>
<td>0.398</td>
</tr>
<tr>
<td>Attractiveness</td>
<td>80 0.0 (-2.0-1.0)</td>
<td>90 0.0 (-2.0-1.0)</td>
<td>0.488</td>
</tr>
<tr>
<td>Frequency Intercourse/week</td>
<td>71 0.0 (-1.0-0.25)</td>
<td>86 0.0 (-0.75-0.25)</td>
<td>0.800</td>
</tr>
<tr>
<td>Total score</td>
<td>81 -5 (-17.0-2.1)</td>
<td>91 -2.0 (-13.0-10.0)</td>
<td>0.086</td>
</tr>
</tbody>
</table>

Table 10. Delta sexual function scores on MFSQ during the final treatment cycle. Data presented as median (IQR).

*The domains of vaginal lubrication and orgasm are presented only for women who reported intercourse during baseline and treatment.

Two domains of sexual function evaluated by the MFSQ were sexual desire and lubrication, both of which were reported to decrease significantly more by the COC users than by the placebo users. However, as shown in Table 10, the mean score differences were small.

The clinical relevance of the small differences seen in change of sexual desire and lubrication are uncertain. We chose to define a clinically relevant deterioration in sexual desire and vaginal lubrication as at least a 30% decrease in the score from
baseline to the last visit. According to this, the proportion of women with clinically relevant impairment of sexual desire or vaginal lubrication did not differ between treatment groups.

We have though not found a reliable previous definition of a clinically relevant size of deterioration and might have underestimated what is clinically relevant.

Moreover, we performed an additional regression analysis on the domains of sexual desire and vaginal lubrication, adjusted for self-rated change in depressive symptoms (MADRS scores). After adjustment, the finding of a decrease in sexual desire remained, whereas the finding of a decrease in vaginal lubrication did not remain. This adjustment should be interpreted with caution due to the different lengths of time assessed by the two tools. The MFSQ evaluates the last four weeks and MADRS only the last three days. Mental wellbeing could be regarded as a potential confounder of sexual function. Changes of scores of MFSQ and changes of scores of MADRS were both outcome measures in the study. Therefore, it could be argued that instead of ΔMADRS we should have adjusted for mental status evaluated prior to inclusion.

Two other randomised studies have suggested that COC might negatively affect sexual desire in women. (86, 87) Nevertheless, neither our study nor the other two referred to, showed a change in total sexual function scores. The detected small change of sexual desire might remain on a statistical level and needs to be confirmed by other studies.

On the other hand, a higher discontinuation rate as well as spontaneously reported sexual side effects were more common among women allocated to the COC treatment group. (Paper III) The flow chart of study participants is presented in the Appendix.

Is testosterone the culprit?
We found a weak correlation between testosterone level changes and change in sexual desire (rho=0.27) as well as change in satisfaction with sexual activities (rho=0.36). (Paper III) However, these associations were only seen in the placebo group where a sub-group of women had greater changes of testosterone levels and FAI during the time of the study.
Figure 7. Spearman’s rank correlations between change in total testosterone and change in sexual function scores in each treatment group.

Levels of total testosterone as well as FAI decreased in the treatment group as expected and in accordance with earlier studies. (68, 88) The levels of testosterone measured in hair did not change. However, our study was the first clinical study to measure testosterone in hair and there might have been yet unknown variables that affected the results.

Our findings suggest that the decrease of testosterone measured in serum during treatment probably does not affect sexual desire change. The absence of testosterone effects in natural cycles found in some other studies suggests there is no substantial regulation of sexual desire by androgen receptors in women. (45, 89) Normal sexual desire levels have been shown in women with androgen insensitivity syndrome, which suggests the same. (90) Exogenous testosterone may still have pharmacological effects on sexual motivation, acting indirectly via oestrogen receptors either after aromatase conversion to oestradiol or by the regulation of binding proteins increasing the bioavailable concentrations of oestradiol. (91)

In summary, testosterone seems not to be the main hormone of importance for COC or HC-induced sexual function changes. A hypothesis for further investigation is that
a sub-group of women is “progestogen sensitive”. This might affect their wellbeing such as premenstrual symptoms in natural cycles induced by progesterone or sexual function and mood changes sometimes associated with HC use, presumably mediated by the different progestins.

**Contraceptive use and contraceptive choice in the light of experienced adverse sexual function**

The question then arises: what is a clinically significant deterioration of sexual desire or of overall sexual function? We might argue that as long as the women do not develop sexual dysfunction by using HC there is no problem to discuss. On the other hand, women reporting that they found their sexual desire negatively affected by contraception compared with women without such side effects were more often dissatisfied with their contraceptive method choice. (Paper I) They were also overrepresented among those reporting they never or almost never felt desire, and they wished more often to change or stop their current contraceptive method. (Paper I) Among HC users, the most common reasons for reconsidering current contraceptive choice were adverse sexual desire effect (33%) and mood changes (22%). (Paper I)

As shown in Figure 6, COC use was less common and ‘not using any contraception’ was more common in the oldest age group (pregnant and nursing women not included). This difference might be explained by reproductive patterns in Sweden. (82) Hormone-free contraception was more common than HC in the oldest age group. One interpretation could be that women who experience side effects, including adverse sexual function effects, eventually choose a hormone-free alternative. However, due to the cross-sectional design, we cannot know whether the use of hormone-free contraceptives truly increase with age or if the change is just seen as observing different age groups. (Study I, Paper I) Nevertheless, in study III (paper IV) women with experiences of adverse mood and sexual function effects while using HC were in many cases describing a timeline-related insight into how their bodies and minds were affected by hormones. Often after years of HC use and periods of no hormonal treatment, they chose a non-hormonal contraceptive alternative, sometimes accepting low efficacy as a consequence.

‘And then it just occurred to me that I would like to try to be without (refers to HC.) and it was when I noticed this great change of my
desire. It wasn’t like I had noticed that it was suppressed before, but what happened afterwards was... I just like “wow, okay, okay (giggling) is this how it is?” So, well, since then I haven’t used any hormones again. I simply just use other methods instead.’ (W4)

The interview study (Paper IV) revealed that women reporting negative effects on sexual function which they thought depended on their contraceptive method, acted in different ways regarding future contraceptive choice. Their long-term aim was to find a method without adverse sexual function effects, but their current choice was often influenced by many other factors.

‘...When I recall when I used the pill, everything was more flat, I mean, sexual desire, irritation, and all that with abdominal pain and tiredness, but (. ) however (. ) in periods without the pill there were more ups and downs. All that was good got even better and all that was bad got even worse. So, (. ) I will for now continue with this new pill even at a cost of having less desire... ‘ (W22)

Contraceptive method choice in the light of sexual function can be illustrated as a scale model (Figure 8). The model suggests that contraceptive counselling might be complicated, but if the contraceptive counsellor is aware of the different and individualised ‘weights’ put on the ‘scale’, both reaching increased self-awareness and the method choice might be alleviated.

‘If you’re 15, you might not be that hard-nosed and tell the midwife that you would like to have something different.(refers to other methods)[... ]With age you get to learn more, you know your body better and you become experienced. It leads you to become more demanding. In a good way. You take the pill to avoid an unplanned pregnancy but there are other important aspects to take into consideration when it comes to method choice. You become more conscious about the whole thing.’(W20)
According to study III and Figure 8, the act of choice was based on the responsibility the women felt for the need to control reproductivity. One of the ‘weights’ on the scale of hormone-free or hormonal contraception choice was the time and experience-based self-awareness of sexual function changes related to intrinsic and extrinsic hormones. Another was mental wellbeing, also dependent on previous experiences and insight, but always put in the first place if women had such experiences.

‘...and even if I had desire and felt like having sex (.) it was as my body didn’t react. I was ...I felt desire, but I didn’t get aroused, I felt no tingling, [...] my body simply didn’t respond physically... And all turned to be better when I removed the implant.’ (W19)

‘I’ve been thinking of, if I might try with another method, just to see if (.) I mean, if these side effects... if I would feel that bad again. But I feel discouraged, I’m afraid to try. I never tried another hormonal...’
method again. I just simply don’t want to. The condom has to be my choice.’ (W8)

Moreover, medical limitations such as heredity for thromboembolism, as well as the social situation and the actual need of reliable contraception, were all put on the scale. Another ‘weight’ on the scale was the influence of friends, media and some sort of internal feeling of wanting to avoid hormonal treatment. Several women also argued that the potential adverse environmental effects of hormones were an important factor to take into consideration. Interestingly, the environmental aspect was not known or elaborated upon by any of the midwives that the 24 women in the interviews ever had discussed with.

Although hormone-free methods were described as having many drawbacks by the women in study III, the women in this group were happy to have such an alternative presented by their contraceptive counsellor.

‘And then she started to ask about our relation and stuff. And I think it’s good overall, but I felt she didn’t really… believed in me. That I really wanted to be with him. So… I didn’t get any help. […] And it became more like a challenge. Like, if it’s really that bad why don’t you just quit. And I got mad and I did! And it turned out well…’ (W12)
Methodological considerations and limitations

Study I
The cross-sectional design has its own limitations; for instance, we cannot draw any conclusions about changes over time by age. Recalling previous experiences, as asked for in the questionnaire is also a potential source of bias. The questionnaire was sent only to women living in Linköping, which makes generalisability questionable. As an example, a geographically closely situated city of similar size has a different socio-demographic profile with different abortion rates and a somewhat different contraceptive counselling and accessibility of contraceptive counselling.(92) The response rate of 50% adds to the uncertainty around generalisability. We might have reached more women and received a greater number of responses by using the email system alone or as an addition to the traditional mailing system.

Women with negative experiences of hormonal contraceptives may be more predisposed to answering a questionnaire addressing sexual function and contraception. This might have biased our results.

The self-constructed questionnaire has its flaws. Although we used a thorough validation process, some important details could have been improved. We had questions about ongoing pregnancy or nursing but unfortunately no question that clarified other reasons for why women currently without contraceptives were not using a contraceptive method. Neither did we have any questions about the duration of the current relationship or an estimation of the quality of the relationship. This prevents us from making further analyses of the finding that having a partner was just as important as the use of hormonal contraception when it comes to experiencing decreased sexual desire.

From the interview study we learned that the experience of insufficient lubrication and non-responsiveness is of key importance when it comes to the overall experience of adverse sexual function effects. The part of our questionnaire evaluating sexual function level unfortunately did not include questions about lubrication.
Study II

The randomised clinical trial design has the potential to render high grade evidence. However, feasibility is restricted by practical and financial considerations which jeopardises the conclusions we can draw from the results.

The study had a non-inferiority design, i.e. the null hypothesis was that the change of mood and aspects of sexual function induced by COC were not greater than the changes induced by placebo. The initial sample size calculation was based on the outcome of mood changes found in two prior studies. The study by Borgström found a difference of four scale-steps between COC users with a history of adverse mood changes while using COC, and COC users without such side effects. The standard deviation (SD) was 2.0 steps. The other study found 3.8±5.3 scale-steps difference between women with an earlier episode of COC-related mood changes compared to women without such side effects.

Both these studies used the Cyclicity Diagnosis scale, evaluating the same symptoms and using approximately the same number of scale steps as the DRSP tool planned for the current study. Since our study had few inclusion criteria and almost no study-specific exclusion criteria, we assumed the included women represented a normal population of young women. Thus, we expected a lower prevalence of women with previous negative experiences of HC use to be included in the study in comparison to the two studies which we based our sample size calculation on.

Altogether, we assumed a change of two scale steps, and an SD of five, which with 120 individuals in each treatment group would yield an 88% power. We expected a 20% drop out rate and therefore aimed to include 150 + 150 study patients in total. After two years of inclusion time we had still not reached the target of 300 study patients. Due to the expiry date of the batch of pills and the high cost for a new batch, the study was closed after 224 women had been assessed for eligibility and of these 202 had been randomised (See flow chart study II in the Appendix.)

An additional sample size calculation for the outcome regarding aspects of sexual function (paper III) was based upon data from Graham and colleagues who reported a 0.3 scale steps difference between COC and placebo. We assumed a twofold SD i.e. 0.6, which yielded a power of 88%, and significance level of 0.05, with a sample size of 80+80 patients. After analysing the results, it appeared that SD was underestimated, and the actual power was well below 80%.
The MFSQ is a well-used questionnaire and has been translated into Swedish. Nevertheless, the lack of information on the psychometrics of the translated questionnaire could be a serious limitation to our investigation of sexuality. Since the questionnaire was developed decades ago, cultural and generational changes might have influenced the answering accuracy.

Several questions in the questionnaire were dependent on sexual activity in the sense of vaginal intercourse, which excluded several women from being included in the evaluation of lubrication and orgasm. This drawback could have been overcome with the use of another tool that allows evaluation of aspects of sexual function including all types of sexual activities.

The MFSQ does not have any pre-set clear-cut scores for clinical conditions or clinically significant minimum changes. There was thus no clear theoretical background indicating what a clinically significant deterioration was in terms of the MFSQ scores. The assumption of a 30% deterioration could have been either too narrow or too wide. It could be argued that we should have decided upon a fixed number of scale-steps as a relevant change. As an alternative, we could have decided to consider as clinically significant at least four steps within the sexual interest domain and three steps within the lubrication domain that were composed of four and three questions respectively. (See Table 4)

The time of follow up in our study was three treatment cycles i.e. approximately three months which can be considered as short. However, a more prolonged study may have led to a selection bias. It may be speculated that the higher discontinuation rate in the COC group could have reduced the differences regarding sexual function changes between the groups.

We might also question whether one month of wash out was enough time for women with an ongoing HC at the time of recruitment to the study. Were they able to adequately fill out the questionnaire as soon as the end of the first cycle without hormonal treatment, at which time they might still have been without a well-functioning menstrual cycle?

Although it has been shown that testosterone can be detected adequately even in minute hair samples (65), maybe in the clinical setting the method to obtain the hair samples and the manual fragmentation of the correct amount of hair, could have been too blunt. Information about potential hair treatments prior to hair sampling was sometimes missing in the study protocol, which made hair treatments difficult to
take into consideration in the analysis process and might have jeopardised the accuracy of the measurement.

Study III
The qualitative design restricts any possibilities for drawing conclusions about causality or hypothesis testing. However, it can reveal a wider range of possible explanations for a certain phenomenon or experience. We used an interpretive approach which of course makes all the conclusions dependent on the researchers and the reliability of the research team.

The interviewers must be adaptable, friendly, responsive, and should make the respondent feel at ease to say anything, even if it is irrelevant. The interviewers must also be careful to be neutral so as not to lead the respondent, hence minimising bias. Some of these demands on the interviewer might occasionally and unintentionally not have been met.

The honesty of the respondents could hypothetically be restrained due to the sensitive nature of the questions or if the respondents did not want to give what they might have believed to be a socially undesirable answer.

We had two interviewers present on almost half of the interview occasions. Even if the women interviewed on those occasions gave assurances that they were not disturbed by the presence of the second interviewer, this way of interviewing is not described in the literature as a method of choice and might thus be questioned.

Five years passed between the questionnaire study and the interviews, which could have been a limitation, at least for the purposeful sampling. Some of the women who in the questionnaire stated adverse sexual function effects due to their hormonal contraceptive method, had an altered or more nuanced perception of this question five years later.

Most women in the interview study had a university education and may in that aspect be considered as selected, which restricts transferability.

In all three studies, all the participants were fluent in the Swedish language and therefore the study groups did not match the ethnic make-up of the present Swedish population.
Specific conclusions

❖ Young Swedish women who use HC reported an adverse sexual desire effect more than twice as often as the women who used hormone-free contraceptive methods. The difference was observed regarding all types of hormonal methods compared to non-hormonal methods.

❖ An adverse sexual desire effect was more commonly reported by Lng-IUS users compared with Cu-IUD users, and the Lng-IUS users reported a lower sexual desire frequency compared with the Cu-IUD users. (This finding evokes the need for further evaluation of a selected group of women who seems to be susceptible to even low systemic dose HC.)

❖ The experience of an adverse sexual desire effect, which the women thought was due to contraceptive use, is a strong predictive factor of method reconsideration. According to our observations, sexual side effects either alone or together with mood side effects were the most common reason for reconsidering the contraceptive method, which stresses the importance of further research on these side-effects.

❖ Reported total sexual function level changes did not differ during COC use compared with placebo. An association was found between the change of sexual desire level and the use of the tested COC, but the clinical relevance of this finding is unclear and needs to be confirmed in future studies.

❖ Weak associations were found between COC-induced serum testosterone level decrease and sexual desire changes. The biologically active fraction of testosterone embedded in hair did not decrease during COC treatment. This finding is inconsistent with the finding of decreased levels of the bioavailable fraction of serum testosterone.

❖ Women reporting negative sexual function effects while using HC described lubrication difficulties and decreased sexual desire associated with both contraceptive use and the menstrual cycle. Associations became obvious with time and experience, and consequently contraceptive choice became easier with age, experience and better understanding. We conclude that the latter could be facilitated by a responsive contraceptive counsellor.
Considerations for future research

For future research there is a need for an updated and modern assessment tool to evaluate female sexual function. The development of such a tool that measures changes in aspects of and total female sexual function level within the range of what is normal function is necessary for future good quality studies that are also comparable to each other.

Owing to the diverse range of existing HC methods and the complexity of female sexual function, perhaps searching for general causality is not achievable or advisable. If we instead recognise the existence of a sub-group of women sensitive to hormonal treatment and the complaint of adverse sexual function effects while using HC, research could be concentrated on deepening the understanding of this group.

Testosterone levels could not be strongly linked to changes of sexual desire. We introduced a new method to analyse testosterone in hair. This method should be further evaluated on clinical samples and hopefully be developed as a future tool for endocrinological studies. If the lack of association between testosterone changes and aspects of sexuality will be confirmed in future studies, it would be an interesting finding that could potentially end the discussion whether changed testosterone levels are the cause of observed or experienced and reported decreased sexual desire.

It is clearly possible that the sexual behavioural impact of exogenous administration of progestogens and/or oestrogens varies between women, which would explain why negative or positive effects are restricted to subgroups. It is not yet possible to predict which women are likely to experience adverse effects of hormonal contraception on their sexuality, nor which oral formulations or non-oral routes of administration are most likely to be responsible.

To compare the effects of different HCs containing different progestins in a selected group of women who previously reported adverse sexual function effects, would be of clinical relevance.

To use mixed-methods, combining for example both randomisation and later interviews with the same women, might be suitable to address the complex issue of sexual function changes.

Suggestions for groups of women to include in future individualised research are women with PMS, women with irregular menstrual cycles, and women with normal
28-day-cycles. Can we identify a ‘progestogen-sensitive’ group? Do these women have common features? How are the aspects of sexual function influenced by hormonal fluctuations in the natural cycle, while using HC, and later in connection to menopausal hormone therapy in the same selected group of women?
Concluding remarks and clinical implications

We found that twice as many young Swedish women using hormonal contraceptives reported that their contraceptive method negatively influenced sexual desire than women using hormone-free alternatives. This experience was a strong predictive factor for stopping or changing contraceptive method, which potentially puts a number of women at risk of being without a contraceptive method or of using less effective methods. Women with adverse sexual function effects described mainly lubrication difficulties and decreased sexual desire which they experienced with both hormonal contraceptive use and during part of the menstrual cycle, possibly associated with hormonal fluctuations. The contraceptive counsellor who recognises these kinds of adverse effects and affirms the affected women, will probably more successfully guide women to find a suitable method and thereby increase compliance.

In an unselected population of young women, COC use compared to placebo, was associated with a small decrease of sexual desire and lubrication, but the clinical significance of these findings is unclear.

Altogether, our findings add valuable knowledge to the field of contraceptive counselling, suggesting further development of individualised counselling. Our findings are also of clinical importance for women who experience sexual function changes and have difficulty to find a suitable contraceptive method, to become ‘happy with the method’.
References


Appendix

I. Questionnaire used in study I.

II. Questionnaire used in study II (MFSQ) Swedish version.

III. The Swedish interview guide used in study III and the translated English version. (Paper IV)

IV. Example of the thematic analysis process. Step 3a and 3b, in Swedish.

V. Final thematic map, in Swedish

VI. Flow chart study II.
FRÅGEFORMULÄR OM PREVENTIVMEDELSANVÄNDNING
OCH BIVERKNINGAR

I följebrevet kan du läsa om syftet med formuläret, hur det hanteras och varför just du har fått det. Använd kulspetspenna och skriv siffror och kryss så tydligt som möjligt. Välj det eller de alternativ som stämmer bäst för Dig och med vad Du tycker.

DEL 1 – BAKGRUNDSFAKTA

1. Ditt födelseår
   - 1991
   - 1988
   - 1985

2. Din vikt
   - kg

3. Din längd
   - cm

4. Röker du dagligen?
   - Ja
   - Nej

5. Hur ofta motionerar du pass om minst 30 minuter?
   - Regelbundet flera ggr i veckan
   - Någon gång i veckan
   - Ibland
   - Aldrig

6. Kryssa för din högsta utbildning
   - Grundskola
   - Gymnasieskola
   - Pågående eftergymnasial utbildning
   - Avslutad eftergymnasial utbildning

7. Vad är din huvudsakliga försörjningskälla?
   - Studiemedel
   - Arbeta
   - Övrigt

8. Anser du dig vara helt frisk?
   - Ja
   - Nej

9. Använder du regelbundet något receptbelagt läkemedel?
   - Ja
   - Nej
   Denna fråga gäller ej p-piller eller annat preventivmedel.

10. Om du svarat Ja, skriv ev läkemedelsnamn nedan:

11. Har du någon behandling mot nedstämdhet?
    - Ja, med läkemedel
    - Ja, med annan behandling
    - Nej

12. Hur många barn har du fött?
    - 0
    - 1
    - 2
    - 3
    - 4 eller fler

13. Är du gravid just nu?
    - Ja
    - Nej

14. Ammar du just nu?
    Du ska svara Ja om du ammar minst 2 ggr om dagen.
    - Ja
    - Nej

DEL 2 – PREVENTIVMEDELSANVÄNDNING
14. Vilket eller vilka preventivmedel använder du för närvarande?

<table>
<thead>
<tr>
<th>Alternativ</th>
<th>Markera</th>
</tr>
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<tbody>
<tr>
<td>Inget alls</td>
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</tr>
<tr>
<td>P-piller</td>
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<tr>
<td>Minipiller</td>
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<tr>
<td>P-plåster</td>
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<td>P-ring</td>
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<td>P-spruta</td>
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<td>P-stav</td>
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<td>Hormonspiral</td>
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<td>Kopparspiral</td>
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<tr>
<td>Kondom</td>
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<tr>
<td>Andra skyddsmedel som pessar, p-skum osv</td>
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<tr>
<td>Steriliserad</td>
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<tr>
<td>Naturlig familjeplanering (säkra perioder)</td>
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<tr>
<td>Avbrutet samlag</td>
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</tbody>
</table>

15. Ungefär hur länge har du använt ditt nuvarande preventivmedel?

<table>
<thead>
<tr>
<th>Alternativ</th>
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<tbody>
<tr>
<td>Mindre än 6 månader</td>
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</tr>
<tr>
<td>Mellan 6 månader och 1 år</td>
<td></td>
</tr>
<tr>
<td>Mer än 1 år</td>
<td></td>
</tr>
<tr>
<td>Använder ej preventivmedel</td>
<td></td>
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</tbody>
</table>

16. Är du nöjd med ditt nuvarande preventivmedelsval?

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<thead>
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<th>Alternativ</th>
<th>Markera</th>
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<tbody>
<tr>
<td>Ja</td>
<td></td>
</tr>
<tr>
<td>Nej</td>
<td></td>
</tr>
<tr>
<td>Använder ej preventivmedel</td>
<td></td>
</tr>
</tbody>
</table>

17. Har du övervägt att sluta använda din nuvarande preventivmedelsmetod, alternativt byta till annat preventivmedel?

<table>
<thead>
<tr>
<th>Alternativ</th>
<th>Markera</th>
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<tbody>
<tr>
<td>Pga graviditetsönskan</td>
<td></td>
</tr>
<tr>
<td>Behövde ej preventivmedel av andra skäl, tex. ingen partner</td>
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<tr>
<td>Av kostnadsskäl</td>
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<tr>
<td>Psykiska biverkningar</td>
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<tr>
<td>Minskad sexlust</td>
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<tr>
<td>Viktökning</td>
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<tr>
<td>Blödningsproblem</td>
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<tr>
<td>Illamående</td>
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<tr>
<td>Underlivssmärta</td>
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<td>Flytningar</td>
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<tr>
<td>Infektion</td>
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<tr>
<td>Okad behåring</td>
<td></td>
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<tr>
<td>Fet hy, akne</td>
<td></td>
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<tr>
<td>Rädsla för biverkningar</td>
<td></td>
</tr>
<tr>
<td>För krångligt att använda sig av denna metod</td>
<td></td>
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<tr>
<td>Annan orsak, ange nedan</td>
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</table>

Om du svarat Ja, ange till höger av vilken eller vilka orsaker? Du kan kryssa i flera alternativ.

18. Har du i samband med tidigare användning av HORMONBASERADE PREVENTIVMEDEL* övervägt att sluta använda denna metod alternativt byta till annat preventivmedel?

<table>
<thead>
<tr>
<th>Alternativ</th>
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<tr>
<td>Pga. graviditetsönskan</td>
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<tr>
<td>Behövde ej preventivmedel av andra skäl tex. ingen partner</td>
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<tr>
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<td>Psykiska biverkningar</td>
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<td>Okad behåring</td>
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<td>Fet hy, akne</td>
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<td>Rädsla för biverkningar</td>
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<tr>
<td>För krångligt att använda sig av denna metod</td>
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<tr>
<td>Annan orsak, ange nedan</td>
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</table>

Ja

Nej

Jag har inte tidigare använt hormonbaserade preventivmedel
**Del 3 – Sexualitet**

| 23. Vilken är din relation till din nuvarande sexualpartner? | Har ingen partner
Make/maka
Sambo
Pojkvän/flickvän
Tillfällig partner/partners |
|-------------------------------------------------------------|-------------------------------------------------|
| 24. Hur ofta har du känt sexuell lust eller sexuellt intresse under de senaste 4 veckorna? | Varje dag
Någon till ett par gånger i veckan
Aldrig eller nästan aldrig |
25. Under de senaste 4 veckorna, hur ofta har du haft sexuell aktivitet eller samlag?

☐ Dagligen
☐ Ett par gånger i veckan
☐ Enstaka gånger
☐ Aldrig

26. Under de senaste 4 veckorna, hur ofta har du fått orgasm genom sexuell stimulans eller samlag?

☐ Samtliga eller nästan samtliga gånger
☐ Mer än halften av gångerna
☐ Mindre än halften av gångerna
☐ Aldrig eller nästan aldrig
☐ Ingen sexuell aktivitet

27. Under de senaste 4 veckorna hur nöjd har du varit med ditt sexliv i allmänhet?

☐ Mycket nöjd
☐ Ganska nöjd
☐ Ganska missnöjd
☐ Mycket missnöjd

28. Är du nöjd med din sexuella lust?

☐ Ja
☐ Nej, jag önskar att den vore större
☐ Nej, jag önskar att den vore mindre

29. Upplever du att ditt nuvarande preventivmedel påverkar din sexlust?

☐ Nej
☐ Ja, till det sämre
☐ Ja, till det bättre
☐ Jag använder inget preventivmedel

30. Kan du tänka dig att bli kontaktad för en eventuell fördjupad intervju om preventivmedel och lust?

☐ Ja
☐ Nej

Om du har svarat att du kan tänka dig att bli kontaktad för en eventuell intervju i framtiden, var då god och fyll i kontaktuppgifter:

Ditt namn: ..........................................................................................................

Telefonnummer: ..............................................................................................

Alternativt telefonnummer: ..............................................................................

Mejladress: ......................................................................................................

Tack för din medverkan!
Appendix II. The McCoy female sexuality questionnaire (MFSQ) used in study II.

McCoy:s enkät om kvinnors sexualitet

Vänligen svara på följande frågor enligt dina upplevelser under de senaste fyra veckorna. I en fråga ska du fylla i en siffra. I andra frågor ska du ringa in en siffra eller ER (ej relevant), vilket betyder att du inte har haft en partner och/eller haft någon form av sexuell aktivitet (inklusive onani, smekning, förspel, samlag etc.) under denna tidsperiod.

1. **Hur njutbar har sexuellt aktivitet varit för dig?**
   - Inte alls
   - Ganska
   - Mycket
   - Njutbar

2. **Hur pass ofta/sällan upplever du att du har haft någon form av sexuell aktivitet?**
   - För sällan
   - Lagom
   - För ofta

3. **Gör en uppskattning av hur ofta du har haft sexuella tankar eller fantasier under de senaste 4 veckorna.**
   - Aldrig
   - En gång i veckan
   - En gång per dag
   - Mer än tiotals gånger per dag

4. **Hur upphetsad har du varit när du haft sex (har du till exempel fått ökad puls/rodnad, andats tungt, etc.)?**
   - Inte alls
   - Ganska
   - Mycket
   - Upphetsad

5. **Beskriv hur intresserad du har varit av sex (dvs. din sexlust) under de senaste 4 veckorna.**
   - Mycket
   - Ganska
   - Lite

6. **Beskriv din naturliga fuktighetsgrad i vaginan (fuktighet vid sexuell upphetsning) under de senaste 4 veckorna.**
   - Ingen
   - Tillräcklig
   - För mycket

**VAR GOD VÅND**
Vänligen svara på följande frågor enligt dina upplevelser under de senaste fyra veckorna. I en fråga ska du fylla i en siffra. I andra frågor ska du ringa in en siffra eller ER (ej relevant), vilket betyder att du inte har haft en partner och/eller haft någon form av sexuell aktivitet (inklusive onani, smekning, förspel, samlag etc.) under denna tidsperiod.

7. Hur sexuellt attraktiv har du ansett dig vara?
   1 2 3 4 5 6 7
   Inte alls sexuellt attraktiv
   Ganska attraktiv
   Mycket sexuellt attraktiv

8. Hur sexuellt attraktiv har du ansett dig vara för din sexpartner?
   1 2 3 4 5 6 7
   ER
   Inte alls sexuellt attraktiv
   Ganska sexuellt attraktiv
   Mycket sexuellt attraktiv

9. Hur ofta har din tillfredsställelse av sexuell aktivitet minskat på grund av att din sexpartner inte har varit tillräckligt sexuellt intresserad av dig?
   1 2 3 4 5 6 7
   ER
   Varje gång
   Ungefärlig varamann gång
   Aldrig

10. Hur nöjd har du varit med din sexpartner som älskare?
    1 2 3 4 5 6
    ER
    Inte alls nöjd
    Ganska nöjd
    Mycket nöjd

11. Hur nöjd har du varit med din partner som människa/vän?
    1 2 3 4 5 6
    ER
    Inte alls nöjd
    Ganska nöjd
    Mycket nöjd

12. Under de senaste 4 veckorna, hur ofta har du haft samlag (vaginal penetration)?

   Aldrig _______ eller _______ gånger per _______ vecka _______ månad
   (kryssa) (antal) (ringa in ett alternativ)

• Om du inte har haft samlag under de senaste 4 veckorna, vänligen avsluta här.

VAR GOD VÄND
13. Hur njutbart har samlag varit för dig?

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inte alls</td>
<td>Ganska</td>
<td>Mycket</td>
<td></td>
<td></td>
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</table>

14. Hur ofta har du fått orgasm under samlag?

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
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<th>5</th>
<th>6</th>
<th>7</th>
</tr>
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<tbody>
<tr>
<td>Aldrig</td>
<td>Ungefär</td>
<td>Alltid</td>
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<td>varannan gång</td>
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</tbody>
</table>

15. Hur njutbar(a) var i genomsnitt den orgasm (de orgasmer) du fått under samlag?

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>ER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ganska</td>
<td>Njutbara</td>
<td>Mycket</td>
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</table>

16. Hur ofta har du behövt ta hjälp av manuell (hand) eller mekanisk (massage) stimulering vid klimax för att nå orgasm under samlag?

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<th>6</th>
<th>7</th>
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</tbody>
</table>

17. Hur ofta har du varit otillräckligt (naturligt) fuktig i vaginan under samlag?

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<td>Alltid</td>
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</table>

18. Hur ofta har du haft ont under samlag?

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alltid</td>
<td>Ungefär</td>
<td>Aldrig</td>
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<tr>
<td>varannan gång</td>
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</tbody>
</table>

19. Hur ofta har du hindrats från att ha samlag för att din partner inte kunde få eller upprätthålla en erektion?

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
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<th>ER</th>
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</thead>
<tbody>
<tr>
<td>Alltid</td>
<td>Ungefär</td>
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</tbody>
</table>

TACK FÖR DIN MEDVERKAN
Appendix III. Interview guide in Swedish and the English translation.

**Intervjuguide**
Översikt över de ämnen intervjun skall beröra. Ordning och formulering är flexibelt.

**Huvudämnen**

1. Nedsatt sexlust / negativa effekter på sexualitet
   - Berätta om din erfarenhet av hormonella preventivmedel genom åren
   - Berätta om hur du märkte av effekterna.
   - Hur påverkade/påverkar det dig?
   - Påverkade / påverkar det ditt förhållande?

2. Välja preventivmedelsmetod
   - Hur hanterade/hanterar du de (specifika) negativa/positiva effekterna?
   - Vad är viktigt för dig när du väljer/byter preventivmedelsmetod?
   - På vilket sätt är du nöjd/missnöjd med nuvarande/tidigare val?
   - Diskuterade du med din barnmorska/läkare? Hur?

---

**Interview guide (translation into English)**

<table>
<thead>
<tr>
<th>Main topics</th>
<th>Questions and prompts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Impaired sexual desire/ negative effects on sexuality</strong></td>
<td>Could you please tell me about your experiences of contraceptive use?</td>
</tr>
<tr>
<td></td>
<td>Tell me about how you noticed [these] negative/positive effects.</td>
</tr>
<tr>
<td></td>
<td>If you can recall, how did or does this affect you?</td>
</tr>
<tr>
<td></td>
<td>How did [this] affect your relationship?</td>
</tr>
<tr>
<td></td>
<td>How did you/do you manage [the specific negative/positive effects]?</td>
</tr>
<tr>
<td></td>
<td>Describe what is important for you when choosing/changing a [contraceptive] method?</td>
</tr>
<tr>
<td></td>
<td>In what way are you content/discontent with [this/your] choice?</td>
</tr>
<tr>
<td><strong>2. Choosing contraceptive method</strong></td>
<td>Did you discuss the side effects with the midwife/doctor? How was the discussion/meeting?</td>
</tr>
</tbody>
</table>
Appendix IV. Example of analysis of interview nr 19 according to the thematic analysis process. Steps 3a (on this page) and 3b (on the next page). In Swedish.
K19:2

Vill ej ofrira sin lust som klart påverkas av tillförda hormoner
Tro på kvinnans jämlikhet, kraft och sexuella utveckling
Lär sig av p metodserfarenhe ter om hur hennes lust och kropp fungerar
Om brist på lust påverkas förhållandet men mannen påverkar inte valet
Njuta av egen cykel
Uteblivet kroppsligt gensvar
Behovet av säkerhet varierar
Vågskålen med pos/neg biverkningar omkalibreras med tiden
Att landa i "ingen metod" som metod
Resan att hitta rätt metod fördjöjd av bristande rådgivning
Önskar att rådgivningen facilitarar för kvinnans egen upptäckt utifrån fas hon är i
Att bli äldre positivt för sexualiteten, att förstå samband och kräva rätt råd
Större möjligheter att ta risken av en oplanerad graviditet
Önskar att rådgivningen facilitarar för kvinnans egen upptäckt utifrån fas hon är i
Om brist på lust påverkas förhållandet men mannen påverkar inte valet
Njuta av egen cykel
Uteblivet kroppsligt gensvar
Behovet av säkerhet varierar
Vågskålen med pos/neg biverkningar omkalibreras med tiden
Att landa i "ingen metod" som metod
Resan att hitta rätt metod fördjöjd av bristande rådgivning
Önskar att rådgivningen facilitarar för kvinnans egen upptäckt utifrån fas hon är i
Att bli äldre positivt för sexualiteten, att förstå samband och kräva rätt råd
Större möjligheter att ta risken av en oplanerad graviditet

Prova sig fram mellan olika p metoder är ett livsprojekt
Behovet av säkerhet varierar
Att landa i "ingen metod" som metod
Vågskålen med pos/neg biverkningar omkalibreras med tiden
Resan att hitta rätt metod fördjöjd av bristande rådgivning
Önskar att rådgivningen facilitarar för kvinnans egen upptäckt utifrån fas hon är i
Att bli äldre positivt för sexualiteten, att förstå samband och kräva rätt råd
Större möjligheter att ta risken av en oplanerad graviditet

Appendix V. The final thematic map of study III. In Swedish.

1. Efter erfarenheten kommer, eller uteblir, insikten. Valet av metod underlättas.


4. Rådgivning/rådgivaren kan vara en potentiell facilitator för kvinnans insikter och/eller egna val av metod

A. Ansvaret att skydda sig oftast kvinnans, acceptans av ojämlikhet och situation

B. Behandling av sjukdom, absoluta begränsningar och faktiskt behov av skydd

C. Inre och yttre miljön, att vilja undvika hormoner Att inte chansa

D. Hormonfritt alternativ, ett dugligt andrahands alternativ
Appendix VI. Flow chart study II.

CONSORT 2010- Flow chart

1. **Enrollment**
   - Assessed for eligibility (n=222)
     - Excluded (n= 20)
       - Not meeting inclusion criteria (n= 1)
       - Declined to participate (n= 18)
       - Others (n= 1)

2. **Allocation**
   - Randomized (n= 202)
     - Allocated to COC (n=102)
       - Received allocated intervention (n=102)
       - Did not receive allocated intervention (give reasons) (n= 0)
     - Allocated to placebo (n=100)
       - Received allocated intervention (n=99)
       - Did not receive allocated intervention (pregnancy) (n= 1)

3. **Follow-Up**
   - Lost to follow-up (n=18)
     - Cycle 1 (n=12) Cycle 2 (n=4) Cycle 3 (n=2)
     - Five discontinued because of adverse effects, others no reasons given.
   - Lost to follow-up (n=5)
     - Cycle 1 (n=3) Cycle 2 (n=1) Cycle 3 (n=1)
     - One discontinued because of pregnancy, others no reasons given.

4. **Analysis**
   - Analysed for primary outcome (n= 81)
     - Excluded from analysis (n= 3) no MFSQ at baseline or at cycle 3 follow up
   - Analysed for primary outcome (n= 91)
     - Excluded from analysis (n= 4) no MFSQ at baseline or at cycle 3 follow up
Papers I-IV
Papers

The papers associated with this thesis have been removed for copyright reasons. For more details about these see:

http://urn.kb.se/resolve?urn=urn:nbn:se:liu:diva-161653
Happy with the method? Sexual function changes in young women using contraception

Agota Malmborg