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Prevalence of sexual dysfunction and impact of contraception in female German medical students

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Meinem lieben Mann Christian und meiner lieben Tochter Rosalie Elli Marie

TABLES OF CONTENTS

1. INTRODUCTION

1.1. The importance of sexuality

It is now widely accepted that sexuality is a fundamental part of human life and that sexual problems have a (clear) negative impact on both quality of life and emotional well-being, regardless of age [1]. Female sexual dysfunction (FSD) is a very common disorder, with an estimated prevalence of having at least one sexual dysfunction of about 40% [2-4].

1.2. Female sexual dysfunction (FSD) and its prevalence

Sexual dysfunction can be subcategorized into diminished desire, interest and sexual fantasies, arousal problems (mental and physical), inability to achieve orgasm and pain associated with intercourse [4]. Interpersonal, psychological, physiological, medical, social, and cultural factors have been identified as associated with FSD [5, 6]. Sexual dysfunction has been linked in particular with age, depression, sexual and physical abuse in adulthood, global mental health function, alcohol [7] and emotional intimacy [8].

In Germany, FSD prevalence of 38% was suggested in 2008 [9], and estimates of 38–43% in adult women have been made in surveys in the USA [2, 7]. Most common was low desire, reported by just under a third of those surveyed, with little variation by age. Based on the well-established Female Sexual Function

Index (FSFI) by Rosen et al. [10], the prevalence of women in heterogeneous populations “at high risk” for FSD ranged from 24% in Pavia, Italy [11], 33% in Finland [12], and 43% in Istanbul, Turkey [13], to 63% for medical students in the USA [14].

1.3. Why female sexual dysfunction prevalences vary to great extent

Such estimates of FSD are, however, very controversial, because they vary up to tenfold across instruments, thereby affecting reported risk factors [15]. Differences between sample types, age range of participants, data collection, time frames, and definitions of sexual dysfunction are responsible for the different estimates [16, 17]. Even with well-established instruments such as the FSFI in relatively similar samples, different cut-offs for female sexual dysfunction result in different estimates. A further complicating factor is that sexual problems are particularly prevalent among women seeking routine gynaecological care, but are less common in community samples [18, 19].

1.4. Oral hormonal contraception (OHC) and female sexual function

Female sexual function is influenced by a multitude of factors including sexual hormones (estrogens, androgens and progestins) which elicit different effects on vaginal tissue and the central nervous system [20]. Oral estrogens and progestins induce Sexual Hormone Binding Globuline (SHBG) – a transport protein for sex hormones – in the liver [21] which can be enhanced or reduced

by adding progestins, depending on their androgenic or anti-androgenic properties. Testosterone has a high affinity for SHBG, and high SHBG serum levels can therefore reduce free testosterone levels, which are important for sexual function. OHC contain the synthetic estrogen ethinylestradiol (EE) and progestins with partial androgenic and antiandrogenic properties that can influence serum SHGB levels [22] and thus potentially also female sexual function.

Oral contraception has also been suggested as a possible modulator of female sexual function [23, 24]. However, published results are controversial, and the extent and nature of the effects remain unclear [25-27].

1.5. Female sexual function in students

Female sexual function in students has been poorly studied. We are aware of only an investigation by Shindel et al. [14] into sexual dysfunction in female medical students in the USA. They found that of 78 women, 63% were at high risk of sexual dysfunction based on validated FSFI scoring, and that problems with the following were reported: pain (39%), orgasms (37%), desire (32%), sexual satisfaction (28%), lubrication (26%), and arousal (24%). This corresponds broadly with normative data for 18–29-year-olds from the 1992 National Health and Social Life Survey [2]. Because it can be assumed that students in general represent a healthy population with only infrequent organic sexual dysfunction, it has been suggested that psychological and emotional

stress may be responsible for the high rate of sexual dysfunction in Schindel's small sample [14].

1.6. Objectives and Rationale

The objective of this survey was to assess sexual function and the prevalence of sexual dysfunction in female medical students in greater numbers than previously using an online survey, and to analyse the potential impact of OHC on sexual function by comparing possible correlations between progestins with androgenic and antiandrogenic properties and ethinylestradiol dosage on the sexual activity of female medical students using OHC.

2. PATIENTS AND METHODS

2.1. Study design

An online questionnaire based on the Female Sexual Function Index (FSFI) with additional questions on contraception, sexual activity and other factors that may influence sexual function was completed by students from six medical schools. The University of Tuebingen Ethics Committee (IRB) approved the study and study protocols were subsequently submitted and approved by the collaborating centres' IRBs.

2.2. Measurements and Parameters

2.2.1. The FSFI – a tool to investigate female sexual function

The FSFI by Rosen et al. [10] was used to analyse female sexual function. This is a well-established tool [28] and was validated in the German language [29]. The FSFI is designed to investigate problems with sexual function during the past 4 weeks and consists of 19 questions that measure six dimensions of female sexual function: desire, arousal, lubrication, orgasm, satisfaction, and pain. The response options on Likert-type scales are used to calculate the separate domain scores and an overall score for sexual function. We are not aware of any instruments especially validated for use in bisexual or homosexual individuals, although the FSFI has been validated for use in lesbians [30]. Thus,

in the introductory text of the questionnaire, homosexual and bisexual women were advised to interpret the questionnaire so as to best accommodate their understanding and definitions of sexual activity.

For the investigation, scores were calculated from submitted questionnaires and statistically analysed. According to Wiegel et al. [27], women with total FSFI scores of less than 26.55 are classified as “at high risk” for sexual dysfunction. Several other cut-offs have been proposed. Shindel et al. [14] suggested a different approach to define cut-offs for the subdomains of the FSFI: an arbitrary score of 33% or less of the maximum score in each domain. We agreed with Shindel et al. that classifying only individuals reporting “rarely/very little” or “never/not all” in any category as potentially dysfunctional was reasonable. We used both approaches in our study.

2.2.2. The online questionnaire

In addition to the FSFI questions, a further 11 questions were concerned with the participants usual means of contraception, changes in contraception, recent sexual activity, factors influencing sexual activity, wish for children, relationship, age, level of education, pregnancies and smoking.

2.2.3. Participants – how to reach to reach them online

Medical students at the Universities of Tuebingen, Munich (Technical University and Ludwig-Maximilians-University), Freiburg, Marburg, Heidelberg and Regensburg were informed about the online study and asked to participate via a standardized circular E-mail sent to the dean's student mailing list and via standardized messages posted on the online bulletin boards of all participating medical schools. All mails were sent and all messages posted in the 48 hours after the online questionnaire was opened for access. The questionnaire was closed exactly 14 days after launch. Anonymity was stressed in all communications. Submission of the completed questionnaire was considered as consent to participate in the study.

2.2.4. Data Handling

All responses were stored in a database. Each participant's responses were automatically scanned for inconsistencies by a programmed algorithm. Data were considered inconsistent if (i) participants negated recent sexual activity at some point and gave answers consistent with recent sexual activity at another point, or (ii) participants gave less than university entrance qualification as the highest educational level since the aim was to form as homogenous a sample of young female medical students as possible. All cases with possible inconsistencies marked by the algorithm were reviewed by two of the authors blinded to scores and excluded from the analyses by consensus.

2.2.5. Classification of Contraceptives

The mean FSFI scores were calculated and statistically compared for OHC containing androgenic progestins and OHC containing antiandrogenic progestins. The effects of OHC were also compared by the following dosage groups: 20 µg EE, 30 µg EE and >30 µg EE.

2.3. Statistical analysis

The distribution of FSFI scores is highly skewed, therefore mainly nonparametric methods were used. Median differences with 95% CIs were calculated for differences between FSFI subgroup scores. Correlations between FSFI scores and numbers (e.g. cigarettes per day) were estimated with Spearman's correlation coefficient rs. Comparisons of subgroup proportions using OHC were described using proportional differences with 95% CIs. The effect of the factors age, former pregnancy, wish for children, method of contraception, partnership and smoking status on total FSFI scores was estimated by an analysis of variance (ANOVA) model. Thereby the response variable was transformed by squaring to achive residuals' normality which was verified by quantile-quantile plots. Homoscedasticity was assessed by residuals by predicted plots and outlieres with high leverage were identified by calculating Cook`s distance. The Kruskal-Wallis test was used to elicit differences in total FSFI scores and subscores for desire and arousal between groups using

different OHC. Quality of fit is recorded as adjusted coefficient of determination (Radj2). The statistical analysis was performed with R version 2.7.2.

3. RESULTS

3.1. Total number of Participants

1,219 respondents submitted completed questionnaires. After screening the data for completeness and unserious responders, 1,086 data sets were included in the analysis.

3.2. Demographic Data

Demographic data are presented in Table 1. Most participants had used contraceptives in the previous 6 months (87.4%), and almost all (97.3%) had been sexually active in the previous 4 weeks. The 3 most common means of contraception were OHC (69.5%), condoms (22.5%), and the vaginal contraceptive ring (7.3%). The majority of respondents (81.1%) were in stable relationships.

Table 1: Demographic data

	All participants		Participants sexually active in past four weeks	
	Number	Percentage	Number	Percentage
Participants (after screening for	1086	*100.0*	1057	*100.0*

unserious responders)				
Contraception in past 6 month				
Yes	945	*87.0*	924	*87.4*
No	141	*13.0*	133	*12.6*
Method of contraception in past 6 month *(multiple answers possible)*				
Oral contraceptives (OHC) total	752	*69.2*	735	*69.5*
Contraceptive implant	8	*0.7*	8	*0.8*
Intrauterine methods	19	*1.7*	18	*1.7*
Vaginal contraceptive ring	78	*7.2*	77	*7.3*
Condoms	243	*22.4*	238	*22.5*
Fertility awareness	17	*1.6*	17	*1.6*
Other contraception	8	*0.7*	8	*0.8*
Sexually active in the past 4 weeks				
Yes	1057	*97.3*	1057	*100 .0*
No	29	*2.7*	0	*0.0*
Age (years)				
< 25	856	*78.8*	830	*78.5*
≥ 25 and < 35	223	*20.5*	220	*20.8*
> 35	7	*0.6*	7	*0.7*
Stable relationship				
Yes	869	*80.0*	857	*81.1*
Mean duration	3.2 (std 2.6) years		3.2 (std 2.6) years	
No	217	*20.0*	200	*18.9*
Pregnancy				
No pregnancy	1046	*96.3*	1019	*96.4*
One pregnancy	29	*2.7*	27	*2.6*

More than one pregnancy	11	*1.0*	11	*1.0*
Pregnant in the last 2 years				
Yes	26	*2.4*	25	*2.4*
No	1060	*97.6*	1032	*97.6*
Active wish for children				
Yes	37	*3.4*	35	*3.3*
No	1049	*96.6*	1022	*96.7*
Smoking				
Yes	131	*12.1*	127	*12.0*
Mean number of cigarettes/day	8.7 (std 6.8) cigarettes / day		8.8 (std 6.7) cigarettes / day	
No	955	*87.9*	930	*88.0*

Among the women using contraception, 752 women were OHC users, of whom 404 used OHC with antiandrogenic progestins and 263 OHC with androgenic progestins. 132 preparations contained 20 µg EE, 450 contained 30 µg, and 62 >30 µg. Table 2 lists the OHC used and classification of the progestins.

Table 2: OHC used with numbers and qualities.

OHC used	**Number of users**	**Percentage of total OHC users**	**EE content (µg)**	**Partial gestagenic property**
Valette	176	23,40%	30	antiandrogenic
Belara	101	13,43%	30	antiandrogenic

Yasmin	65	8,64%	30	antiandrogenic
Leios	44	5,85%	20	androgenic
Petibelle	41	5,45%	30	antiandrogenic
LAMUNA	34	4,52%	20/30	androgenic
Miranova	27	3,59%	20	androgenic
Desmin	25	3,32%	20	androgenic
Microgynon	23	3,06%	30	androgenic
Minisiston	23	3,06%	30	androgenic
Diane35	20	2,66%	35	antiandrogenic
MonoStep	19	2,53%	30	androgenic
Novial	15	1,99%	30/35	androgenic
Biviol	14	1,86%	40	androgenic
Femigoa	11	1,46%	30	androgenic
BellaHEXAL	9	1,20%	35	antiandrogenic
Neo-Eunomin	8	1,06%	50	antiandrogenic
Cilest	7	0,93%	35	androgenic
Lovelle	7	0,93%	20	androgenic
NovaStep	4	0,53%	30	androgenic
Cyproderm	3	0,40%	35	antiandrogenic
Triquilar	3	0,40%	30/40	androgenic
Marvelon	2	0,27%	30	androgenic
Pramino	2	0,27%	35	androgenic
Triette	2	0,27%	30/40	androgenic
Trigoa	2	0,27%	30/40	androgenic
Conceplan	1	0,13%	30	androgenic
Cyclosa	1	0,13%	50	androgenic
EVRA	1	0,13%	600 (patch)	androgenic
Femovan	1	0,13%	30	androgenic

TriNovum	1	0,13%	35	androgenic
Other OHCs*	60	7,98%	N/A	N/A
Sum	752	100,00%		

* OHC with controversially discussed partial gestagenic properaties

3.3. Sexual Dysfunction

The subscores for arousal, lubrication, orgasm und pain and therefore also the total FSFI score for women who were not sexually active in the past 4 weeks have to be interpreted differently from those who were sexually active and were therefore excluded from the analysis of the FSFI scores. Table 3 shows the FSFI scores and the proportion of participants who were below the cut-offs for sexual dysfunction and therefore at high risk for FSD. For the total FSFI score, the cut-off of 26.55 by Weigel et al. was used, and a cut-off of 33% was used for the subscores. 342 (32.4%) participants were considered at high risk for sexual dysfunction based on the total FSFI score. If a cut-off of 33% the score was applied for the FSFI total score, the at-risk fraction would be 0.3%. For the subscores, 61 (5.8%) were considered at high risk for sexual desire dysfunction, 11 (1.0%) for arousal, 13 (1.2%) for lubrication, 92 (8.7%) for orgasm, 28 (2.6%) for satisfaction and 12 (1.1%) for pain dysfunction.

Table 3: FSFI scores in participants (sexually active in past four weeks) and proportion at risk for sexual dysfunction

SCORES	Median	First Quartile	Third Quartile	Range	Number analysed	Number "at risk for sexual dys-function"	Percentage "at risk for sexual dys-function"
FSFI total	28.6	25.5	31.6	9.5–36.0	1057	342	*32.4*
Desire	3.6	3	4.2	1.2–6.0	1057	61	*5.8*
Arousal	5.1	4.2	5.7	1.2–6.0	1057	11	*1.0*
Lubrication	5.7	4.8	6.0	1.2–6.0	1057	13	*1.2*
Orgasm	4.8	3.6	5.6	0.8–6.0	1057	92	*8.7*
Satisfaction	5.2	4.0	6.0	1.2–6.0	1057	28	*2.6*
Pain	5.2	4.4	6.0	1.2–6.0	1057	12	*1.1*

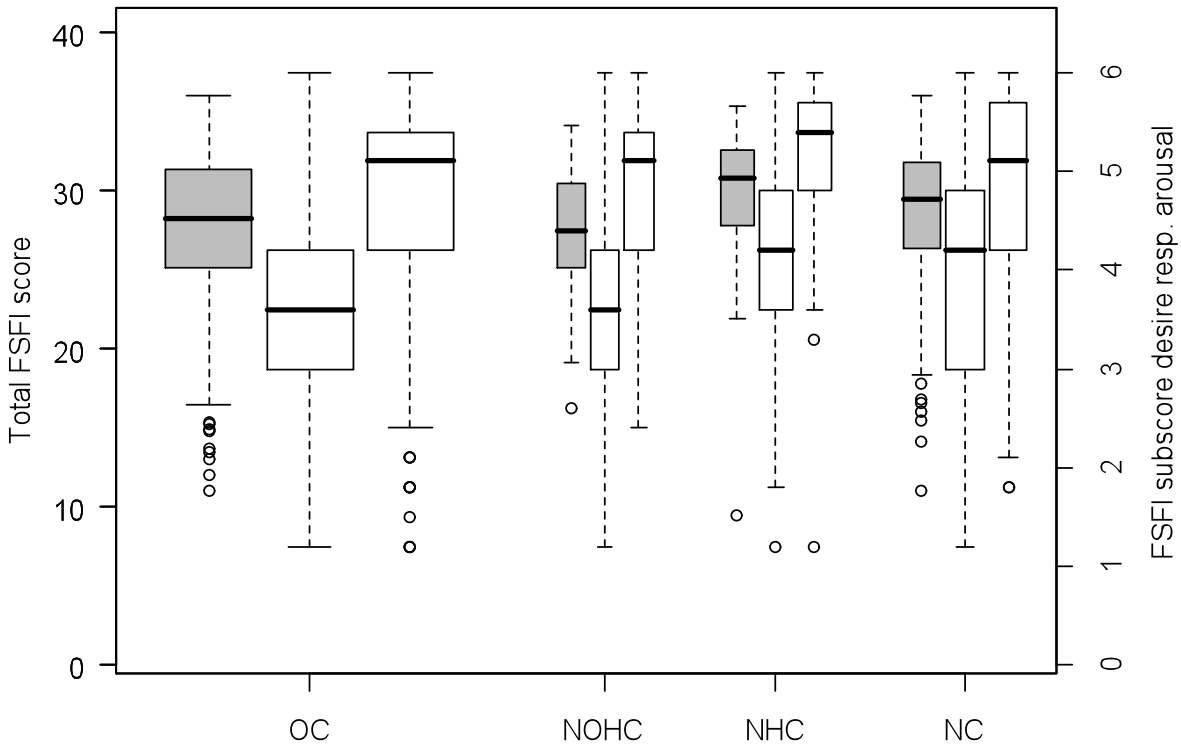
3.4. Contraception and sexual function

3.4.1. Impact of different forms of contraception on sexual function

The total FSFI score and subscores for desire and arousal were compared between participants with different methods of contraception: oral (hormonal) contraception (OHC), non-oral hormonal contraception (NOHC), non-hormonal contraception (NHC), and no contraception (NC) (Figure 1). All 3 scores differed between contraception methods. The highest total FSFI score was found for NHC, followed by NC and OHC, and NOHC was lowest. For desire, NC and NHC had the same score, followed by OHC and NOHC, and for arousal, the highest score was found for NHC, followed by NOHC, NC and OHC. ANOVA

models with or without interactions showed a signifikant effect of the method of contraception and also of smoking status on total FSFI Scores (p-value < 0.0001 resp. p-value = 0.005) with higher total FSFI scores for smokers. Other factors included, namely age, former pregnancy, wish for children and partnership status had no significant effect (all p-values > 0.15). The coefficient of determination R_{adj}^2 was 0.03 and 11 women were excluded that used different methods of contraception, leaving 1046 women in this analysis.

Figure 1: Boxplots of FSFI total scores of different contraception groups (oral [hormonal]) contraception [OHC], non-oral hormonal contraception [NOHC], non-hormonal contraception [NHC] and no contraception [NC]. Box size is proportional to the number of observations in each group. Medians, quartiles and ranges are shown. Circles indicate outliers: more than 1.5 times the interquartile range from the box. The total FSFI score is grey, desire and arousal subscores are white.



3.4.2. Comparison of different kinds of oral hormonal contraceptives

3.4.2.1. Androgenic versus antiandrogenic progestins

Figure 2 shows the total FSFI scores for the groups with androgenic and antiandrogenic progestins. The median scores of 28.3 and 28.5 and were not statistically significantly different. Table 4 lists the medians for the FSFI subscores, which also did not differ significantly.

Fig. 2: Box-Whisker plot for total FSFI score for oral contraceptives containing progestins with partial androgenic or antiandrogenic properties

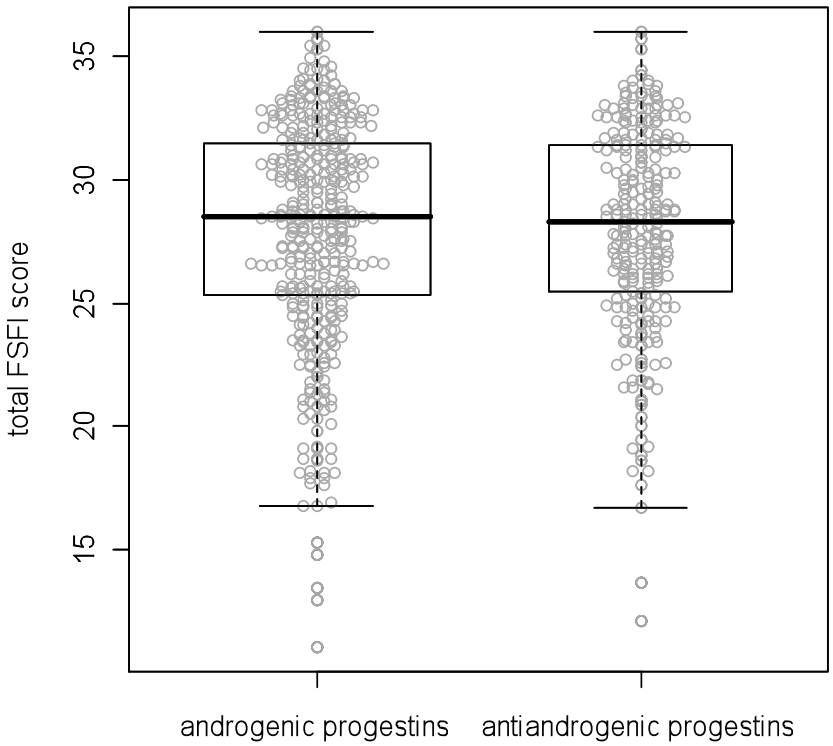


Table 4: FSFI-subscores for oral contraceptives containing progestins with partial androgenic or antiandrogenic properties and for oral contraceptives with different dosages of ethinylestradiol (EE).

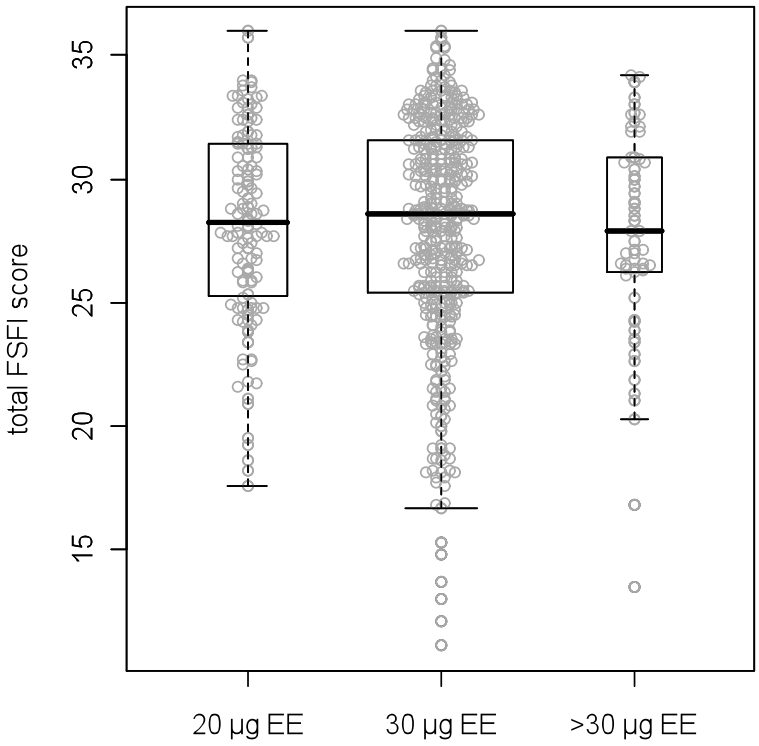
	Q5-6 Median (25/75 percentile)	*Q7-10 Median (25/75 percentile)*	*Q11-14 Median (25/75 percentile)*	*Q15-17 Median (25/75 percentile)*	*Q18-20 Median (25/75 percentile)*	*Q21-23 Median (25/75 percentile)*
Progestins-androgenic N=263	3.6 (3.0/4.2)	5.1 (4.2/5.4)	5,7 (5.1/6.0)	4.8 (3.6/5.6)	5.2 (4.4/5.6)	5.2 (4.4/6.0)

Progestins-antiandrogenic N=404		3,6 (3.0/4.2)	5.1 (4.2/5.4)	5.7 (4.8/6.0)	4.8 (3.2/5.6)	5.2 (4.0/6.0)	5.2 (4.4/6.0)
EE dosages	20µg n= 149	3.6 (3.0/4.2)	5.1 (4.2/5.4)	5.7 (5.1/6.0)	4.6 (3.6/5.6)	5.2 (4.4/6.0)	5.2 (4.4/6.0)
	30µg n=509	3.6 (3.0/4.2)	5.1 (4.2/5.4)	5.7 (4.8/6.0)	4.8 (3.6/5.6)	5.2 (4.0/6.0)	5.2 (4.4./6.0)
	>30µg n=70	3.6 (2.4/4.2)	5.1 (3.9/5.7)	5.7 (5.1/6.0)	4.8 (4.4/5.6)	5.2 (4.4/5.6)	5.2 (4.4/6.0)

3.4.2.2. Impact of different EE dosages

Figure 3 shows the total FSFI scores by EE dosage. The median total score for the 20 µg group was 28.3, for 30 µg group 28.6, and for the >30 µg group 27.3. The scores did not differ significantly. Table 4 summarizes the medians for the subscores, which also did not differ significantly.

Fig. 3: Box-Whisker plot for total FSFI score for oral contraceptives with different ethinylestradiol dosages



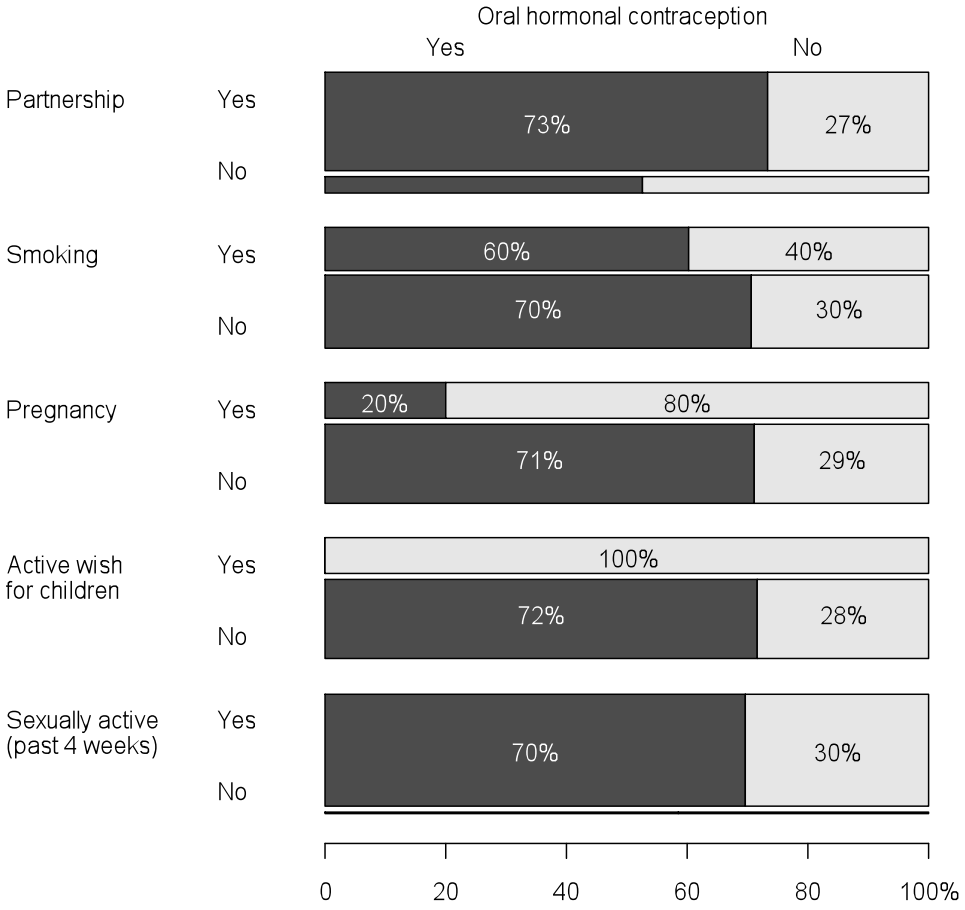
3.5. Epidemiological factors and sexual function

Comparison of median scores and CIs showed that women not in stable relationships had higher desire scores (0.6 [0.6,0.6]) but lower orgasm scores (-0.4 [-0.8,-0.2]). Smokers had a higher median total FSFI score (1.5 [2.3,0.2]) and higher median pain score (0.8 [0.8,0.4]) than non-smokers. 70.4% of non-smokers used OHC for birth control as opposed to 60.3% of smokers. A history of pregnancy and age higher than 25 years were associated with a lower median pain score (-0.8 [-0.8,-0.4], respectively -0.4 [-0.4,-0.8]). The scores for women with and without an active wish for children differed only slightly.

Women who reported a strong negative influence of stress also had a low median FSFI subscore for desire (r_s=-0.31). Those who stated a strong negative influence of their partner had a low median total FSFI score (r_s=-0.28) and low median satisfaction subscore (r_s=-0.40). An increase in intercourse frequency in the past 6 months correlated positively with the total FSFI score (r_s=0.29) and satisfaction subscore (r_s=0.38), and an increase in ability to reach orgasm correlated positively with total FSFI score (r_s=0.33) and the desire (r_s=0.29), arousal (r_s=0.32) and orgasm subscores (r_s=0.25). The length of the relationship correlated negatively with the desire subscore for women in a stable relationship (r_s=-0.26). All other factors (e.g. number of cigarettes per day) correlated only weakly or not at all with the total FSFI score.

Women in stable relationships were more likely to use oral rather than other or no contraception (Figure 4). Also non-smokers, women who have not been pregnant and those with no active wish for children were more likely to use OHC than other or no contraception. All participants were included in this analysis.

Figure 4: Proportion of patients using oral contraception by selected factors. Bar widths are proportional to numbers in each group.


Oral hormonal contraception
Yes
No
Partnership
Yes
No
73%
27%
Smoking
Yes
No
60%
40%
70%
30%
Pregnancy
Yes
No
20%
80%
71%
29%
Active wish for children
Yes
No
100%
72%
28%
Sexually active (past 4 weeks)
Yes
No
70%
30%
0
20
40
60
80
100%

4. DISCUSSION

4.1. Problem Statement

This survey assessed sexual function in female German medical students and the effects of contraception on sexual function using datasets from 1,068 completed questionnaires based on the German FSFI.

Only four published surveys have so far specifically studied sexuality in medical students. Two of these were conducted almost 40 years ago [31, 32], the third dealt with Chinese students' attitude towards sexuality rather than sexual function [33], and the fourth was a pilot study in only 78 women [14].

Moreover, an association between oral contraceptives (OHC) and sexual dysfunction has been suggested [23], although the extent of the effects remains unclear [26, 34]. OHC contain the synthetic estrogen ethinylestradiol (EE) and progestins with partial androgenic and antiandrogenic properties that can influence serum SHGB levels [22] and thus potentially also female sexual function.

The aim of this study was to shed light on the sexual life of German medical students, to analyse the prevalence of sexual dysfunction and to investigate the impact of contraception on sexual function.

4.2. Interpretation of results

4.2.1. Patient Demographics

Almost 90% of our participants had used contraception and almost all had been sexually active in the previous 4 weeks. 80% were in a stable relationship. The three most common means of contraception were OHC, condoms and the vaginal contraceptive ring. Users of hormonal contraception were more likely to be women in stable relationships who were non-smokers, had not been pregnant before and did not have an active wish for children, which might be expected given the contraindications for OHC.

4.2.2. Prevalence of sexual dysfunction

Based on the total FSFI score, 32.4% of participants were “at high risk” for sexual dysfunction. With regard to subscores, this was the case for 8.7% for orgasm, 5.8% for desire, 2.6% satisfaction, 1.2% for lubrication, 1.1% for pain, and 1.0% for arousal. When interpreting these numbers, however, it has to be borne in mind that the cut-off for the total FSFI score suggested by Wiegel et al. in wide use does not necessarily apply for our study sample [27] and that the cut-offs for subscores suggested by Shindel et al. [11]. are purely speculative. Furthermore, it has to be considered that these are different cut-offs and that therefore the numbers of at-risk fractions for the total score and the subscores differ greatly. Despite the FSFI’s widespread use and its descriptive validity, it

does not measure the individual distress related to the sexual function or dysfunction. It is therefore to be stressed that these numbers are based mainly on quantitative ratings of events over a 4-week period.

Estimates of the prevalence of sexual dysfunction differ greatly because of different sample sizes, populations, age ranges and instruments [15-17], and also because of different cut-off levels for the same instrument. Moreover, sexual problems tend to be higher in clinical samples and women seeking medical attention than in community samples [13, 18, 19]. This is further complicated because physicians are not confident in diagnosing hypoactive sexual desire disorder and rarely screen patients for this [35].

The prevalence of FSD in our German medical students based on the total FSFI score was similar to that in some studies [9, 25], but was lower than the 43% determined by the 1992 National Health and Social Life Survey (NHSLS) in the USA in women aged 18–59 [2], and much lower than the 63% found by Shindel et al. in their sample of 78 female US medical students [14]. Shindel's figures for problems with pain, orgasms, desire, sexual satisfaction, lubrication, and arousal, although similar to normative data for 18–29-year olds in the 1992 NHSLS study, also differed greatly from our findings. In a review in 1990, however, a prevalence of 5–10% for inhibited female orgasm was given for community samples [19], which agrees with our prevalence of orgasm disorder of 8.7%. The most common types of sexual dysfunction in the literature and in our patients were problems with orgasm [36, 37] and low sexual desire [2, 38,

39]. One reason for these differences may be that we studied a large but relatively homogenous collective as opposed to the other studies or it may be a selection bias towards students who decided to participate in our study or cultural differences in the perception of sexual dysfunction. Also, the difference in the applied instruments may contribute to this disparity.

4.2.3. Contraception and sexual funcion

4.2.3.1. Impact of different forms of contraception on sexual function

Contraception had a significant impact on sexual function as indicated by FSFI scores in German medical students. Women using non-hormonal contraception or no contraception had higher total, desire and arousal scores than women using OHC. In our model, not all variables such as smoking, stress etc. could be adequately controlled, which complicates interpretation. The possible association between contraceptives and sexual function remains controversial in the literature. In a prospective observational study in 365 women, Lit et al. found that combined OHC and intrauterine contraceptive devices did not have an impact on sexual function, whilst sterilization improved both sexual satisfaction and sexual drive. In a Finnish sample of 2,081 women aged 33–43 years, the usage of OHC had no significant effects on sexual function. The use of hormone-based intrauterine systems was, however, significantly associated with less pain and more desire, arousal, and satisfaction [25]. In a validation study in 568 women, Wiegel et al. found that OHC did not influence any sexual

function domains of the FSFI, but that intrauterine devices were associated with fewer arousal, satisfaction, and pain problems [27]. In 1997, McCoy al. [24] found OHC users to have more desire but less lubrication than nonusers, but the association varied with the type. Bitzer et al. reported that OHC had a possible impact on female desire (increasing or decreasing) and that the impact also depended on the kind of OHC used [23, 40]. Cultural differences have also been reported [41]. Davies et al. summarised the controversy in their 2004 review, reporting that overall, women experience positive effects, negative effects, and no effects on libido during OHC use [26].

Our data suggest either a negative effect of OHC on female sexuality, and desire and arousal in particular, or one or more relevant difference between women using contraceptives or no contraceptives such the ability to enjoy oneself or the perception of one's own body. Furthermore, the complexity of sexual desire and other complicating factors such as positive and negative influences in relationships have to be considered. The fact that this is a cross sectional study without randomization further limits conclusions concerning the relationship between contraceptive methods and sexual function or dysfunction. Finally, the low coefficient of determination of the ANOVA model suggests that the factors considered can only explain a small fraction of the variability of total FSFI scores. Therefore, other factors that are not covered in the model must have an influence, too. It might be the case that there exists a multitude of factors with each only very little impact.

4.2.3.2. Comparison of different kinds of oral hormonal contraceptives

Ovarian dysfunction and hormonal dysbalance of endogenous or iatrogenic origin are associated with reduced sexual desire and disturbance of sexual arousal [42]. Especially testosterone may play a key role in mediating hormonal effects on sexual function, as may factors that induce changes in free testosterone serum levels. Compounds that bind to the androgen receptor and trigger androgenic effects may also be involved. Progestins used in OHC possess partial androgenic or antiandrogenic properties [21], and these progestins can modulate the synthesis of SHBG, an important regulator of free testosterone serum levels. It is well known that EE can influence the synthesis of various liver proteins, including SBHG, and that SHBG synthesis may be dependent on the EE dose [21]. These hormonal functions led to the hypothesis that the sex hormones in OHC might influence female sexual function via their modes of action, and that these influences may be dose-dependent.

Graham et al. investigated the serum levels of a number of hormones during OHC intake using the same progestin [43]. Significant decreases were found after 3 months. Their findings also suggested a statistical correlation between low sex hormone levels and the frequency of sexual thoughts. However, some women showed no loss of sexual interest despite low testosterone levels. The authors concluded that some women may be more sensitive to changes in testosterone levels. Free testosterone (FT) serum levels under 25 and 35 µg EE

were investigated by Greco et al. [44], who found that the lower EE dosage was associated with a smaller reduction in FT. Two recent investigations studied the effect of oral OHC on SHBG serum levels and the possible correlation with sexual function. Panzer et al. [45] investigated SHBG serum levels in 124 women with sexual dysfunction who were users or non-user of OHC. The SHBG levels were up to four-times higher in users, and total FSFI scores were also lower. Warnock et al. [46] measured SHBG, total testosterone and free testosterone serum levels in 106 women with sexual dysfunction, 43 of whom were OHC users. Amongst OHC users, SHBG levels were higher and total and free testosterone levels lower than in non-users.

In our Internet-based study based on the validated and well-established FSFI [10, 34], we found no significant difference between OHC containing androgenic and antiandrogenic progestins, nor did we observe any relationship between EE dosage and sexual function, which was not consistent with some of the studies mentioned above. However, the effects in those studies were found in women with diagnosed sexual dysfunction, whereas we studied a large homogenous sample of healthy, young female medical students. It is worth noting in this context that sexual problems have been reported to be particularly prevalent among women seeking routine gynecological care [18], whereas they are more scarce in community samples. One review showed the prevalence of inhibited female orgasm to range from 18% to 76% in clinic settings, but only 5% to 20% in community samples [18, 19].

Comparison of total FSFI scores in student OHC users and those using non-hormonal contraception or no contraceptives showed that OHC had a negative influence on sexual function. The influence of OHC on sexual function, and desire in particular, is controversial [23, 34]. A review by Davis et al. [26] found very variable results in controlled and uncontrolled studies, with both positive and negative effects.

4.2.4. Epidemiological factors and their association with sexual function

4.2.4.1. Stress

One factor that had a clear impact on desire in our study was stress: increases in perceived stress were associated with lower desire scores. This agrees with Witting's finding that psychological distress was positively associated with every dimension of the FSFI, except desire [12]. Interestingly, Bancroft et al. [8] found that the best predictors of sexual distress were mental and physical health and not sexual function problems.

4.2.4.2. Relationship

Studies have shown that greater satisfaction with a relationship overall was associated with greater sexual satisfaction and fewer sexual function problems [25]: the stronger the emotional intimacy with the partner, the less the sexual

distress [8]. In our study, women in stable relationships had higher orgasm scores but lower desire scores. However, the longer the partnership lasted, the more the desire scores decreased. An increase in intercourse frequency was associated with higher FSFI total and satisfaction scores, while an increase in ability to achieve orgasm was associated with higher total, desire, arousal and orgasm scores. This seems plausible, given that sexual desire was reported as increased in new relationships [47], but differs from Shindel's finding that women in relationships had higher FSFI scores for desire and satisfaction [14]. Again, this may have been attributable to the different sample sizes and instruments applied.

4.2.4.3. Smoking

Interestingly, in our sample, smokers had a higher total FSFI total score. An explanation might be that smokers tend to have lower oestrogen levels than non-smokers [48], which may lead to lower SHBG levels and, in turn, to increased free testosterone levels. Another possible explanation could be that smokers might have greater ability to enjoy themselves.

4.2.4.4. Pregnancy

A further factor that can affect female sexual function is pregnancy. Witting et al. reported that multiparous women had fewer orgasm problems than nulliparous women. Nulliparous women had more pain problems and were less sexually

satisfied [25]. We were unable to confirm either of these findings, as only 3.6% of our participants had been pregnant.

4.2.4.5. Age

The link between age and sexual dysfunction [49] is controversial. Laumann et al. [2] suggested that sexual dysfunction declines with age, whilst Abdo et al. found age to be associated with increased reaching of orgasm and desire [38], which was supported by Witting et al. [25]. Ponholzer et al. reported that sexual desire was at its peak between 20 and 40 years of age, with pain and orgasm problems being the most frequent difficulties in the this age group [36]. The age range of our participants was too narrow to establish associated differences.

4.3. Discussion of methodology and its limitations

4.3.1. Discussion of the use of an online questionnaire

We decided on an online approach to maximise access to the medical student community because all collaborating medical schools offer Internet access. Numerous instruments have been reported to be equally as reliable as paper when administered via the Internet [50, 51]. Internet findings have also been shown to be superior to paper questionnaires with respect to completeness of data [51, 52]. Furthermore, internet participation in online surveys is at least as good as if not better than paper surveys, with less recruitment and follow-up

effort [50]. Joinson et al. reported in 1999 that online surveys may even result in more honest answers [53]. Potential disadvantages of online questionnaires are unserious and repeat responders. It has, however, been reported that Internet findings are not adversely affected by these groups [51]. Because we took measures to detect unserious responders (inconsistent responses), we feel confident that our results accurately represent the population studied. We also assume that serious participants entered true information since anonymity was assured.

4.3.2. Discussion of the study design and selection bias

Despite our strict plausibility checks, however, selection bias cannot be ruled out. We felt that a homogenous sample was imperative in meeting the study's objectives, and that this outweighed the risk of selection bias. Almost all participants excluded because the education level was too low met other exclusion criteria. Another further form of selection bias that we considered was that women with perceived sexual problems might have felt more inclined to participate than women with no sexual problems or that students with oral contraceptive use exposed recently to publications about a possible negative impact of these contraceptives on desire etc. may be overrepresented. Moreover, the possibility of reporting bias cannot be ignored, although whether participants would tend to over or underreport sexual difficulties is open to speculation. We can only assume that the relatively large number of participants counteract these biases.

When interpreting the results, the design (cross sectional study) has to be considered as well. We had no control group and were only able to compare our findings to prior studies. Also, the FSFI questionnaire uses the Likert approach, unlike many community studies in which the results are collected with yes/no questions. The extent of comparison of our findings with other findings was therefore limited. Finally, our investigation was targeted at medical students and the age range was therefore narrow. Although this reduces variation in responses, it also restricts generalisation to other age groups.

4.3.3. Discussion of the methodology of contraceptive comparisons

We did not collect laboratory measurements to support our clinical findings (FSFI scores). Because both hormone and SHBG levels can vary widely and can be influenced by many factors, we cannot rule out that OHCs may influence sexual function and may have different effects depending on the EE dosage and type and dosage of progestin, and to establish this was one aim of our study. To our knowledge, however, such a key study has never been performed in patient samples large enough to test this important hypothesis.

OHCs contain either androgenic or antiandrogenic progestogens, classified according to their behaviour with regard to progesterone receptors and SHBG, as described above. In addition to this, we analysed the effects of OHCs depending on EE dosage. Progestogens were classified according to the

general classification based on the Hersberger test, i.e. according to animal experiments. Clinically, the effects of progestogens may vary, since other partial functions, such as their influence on the conversion of testosterone into dihydrotestosterone, may also play an important role in their overall effect. It is therefore possible that they may exert a different net effect depending on the combination of hormones. For instance, an OHC with a high EE dosage and an androgenic progestogen may actually have antiandrogenic effects. The same applies to triphasic preparations with up to 40 µg EE. However, only 8 of our participants used OHCs that fall into these categories, and we therefore disregarded this possible effect. It could, however, be claimed that the effects of the antiandrogenic preparations may have had a strong impact on sexual function in our study, since a large number of participant used combinations of antiandrogenic progestogens with high EE dosages (e.g. Neo-Eunomin 50 µg, and Diane 35 or 35 µg EE), which may markedly reduce free testosterone levels. Furthermore, in Germany, preparations such as ‘Valette’ are often used for ‘‘long-term’ application (i.e. without a hormonal pause), and with these the enhancement of the antiandrogenic effect might be even greater due to more marked central inhibitory actions. Our results, however, showed that the effects of the EE dosage (and the consequent effects on SHBG levels) appear to be irrelevant in the population of women we studied, indicating that the combined effects discussed above also have no clinical impact.

4.4. Conclusions

To our knowledge, this is by far the largest study with a validated instrument to assess sexual dysfunction in female medical students. The prevalence of students at high risk for FSD in this multi-institutional study was consistent with the literature, although domain subscores differed from previous investigations. Women using contraception, especially hormonal contraception, had significantly lower sexual functioning scores. However, neither androgenic nor antiandrogenic progestins in OHC nor the EE dosage in the OHC used significantly influenced sexual function in German medical students. Stress, relationship, smoking and pregnancy among other variables were found to be associated with sexual function and may assist in elucidating the reasons for sexual disorders when specifically evaluated in future studies.

5. SUMMARY

This study's objective was to investigate the prevalence and types of female sexual dysfunction (FSD) and the relationship between hormonal contraception and FSD in female German medical students. Moreover, the influence of sex hormones in oral contraceptives on female sexual function was compared.

An online questionnaire based on the Female Sexual Function Index (FSFI) with additional questions on contraception, sexual activity and other factors that may influence sexual function was completed by students from six medical schools. Obtained data was screened for inconsistencies by programmed algorithms. FSFI scores for all relevant subscores were calculated and numbers of women at risk for sexual dysfunction compared determined. The effects of different contraceptive methods on sexual function as well as different types of oral hormonal contraceptives (classified into those containing androgenic or antiandrogenic progestins and by ethinylestradiol (EE) dosage (20 µg, 30 µg and >30 µg) were compared against each other and against control groups.

1,219 completed questionnaires were received and 1,086 included in the analyses after screening. The mean total FSFI score was 28.6 +/- 4.5. 32.4% of women were at risk for FSD according to FSFI definitions. Based on domain scores, 8.7% for were at risk for FSD concerning orgasm, 5.8% for desire, 2.6% for satisfaction, 1.2% for lubrication, 1.1% for pain and 1.0% for arousal. The method of contraception and smoking were factors with significant effect on the

total FSFI score whereby hormonal contraception was associated with lower total FSFI scores and lower desire and arousal scores than no contraception and non-hormonal contraception only. Other variables such as stress, pregnancy, smoking, relationship and wish for children had an important impact on sexual function as expected according to earlier studies. No statistically significant differences in FSFI scores were found between women using OHCs containing androgenic or antiandrogenic progestins, nor were any seen between different EE dosages.

In conclusion, the prevalence of students at high risk for FSD was consistent with the literature although domain subscores differed from samples previously described. Women using contraception, especially hormonal contraception, had lower sexual functioning scores. However, the impact of an androgenic or antiandrogenic progestin content or different dosages of EE as modulating factors of female sexual function seemed negligible. Stress, relationship and smoking among other variables were found to be associated with sexual function and may thus provide insight into the aetiology of sexual disorders.

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7. PRESENTATIONS AND PUBLICATIONS

Presentations:

- Oral presentation at the XXI. German Full Professor Conference for OB/GYN (25.-26.09.2009, Innsbruck, Austria)
- Oral presentation at the XIV. World Congress of the International Society of Gynecological Endocrinology (04.-07.03.2010, Firenze, Italy)

Publications:

- Prevalence of sexual dysfunction and impact of contraception in female German medical students; J Sex Med. 2010 Jun;7(6):2139-48. Epub 2010 Apr 12.
- Effects of sex hormones in oral contraceptives on the female sexual function score: a study in German female medical students; Contraception. 2010 Aug;82(2):155-9. Epub 2010 Feb 10.

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9. CURRICULUM VITAE

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- Gynäkologie und Geburtshilfe (Prof. Friese, Direktor der I. Frauenklinik der LMU, München)
- Innere Medizin (Prof. Reincke, Direktor der Medizinischen Poliklinik der LMU, München)

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09/02 – 03/03	Abschluss als Gesellin für Damenschneiderei
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09/93 – 07/98	Gymnasium Seligenthal Landshut
09/89 – 07/93	Grundschule Seligenthal, Landshut

10.ADDENDUM

- Prevalence of sexual dysfunction and impact of contraception in female German medical students; J Sex Med. 2010 Jun;7(6):2139-48. Epub 2010 Apr 12.
- Effects of sex hormones in oral contraceptives on the female sexual function score: a study in German female medical students; Contraception. 2010 Aug;82(2):155-9. Epub 2010 Feb 10.

Prevalence of Sexual Dysfunction and Impact of Contraception in Female German Medical Students

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ABSTRACT

Introduction. Female sexual dysfunction (FSD) is a very common disorder, with an estimated prevalence of having at least one sexual dysfunction of about 40%.

Aim. To investigate the prevalence and types of FSD and the relationship between hormonal contraception (HC) and FSD in female German medical students.

Main Outcome Measures. Female Sexual Function Index (FSFI) with additional questions on contraception, sexual activity, and other factors that may influence sexual function.

Methods. An online questionnaire based on the FSFI was completed by students from six medical schools. Obtained data were screened for inconsistencies by programmed algorithms.

Results. A total of 1,219 completed questionnaires were received, and 1,086 were included in the analyses after screening. The mean total FSFI score was 28.6 +/– 4.5. 32.4% of women were at risk for FSD according to FSFI definitions. Based on domain scores, 8.7% for were at risk for FSD concerning orgasm, 5.8% for desire, 2.6% for satisfaction, 1.2% for lubrication, 1.1% for pain and 1.0% for arousal. The method of contraception and smoking were factors with significant effect on the total FSFI score whereby hormonal contraception was associated with lower total FSFI scores and lower desire and arousal scores than no contraception and non-hormonal contraception only. Other variables such as stress, pregnancy, smoking, relationship and wish for children had an important impact on sexual function as expected according to earlier studies.

Conclusions. The prevalence of students at high risk for FSD was consistent with the literature although domain subscores differed from samples previously described. The contraception method has a significant effect on the sexual functioning score and women using contraception, especially hormonal contraception, had lower sexual functioning scores. Stress and relationship among other variables were found to be associated with sexual function and may thus provide insight into the etiology of sexual disorders. **Wallwiener CW, Wallwiener L-M, Seeger H, Mück AO, Bitzer J, and Wallwiener M. Prevalence of sexual dysfunction and impact of contraception in female german medical students. J Sex Med **;**:**–**.**

Key Words. Female Sexual Dysfunction; Contraception; Libido; FSFI; Desire

Introduction

It is now widely accepted that sexuality is a fundamental part of human life and that sexual problems have a (clear) negative impact on both quality of life and emotional well-being, regardless of age [1]. Female sexual dysfunction (FSD) is a

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very common disorder, with an estimated prevalence of having at least one sexual dysfunction of about 40% [2–4].

In Germany, FSD prevalence of 38% was suggested in 2008 [5], and estimates of 38–43% in adult women have been made in surveys in the USA [2,6]. Most common was low desire, reported by just under a third of those surveyed, with little variation by age. Based on the well-established Female Sexual Function Index (FSFI) by Rosen et al. [7], the prevalence of women in heterogeneous populations "at high risk" for FSD ranged from 24% in Pavia, Italy [8], 33% in Finland [9], and 43% in Istanbul, Turkey [10], to 63% for medical students in the USA [11].

Such estimates of FSD are, however, very controversial, because they vary up to tenfold across instruments, thereby affecting reported risk factors [12]. Differences between sample types, age range of participants, data collection, time frames, and definitions of sexual dysfunction are responsible for the different estimates [13,14]. Even with well-established instruments such as the FSFI in relatively similar samples, different cutoffs for female sexual dysfunction result in different estimates. A further complicating factor is that sexual problems are particularly prevalent among women seeking routine gynecological care, but are less common in community samples [15,16].

Oral contraception (OC) has been suggested as a possible modulator of female sexual function [17,18]. However, published results are controversial, and the extent and nature of the effects remain unclear [19–21].

Female sexual function in today's medical students has been poorly studied, although they represent a relatively homogenous, young and healthy study population. We are aware of only an investigation by Shindel et al. [11] into sexual dysfunction in female medical students in the USA. While this study provided interesting results, they cannot be extrapolated to other population subgroups because the sample was so small. Shindel et al. found that of 78 women, 63% were at high risk of sexual dysfunction based on validated FSFI scoring, and that problems with the following were reported: pain (39%), orgasms (37%), desire (32%), sexual satisfaction (28%), lubrication (26%), and arousal (24%). This corresponds broadly with normative data for 18–29-year-olds from the 1992 National Health and Social Life Survey [2].

The objective of this survey was to assess sexual function and the prevalence of sexual dysfunction in female medical students in greater numbers than previously using an online survey, and to analyze the potential impact of OC on sexual function.

Methods and Main Outcome Measures

The University of Tuebingen Ethics Committee (IRB) approved the study and study protocols were subsequently submitted and approved by the collaborating centers' IRBs.

Medical students at the Universities of Tuebingen, Munich (Technical University and Ludwig-Maximilians-University), Freiburg, Marburg, Heidelberg, and Regensburg were informed about the online study and asked to participate via a standardized circular e-mail sent to the dean's student mailing list and via standardized messages posted on the online bulletin boards of all participating medical schools. All mail was sent and all messages posted in the 48 hours after the online questionnaire was opened for access. The questionnaire was closed exactly 14 days after launch. Anonymity was stressed in all communications. Submission of the completed questionnaire was considered as consent to participate in the study.

The FSFI by Rosen et al. [7] was used to analyze female sexual function. This is a well-established tool [22] and was validated in the German language [23]. The FSFI is designed to investigate problems with sexual function during the past 4 weeks and consists of 19 questions that measure six dimensions of female sexual function: desire, arousal, lubrication, orgasm, satisfaction, and pain. The response options on Likert-type scales are used to calculate the separate domain scores and an overall score for sexual function. We are not aware of any instruments especially validated for use in bisexual or homosexual individuals, although the FSFI has been validated for use in lesbians [24]. Thus, in the introductory text of the questionnaire, homosexual and bisexual women were advised to interpret the questionnaire so as to best accommodate their understanding and definitions of sexual activity.

Scores were then calculated and statistically analyzed. According to Wiegel et al. [21], women with total FSFI scores of less than 26.55 are classified as "at high risk" for sexual dysfunction. Several other cutoffs have been proposed. Shindel et al. [11] suggested a different approach to define cutoffs for the subdomains of the FSFI: an arbitrary score of 33% or less of the maximum score in each domain. We agreed with Shindel et al. that

classifying only individuals reporting "rarely/very little" or "never/not all" in any category as potentially dysfunctional was reasonable. We used both approaches in our study.

In addition to the FSFI questions, a further 11 questions were asked. Five dichotomous questions inquired whether participants had been sexually active in the last 4 weeks, wanted children, had been in a relationship for the past 6 months, were currently pregnant, or had been pregnant in the past, and whether they were smokers. Participants were provided option menus to select their usual means of contraception and changes in contraception, age, and level of education. In a further question, participants were asked to rate changes in the frequency of intercourse, presence of sexual ideation, sexual desire, ability to orgasm, lubrication, and pain associated with vaginal penetration over the past 4 weeks on a scale from "strongly decreased" to "strongly increased" or to choose the option "no change". Finally, participants judged the influence of stress and their partner on their sex life over the past 4 weeks in two questions on a scale from "very strongly" to "not at all".

All responses were stored in a database. Software to collect and store the data was purchased from Aescon Medical (Tuebingen, Germany). Each participant's responses were automatically scanned for inconsistencies by a programmed algorithm. Data were considered inconsistent if (i) participants negated recent sexual activity at some point and gave answers consistent with recent sexual activity at another point, or (ii) participants gave less than university entrance qualification as the highest educational level since the aim was to form as homogenous a sample of young female medical students as possible. All cases with possible inconsistencies marked by the algorithm were reviewed by two of the authors blinded to scores and excluded from the analyses by consensus.

Statistical Analysis

The distribution of FSFI scores is left skewed. Medians, ranges, and quartiles were therefore chosen to describe this variable. For median differences between FSFI subgroup scores, 95% confidence intervals (CIs) were calculated using bootstrap methods. Correlations between FSFI scores and numbers (e.g., cigarettes per day) were estimated with Spearman's correlation coefficient rs. Comparisons of subgroup proportions using OC were described using proportional differences with 95% CIs. The differences in total FSFI scores by factors age, former pregnancy, wish for children, method of contraception, partnership, and smoking status were estimated by a multifactorial linear regression model where the response variable was transformed by squaring to achieve residual normality, which was verified by quantile-quantile plots. Homoscedasticity was assessed by residuals by predicted plots, and outliers with high leverage were identified by calculating Cook's distance. Quality of fit is recorded as the adjusted coefficient of determination (R_{adj2}). We show here the corresponding multifactorial analysis of variance (ANOVA) model and spare regression coefficients which are not easily identifiable as a result of the transformation. A significance level of 5% was chosen. Tukey's Honestly Significant Difference test was used as post hoc test. All statistical analysis was performed with R version 2.7.2.

Results

1,219 respondents submitted completed questionnaires. After screening the data for completeness and unserious responders, 1,086 data sets were included in the analysis. The response rate was between 15 and 20% and the data represent roughly 2.5% of the overall female German medical student population.

Demographic data are presented in Table 1. Most participants had used contraceptives in the previous 6 months (87.4%), and almost all (97.3%) had been sexually active in the previous 4 weeks. The three most common means of contraception were OC (69.5%), condoms (22.5%), and the vaginal contraceptive ring (7.3%). The majority of respondents (81.1%) were in stable relationships (had the same partner for at least the past 6 months).

Sexual Dysfunction

The subscores for arousal, lubrication, orgasm und pain and therefore also the total FSFI score for women who were not sexually active in the past 4 weeks have to be interpreted differently from those who were sexually active and were therefore excluded from the analysis of the FSFI scores. Table 2 shows the FSFI scores and the proportion of participants who were below the cutoffs for sexual dysfunction and therefore at high risk for FSD. For the total FSFI score, the cutoff of 26.55 by Weigel et al. was used, and a cutoff of 33% was used for the subscores. 342 (32.4%) participants were considered at high risk for sexual dysfunction based on the total FSFI score. If a cutoff of 33% of the maximal possible score was applied for the

Table 1 Demographic data

	All participants	
Participants (after screening for unserious responders)	Number 1,086	Percentage 100.0
Contraception in past 6 month		
Yes	945	87.0
No	141	13.0
Method of contraception in past 6 month(multiple answers possible)		
Oral contraceptives (OC) total	752	69.2
Contraceptive implant	8	0.7
Intrauterine methods	19	1.7
Vaginal contraceptive ring	78	7.2
Condoms	243	22.4
Fertility awareness	17	1.6
Other contraception	8	0.7
Sexually active in the past 4 weeks		
Yes	1,057	97.3
No	29	2.7
Age (years)		
<25	856	78.8
≥25 and <35	223	20.5
>35	7	0.6
Stable relationship		
Yes	869	80.0
Mean duration	3.2 (std 2.6) years	
No	217	20.0
Pregnancy		
No pregnancy	1,046	96.3
One pregnancy	29	2.7
More than one pregnancy	11	1.0
Pregnant in the last 2 years		
Yes	26	2.4
No	1,060	97.6
Active wish for children		
Yes	37	3.4
No	1,049	96.6
Smoking		
Yes	131	12.1
Mean number of cigarettes/day	8.7 (std 6.8) cigarettes / day	
No	955	87.9

FSFI total score, the at-risk fraction would be 0.3%. For the subscores, 61 (5.8%) were considered at high risk for sexual desire dysfunction, 11 (1.0%) for arousal, 13 (1.2%) for lubrication, 92 (8.7%) for orgasm, 28 (2.6%) for satisfaction, and 12 (1.1%) for pain dysfunction.

Contraception and Sexual Function

In this analysis, 11 women were excluded who used both oral and non-oral hormonal contraception or hormonal and nonhormonal contraception, leaving 1,046 participants. The total FSFI score and subscores for desire and arousal were compared between participants with different methods of contraception: oral (hormonal) contraception (OC), non-oral hormonal contraception (NOHC), nonhormonal contraception (NHC), and no contraception (NC) (Figure 1). All three scores differed between contraception methods. The highest total FSFI score was found for NHC, followed by NC and OC, and NOHC was lowest. For desire, NC and NHC had the same score, followed by OC and NOHC, and for arousal, the highest score was found for NHC, followed by NOHC, NC, and OC.

In a multifactorial ANOVA model, the method of contraception and also the smoking status were significant factors for the total FSFI scores (P-values < 0.0001 and 0.005) with higher total FSFI scores for smokers (Table 3). Other factors included-age, former pregnancy, wish for children, and partnership status-were no significant (all P-values > 0.15). The coefficient of determination R_{adj} [2] was 0.03. Post hoc tests showed a significant difference for total FSFI between the NHC group and NC, NOHC, and NC (P-values < 0.01), all other pairwise comparisons were not significant (P-values > 0.4). A model including also interactions of degree 2 gave the same result (not shown).

Epidemiological Factors and Sexual Function

Comparison of median scores and CIs showed that women not in stable relationships had higher desire scores (difference of the medians was 0.6

Table 2 FSFI scores in participants (sexually active in past 4 weeks) and proportion at risk for sexual dysfunction

Scores	Median	25% quartile	75% quartile	Range	Number analyzed	Number "at risk for sexual dysfunction"	Percentage "at risk for sexual dysfunction"
FSFI total	28.6	25.5	31.6	9.5–36.0	1,057	342	32.4
Desire	3.6	3.0	4.2	1.2–6.0	1,057	61	5.8
Arousal	5.1	4.2	5.7	1.2–6.0	1,057	11	1.0
Lubrication	5.7	4.8	6.0	1.2–6.0	1,057	13	1.2
Orgasm	4.8	3.6	5.6	0.8–6.0	1,057	92	8.7
Satisfaction	5.2	4.0	6.0	1.2–6.0	1,057	28	2.6
Pain	5.2	4.4	6.0	1.2–6.0	1,057	12	1.1

FSFI = Female Sexual Function Index.

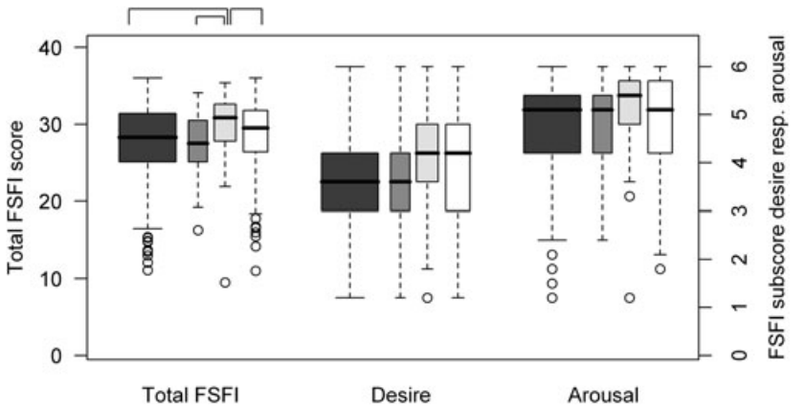

Figure 1 Boxplots of FSFI total scores and subscores for desire and arousal of different contraception groups. Oral (hormonal) contraception (OC) is shown in darkgrey, non-oral hormonal contraception (NOHC) in grey, nonhormonal contraception (NHC) in lightgrey, and no contraception (NC) in white. Box size is proportional to the number of observations in each group. Medians, quartiles, and ranges are shown. Circles indicate outliers: more than 1.5 times the interquartile range from the box. On the top, pairwise comparisons of total FSFI scores of contraception groups significant in an ANOVA post hoc test are indicated.

[95% CI 0.6–0.6]) but lower orgasm scores (–0.4 [95% CI –0.8 –0.2]). Smokers had a higher median total FSFI score (1.5 [95% CI 2.3–0.2]) and higher median pain score (0.8 [95% CI 0.8–0.4]) than nonsmokers. 70.4% of nonsmokers used OC for birth control as opposed to 60.3% of smokers. A history of pregnancy and age higher than 25 years were associated with a lower median pain score (–0.8 [95% CI –0.8–0.4], respectively, –0.4 [95% CI—0.4–0.8]). The scores for women with and without an active wish for children differed only slightly.

Women who reported a strong negative influence of stress also had a low median FSFI subscore for desire ($r_s = -0.31$). Those who stated a strong negative influence of their partner had a low median total FSFI score ($r_s = -0.28$) and low median satisfaction subscore ($r_s = -0.40$). An increase in intercourse frequency in the past 6 months correlated positively with the total FSFI score ($r_s = 0.29$) and satisfaction subscore ($r_s = 0.38$), and an increase in ability to reach orgasm correlated positively with total FSFI score ($r_s = 0.33$) and the desire ($r_s = 0.29$), arousal ($r_s = 0.32$) and orgasm subscores ($r_s = 0.25$). The length of the relationship correlated negatively with the desire subscore for women in a stable relationship ($r_s = -0.26$). All other factors (e.g., number of cigarettes per day) correlated only weakly or not at all with the total FSFI score.

Women in stable relationships were more likely to use oral rather than other or no contraception (Figure 2). Also nonsmokers, women who have not been pregnant and those with no active wish for children were more likely to use OC than other or no contraception. All participants were included in this analysis.

Discussion

This survey assessed sexual function in female German medical students and the effects of contraception on sexual function using datasets from 1,068 completed questionnaires based on the

Table 3 Multifactorial ANOVA model results for response total FSFI score

Factor	Df	Sum of squares	Mean square error	F-value	*P*-value
Age	1	25,978	25,978	0.478	0.489
Partner	1	112,292	112,292	2.066	0.151
Preg	1	88,572	88,572	1.630	0.202
Kiwu	1	29,516	29,516	0.543	0.461
Smoke	1	428,326	428,326	7.881	0.005
Contraception	3	1,561,254	520,418	9.576	<0.0001
Residuals	1,037	56,357,958	54,347		

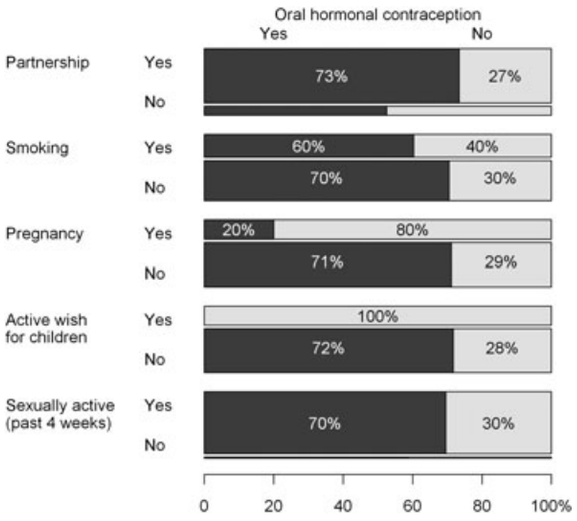

Figure 2 Proportion of patients using oral contraception by selected factors. Bar widths are proportional to numbers in each group.

German FSFI. Only four published surveys have so far specifically studied sexuality in medical students. Two of these were conducted almost 40 years ago [25,26], the third dealt with Chinese students' attitude towards sexuality rather than sexual function [27], and the fourth was a pilot study in only 78 women [11].

Almost 90% of our participants had used contraception and almost all had been sexually active in the previous 4 weeks. 80% were in a stable relationship. The three most common means of contraception were OC, condoms, and the vaginal contraceptive ring. Users of hormonal contraception were more likely to be women in stable relationships who were nonsmokers, had not been pregnant before, and did not have an active wish for children, which might be expected given the contraindications for OC.

In general, sexual dysfunction can be subcategorized into diminished desire, interest and sexual fantasies, arousal problems (mental and physical), inability to achieve orgasm, and pain associated with vaginal penetration [4]. Interpersonal, psychological, physiological, medical, social, and cultural factors have been identified as associated with FSD [28,29]. Sexual dysfunction has been linked in particular with age, depression, sexual and physical abuse in adulthood, global mental health function, and alcohol [6] and emotional intimacy [30].

Based on the total FSFI score, 32.4% of participants were "at high risk" for sexual dysfunction. With regard to subscores, this was the case for 8.7% for orgasm, 5.8% for desire, 2.6% satisfaction, 1.2% for lubrication, 1.1% for pain, and 1.0% for arousal. When interpreting these numbers, however, it has to be borne in mind that the cutoff for the total FSFI score suggested by Wiegel et al. in wide use does not necessarily apply for our study sample [21] and that the cutoffs for subscores suggested by Shindel et al. [11] are purely speculative. Furthermore, it has to be considered that these are different cutoffs and that therefore the numbers of at-risk fractions for the total score and the subscores differ greatly. Despite the FSFI's widespread use and its descriptive validity, it does not measure the individual distress related to the sexual function or dysfunction. It is therefore to be stressed that these numbers are based mainly on quantitative ratings of events over a 4-week period.

Estimates of the prevalence of sexual dysfunction differ greatly because of different sample sizes, populations, age ranges, and instruments [12–14], and also because of different cutoff levels for the same instrument. Moreover, sexual problems tend to be higher in clinical samples and women seeking medical attention than in community samples [10,15,16]. This is further complicated because physicians are not confident in diagnosing hypoactive sexual desire disorder and rarely screen patients for this [31]. Here, it has been suggested that both physicians' attitudes to sex and their sex education during their medical training play an important role [32,33].

The prevalence of FSD of 32% in our German medical students based on the total FSFI score was similar to that in some studies [5,19], but was lower than the 43% determined by the 1992 National Health and Social Life Survey (NHSLS) in the USA in women aged 18–29 [2], and much lower than the 63% found by Shindel et al. in their sample of 78 female US medical students [11]. Compared with Laumann's normative data, we found lower rates of dysfunctions for desire (6% vs. 32%), orgasm (9% vs. 26%), pain associated with vaginal penetration (1% vs. 21%), and lubrication (1% vs. 19%) [2]. Shindel's figures for problems with pain, orgasms, desire, sexual satisfaction, lubrication, and arousal, although similar to normative data for 18–29-year olds in the 1992 NHSLS study, also differed greatly from our findings. In a review in 1990, however, a prevalence of 5–10% for inhibited female orgasm was given for community samples [16], which agrees with our prevalence of orgasm disorder of 8.7%. The most common types of sexual dysfunction in the literature and in our

patients were problems with orgasm [34,35] and low sexual desire [2,36,37]. One reason for these differences may be that we studied a large but relatively homogenous collective as opposed to the other studies or it may be a selection bias towards students who decided to participate in our study or cultural differences in the perception of sexual dysfunction. Also, the difference in the applied instruments may contribute to this disparity.

Different methods of contraception were associated with significant differences in sexual function, as indicated by FSFI scores in female German medical students. Women using nonhormonal contraception or no contraception had higher total, desire and arousal scores than women using OC. The possible association between contraceptives and sexual function remains controversial in the literature. It has been reported that women experience positive effects [18,19,21], negative effects [17,38], and no effects [9,19,21,39] on libido and sexual function during OC use, a controversy summarized by Davies et al. in their 2004 review [20]. Further complicating this discussion are reports of cultural differences in the impact of contraceptives [40].

Our data show that hormonal contraception in particular, was associated with lower desire and arousal scores when compared with other contraceptives. Whether there exists an underlying effect of contraceptives or this is simply because of one or more relevant differences between women using contraceptives or no contraceptives such as the ability to enjoy oneself or the perception of one's own body, is speculative. Furthermore, the complexity of sexual desire and other complicating factors such as positive and negative influences in relationships have to be considered. The fact that this is a cross-sectional study without randomization further limits conclusions concerning the relationship between contraceptive methods and sexual function or dysfunction. One explanation for a possible impact of OC on sexual function may be that they have been found to decrease the circulating levels of androgens by direct inhibition of androgen production in the ovaries and by a marked increase in the hepatic synthesis of sexual hormone binding globulin (SHBG), the major binding protein for gonadal steroids in the circulation [41]. The combination of these two mechanisms may lead to low circulating levels of free and bioavailable testosterone [42–45] which is needed to (i) stimulate sexual desire and (ii) regulate genital blood flow and the structural and functional integrity of the genitals.

One factor that had a clear association with desire in our study was stress: increases in perceived stress were associated with lower desire scores. This agrees with Witting's finding that psychological distress was positively associated with every dimension of the FSFI, except desire [9]. Interestingly, Bancroft et al. [30] found that the best predictors of sexual distress were mental and physical health and not sexual function problems.

Studies have shown that greater satisfaction with a relationship overall was associated with greater sexual satisfaction and fewer sexual function problems [19]: the stronger the emotional intimacy with the partner, the less the sexual distress [30]. In our study, women in stable relationships had higher orgasm scores but lower desire scores. However, the longer the partnership lasted, the more the desire scores decreased. An increase in intercourse frequency was associated with higher FSFI total and satisfaction scores, while an increase in ability to achieve orgasm was associated with higher total, desire, arousal, and orgasm scores. This seems plausible, given that sexual desire was reported as increased in new relationships [46], but differs from Shindel's finding that women in relationships had higher FSFI scores for desire and satisfaction [11]. Again, this may have been attributable to the different sample sizes and instruments applied.

A further factor that can affect female sexual function is pregnancy. Witting et al. reported that multiparous women had fewer orgasm problems than nulliparous women. Nulliparous women had more pain problems and were less sexually satisfied [19]. In our study, a history of pregnancy was associated with less pain, which confirms the finding by Witting et al. However, only 3.6% of our participants had been pregnant.

Interestingly, in our sample, smokers had a higher total FSFI total score. One possible explanation is that smokers might have greater ability to enjoy themselves or that the association with smoking is confounded by other factors. Another speculative explanation is based on reports that smokers have lower estrogen levels than nonsmokers [47]. While it has been demonstrated that elevated estrogen levels induced by OC [41] lead to decreased free-testosterone levels via an increase in SHBG [42–45], the reverse may be true for smokers: lower estrogen levels might result in higher free-testosterone levels. Alternatively, in our group, smokers were less likely to use OC and may therefore, as a group, lack the estrogen-

inducing and thereby testosterone-lowering OC effect. All of these explanations represent only a little part of all possible mechanisms.

The link between age and sexual dysfunction [48] is controversial, with studies suggesting that sexual dysfunction declines with age [2] and others suggesting the opposite [19,36]. The age range of our participants was too narrow to establish associated differences.

Limitations

We decided on an online approach to maximize access to the medical student community because all collaborating medical schools offer Internet access. Numerous instruments have been reported to be equally as reliable as paper when administered via the Internet [49,50]. Internet findings have also been shown to be superior to paper questionnaires with respect to completeness of data [50,51]. Furthermore, internet participation in online surveys is at least as good as if not better than paper surveys, with less recruitment and follow-up effort [49]. Joinson et al. reported in 1999 that online surveys may even result in more honest answers [52]. Potential disadvantages of online questionnaires are unserious and repeat responders. It has, however, been reported that Internet findings are not adversely affected by these groups [50]. Because we took measures to detect unserious responders (inconsistent responses), we feel confident that our results accurately represent the population studied. We also assume that serious participants entered true information since anonymity was assured.

Despite our strict plausibility checks, however, selection bias cannot be ruled out. We felt that a homogenous sample was imperative in meeting the study's objectives, and that this outweighed the risk of selection bias. Almost all participants excluded because the education level was too low met other exclusion criteria. A further form of bias that we considered was participation bias: Women with perceived sexual problems might have felt more inclined to participate than women with no sexual problems or that students with oral contraceptive use exposed recently to publications about a possible effect of these contraceptives on desire, etc. may be overrepresented. Moreover, the possibility of reporting bias cannot be ignored, although whether participants would tend to over or underreport sexual difficulties is open to speculation. It also has to be borne in mind that sexual function is influenced by sexual attitude. In this context, Papaharitou et al. demonstrated that the sexual attitude of female students in the health professions was more conservative than the attitude of male students [53]. As sex education of medical students may affect sexual attitude, this factor also has to be taken into consideration [33]. It is not possible to estimate the impact of these effects on our study.

When interpreting the results, the design (cross-sectional study) has to be considered as well as the fact that this is a convenience sample rather than a random sample. We had no control group and were only able to compare our findings to prior studies. Also, the FSFI questionnaire uses the Likert-scale approach, unlike many community studies in which the results are collected with yes/no questions. The extent of comparison of our findings with other findings was therefore limited. Also, our investigation was targeted at medical students and the age range was therefore narrow. Although this reduces variation in responses, it also restricts generalization to other age groups. Finally, the low coefficient of determination of the ANOVA model suggests that the factors considered can only explain a small fraction of the variability of total FSFI scores. Therefore, other factors that are not covered in the model must have an influence, too. It might be the case that there exists a multitude of factors with each only very little impact.

Conclusion

To our knowledge, this is by far the largest study with a validated instrument to assess sexual dysfunction in female medical students. The prevalence of students at high risk for FSD in this multi-institutional study was consistent with the literature, although domain subscores differed from previous investigations. Women using contraception, especially hormonal contraception, had significantly lower sexual functioning scores. Stress, relationship, smoking, and pregnancy among other variables were found to be associated with sexual function and may assist in elucidating the reasons for sexual disorders when specifically evaluated in future studies.

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Original research article

Effects of sex hormones in oral contraceptives on the female sexual function score: a study in German female medical students☆,☆☆,★

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Abstract

Background: The survey was conducted to compare the influence of sex hormones in oral contraceptives (OCs) on female sexual function.
Methods: One thousand eighty-six female German medical students completed an online-based questionnaire incorporating the Female Sexual Function Index (FSFI). Oral contraceptives used were classified into those containing androgenic or antiandrogenic progestins and by ethinylestradiol (EE) dosage (20 mcg, 30 mcg and >30 mcg). Female Sexual Function Index scores in women using OCs were compared to those in nonusers.
Results: Seven hundred fifty-two of 1086 participating women used OCs. No statistically significant differences in FSFI scores were found among women using OCs containing androgenic or antiandrogenic progestins, nor were any seen between different EE dosages. In general, OC users had lower FSFI scores than nonusers.
Conclusion: Female Sexual Function Index scores were negatively influenced by the use of OCs. However, the impact of an androgenic or antiandrogenic progestin content or different dosages of EE as modulating factors of female sexual function seems negligible.

Keywords: Libido; Contraception; Female sexual dysfunction; Desire; Arousal; FSFI; Online study

1. Introduction

Female sexual function is influenced by a multitude of factors including sexual hormones (estrogens, androgens and progestins), which elicit different effects on vaginal tissue and the central nervous system [1]. Oral estrogens increase sex hormone-binding globulins (SHBG) — a transport protein for sex hormones — in the liver [2], which can be enhanced or reduced by adding progestins, depending on their androgenic or antiandrogenic properties. Testosterone has a high affinity for SHBG, and high SHBG serum levels can therefore reduce free testosterone levels, which are important for sexual function.

An association between oral contraceptives (OCs) and sexual dysfunction has already been suggested [3], although the extent of the effects remains unclear [4,5]. Oral contraceptives contain the synthetic estrogen ethinylestradiol (EE) and progestins with partial androgenic and antiandrogenic properties that can influence serum SHBG levels [6] and, thus, potentially also female sexual function.

The aim of this investigation was to study and compare possible correlations between progestins with androgenic and antiandrogenic properties and EE dosage on the sexual activity of female medical students using OCs. The evaluation was conducted using an Internet-based questionnaire incorporating a validated scale for female sexual function.

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2. Methods

This study was approved by the University of Tuebingen's Ethics Committee (institutional review board [IRB]) and subsequently submitted to and approved by the collaborating centers' IRBs.

We used the well-established Female Sexual Function Index (FSFI) by Rosen et al. [7] to analyze female sexual function [8]. The questionnaire was validated in the German language [9]. In brief, a total score (Questions 1–19) is obtained in addition to six subscores: desire (Q1–2), arousal (Q3–6), lubrication (Q7–10), orgasm (Q11–13), satisfaction (Q14–16) and pain (Q17–19). In addition to the FSFI questions, we also asked 11 questions concerning the participants' means of contraception and changes in contraception and recent sexual activity.

The resulting questionnaire was implemented as an online version, and medical students at the Medical Schools of the Universities of Tuebingen, Munich (Technical University and Ludwig-Maximilians-University), Fribourg, Marburg, Heidelberg and Regensburg were informed about the study, and women were asked to participate via a standardized circular E-mail sent to the Dean's student mailing list and via standardized messages posted on the online bulletin boards of all participating medical schools. Submitting the completed questionnaire was considered consent to participate in the study.

The answers from each participant were then automatically scanned for inconsistencies by a programmed algorithm. Data were considered inconsistent if (i) participants denied recent sexual activity at some point and gave answers consistent with recent sexual activity at another point or (ii) gave less than university entrance qualification as the highest level of education. All cases with possible inconsistencies flagged by the algorithm were reviewed by two of the authors blinded to the scores and were excluded from the analyses by consensus.

The mean FSFI scores were calculated and statistically compared for OCs containing androgenic progestins and OCs containing antiandrogenic progestins. The effects of OCs were also compared by the following dosage groups: 20 mcg EE, 30 mcg EE and >30 mcg EE.

The Kruskal–Wallis and Mann–Whitney tests were used for statistical analysis. A p value <.5 was set as statistically significant. When comparing groups using OCs vs. women not using OCs, the FSFI scores were described using median differences with 95% confidence intervals (CIs). The statistical analysis was performed with R version 2.7.2 (R Project; R Foundation, Vienna, Austria).

3. Results

After screening for inconsistencies, 1086 completed questionnaires were included in the analysis.

3.1. Demographic data

Age distribution revealed 856 women were under 25 years, 223 between 25 and 35 years and 7 older than 35 years. Of all women participating, 945 were using contraception and 141 women were not. Among the women using contraception, 752 women were OC users, of whom 404 used OCs with antiandrogenic progestins and 263 OCs with androgenic progestins. One hundred thirty-two preparations contained 20-mcg EE, 450 contained 30 mcg and 62 contained >30 mcg. Table 1 lists the OCs used and their classification.

3.2. Androgenic vs. antiandrogenic progestins

Fig. 1 shows the total FSFI scores for the groups with androgenic and antiandrogenic progestins. The median scores were 28.3 and 28.5 and were not statistically significantly different. Table 2 lists the medians for the FSFI subscores, which also did not differ significantly.

3.3. Impact of different EE dosages

Fig. 2 shows the total FSFI scores by EE dosage. The median total score for the 20-mcg group was 28.3, for 30-mcg group, 28.6, and for the >30-mcg group, 27.3. The scores did not differ significantly. Table 2 sum-

Table 1
Oral contraceptives used with numbers and qualities

OC used	No. of users	Percentage of total OC users	EE content (mcg)
Antiandrogenic gestagenic property			
Dienogest	176	23.40%	30
Chlormadinone acetate	101	13.43%	30
Drospirenone	106	14.09%	30
Cyproterone acetate	32	4.26%	35
Chlormadinone acetate	8	1.06%	50
Androgenic gestagenic property			
Levonorgestrel	80	10.64%	30
Levonorgestrel	71	9.44%	20
Desogestrel	34	4.52%	20/30
Desogestrel	32	4.25%	20
Desogestrel	15	1.99%	30/35
Desogestrel	14	1.86%	40
Norgestimate	9	1.20%	35
Levonorgestrel	7	0.94%	30/40
Desogestrel	2	0.27%	30
Norethindrone	1	0.13%	30
Desogestrel	1	0.13%	50
Norelgestromin	1	0.13%	600 (patch)
Gestodene	1	0.13%	30
Norethindrone	1	0.13%	35
Other OCs[a]	60	7.98%	NA
Sum	752	100.00%	

NA indicates not applicable.

[a] Oral contraceptives with controversially discussed partial gestagenic properties.

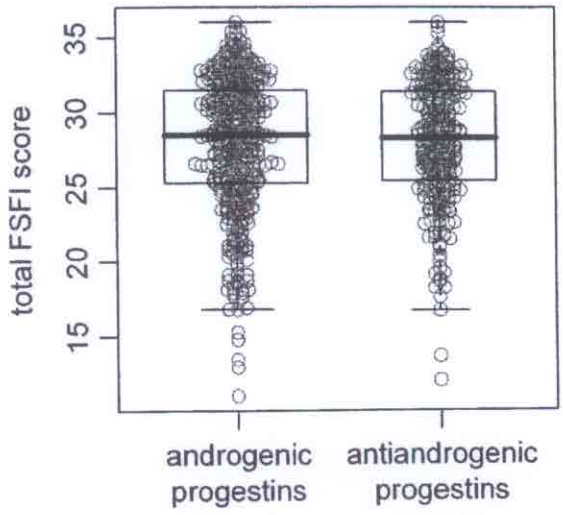

Fig. 1. Box-whisker plot for total FSFI score for OCs containing progestins with partial androgenic or antiandrogenic properties. Box size is proportional to the number of observations in each group. Horizontal lines represent medians, quartiles and ranges. Circles indicate outliers: more than 1.5 times the interquartile range from the box.

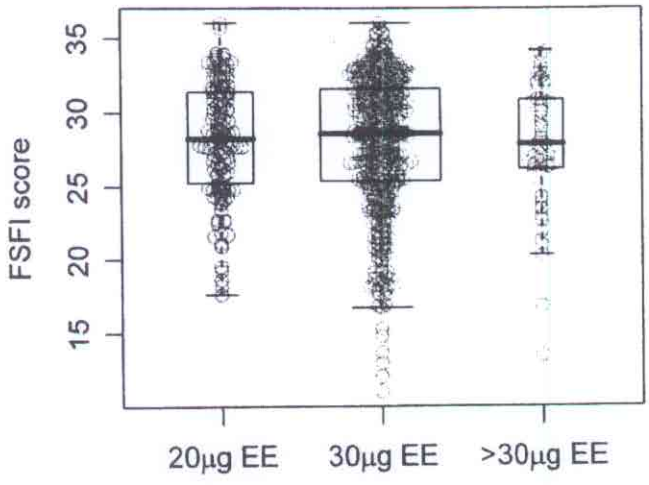

Fig. 2. Box-whisker plot for total FSFI score for OCs with different EE dosages. Box size is proportional to the number of observations in each group. Horizontal lines represent medians, quartiles and ranges. Circles indicate outliers: more than 1.5 times the interquartile range from the box.

marizes the medians for the subscores, which also did not differ significantly.

3.4. *Oral contraceptives vs. nonhormonal contraception and no contraception at all*

OC users had lower median FSFI scores than those using nonhormonal contraception or no contraception at all. Since the 95% CIs of the differences in median FSFI scores do not include 0, differences would be considered significant. Table 3 lists the differences expressed as medians with 95% CIs.

4. Discussion

It has been reported that female sexual dysfunction had a prevalence of 38% in German women between 20 and 80 years old, and the frequency increased with age [10].

Ovarian dysfunction and hormonal disbalance of endogenous or iatrogenic origin are associated with reduced sexual desire and disturbance of sexual arousal [11]. Testosterone may play a key role in mediating hormonal effects on sexual function, as may factors that induce changes in free testosterone serum levels [12]. Compounds that bind to the androgen receptor and trigger androgenic effects may also be involved. Progestins used in OCs possess partial androgenic or antiandrogenic properties [2], and these progestins can modulate the synthesis of SHBG, an important regulator of free testosterone serum levels. It is well known that EE can influence the synthesis of various liver proteins, including SHBG, and that SHBG synthesis may be dependent on the EE dose [2]. These hormonal functions led to the hypothesis that the sex hormones in OCs might influence female sexual function via their modes of action, and that these influences may be dose dependent.

Graham et al. [13] investigated the serum levels of total testosterone, free testosterone and dehydroepiandrosterone sulfate during OC intake using the same progestin. Significant decreases were found after 3 months. Their findings also suggested a statistical correlation between low total testosterone and free testosterone levels and the frequency of sexual thoughts. However, some women showed no loss of sexual interest despite low testosterone

Table 2
Female Sexual Function Index subscores for OCs containing progestins with partial androgenic or antiandrogenic properties and for OCs with different dosages of EE

		Q1–2	Q3–6	Q7–10	Q11–13	Q14–16	Q17–19
		Median (25/75 percentile)	Median (25/75 percentile)	Median (25/75 percentile)	Median (25/75 percentile)	Median (25/75 percentile)	Median (25/75 percentile)
Progestins–androgenic, n=263		3.6 (3.0/4.2)	5.1 (4.2/5.4)	5.7 (5.1/6.0)	4.8 (3.6/5.6)	5.2 (4.4/5.6)	5.2 (4.4/6.0)
Progestins–antiandrogenic, n=404		3.6 (3.0/4.2)	5.1 (4.2/5.4)	5.7 (4.8/6.0)	4.8 (3.2/5.6)	5.2 (4.0/6.0)	5.2 (4.4/6.0)
EE dosages	20 mcg, n=149	3.6 (3.0/4.2)	5.1 (4.2/5.4)	5.7 (5.1/6.0)	4.6 (3.6/5.6)	5.2 (4.4/6.0)	5.2 (4.4/6.0)
	30 mcg, n=509	3.6 (3.0/4.2)	5.1 (4.2/5.4)	5.7 (4.8/6.0)	4.8 (3.6/5.6)	5.2 (4.0/6.0)	5.2 (4.4./6.0)
	>30 mcg, n=70	3.6 (2.4/4.2)	5.1 (3.9/5.7)	5.7 (5.1/6.0)	4.8 (4.4/5.6)	5.2 (4.4/5.6)	5.2 (4.4/6.0)

Table 3
Median FSFI scores of OC vs. nonhormonal contraception or no contraception at all

Group	Median FSFI scores	Difference in medians with 95% CI	No.
OC	28.3	1.2 (0.3–2.0)[a]	735
No contraception	29.5		133
OC	28.3	2.7 (1.9–3.6)[a]	735
Nonhormonal contraception	31.0		98

[a] 95% CIs of the differences in median FSFI scores but do include zero. Differences are therefore significant for OC vs. no contraception and for OC vs. nonhormonal contraception.

levels. The authors concluded that some women might be more sensitive to changes in testosterone levels. Free testosterone serum levels with use of 25- and 35-mcg EE and the same progestin were investigated by Greco et al. [14], who found that the lower EE dosage was associated with a smaller reduction in free testosterone. Two recent investigations studied the effect of oral OCs on SHBG serum levels and the possible correlation with sexual function. Panzer et al. [15] investigated SHBG serum levels in 124 women with sexual dysfunction who were users or nonuser of OCs. The SHBG levels were up to four times higher in users, and total FSFI scores were also lower. Warnock et al. [16] measured SHBG, total testosterone and free testosterone serum levels in 106 women with sexual dysfunction, 43 of whom were OC users. Among OC users, SHBG levels were higher and total and free testosterone levels lower than in nonusers, but both had sexual dysfunctions.

In our Internet-based study based on the validated and well-established FSFI [5,7], we found no significant difference between OCs containing androgenic and antiandrogenic progestins, nor did we observe any relationship between EE dosage and sexual function, which was not consistent with some of the studies mentioned above. However, the effects in those studies were found in women with diagnosed sexual dysfunction, whereas we studied a large homogenous sample of healthy young female medical students. It is worth noting in this context that sexual problems have been reported to be particularly prevalent among women seeking routine gynecological care [17], whereas they are less frequent in community samples. One review showed the prevalence of inhibited female orgasm to range from 18% to 76% in clinic settings, but only 5% to 20% in community samples [17,18].

Comparison of total FSFI scores in student OC users and those using nonhormonal contraception or no contraceptives showed that OCs had a negative influence on sexual function. The influence of OCs on sexual function and desire, in particular, is controversial [3,5]. A review by Davis and Castano [4] found variable results in controlled and uncontrolled studies, with both positive and negative effects.

Our study had several limitations. First, the results were collected in a narrowly defined population, female medical students. Although this simplifies interpretation for this specific group, the results cannot be applied to broader populations. Second, Internet-based data collection may differ from traditional methods with respect to response rate and data quality, although Web-based studies have been demonstrated to be reliable [19,20]. Third, we did not collect laboratory measurements to support our clinical findings (FSFI scores). Because both hormone and SHBG levels can vary widely and can be influenced by many factors, we cannot rule out that OCs may influence sexual function and may have different effects depending on the EE dosage and type and dosage of progestin, and to establish this was one aim of our study. To our knowledge, however, such a key study has never been performed in patient samples large enough to test this important hypothesis.

OCs contain either androgenic or antiandrogenic progestogens, classified according to their behavior with regard to progesterone receptors and SHBG, as described above. In addition to this, we analyzed the effects of OCs depending on EE dosage. Progestogens were classified according to the general classification based on the Hershberger test, that is, according to animal experiments. Clinically, the effects of progestogens may vary, since other partial functions, such as their influence on the conversion of testosterone into dihydrotestosterone, may also play an important role in their overall effect. It is therefore possible that they may exert a different net effect depending on the combination of hormones. For instance, an OC with a high EE dosage and an androgenic progestogen may actually have antiandrogenic effects. The same applies to triphasic preparations with up to 40-mcg EE. However, only eight of our participants used OCs that fall into these categories, and we therefore disregarded this possible effect. It could, however, be claimed that the effects of the antiandrogenic preparations may have had a strong impact on sexual function in our study, since a large number of participant used combinations of antiandrogenic progestogens with high EE dosages (e.g., chlormadinone acetate with 50-mcg EE and cyproterone acetate with 35-mcg EE), which may markedly reduce free testosterone levels. Furthermore, in Germany, preparations such as dienogest with 30 mcg EE are often used for "long-term" application (i.e., without a hormonal pause), and with these, the enhancement of the antiandrogenic effect might be even greater due to more marked central inhibitory actions. Our results, however, showed that the effects of the EE dosage (and the consequent effects on SHBG levels) appear to be irrelevant in the population of women we studied, indicating that the combined effects discussed above also have no clinical impact.

In conclusion, according to our online investigation, neither androgenic or antiandrogenic progestins in OCs nor the EE dosage in the OCs used significantly influenced sexual function in German medical students. Oral contraceptive users, however, did have lower FSFI scores than users of nonhormonal contraceptives or no contraception at all. These results could be explained by two alternative

hypothesis: (1) The difference in FSFI scores between users and nonusers of OCs is not due to biological actions of the steroids but due to differences in psychosocial variables (personality, relationship, sexual script, etc.) between the two groups. (2) The difference in FSFI scores may indicate that even small dosages of steroids have a direct influence on the sexual response of women. This effect would then not be dose or type dependent. We will need further studies to understand these interactions better and to clarify which hypothesis holds true.

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