Intrauterine device prescribing patterns and types in Europe – a cross-sectional analysis of the European Active Surveillance LCS12 Study

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ABSTRACT

Background and purpose: To give an overview of how the World Health Organization's Medical Eligibility Criteria (WHO MEC) recommendations are followed in Europe and to investigate the prescription behavior of health care professionals (HCPs) regarding the selective choice of intrauterine devices (IUDs) in routine medical practice.

Methods: Cross-sectional analysis of baseline data from the ongoing, prospective cohort study 'European Active Surveillance Study on LCS12' (EURAS-LCS12). The study population consisted of EURAS-LCS12 participants from ten European countries who used a new IUD solely for reasons of birth control. IUD insertions observed within the study population were compared with the WHO MEC recommendations. The association between women's baseline parameters and the characteristics of the IUDs prescribed by the HCPs was assessed.

Results: The WHO MEC guideline was followed in most European countries, although no further recommendations exist on what specific IUD model to insert. A woman's parity appeared to be the most important factor influencing the choices of IUD made by the HCPs.

Conclusions: Due to the great variety of IUDs available on the European market, guidance for HCPs is strongly needed to support them in their decision-making process. The ongoing EURAS-LCS12 study will provide data on the basis of which recommendations regarding differential use may be made.

KEYWORDS

Copper IUD, Europe, hormonal IUD, intrauterine device, levonorgestrel-releasing IUS, prescription patterns, prospective cohort study, routine medical practice, WHO MEC.

Introduction

According to data from the United Nations published in 2019, 8.1% of European women of reproductive age (i.e., 15-49 years) use an intrauterine device (IUD) for contraception, and thus IUDs are ranked as the third most commonly used contraceptive method in Europe [1].

Health care professionals (HCPs) can turn to the World Health Organization (WHO) guideline 'Medical Eligibility Criteria for Contraceptive Use' (MEC) to support them in determining whether a woman with underlying medical conditions or particular characteristics can safely use an IUD [2]. Country-specific guidelines on IUD use are available only in some European countries (e.g., United Kingdom, France, Italy). However, these guidelines are mainly based on the WHO's MEC global guideline or follow similar recommendations [3-7]. Where no country-specific guidelines exist (e.g., Germany), most HCPs use the WHO MEC recommendations in routine medical practice [8]. Today, IUDs, especially copper IUDs, are available in a variety of models on the European market, with different characteristics.

However, there are no official recommendations describing which IUD model is the most appropriate for a particular woman or clinical scenario. Existing guidelines only distinguish between copper IUDs and levonorgestrel-releasing intrauterine systems (LNG-IUSs), without providing any further specification on the IUS/IUD model. In this paper, if copper IUDs and LNG-IUSs are not explicitly designated as such, then they are generally identified as IUDs.

In this article we give an overview of how the WHO MEC recommendations are followed across European countries. Furthermore, with regard to IUDs, we describe the differential prescription behavior of HCPs in routine medical practice, as influenced by various factors.

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Methods

We conducted a cross-sectional analysis of baseline data from the ongoing, prospective, non-interventional "European Active Surveillance Study on LCS12" (EURAS-LCS12

[NCT02146950]). Women were recruited, following the decision to insert an IUD, via a network of about 1,200 HCPs. An informed consent form was signed at baseline. Study participants consisted of women from ten European countries (Austria, Germany, Poland, Czech Republic, Spain, Italy, United Kingdom, France, Sweden, Finland) who had a new IUD inserted. There were no specific medical inclusion and exclusion criteria. Ethical approval for the study was acquired following the rules in the respective countries.

Some copper IUDs are prescribed for emergency contraception, whereas some LNG-IUSs are additionally indicated for heavy menstrual bleeding or hormone replacement therapy. However, for this analysis, we restricted the study population to women who used their IUD exclusively for birth control reasons, so as to create the same initial situation for all participants.

The WHO "Medical Eligibility Criteria for Contraceptive Use"

The comparison of the WHO MEC recommendations and real-life use of IUDs in the EURAS-LCS12 study population was based on the following twelve observed parameters: age, obesity, parity, postpartum, endometriosis, sexually transmitted infections (STIs), anatomical abnormalities, smoking, history of pelvic inflammatory disease (PID), history of deep vein thrombosis (DVT) or pulmonary embolism (PE), history of ectopic pregnancy, and history of breast cancer.

Statistical analysis

We compared WHO MEC items descriptively with IUD users' baseline characteristics stratified by IUD type and country. Results are presented as proportions and percentages.

Multiple linear, multinomial, and logistic regression models were respectively applied per country to investigate the association between IUD users' baseline parameters and characteristics of devices chosen for insertion. Point estimates and corresponding two-sided 95% confidence intervals (CI) are provided. The outcome variables used for regression analyses were:

– Shape
– Size
– Labeled duration of use
– Copper surface area
– Additional gold/silver coating

Women's baseline parameter considered potentially relevant for analysis of physician prescription behavior were the following:

– Age
– BMI
– Monthly household income
– Marital status
– Parity status
– Previous use of hormonal contraception other than IUS
– Previous IUD use
– Smoking status
– Sexual history (i.e., number of sexual partners within the last 12 months)

Marginally associated ($p<0.1$) factors, identified by bivariable analyses, were included in the specified multiple regression models. All statistical analyses were performed using the statistical package SAS® release 9.4.

Results

In total 46,326 (83.0%) out of 55,793 women recruited between June 2014 and August 2019 used an IUD (28,050 [60.5%] LNG-IUS; 18,276 [39.5%] copper IUD) exclusively for birth control reasons and were included in this analysis (Table 1). Most recruited participants were from Germany (28.4%), United Kingdom (21.5%), and Sweden (15.9%), followed by France (9.5%), Czech Republic (8.6%), and Austria (6.3%).

Table 1 Selected baseline characteristics of intrauterine device users.

	LNG-IUS 28,050 (100%)	Copper IUD 18,276 (100%)	Total 46,326 (100%)
Age (years) Mean (SD)	32.5 (7.99)	30.5 (6.94)	31.7 (7.65)
BMI (kg/m²) Mean (SD)	24.9 (4.96)	24.5 (4.82)	24.7 (4.91)
Gravidity			
Nulligravid	6,971 (24.9%)	6,068 (33.2%)	13,039 (28.2%)
Gravid	21,079 (75.1%)	12,208 (66.8%)	33,287 (71.8%)
Parity			
Nulliparous	8,056 (28.7%)	7,193 (39.4%)	15,249 (32.9%)
Parous	19,994 (71.3%)	11,083 (60.6%)	31,077 (67.1%)
Ever used IUD	11,565 (41.2%)	6,372 (34.9%)	17,937 (38.7%)
Ever used hormonal contraception	23,689 (84.5%)	14,670 (80.3%)	38,359 (82.8%)
Educational level [a]			
Low	8,113 (28.9%)	4,382 (24.0%)	12,495 (27.0%)
High	19,407 (69.2%)	13,496 (73.9%)	32,903 (71.0%)
Missing	530 (1.9%)	398 (2.1%)	928 (2.0%)
Monthly household income [b]			
Low	12,047 (43.0%)	9,884 (54.1%)	21,931 (47.3%)
High	13,257 (47.3%)	6,989 (38.2%)	20,246 (43.7%)
Missing	2,746 (9.7%)	1,403 (7.7%)	4,149 (9.0%)
Smoking			
Yes	5,599 (20.0%)	3,962 (21.7%)	9,561 (20.6%)
No	22,264 (79.4%)	14,192 (77.7%)	36,456 (78.7%)
Missing	187 (0.6%)	122 (0.6%)	309 (0.7%)
Marital status			
Single	6,191 (22.1%)	4,960 (27.1%)	11,151 (24.1%)
Living with a spouse or partner	21,135 (75.4%)	12,874 (70.5%)	34,009 (73.4%)
Missing	724 (2.5%)	442 (2.4%)	1,166 (2.5%)
Sexual history in the past 12 months			
0-1 partner	23,853 (85.0%)	15,033 (82.3%)	38,886 (83.9%)
2+ partner	3,417 (12.2%)	2,838 (15.5%)	6,255 (13.5%)
Missing	780 (2.8%)	405 (2.2%)	1,185 (2.6%)

[a] *Low educational level = less than university entrance level; High educational level = university entrance level or higher.*
[b] *Monthly household income categories were defined with respect to the income standards in the different countries.*

Lower recruitment rates were observed in Poland (4.0%), Finland (3.7%), as well as in Spain (2.0%) and Italy (0.3%), which joined the study only 12 months before this cross-sectional analysis. Data from Italy were excluded from the regression analyses due to an insufficient number of recruitments.

WHO MEC recommendations vs. real-life use in Europe

Most IUD insertions observed in the EURAS-LCS12 study were performed following the WHO MEC recommendations. Therefore, IUDs were appropriately used regardless of BMI, endometriosis, anatomical abnormalities, history of ectopic pregnancy, PID or DVT/PE, and smoking status (Tables 2 and 3). In accordance with the guideline, most IUD users were older than 20 years (>89%) and parous (55.3% - 91.4% for LNG-IUSs; 38.1% - 97.5% for copper IUDs) across countries (Tables 2 and 3). We observed that the recommendation for postpartum IUD insertion (<48h or >4 weeks) was followed in 95% of insertions. We furthermore observed a few cases of chlamydial infections at baseline and one gonorrhea case in a copper IUD user from the United Kingdom. However, the proportion of women undergoing any screening test at all was low (22.5%). In contrast to copper IUDs, LNG-IUS usage is not appropriate for women who have had breast cancer. About 0.1% of LNG-IUS and 0.4% of copper IUD users were found to have a history of breast cancer.

HCP prescription behavior

About 130 copper IUD brands and five LNG-IUSs (i.e., Mirena®, Jaydess®, Kyleena®, Levosert®, Fibroplant®) were used in

Table 2 Distribution of selected baseline characteristics of LNG-IUS users in the EURAS-LCS12 cohort with respective WHO MEC category.

	Germany 8,293 (100%)	Spain 307 (100%)	Austria 1,326 (100%)	United Kingdom 5,359 (100%)	France 2,074 (100%)	Italy 66 (100%)	Finland 1,419 (100%)	Poland 988 (100%)	Sweden 5,341 (100%)	Czech Republic 2,877 (100%)	Total 28,050 (100%)	WHO MEC[a] category[b]
Age												
<20 years	419 (5.1%)	9 (2.9%)	143 (10.8%)	164 (3.1%)	50 (2.4%)	1 (1.5%)	94 (6.6%)	14 (1.4%)	533 (10%)	115 (4%)	1,542 (5.5%)	2
≥20 years	7,874 (94.9%)	298 (97.1%)	1,183 (89.2%)	5,195 (96.9%)	2,024 (97.6%)	65 (98.5%)	1,325 (93.4%)	974 (98.6%)	4,808 (90%)	2,762 (96%)	26,508 (94.5%)	1
Obesity												
BMI ≥30	1,167 (14.1%)	31 (10.1%)	114 (8.6%)	1,101 (20.5%)	255 (12.3%)	2 (3%)	275 (19.4%)	93 (9.4%)	567 (10.6%)	312 (10.8%)	3,917 (14%)	1
Parity												
Nulliparous	2,296 (27.7%)	103 (33.6%)	431 (32.5%)	1,577 (29.4%)	286 (13.8%)	14 (21.2%)	406 (28.6%)	85 (8.6%)	2,387 (44.7%)	471 (16.4%)	8,056 (28.7%)	2
Parous	5,997 (72.3%)	204 (66.4%)	895 (67.5%)	3,782 (70.6%)	1,788 (86.2%)	52 (78.8%)	1,013 (71.4%)	903 (91.4%)	2,954 (55.3%)	2,406 (83.6%)	19,994 (71.3%)	1
There of												
Postpartum												
<48h	1 (0%)	-	-	-	-	-	-	-	-	-	1 (0%)	1 / 2
48h - 4 weeks	7 (0%)	-	-	8 (0.2%)	1 (0.1%)	-	1 (0.1%)	2 (0.2%)	5 (0.1%)	1 (0%)	25 (0.1%)	3
≥4 weeks	5,928 (98.8%)	198 (97.1%)	885 (98.9%)	3,745 (98%)	1,756 (98.2%)	51 (98.1%)	1,010 (99.7%)	885 (98%)	2,934 (99.3%)	2,395 (99.5%)	19,787 (99%)	1
Endometriosis	3 (0%)	-	-	1 (0%)	-	-	1 (0.1%)	-	-	-	5 (0%)	1
STIs												
Chlamydia	6 (0.1%)	0 (0%)	1 (0.1%)	14 (0.3%)	4 (0.2%)	0 (0%)	1 (0.1%)	0 (0%)	14 (0.3%)	0 (0%)	40 (0.1%)	4
Gonorrhea	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4
Viral hepatitis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1
Other	7 (0.1%)	0 (0%)	1 (0.1%)	17 (0.3%)	2 (0.1%)	0 (0%)	1 (0.1%)	1 (0.1%)	6 (0.1%)	6 (0.2%)	41 (0.1%)	2
Anatomical abnormalities	677 (8.2%)	8 (2.6%)	77 (5.8%)	716 (13.4%)	99 (4.8%)	4 (6.1%)	207 (14.6%)	121 (12.3%)	324 (6.1%)	209 (7.3%)	2,442 (8.7%)	2
History of ectopic pregnancy	106 (1.3%)	7 (2.3%)	22 (1.7%)	71 (1.3%)	48 (2.3%)	4 (6.1%)	27 (1.9%)	14 (1.4%)	66 (1.2%)	45 (1.6%)	410 (1.5%)	1
History of PID	40 (0.5%)	-	9 (0.7%)	34 (0.6%)	9 (0.4%)	1 (1.5%)	46 (3.2%)	7 (0.7%)	52 (1%)	7 (0.2%)	205 (0.7%)	1 / 2
History of DVT or PE	107 (1.3%)	1 (0.3%)	16 (1.2%)	46 (0.9%)	16 (0.8%)	-	15 (1.1%)	6 (0.6%)	43 (0.8%)	47 (1.6%)	297 (1.1%)	2
History of breast cancer	8 (0.1%)	-	-	3 (0.1%)	1 (0.1%)	-	-	-	3 (0.1%)	2 (0.1%)	17 (0.1%)	3
Smoking	2,047 (24.7%)	85 (27.7%)	359 (27.1%)	945 (17.6%)	723 (34.9%)	21 (31.8%)	272 (19.2%)	157 (15.9%)	510 (9.6%)	480 (16.7%)	5,599 (20.0%)	1

[a] *WHO MEC = World Health Organization Medical Eligibility Criteria for Contraceptive Use*

[b] ***Category 1** = No restriction; **Category 2** = Advantages generally outweigh the theoretical or proven risks; **Category 3** = Theoretical or proven risks usually outweigh the advantages; **Category 4** = Unacceptable health risk*

Table 3 Distribution of selected baseline characteristics of copper IUD users in the EURAS-LCS12 cohort with respective WHO MEC category.

	Germany 4,857 (100%)	**Spain** 629 (100%)	**Austria** 1,582 (100%)	**United Kingdom** 4,579 (100%)	**France** 2,318 (100%)	**Italy** 55 (100%)	**Finland** 278 (100%)	**Poland** 854 (100%)	**Sweden** 2,040 (100%)	**Czech Republic** 1,084 (100%)	**Total** 18,276 (100%)	**WHO MEC[a] category[b]**
Age												
<20 years	371 (7.6%)	27 (4.3%)	109 (6.9%)	191 (4.2%)	69 (3%)	2 (3.6%)	15 (5.4%)	6 (0.7%)	53 (2.6%)	31 (2.9%)	874 (4.8%)	2
≥20 years	4,486 (92.4%)	602 (95.7%)	1,473 (93.1%)	4,388 (95.8%)	2,249 (97%)	53 (96.4%)	263 (94.6%)	848 (99.3%)	1,987 (97.4%)	1,053 (97.1%)	17,402 (95.2%)	1
Obesity												
BMI ≥30	444 (9.1%)	98 (15.6%)	86 (5.4%)	843 (18.4%)	261 (11.3%)	6 (10.9%)	39 (14%)	92 (10.8%)	204 (10%)	156 (14.4%)	2,229 (12.2%)	1
Parity												
Nulliparous	2,600 (53.5%)	148 (23.5%)	979 (61.9%)	1,827 (39.9%)	747 (32.2%)	9 (16.4%)	93 (33.4%)	21 (2.5%)	606 (29.7%)	163 (15%)	7,193 (39.4%)	2
Parous	2,257 (46.5%)	481 (76.5%)	603 (38.1%)	2,752 (60.1%)	1,571 (67.8%)	46 (83.6%)	185 (66.6%)	833 (97.5%)	1,434 (70.3%)	921 (85%)	11,083 (60.6%)	1
There of												
Postpartum												
<48h	1 (0%)	-	-	1 (0%)	1 (0.1%)	-	-	-	1 (0.1%)	-	4 (0%)	1
48h - 4 weeks	-	-	-	9 (0.3%)	4 (0.3%)	-	-	2 (0.2%)	1 (0.1%)	2 (0.2%)	18 (0.2%)	3
≥4 weeks	2,232 (98.9%)	471 (97.9%)	599 (99.3%)	2,718 (98.8%)	1,531 (97.5%)	44 (95.7%)	185 (100%)	800 (96%)	1,416 (98.7%)	917 (99.6%)	10,913 (98.5%)	1
Endometriosis	-	-	-	1 (0%)	-	-	-	-	-	-	1 (0%)	2
STIs												
Chlamydia	6 (0.1%)	0 (0%)	0 (0%)	3 (0.1%)	11 (0.5%)	0 (0%)	0 (0%)	1 (0.1%)	1 (0%)	0 (0%)	22 (0.1%)	4
Gonorrhea	0 (0%)	0 (0%)	0 (0%)	1 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0%)	4
Viral hepatitis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1
Other	3 (0.1%)	1 (0.2%)	1 (0.1%)	15 (0.3%)	2 (0.1%)	0 (0%)	1 (0.4%)	0 (0%)	1 (0%)	8 (0.7%)	32(0.2%)	2
Anatomical abnormalities	365 (7.5%)	15 (2.4%)	95 (6%)	755 (16.5%)	155 (6.7%)	-	41 (14.8%)	59 (6.9%)	113 (5.5%)	63 (5.8%)	1,661 (9.1%)	2
History of ectopic pregnancy	44 (0.9%)	11 (1.8%)	19 (1.2%)	59 (1.3%)	47 (2%)	-	4 (1.4%)	5 (0.6%)	31 (1.5%)	15 (1.4%)	235 (1.3%)	1
History of PID	40 (0.8%)	-	10 (0.6%)	19 (0.4%)	8 (0.4%)	-	9 (3.2%)	7 (0.8%)	8 (0.4%)	2 (0.2%)	103 (0.6%)	1 / 2
History of DVT or PE	82 (1.7%)	1 (0.2%)	21 (1.3%)	44 (1%)	26 (1.1%)	1 (1.8%)	2 (0.7%)	9 (1.1%)	18 (0.9%)	30 (2.8%)	234 (1.3%)	1
History of breast cancer	15 (0.3%)	1 (0.2%)	7 (0.4%)	26 (0.6%)	10 (0.4%)	-	2 (0.7%)	5 (0.6%)	5 (0.3%)	1 (0.1%)	72 (0.4%)	1
Smoking	1,045 (21.5%)	155 (24.6%)	461 (29.1%)	839 (18.3%)	713 (30.8%)	13 (23.6%)	39 (14%)	219 (25.6%)	191 (9.4%)	287 (26.5%)	3,962 (21.7%)	1

[a] *WHO MEC = World Health Organization Medical Eligibility Criteria for Contraceptive Use*
[b] ***Category 1** = No restriction; **Category 2** = Advantages generally outweigh the theoretical or proven risks; **Category 3** = Theoretical or proven risks usually outweigh the advantages; **Category 4** = Unacceptable health risk*

the study population (data not shown). However, the number of copper IUDs available on some country-specific markets was much higher. The proportion of copper IUD subtypes used among those available on the market ranged from 6.7% in Finland (4 types used) to 60.2% in Germany (56 types used).

Characteristics of LNG-IUSs and copper IUDs are described in Table 4. Except for the hormonal thread Fibroplant®, all other LNG-IUSs were T-shaped, having a similar size and a labeled duration of use of three (Jaydess®), five (Kyleena®, Fibroplant®), or six years (Mirena®, Levosert®). However, the characteristics of copper IUDs vary widely. In this study, there were five different shapes, with a composition of copper only or copper with silver or gold alloy; they varied in size, and had a labeled duration of use ranging from three to ten years (Table 4).

In total, 18,276 copper IUDs were inserted by 637 HCPs (data not shown). The main factor in an HCP's choice to insert a particular IUD model was found to be the woman's parity status. We observed that, in all countries, parous women used larger devices ($p<0.02$) compared with nulliparous women (Fig.1A).

Furthermore, the copper surface area, as well as the labeled duration of use, was significantly higher in IUDs used by parous women in several European countries (Fig. 1B, C). Most of the copper IUDs were T-shaped, and therefore we chose the T-shape as the reference category for regression analyses. Across countries, there was a trend whereby frameless devices (i.e., copper chains or balls) were more likely to be inserted in nulliparous women, whereas Y- and Omega-shaped devices were more frequently used in parous women (Fig. 1D).

Table 4 Characteristics of intrauterine systems/devices used in the study population

	LNG-IUS 28,050 (60.6%)	Copper IUD 18,276 (39.5%)
Length (mm)		
Min	30	20
Mean (SD)	31.4 (0.92)	31.6 (3.97)
Max	35	38
Width (mm)		
Min	28	18
Mean (SD)	30.8 (1.85)	29.8 (4.04)
Max	32	37
Shape		
T	28,048 (100%)	12,524 (68.5%)
Omega	-	1,838 (10.1%)
Chain	2 (0%)	2,189 (12%)
Ball	-	582 (3.2%)
Y	-	1,121 (6.1%)
Not specified	-	22 (0.12)
Labeled duration of use (months)		
36	5,252 (18.7%)	391 (2.1%)
48	-	27 (0.2%)
60	3,161 (11.3%)	14,468 (79.2%)
72	18,853 (67.2%)	-
84	-	5 (0%)
120	-	3,174 (17.4%)
Not specified	2 (0%)	211 (1.2%)
Copper surface area (mm²)		
200	-	2,050 (11.2%)
240	-	17 (0.1%)
250	-	140 (0.8%)
300	-	1,481 (8.1%)
330	-	416 (2.3%)
375	-	2,198 (12%)
380	-	11,972 (65.5%)
Not specified	-	2 (0%)
Additional coating		
Copper only	-	12,233 (66.9%)
Silver	-	5,007 (27.4%)
Gold	-	732 (4%)
Not specified	-	304 (1.7%)

However, not all results reached statistical significance. Parity status also showed an influence on the choice of an additional coating of gold or silver (Fig. 1E). In Austria, Germany, United Kingdom, and Finland, silver and gold alloys were significantly more likely to be prescribed to parous compared with nulliparous women (range of ORs: 1.4-4.2). Conflictingly, copper-gold IUDs were used less frequently for parous women in the Czech Republic (OR 0.53, 95% CI [0.40; 0.98]).

Participant age occasionally showed significant associations with IUD size, labeled duration of use, and copper surface area (Suppl. figures 1-4).

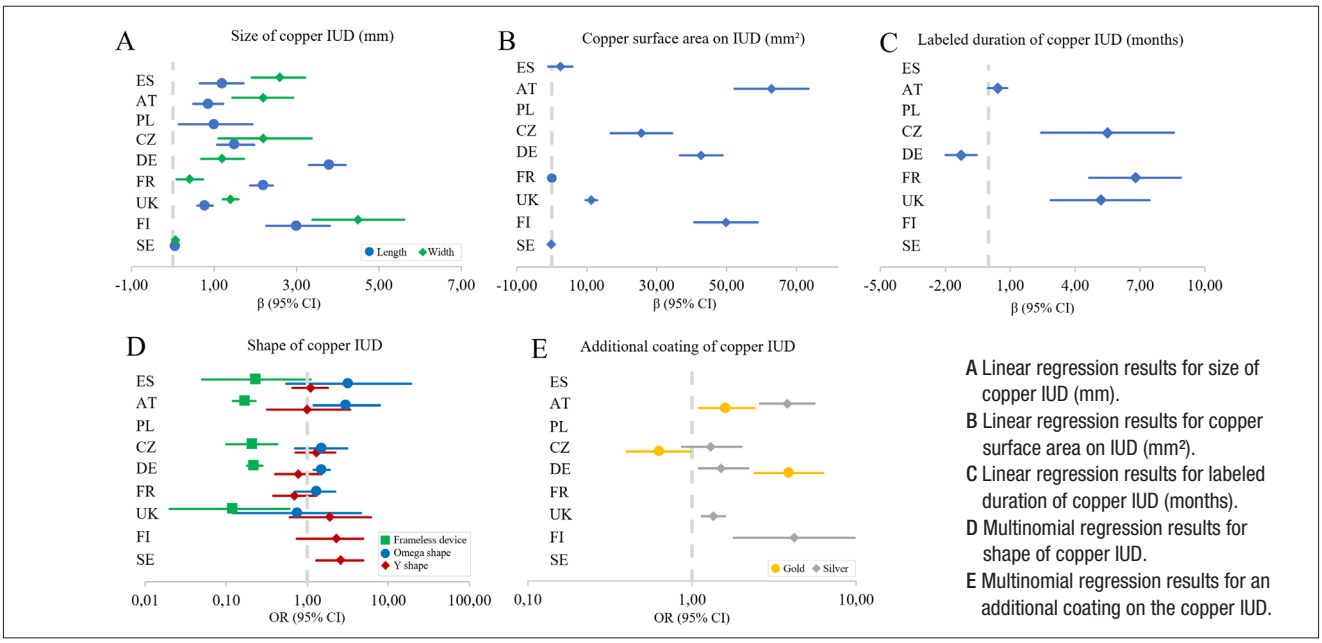
In some countries, IUD size, as well as the copper surface area and the labeled duration of use, increased with increasing age. In a few countries, the size of an IUD and the copper surface area increased slightly with increasing BMI (Suppl. figures 1-3).

Furthermore, in the United Kingdom, a high monthly household income was statistically significant for the decision to insert a longer IUD ($p<0.001$) with a greater copper surface area ($p=0.02$) and a prolonged duration of use ($p<0.01$) (Suppl. figures 1-4). In contrast, for some other countries, such as Germany and Poland, a high income was associated with decreasing size and copper surface area, as well as a shorter labeled duration of use (Suppl. figures 1-4).

Moreover, we observed a trend whereby women with a high income were more likely to use frameless devices, whereas the results for other IUD shapes were inconsistent (Suppl. table 1). Other factors, such as previous use of hormonal contraceptive or IUD, marital status, sexual history, and smoking, showed conflicting results in a few countries and therefore did not allow us to draw firm conclusions (Suppl. figures 1-4; Suppl. tables 1,2).

As only five types of LNG-IUS are currently available on the market, and Mirena® was the predominant IUS prescribed (67.2%), we do not present regression analysis results for LNG-IUS characteristics.

Figure 1 Association of women's parity status and characteristics of copper IUDs inserted.



A Linear regression results for size of copper IUD (mm).
B Linear regression results for copper surface area on IUD (mm²).
C Linear regression results for labeled duration of copper IUD (months).
D Multinomial regression results for shape of copper IUD.
E Multinomial regression results for an additional coating on the copper IUD.

Discussion

Observational data from the EURAS-LCS12 study show that the WHO MEC recommendations selected for comparison were followed in most European countries. However, the majority of analyzed items were defined as category 1 or 2 in the MEC system (indicating: use the method), while only a few were category 3 or 4 ones (indicating: do not use the method). Given that the EURAS-LCS12 study was not designed to investigate WHO MEC compliance and further category 3 and 4 items could not be checked, it is unlikely that the results can be generalized to all WHO MEC recommendations. According to the WHO, IUD insertion carries an unacceptable health risk for women with a chlamydial infection or gonorrhea, whereas insertion is acceptable for other STIs. We observed a few subjects with a positive test result for chlamydial infection and one for gonorrhea. However, the results on STIs in the study population need to be interpreted carefully as screening tests were performed in only 22.5% of the women.

IUDs are still underrepresented in adolescents and nulliparous women, even though IUD use is shown to be safe and effective for these subgroups [9,10]. This result is consistent with other published data showing that only 53%-67% of HCPs recommend IUDs to nulliparous women and an even smaller percentage (38-43%) to adolescents [11,12]. Furthermore, insufficient knowledge of the WHO MEC classification system may also explain HCP prescription behavior. Previous studies reported that only 30%-61% of participating HCPs recognized that IUD use in nulliparous women was defined as category 2 in the WHO classification system [13,14].

However, non-compliance with the WHO MEC guideline may also occur due to inconsistent recommendations within country-specific guidelines. Chlamydial infection, for example, is ranked as category 4 in WHO MEC, but national guidelines from the United Kingdom and France suggest that in asymptomatic women there is no need to wait for STI screening results provided the woman can be contacted and treated promptly in the event of a positive test result [4,7]. Furthermore, there is a common view that only women with risk factors for STI such as previous STI or multiple sexual partners need a laboratory test [15].

Although there are no official recommendations regarding which IUD model to insert, a woman's parity appeared to be a factor influencing the copper IUD types chosen by HCPs. We observed that larger IUDs having a higher copper surface area and a prolonged labeled duration of use were more likely to be inserted in parous compared with nulliparous women. Defining the optimal size of an IUD may reduce device expulsion or uterine perforation. However, previous studies reported controversial findings when investigating associations between these side effects and uterine cavity size [16-19]. The use of larger devices in parous women may be related to a usually larger uterus cavity in these women as compared with nulliparous women. Frameless IUDs were promoted specifically to fit into small uteri and this may explain their frequent use in nulliparous women [20,21]. An additional coating, as well as a larger copper surface area, has been associated with a prolonged labeled duration of use [22,23]. We hypothesize that women who have given birth are more likely to use IUDs that have a prolonged duration of use (due to a greater copper surface area or a gold or silver coating), since these women may have already completed their families.

The relevance of women's monthly household income showed conflicting results across countries, which is likely due to differences between health care systems in Europe [24]. Depending on the country, the cost of an IUD and its placement might be charged to the health care system, insurance companies, nonprofit organizations, or to women themselves. The United Kingdom was the only country investigated where copper IUD purchase and placement are fully funded through the National Health Service for all women. Thus, HCP provision of IUDs is more likely influenced by country-specific guidelines that, irrespective of participant characteristics, advise insertion of an IUD with the longest duration of use so as to reduce the risks of infection, perforation and expulsion associated with reinsertion [24,25]. In countries where women had to pay, at least partially, the costs of an IUD, we observed a trend whereby frameless devices were more likely to be used in women with a high income. This might be explained by the much higher costs of frameless IUDs compared with T-shaped devices.

Other confounding factors with regard to HCP prescription behavior might be: product information (i.e., required depth of the uterine cavity), HCPs' own preferences in relation to ease of insertion or training in the insertion of different IUD types, and women's wishes.

EURAS-LCS12 is an observational study and the methodological limitations of this study design are such that the possibility of bias and residual confounding can never be eliminated fully. The study was not specifically designed to capture HCP prescription behavior concerning IUD model characteristics as presented in this paper. Furthermore, the analyzed data concerned only ten European countries. Due to the geographical variance observed, it is unlikely that the results can be generalized to a global population. As the present analyses were explorative, no adjustments were made for the possibility of type one error, and this may have affected the results. Thus, relevant factors for HCP choices of specific IUD models may be association signals rather than causal effects. Other potential confounders, such as country-specific guidelines, product information, and HCPs' or women's own preferences, may also have had an impact on the results. Moreover, some IUD characteristics are correlated to different degrees, and this may lead to overlapping effects.

Notwithstanding these limitations, this analysis has many strengths. EURAS-LCS12 is a multinational prospective cohort study with a sample size of more than 50,000 women. To our knowledge, it is the first non-interventional cohort study to have collected detailed information on the characteristics of IUDs initially inserted. With this comprehensive dataset, it was possible to investigate prescription patterns in several European countries. Selection bias is not a major issue in this analysis since the participating HCPs are a representative mix of those who prescribe and insert IUDs. Thanks to the use of a subsample of the EURAS-LCS12 population for the present analysis, i.e., women who used IUDs for contraception only, all women had the same starting point for this analysis and thus,

a potential bias in terms of preselection of IUD characteristics was reduced.

In conclusion, the results of this analysis showed that most IUD insertions in the EURAS-LCS12 study were performed in accordance with the WHO MEC guideline. The ongoing EURAS-LCS12 study will provide data on the basis of which recommendations regarding differential use of IUDs may be made.

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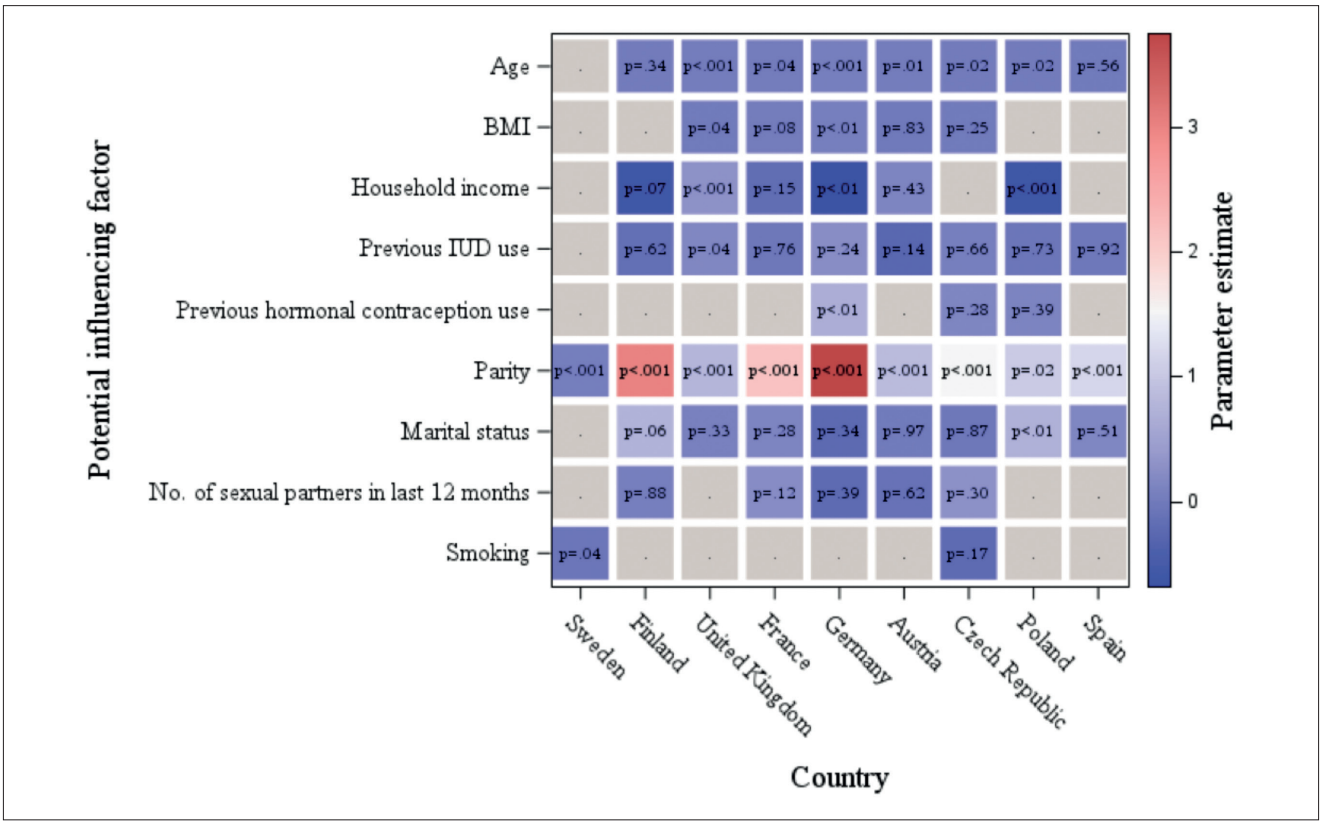
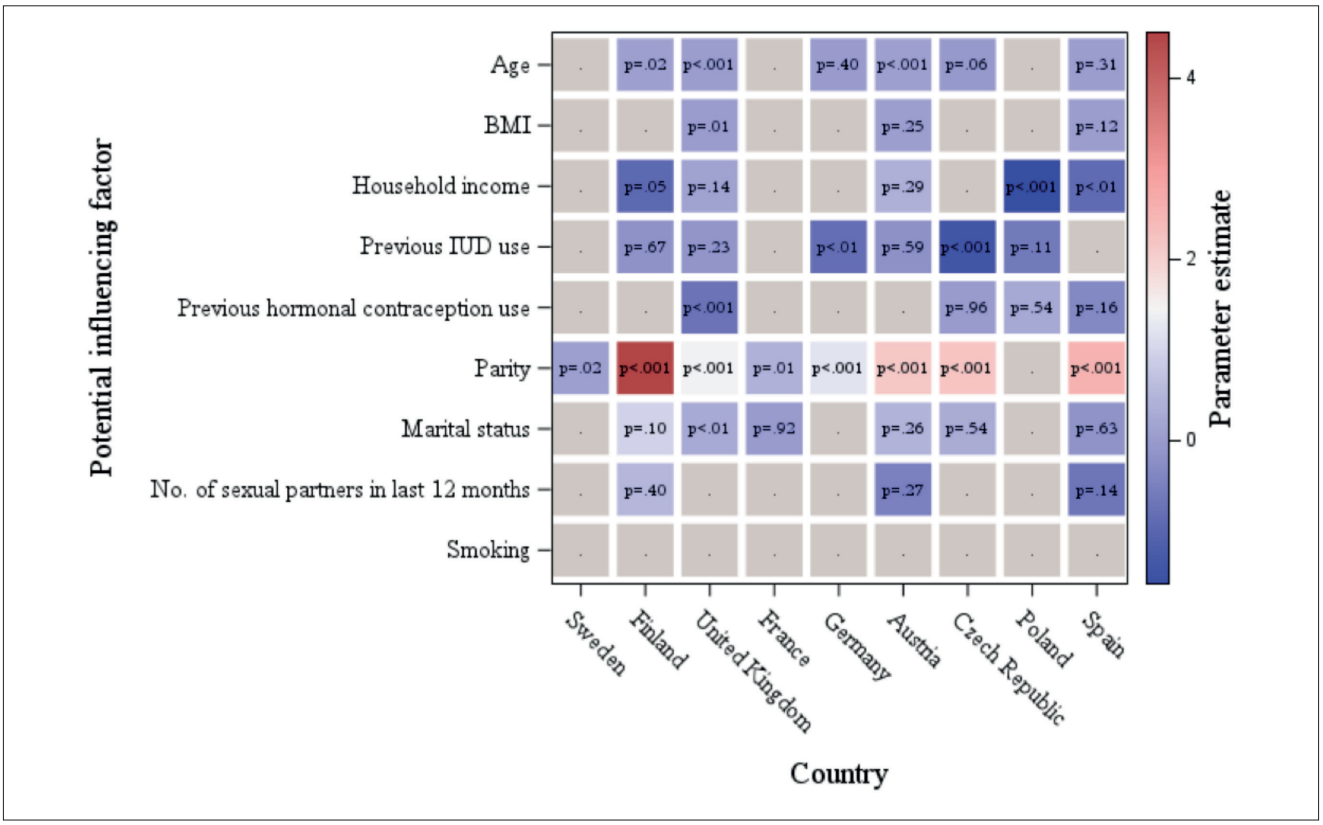
Supplemental material

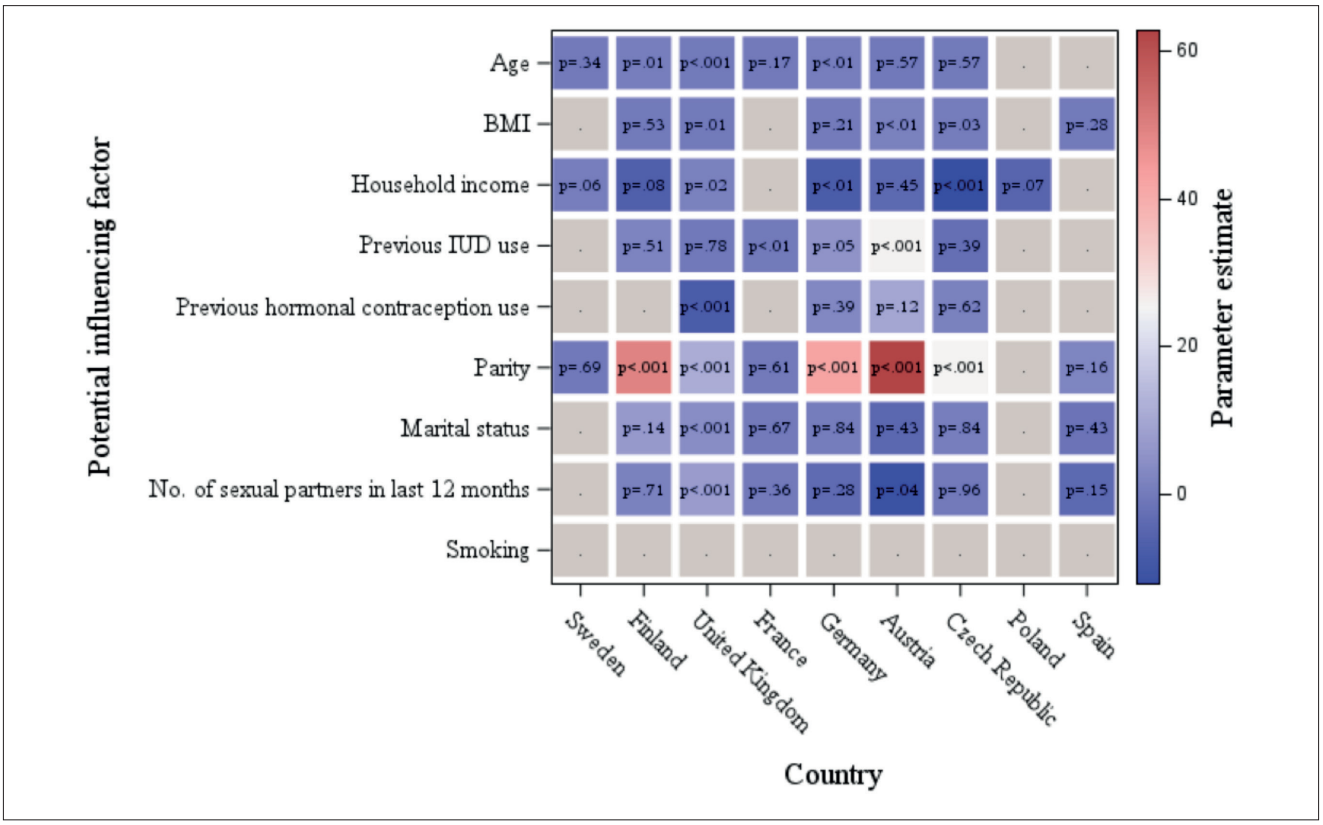
Suppl. fig. 1. Heatmap on women's baseline characteristics associated with the length of copper IUDs determined by multiple linear regression models.



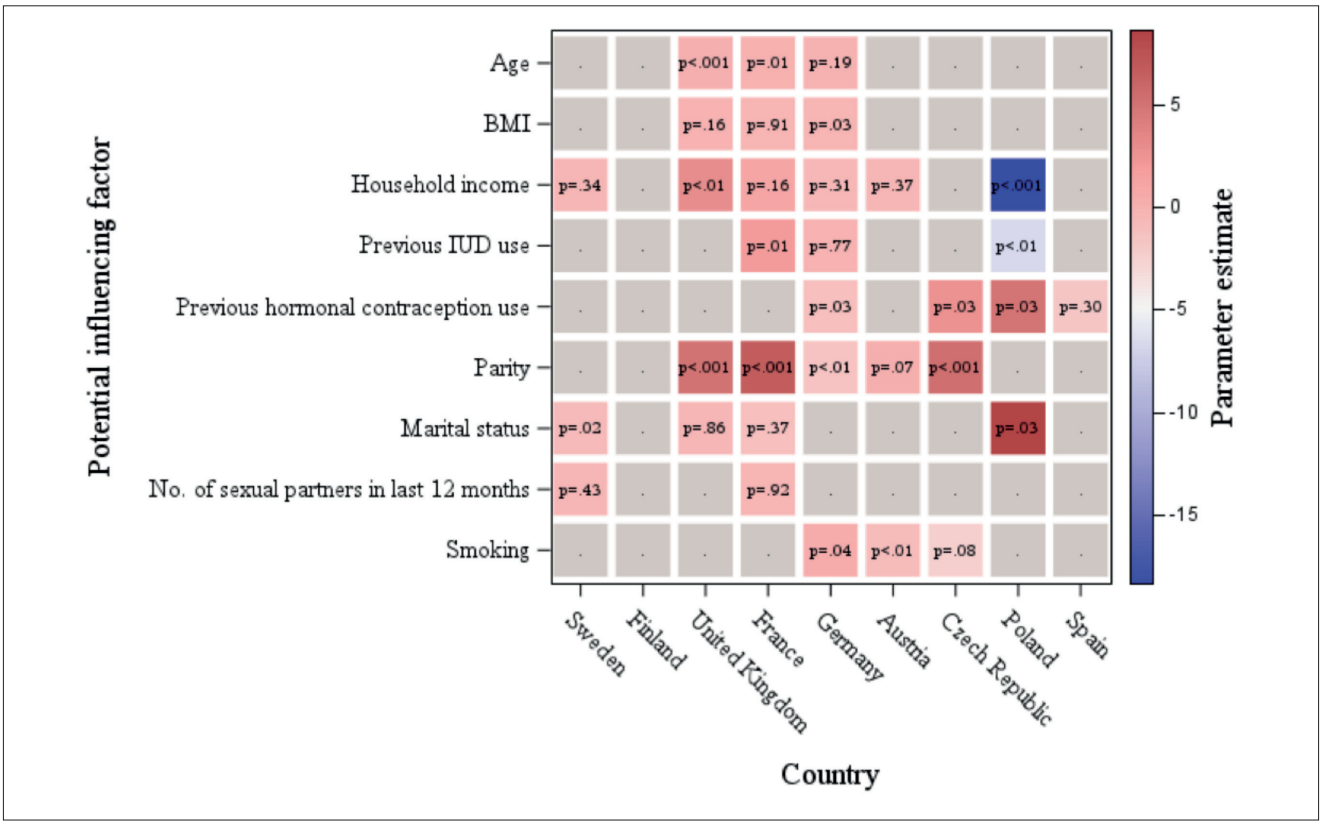
Suppl. fig. 2. Heatmap on women's baseline characteristics associated with the width of IUD determined by multiple linear regression models.



Suppl. fig. 3. Heatmap on women's baseline characteristics associated with the copper surface area of IUDs determined by multiple linear regression models.



Suppl. fig. 4. Heatmap on women's baseline characteristics associated with the labeled duration of use of IUD determined by multiple linear regression models.



Suppl. table 1. Women's baseline characteristics associated with an additional coating on the IUD determined by multiple (multinomial) logistic regression models.

	SWEDEN Silver	FINLAND Silver	UNITED KINGDOM Silver	FRANCE Silver	GERMANY Gold	GERMANY Silver
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age	1.1 (0.99-1.3)	1.1 (0.99-1.1)	-	-	1.0 (0.98-1.0)	0.99 (0.96-1.0)
BMI	-	1.0 (0.95-1.1)	1.00 (0.99-1.0)	-	1.0 (0.97-1.0)	1.0 (0.99-1.0)
Household income high vs low	4.4 (1.00-19.6)	0.51 (0.25-1.0)	0.79 (0.68-0.91)	-	1.1 (0.77-1.5)	0.82 (0.60-1.1)
Previous IUD use yes vs. no	-	1.4 (0.78-2.6)	1.1 (0.99-1.3)	1.2 (0.94-1.6)	0.88 (0.60-1.3)	1.2 (0.86-1.6)
Previous hormonal contraception use yes vs. no	-	-	1.7 (1.4-2.0)	0.71 (0.50-1.0)	-	-
Parity nulliparous vs. parous	-	4.2 (1.8-9.8)	1.4 (1.1-1.6)	-	3.9 (2.4-6.3)	1.5 (1.1-2.2)
Marital status living with partner vs. single	1.1 (0.31-3.9)	1.6 (0.70-3.6)	1.1 (0.93-1.3)	1.3 (0.97-1.7)	-	-
No. of sexual partners in last 12 months >1 vs. 0-1 partner	-	-	0.96 (0.78-1.2)	-	0.93 (0.55-1.6)	0.76 (0.52-1.1)
Smoking yes vs. no	-	-	1.1 (0.96-1.4)	-	-	-

Note: Copper-only composition was chosen as the reference category.

Suppl. table 1. (continued)

	AUSTRIA Gold	AUSTRIA Silver	CZECH REPUBLIC Gold	CZECH REPUBLIC Silver	POLAND Gold	POLAND Silver	SPAIN Gold	SPAIN Silver
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age	0.98 (0.96-1.0)	1.0 (1.0-1.1)	-	-	-	-	-	-
BMI	1.0 (1.00-1.1)	1.1 (1.0-1.1)	-	-	-	-	-	-
Household income high vs low	1.1 (0.77-1.7)	1.2 (0.84-1.7)	-	-	2.2 (0.14-36.7)	3.8 (1.7-8.2)	-	-
Previous IUD use yes vs. no	0.52 (0.35-0.75)	0.72 (0.51-1.0)	-	-	<0.001 (<0.000->999.999)	0.59 (0.29-1.2)	-	-
Previous hormonal contraception use yes vs. no	-	-	1.8 (1.1-2.9)	1.2 (0.85-1.6)	<0.001 (<0.000->999.999)	1.7 (0.81-3.5)	-	-
Parity nulliparous vs. parous	1.6 (1.1-2.4)	3.8 (2.6-5.6)	0.63 (0.40-0.98)	1.3 (0.87-2.0)	-	-	-	-
Marital status living with partner vs. single	0.94 (0.64-1.4)	1.3 (0.80-2.0)	-	-	-	-	-	-
No. of sexual partners in last 12 months >1 vs. 0-1 partner	0.61 (0.40-0.93)	0.71 (0.43-1.2)	-	-	-	-	1.5 (0.33-6.6)	<0.001 (<0.000->999.999
Smoking yes vs. no	-	-	0.58 (0.37-0.89)	0.64 (0.47-0.88)	-	-	-	-

Note: Copper-only composition was chosen as the reference category.

Suppl. table 2. Women's baseline characteristics associated with shape of IUD determined by multiple (multinomial) logistic regression models

	SWEDEN		FINLAND	UNITED KINGDOM			FRANCE	
	Frameless device[a] OR (95% CI)	Y OR (95% CI)	Y OR (95% CI)	Frameless device[a] OR (95% CI)	Omega OR (95% CI)	Y OR (95% CI)	Omega OR (95% CI)	Y OR (95% CI)
Age	-	-	-	-	-	-	1.0 (0.99-1.1)	1.0 (0.99-1.1)
BMI	-	-	-	-	-	-	0.98 (0.94-1.0)	1.0 (0.97-1.1)
Household income high vs low	-	-	-	-	-	-	-	-
Previous IUD use yes vs. no	-	-	1.5 (0.74-3.0)	22.6 (5.0-102.9)	0.86 (0.15-4.9)	0.57 (0.20-1.6)	1.8 (1.2-2.8)	2.1 (1.3-3.4)
Previous hormonal contraception use yes vs. no	-	-	-	-	-	-	-	-
Parity nulliparous vs. parous	<0.000 (<0.000->999.999)	2.6 (1.3-4.9)	2.3 (0.84-6.0)	0.12 (0.02-0.60)	0.75 (0.12-4.6)	1.9 (0.61-6.1)	1.3 (0.70-2.2)	0.70 (0.38-1.3)
Marital status living with partner vs. single	<0.000 (<0.000->999.999)	0.62 (0.35-1.1)	2.7 (0.77-9.7)	0.64 (0.15-2.8)	3.0 (0.31-29.3)	2.7 (0.77-9.5)	0.92 (0.55-1.6)	1.3 (0.70-2.4)
No. of sexual partners in last 12 months >1 vs. 0-1 partner	-	-	-	7.2 (1.9-27.1)	<0.001 (<0.000->999.999)	3.3 (0.85-12.8)	0.69 (0.35-1.4)	0.53 (0.22-1.2)
Smoking yes vs. no	-	-	-	-	-	-	-	-

Note: T-shape was chosen as the reference category. [a] Frameless device includes chains and balls.

Suppl. table 2 (continued)

	GERMANY			AUSTRIA		
	Frameless device[a] OR (95% CI)	Omega OR (95% CI)	Y OR (95% CI)	Frameless device[a] OR (95% CI)	Omega OR (95% CI)	Y OR (95% CI)
Age	0.98 (0.97-1.00)	1.0 (1.0-1.0)	0.96 (0.91-1.0)	1.0 (0.99-1.0)	0.99 (0.94-1.1)	0.97 (0.89-1.1)
BMI	0.99 (0.97-1.0)	1.00 (0.98-1.0)	1.0 (0.95-1.1)	0.95 (0.92-0.98)	0.98 (0.90-1.1)	1.1 (0.97-1.2)
Household income high vs low	1.6 (1.3-1.9)	0.97 (0.80-1.2)	1.2 (0.67-2.3)	1.1 (0.83-1.5)	1.4 (0.63-2.9)	0.56 (0.15-2.1)
Previous IUD use yes vs. no	0.78 (0.64-0.96)	0.79 (0.65-0.97)	0.72 (0.38-1.4)	2.2 (1.6-2.9)	1.4 (0.67-3.1)	1.7 (0.60-5.0)
Previous hormonal contraception use yes vs. no	1.4 (1.0-1.8)	0.86 (0.67-1.1)	0.82 (0.41-1.7)	-	-	-
Parity nulliparous vs. parous	0.22 (0.18-0.28)	1.5 (1.2-1.9)	0.78 (0.40-1.5)	0.17 (0.12-0.23)	-	-
Marital status living with partner vs. single	1.0 (0.83-1.3)	0.98 (0.77-1.3)	0.93 (0.51-1.7)	0.99 (0.74-1.3)	0.72 (0.29-1.8)	1.1 (0.29-4.3)
No. of sexual partners in last 12 months >1 vs. 0-1 partner	1.0 (0.83-1.3)	1.1 (0.88-1.5)	1.3 (0.69-2.4)	1.3 (0.95-1.8)	3.1 (1.3-7.7)	0.30 (0.04-2.5)
Smoking yes vs. no	0.74 (0.61-0.90)	1.0 (0.84-1.2)	1.3 (0.75-2.2)	-	-	-

Note: T-shape was chosen as the reference category. [a] Frameless device includes chains and balls.

Suppl. table 2 (continued)

	Czech Republic			Poland			Spain		
	Frameless device[a] OR (95% CI)	Omega OR (95% CI)	Y OR (95% CI)	Frameless device[a] OR (95% CI)	Omega OR (95% CI)	Y OR (95% CI)	Frameless device[a] OR (95% CI)	Omega OR (95% CI)	Y OR (95% CI)
Age	0.97 (0.92-1.0)	1.0 (0.98-1.1)	0.96 (0.93-0.99)	-	-	-	1.1 (0.96-1.2)	0.97 (0.88-1.1)	0.96 (0.92-0.99)
BMI	0.95 (0.89-1.0)	1.0 (0.98-1.1)	1.00 (0.97-1.0)	-	-	-	0.87 (0.73-1.0)	0.94 (0.83-1.1)	0.99 (0.95-1.0)
Household income high vs low	3.7 (2.0-6.8)	0.60 (0.40-0.88)	0.79 (0.57-1.1)	2.8 (0.50-15.5)	2.0 (1.4-3.0)	2.9 (1.4-5.9)	5.2 (1.4-19.5)	2.7 (0.81-9.0)	2.3 (1.5-3.6)
Previous IUD use yes vs. no	0.78 (0.42-1.4)	0.71 (0.47-1.1)	1.4 (1.0-2.0)	0.22 (0.03-1.9)	0.79 (0.54-1.1)	0.52 (0.25-1.1)	-	-	-
Previous hormonal contraception use yes vs. no	-	-	-	1.6 (0.29-8.9)	1.2 (0.84-1.8)	3.5 (1.5-8.2)	1.4 (0.34-5.4)	0.64 (0.22-1.9)	0.54 (0.37-0.77)
Parity nulliparous vs. parous	0.21 (0.10-0.43)	1.5 (0.71-3.1)	1.3 (0.72-2.2)	-	-	-	0.23 (0.05-1.1)	3.2 (0.55-19.0)	1.1 (0.66-1.8)
Marital status living with partner vs. single	0.72 (0.32-1.6)	0.82 (0.44-1.5)	1.1 (0.68-1.9)	-	-	-	0.39 (0.08-2.0)	0.87 (0.20-3.8)	0.72 (0.45-1.1)
No. of sexual partners in last 12 months >1 vs. 0-1 partner	0.82 (0.35-1.9)	0.32 (0.12-0.86)	0.74 (0.39-1.4)	-	-	-	4.3 (0.83-22.3)	5.2 (1.0-26.9)	1.7 (0.81-3.5)
Smoking yes vs. no	-	-	-	-	-	-	0.32 (0.06-1.6)	1.2 (0.41-3.6)	0.58 (0.38-0.87)

Note: T-shape was chosen as the reference category. Frameless device includes chains and balls.