JAMA | Original Investigation

Association of Hysteroscopic vs Laparoscopic Sterilization With Procedural, Gynecological, and Medical Outcomes

Kim Bouillon, MD, PhD; Marion Bertrand, MSc; Georges Bader, MD; Jean-Philippe Lucot, MD; Rosemary Dray-Spira, MD, PhD; Mahmoud Zureik, MD, PhD

IMPORTANCE Safety of hysteroscopic sterilization has been recently questioned following reports of general symptoms such as allergy, tiredness, and depression in addition to associated gynecological results such as pelvic pain, perforation of fallopian tubes or uterus, and unwanted pregnancy.

OBJECTIVE To compare the risk of reported adverse events between hysteroscopic and laparoscopic sterilization.

DESIGN, SETTING, AND PARTICIPANTS French nationwide cohort study using the national hospital discharge database linked to the health insurance claims database. Women aged 30 to 54 years receiving a first hysteroscopic or laparoscopic sterilization between 2010 and 2014 were included and were followed up through December 2015.

EXPOSURES Hysteroscopic sterilization vs laparoscopic sterilization.

MAIN OUTCOMES AND MEASURES Risks of procedural complications (surgical and medical) and of gynecological (sterilization failure that includes salpingectomy, second sterilization procedure, or pregnancy; pregnancy; reoperation) and medical outcomes (all types of allergy; autoimmune diseases; thyroid disorder; use of analgesics, antimigraines, antidepressants, benzodiazepines; outpatient visits; sickness absence; suicide attempts; death) that occurred within 1 and 3 years after sterilization were compared using inverse probability of treatment–weighted Cox models.

RESULTS Of the 105 357 women included (95.5% of eligible participants; mean age, 41.3 years [SD, 3.7 years]), 71 303 (67.7%) underwent hysteroscopic sterilization, and 34 054 (32.3%) underwent laparoscopic sterilization. During the hospitalization for sterilization, risk of surgical complications for hysteroscopic sterilization was lower: 0.13% for hysteroscopic sterilization vs 0.78% for laparoscopic sterilization (adjusted risk difference [RD], −0.64; 95% CI, −0.67 to −0.60) and was lower for medical complications: 0.06% vs 0.11% (adjusted RD, −0.05; 95% CI, −0.08 to −0.01). During the first year after sterilization, 4.83% of women who underwent hysteroscopic sterilization had a higher risk of sterilization failure than the 0.69% who underwent laparoscopic sterilization (adjusted hazard ratio [HR], 7.11; 95% CI, 5.92 to 8.54; adjusted RD, 4.23 per 100 person-years; 95% CI, 3.40 to 5.22). Additionally, 5.65% of women who underwent hysteroscopic sterilization required gynecological reoperation vs 1.76% of women who underwent laparoscopic sterilization (adjusted HR, 3.26; 95% CI, 2.90 to 3.67; adjusted RD, 4.63 per 100 person-years; 95% CI, 3.38 to 4.75); these differences persisted after 3 years, although attenuated. Hysteroscopic sterilization was associated with a lower risk of pregnancy within the first year of the procedure but was not significantly associated with a difference in risk of pregnancy by the third year (adjusted HR, 1.04; 95% CI, 0.83-1.30; adjusted RD, 0.01 per 100 person-years; 95% CI, −0.04 to 0.07). Risks of medical outcomes were not significantly increased with hysteroscopic sterilization compared with laparoscopic sterilization.

CONCLUSIONS AND RELEVANCE Among women undergoing first sterilization, the use of hysteroscopic sterilization was significantly associated with higher risk of gynecological complications over 1 year and over 3 years than was laparoscopic sterilization. Risk of medical outcomes was not significantly increased over 1 year or over 3 years. These findings do not support increased medical risks associated with hysteroscopic sterilization.

JAMA. 2018;319(4):375-387. doi:10.1001/jama.2017.21269

Editorial page 347

Supplemental content

Author Affiliations: Department of Epidemiology of Health Products, French National Agency for Medicines and Health Products Safety (ANSM), Saint-Denis, France (Bouillon, Bertrand, Dray-Spira, Zureik); Department of Obstetrics and Gynecology and Reproductive Medicine, Poissy Hospital, Poissy, France (Bader); Department of Gynecology and Obstetrics, Centre Hospitalier de Bethune, Bethune, France (Lucot); University Versailles St-Quentin-en-Yvelines, Montigny le Bretonneux, France (Zureik).

Corresponding Author: Mahmoud Zureik, MD, PhD, Department of Epidemiology of Health Products, French National Agency for Medicines and Health Products Safety (ANSM), 143-147 boulevard Anatole France, F-93285 Saint-Denis cedex, France (mahmoud.zureik@ansm.sante.fr).

In developed countries, 2 main types of female sterilization are available: laparoscopic and hysteroscopic sterilization, the latter performed using Essure (Bayer) implants marketed since 2002. This device, a 4-cm-long nitinol coil, is implanted in both fallopian tubes during a hysteroscopic procedure. Approximately 1 million women have undergone this procedure worldwide.[1,2] The main advantages of hysteroscopic sterilization are that the insertion does not necessitate general anesthesia nor does it carry the risks related to laparoscopy. However, it becomes effective when occlusive tubal fibrosis occurs 3 months following insertion. This leads to 2 constraints: women must use contraception and undergo an examination to confirm that the implants remained correctly placed at 3 months. In the United States, such examination is performed using hysterosalpingogram. In France, a pelvic x-ray was recommended until 2016. Placement was considered satisfactory when both devices appeared to be within the tubal lumen, had a symmetrical appearance, and the distance between the intrauterine ends was no more than 4 cm. If it was inconclusive, a pelvic ultrasound was performed with recourse to hysterosalpingogram if necessary.

Safety concerns related to hysteroscopic sterilization were raised in the United States in 2015 by women who reported to the US Food and Drug Administration (FDA) large numbers of adverse events including bleeding, perforation of fallopian tubes or uterus, unwanted pregnancy, hysterectomies, abdominal pain, migraine, depression, suicide attempts, allergy or hypersensitivity reactions, autoimmune diseases, thyroid disorder, and death.[2,3] These concerns have also been reported in other countries,[4-6] including France, the country with the second largest number of women using this method after the United States.

To investigate a possible role of hysteroscopic sterilization in these events, a comparative design is needed.[2] Four published studies[7-10] compared procedural and gynecological outcomes between hysteroscopic and laparoscopic sterilization, but none of them examined nongynecological outcomes.

To compare the risk of reported events between hysteroscopic and laparoscopic sterilization, a French nationwide cohort study was conducted.

Key Points

Question Are there clinically important risks associated with hysteroscopic sterilization compared with laparoscopic sterilization?

Findings In this cohort study of 105 357 women who underwent a first sterilization, the use of hysteroscopic sterilization was significantly associated with lower immediate risk of procedural complications than laparoscopic sterilization (0.13% vs 0.78% for surgical complications and 0.06% vs 0.11% for medical complications); and higher risk of gynecological complications with 4.83% vs 0.69% for sterilization failure and 5.65% vs 1.76% for gynecological reoperation over 1 year; these differences persisted over 3 years, although attenuated. Risk of medical outcomes was not significantly increased over 1 year or over 3 years.

Meaning These findings do not support an increased risk of medical outcomes related to hysteroscopic sterilization.

Methods

Data Sources

The national hospital discharge database (Programme de Médicalisation des Systèmes d'Information [PMSI]) and health insurance claim database (Système National d'Information Inter-Régimes de l'Assurance Maladie [SNIIRAM]) contain information on at least 99% of the French population. Health insurance is divided into various coverage plans based on individuals' occupational status. The general insurance coverage provides exhaustive information on health care use and vital status of approximately 75% of the French population. Various pharmacoepidemiological studies have already used these databases.[11-23]

The PMSI database contains details of all admissions, outpatient appointments, and accident and emergency attendances at all public and private hospitals in France. It contains dates of hospital admission and discharge, discharge diagnoses coded in the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10)*, and type of medical or surgical acts including imaging procedures coded using a common classification of medical procedures (Classification Commune des Actes Médicaux [CCAM]). An anonymous, unique identifier for each subject links PMSI information to the SNIIRAM database.

The SNIIRAM database contains individual data on all reimbursements for patients' health expenditures including medicinal products and outpatient medical care, prescribed or provided by health care professionals.

There is no formal clinical validation of the SNIIRAM and PMSI data. In France, all individuals have a lifelong social security number, which is needed every time an individual seeks health care services. The reimbursement procedure is automated through the social security card, Carte Vitale. In addition, hospital data are collected, validated, and transmitted to paying and controlling institutions by physicians working in private and public hospitals. Therefore, data used in this study are exhaustive and can be considered accurate.

This study was approved by the French Data Protection Supervisory Authority (Commission Nationale de l'Informatique et des Libertés), which did not require informed consent because data are anonymized.

Study Population

Women were included in the study if they had undergone a first hysteroscopic or laparoscopic sterilization between 2010 and 2014 based on CCAM (JJPE001 for hysteroscopic and JJPC003 for laparoscopic sterilization) and *ICD-10* codes (Z30.2: encounter for sterilization), were between 30 and 54 years old, and were registered in the general insurance coverage program. To restrict the study population to women

primarily seeking tubal sterilization, we excluded women who (1) were pregnant or had given birth within 3 months, (2) had been recently diagnosed with a cancer (<1 year prior to inclusion), (3) were receiving fertility treatments, (4) had a mastectomy or salpingectomy along with the sterilization procedure, and (5) had a delay of more than 1 day between the date of hospital admission and the date of the sterilization procedure. Women who had not received health care within the 3 years following the sterilization procedure (who possibly had incomplete information) were also excluded. Detailed definitions on exclusion criteria are described in eTable 1 in the Supplement.

Outcomes Definition and Identification

Outcomes included procedural (surgical and medical) complications occurring during their hospital stay for the sterilization procedure and gynecological and medical outcomes events occurring at the 1-year and 3-year follow-up. Detailed definition of outcome variables are described in eTables 2 through 7 in the Supplement.

Procedural surgical complications included acute hemorrhage, abdominal injury, complications related to the placement of a prosthesis or implant, debridement, evacuation, ablation of a foreign body, and other surgical complications. Procedural medical complications included acute myocardial infarction and cardiac arrest, stroke, peripheral arterial thromboembolism, deep vein thrombosis or pulmonary embolism, anesthetic or anaphylactic shock, respiratory complications, infection, and death.

Gynecological events were categorized as tubal disorder or surgery (complications related to the placement of a prosthesis or implant, or salpingectomy), uterine disorder (hysterectomy, genital hemorrhage, endometrectomy or curettage, or myomectomy), second sterilization procedure (hysteroscopic, laparoscopic, other types of sterilization), and pregnancy. Two composite gynecological outcomes were also defined: sterilization failure (including salpingectomy, second sterilization procedure, and pregnancy) and reoperation (including salpingectomy, hysterectomy, endometrectomy or curettage, myomectomy, or second sterilization procedure). Individual components of composite outcomes were also examined.

Based on safety concerns reported to the FDA,[2,3] medical outcomes included allergic reactions (diagnosed during a hospital stay; desensitized; tested using a patch test, prick test, or intradermal reaction test; or treated with an antihistamine); autoimmune diseases (including demyelinating diseases of the central nervous system; Guillain-Barré syndrome; cutaneous or systemic lupus; localized or systemic scleroderma; vasculitis; rheumatoid or juvenile arthritis; myositis, polymyositis, or dermatomyositis; Gougerot-Sjögren syndrome; idiopathic thrombocytopenic purpura; chronic inflammatory bowel disease; celiac disease; type 1 diabetes; and pancreatitis); thyroid disorders; use of analgesics, antimigraines, antidepressants, and benzodiazepines (as defined by at least 2 annual reimbursements for antihistamines and analgesics, and at least 2 reimbursements during follow-up for antimigraines, antidepressants, and benzodiazepines); suicide attempts; and death. Outcomes also included the number of physician office and outpatient visits and the number of days missed from work due to sickness or injury.

Covariates

Detailed definitions of covariates are described in eTable 7 in the Supplement. Sociodemographic characteristics included age, supplementary universal health coverage (supplementary insurance free of charge for people with a low income), and social deprivation index (level of deprivation in an area).[24]

Variables on lifestyle, medical, surgical, and gynecological history were defined using information collected during the 5-year period preceding the date of sterilization except for nonintrauterine contraceptive methods (1 reimbursement within 1 year prior to the inclusion). Lifestyle variables included alcohol abuse and tobacco and psychoactive substance use. Medical and surgical history included diabetes, obesity, circulatory system disease, allergy (allergy diagnosed during a hospital stay; desensitized; tested using a patch test, prick test, or intradermal reaction test; or treated with an antihistamine), autoimmune disease, thyroid disorder, nongynecological cancers, suicide attempts, and abdominal surgery. Gynecological history included breast cancer, gynecological cancer, gynecological surgery, pelvic inflammatory disease, noninflammatory pelvic disorder, congenital malformation of the uterus or cervix, endometrectomy or curettage, leiomyoma of the uterus, diagnostic or therapeutic hysteroscopy, pregnancy, and contraceptive method (oral contraceptive pill, transdermal patch, vaginal ring, subdermal implant, or intrauterine device).

Consumption of analgesics (opioids, nonsteroidal anti-inflammatory drugs, or other), antimigraines, antifibrinolytics, oral irons, antidepressants, benzodiazepines, and oral corticosteroids were each defined by the existence of at least 2 reimbursements within the 6-month period preceding the date of sterilization.

Characteristics of the sterilization procedure included status of hospital (public or private), region of hospital location, anesthetic procedure (including intravenous sedation or local, regional, or general anesthesia), duration of hospital stay, level of experience with sterilization procedures of the hospital and physician (number of hysteroscopic or laparoscopic sterilizations within the year prior to date of sterilization). A physician's level of experience was estimated for private hospitals for which an anonymous physician's unique identifiers were linked to patients' data. This information was not available for public hospitals.

Statistical Analysis

The frequency of the various outcomes was compared between women with hysteroscopic and laparoscopic sterilization. Multivariable logistic regression was used to study procedural complications occurring during the hospitalization for sterilization providing adjusted odds ratios (ORs) with 95% CIs. Assumptions of logistic regression models

were verified as follows: fit of the models was tested using the Hosmer-Lemeshow test; multicolinearity was assessed calculating variance inflation factors; all interactions terms between sterilization and covariates were tested; and overfitting was assessed using a backward selection procedure. Overall, these assumptions were met. Cox proportional hazards regression models were used for outcomes occurring at 1 and 3 years of follow-up providing adjusted hazard ratios (HRs) with 95% CIs. The proportional hazards assumption for the Cox models was assessed for studied outcomes by (1) testing interaction term type of sterilization × log (follow-up) and (2) graphically drawing curves log (−log [survival]) vs survival time. Except for uterine disorder, the proportional assumption was met. For this outcome, a multivariable logistic regression was conducted to verify that the adjusted OR (95% CIs) were close to the adjusted HR (95% CIs) found using the Cox model. Patients were followed up from the hospital discharge date after sterilization through the date of the occurrence of the event of interest for those experiencing this event. Those without such an event were censored on the date of the following events, whichever came first: the date of maximal time of follow-up, death, or December 31, 2015.

To account for differences between the comparison groups, models were adjusted for baseline covariates including age, medical (gynecological and nongynecological) history, and medication use and were weighted for inverse probability of treatment weighting using a propensity score for 11 characteristics related to women (supplementary universal health coverage, index of deprivation, indicators of alcoholism and of tobacco use, obesity, diabetes, history of psychoactive substance use, and suicide attempts) and related to sterilization sites (region of hospital location [n = 26], status of hospital (public or private), and hospital's level of experience with sterilization procedures (number of hysteroscopic or laparoscopic sterilizations within the year prior to date of sterilization categorized into quintiles). The inverse probability of treatment weighting using the propensity score was applied to account for indication bias. The propensity score was the probability that a woman received either hysteroscopic or laparoscopic sterilization calculated using logistic regression considering the aforementioned covariates.[25] To assess the balance of individual covariates before and after inverse probability of treatment weighting, standardized differences were calculated as the difference in means or proportions divided by the pooled standard deviation. The negligible difference was defined as an absolute standardized difference of less than 0.1.[26]

A sensitivity analysis was conducted examining composite gynecological outcomes (sterilization failure and reoperation) without salpingectomy because this intervention could have been performed along with laparoscopic sterilization for ovarian cancer prevention as promoted by North American Obstetricians and Gynecologists since 2013.[27]

The adjusted risk difference (RD), or difference in the cumulative incidence of gynecological and medical outcomes at 1 and 3 years of follow-up between hysteroscopic and laparoscopic groups was calculated as (adjusted HR−1) × unadjusted incidence rate per 100 person-years in the laparoscopic group. The 95% CIs were calculated analogously. For procedural (surgical and medical) complications, adjusted RDs (95% CIs) were estimated similarly replacing adjusted HR by an adjusted OR, which can be a good approximation of an adjusted HR when an outcome of interest is rare.

Interactions with the following covariates were tested: age, medical history related to studied outcome, and allergy history.

Because exhaustive and systematically collected data were analyzed, use of a technique to account for missing values at baseline was unnecessary. Missing information on follow-up was handled by excluding women with no health care use within the 3 years following the sterilization procedure. This criterion concerned only 322 women (0.29%) of the initial population.

Because of the large number of end points assessed and analyses conducted, the potential for type I error for positive findings needs to be considered in their interpretation.

All analyses were performed using SAS software, version 9.4 (SAS Institute Inc). Statistical significance was defined as $P < .05$; all alternative hypotheses were 2-sided.

Results

Of 110 299 eligible women who underwent a primary tubal sterilization procedure between January 2010 and December 2014, 105 357 (95.5%) were included: 71 303 (67.7%) underwent hysteroscopic and 34 054 (32.3%) laparoscopic sterilization. Of the possible reasons for exclusion, 4942 women (4.5%) met at least 1 of exclusion criterion: obstetric history 3 months prior to inclusion (n = 2505), a history of recent cancer (n = 1794), a delay between date of hospital admission for sterilization and date of sterilization of more than a day (n = 177), a concomitant mastectomy (n = 63) or salpingectomy (n = 131) at time of sterilization, or not using health care services for 3 or more years after sterilization (n = 322).

Women in the hysteroscopic sterilization group were slightly older (mean [SD] age, 41.5 years [3.5] vs 40.8 [3.9]), had a higher socioeconomic status, a more healthful lifestyle, more likely to have diabetes, and more likely to be obese; less likely to have a history of allergy, suicide attempts, gynecological history, and prior pregnancy and were less likely to use an intrauterine contraceptive device (**Table 1**). Prior to inclusion, the hysteroscopic group consumed few medications, consulted a general practitioner less often (mean [SD] number of consultations, 5.27 [4.9] vs 5.69 [5.2]) but consulted a gynecologist more often (mean [SD], 1.56 [1.5] vs 1.51 [1.5]) and had a lower mean number of sick days than did those in the laparoscopic group (mean [SD], 7.0 [27.4]) vs 8.1 [30.3]). Although these characteristics were statistically different, their absolute difference in percentages or means were small. eTable 8 in the Supplement

Table 1. Baseline Characteristics of Participants

Sociodemographic Characteristics	No. (%) of Women		*P* Value
	Hysteroscopic Sterilization (n = 71 303)	Laparoscopic Sterilization (n = 34 054)	
Age, mean (SD), y	41.5 (3.5)	40.8 (3.9)	<.001
Age category, y			
30-39	18 114 (25.4)	11 795 (34.6)	<.001
40-41	16 565 (23.2)	7119 (20.9)	
42-44	22 220 (31.2)	9309 (27.3)	
≥45	14 404 (20.2)	5831 (17.1)	
Supplementary universal insurance[a]	5140 (7.2)	3404 (10.0)	<.001
Social deprivation index (quintiles)			
1 (the least deprivation)	9972 (14.8)	3736 (11.6)	<.001
2	14 164 (21.1)	6213 (19.3)	
3	14 551 (21.6)	6854 (21.3)	
4	14 867 (22.1)	7445 (23.1)	
5 (the most deprivation)	13 699 (20.4)	7912 (24.6)	
Missing data	4050 (5.7)	1894 (5.6)	
Conditions			
History of allergy	9970 (14.0)	5493 (16.1)	<.001
Tobacco use	6024 (8.4)	3687 (10.8)	<.001
Circulatory system disease	5762 (8.1)	2765 (8.1)	.83
Obesity[b]	5361 (7.5)	2330 (6.8)	<.001
Thyroid disorders	4373 (6.1)	1986 (5.8)	.06
Diabetes	3492 (4.9)	1567 (4.6)	.04
Abdominal surgery	3420 (4.8)	1594 (4.7)	.41
Autoimmune disease	1625 (2.3)	834 (2.4)	.09
Alcohol abuse	646 (0.9)	443 (1.3)	<.001
Suicide attempt	567 (0.8)	422 (1.2)	<.001
Nongynecological cancers	402 (0.6)	195 (0.6)	.86
Psychoactive substance use	207 (0.3)	119 (0.3)	.11
Gynecologic history			
Contraceptive method	32 371 (45.4)	16 251 (47.7)	<.001
Intrauterine device	24 804 (34.8)	12 831 (37.7)	<.001
Other[c]	9583 (13.4)	4443 (13.0)	.08
Prior pregnancy	20 309 (28.5)	10 663 (31.3)	<.001
Noninflammatory pelvic disorder	3175 (4.5)	1990 (5.8)	<.001
Gynecologic surgery	3086 (4.3)	1693 (5.0)	<.001
Diagnostic or therapeutic hysteroscopy	2800 (3.9)	1763 (5.2)	<.001
Endometrectomy or curettage	1161 (1.6)	840 (2.5)	<.001
Pelvic inflammatory disease	749 (1.1)	905 (2.7)	<.001
Breast cancer	446 (0.6)	229 (0.7)	.37
Leiomyoma of uterus	462 (0.6)	211 (0.6)	.59
Gynecologic cancer	189 (0.3)	118 (0.3)	.02
Congenital malformation of uterus or cervix	43 (0.1)	24 (0.1)	.54
Concomitant medications			
Analgesic drugs	25 174 (35.3)	12 374 (36.3)	.001
Antidepressant drugs	6008 (8.4)	3236 (9.5)	<.001
Benzodiazepines	5404 (7.6)	3144 (9.2)	<.001
Oral corticosteroids	2370 (3.3)	1367 (4.0)	<.001
Antimigraine drugs	1837 (2.6)	1023 (3.0)	<.001
Oral iron	1562 (2.2)	732 (2.1)	.67
Antifibrinolytic drugs	410 (0.6)	246 (0.7)	.004

[a] Supplementary universal medical coverage is a supplementary insurance free of charge for people with a low income.

[b] Obesity was defined based on the use of antiobesity products or obesity-related hospitalization. For further details, see eTable 7 in the Supplement.

[c] Contraceptive pill, transdermal patch, vaginal ring, subdermal implant.

Table 2. Description of Management of Sterilization in Hospitals at Inclusion

	Hysteroscopic Sterilization (n = 71 303)	Laparoscopic Sterilization (n = 34 054)	*P* Value
No. of hospitals	654	814	
Type of hospital, No. (%) of women			
Public	41 404 (58.2)	18 977 (55.9)	<.001
Private	29 785 (41.8)	14 997 (44.1)	
Missing data	114	80	
Anesthetic procedure[a]	52 196 (73.2)	33 876 (99.5)	<.001
Duration of hospitalization, d			
Median (IQR; range)	0 (0-0; 0-6)	0 (0-1; 0-20)	
Mean (SD)	0.01 (0.1)	0.57 (0.7)	<.001
No. of days in hospital			
0	70 406 (98.7)	17 600 (51.7)	<.001
1	890 (1.2)	14 163 (41.6)	
>1	7 (<1)	2291 (6.7)	
No. of procedures performed within year of sterilization date, median (IQR)			
Hospital			
Laparoscopic	21 (11-38)	31 (17-51)	<.001
Hysteroscopic	60 (33-102)	36 (17-67)	<.001
Physician[b]			
Laparoscopic	6 (3-12)	11 (6-20)	<.001
Hysteroscopic	24 (13-43)	10 (4-21)	<.001

Abbreviation: IQR, interquartile range.

[a] Including intravenous sedation or local, regional, or general anesthesia.

[b] Physican records were only available from private hospitals.

summarizes the balance of covariates between groups before and after applying inverse probability of treatment weighting. All covariates included in the inverse probability of treatment-weighting analysis were well-balanced in both groups (standardized differences value <0.1). This was also the case for all other covariates not included in inverse probability of treatment weighting analysis except for pelvic inflammatory disease (standardized differences value, 0.112). This small difference was taken into account in multivariable analyses because this variable was systematically adjusted for.

The sterilization procedures of women included in the study were conducted in 831 hospitals located throughout all 26 French regions. Hospitals in which hysteroscopic sterilization had been performed differed from those in which laparoscopic sterilization had been performed in terms of status (58.2% public for hysteroscopic sterilization vs 55.9% public for laparoscopic sterilization), level of experience in hysteroscopic sterilization (median number performed during the preceding year, 60 vs 36, respectively) (**Table 2**), and region (eTable 9 in the Supplement).

Overall, 105 318 women (99.96%) were followed-up for at least 1 year and 54 232 (51.5%) for at least 3 years. The mean (SD) follow-up time up to 3 years was 2.5 years (0.6 years).

Procedural Complications

At the time of the procedure, inhospital surgical complications occurred in 0.13% of women in hysteroscopic and 0.78% in laparoscopic groups.

Medical complications occurred in 0.06% in hysteroscopic and 0.11% in laparoscopic group.

In multivariable analysis, hysteroscopic sterilization was associated with a significantly lower risk of surgical complications than was laparoscopic sterilization (adjusted OR, 0.18; 95% CI, 0.14 to 0.23; adjusted RD, −0.64; 95% CI, −0.67 to −0.60) and medical (adjusted OR, 0.51; 95% CI, 0.30 to 0.89; adjusted RD, −0.05; 95% CI, −0.08 to −0.01) complications of the sterilization procedure. Description of each condition is provided in **Table 3**. No deaths occurred during the sterilization procedure in either group.

Gynecologic Outcomes

At the 1-year follow-up, the risk of tubal disorder or surgery, complications related to the placement of a prosthesis or implant, or salpingectomy, was 0.70% in women who underwent hysteroscopic sterilization and 0.23% in women who underwent laparoscopic sterilization; these disorders were mostly salpingectomies (**Table 4**). After adjustment, hysteroscopic sterilization was associated with a significantly higher risk of tubal disorder or surgery than was laparoscopic sterilization (adjusted HR, 2.98; 95% CI, 2.17 to 4.10; adjusted RD, 0.47 per 100 person-years; 95% CI, 0.28 to 0.73). This heightened risk persisted at the 3-year follow-up although was less pronounced (Table 4).

Hysteroscopic sterilization was associated with a significantly lower risk of uterine disorder at 1 year than was laparoscopic sterilization (1.28% vs 1.50%; adjusted HR, 0.85; 95% CI, 0.74 to 0.98; adjusted RD, −0.23 per 100 person-years; 95% CI, −0.39 to −0.03), with fewer hysterectomies and fewer occurrences of genital hemorrhage but with more myomectomies (Table 4). This lower risk of uterine disorder persisted at 3 years (Table 4).

Table 3. Surgical and Medical Complications After Hysteroscopic and Laparoscopic Sterilization, 2010-2014, France

	No. (%) of Women		Adjusted (95% CI)[a]		
	Hysteroscopic Sterilization (n = 71 303)	Laparoscopic Sterilization (n = 34 054)	Risk Difference	Odds Ratio	*P* Value
Surgical complication[b]	96 (0.13)	265 (0.78)	−0.64 (−0.67 to −0.60)	0.18 (0.14 to 0.23)	<.001
Acute hemorrhage	5 (0.01)	56 (0.16)			<.001
Abdominal injury	30 (0.04)	117 (0.34)			<.001
Complications from prosthesis or implant placement	35 (0.05)	20 (0.06)			.52
Debridement, evacuation, ablation of a foreign body	7 (0.01)	37 (0.11)			<.001
Other	19 (0.03)	62 (0.18)			<.001
Medical complication[b]	41 (0.06)	39 (0.11)	−0.05 (−0.08 to −0.01)	0.51 (0.30 to 0.89)	.002
Acute myocardial infarction or cardiac arrest	11 (0.02)	2 (0.01)			.19
Stroke	1 (<0.01)	2 (0.01)			.20
Hemorrhagic	0	0			
Ischemic	1 (0.00)	2 (0.01)			.20
Peripheral arterial thromboembolism	1 (0.00)	2 (0.01)			.20
Deep vein thrombosis or pulmonary embolism	18 (0.03)	14 (0.04)			.17
Deep vein thrombosis	14 (0.02)	11 (0.03)			.21
Pulmonary embolism	4 (0.01)	3 (0.01)			.55
Anesthetic or anaphylactic shock	1 (<0.01)	5 (0.01)			.008
Respiratory complications	2 (<0.01)	8 (0.02)			.001
Infection	8 (0.01)	9 (0.03)			.07
Death	0	0			

[a] Laparoscopic group is the reference group for comparisons. Adjusted for age, propensity score for socioeconomic characteristics, medicines use, and medical, surgical, gynecological history.

[b] Numbers may not sum because some patients had more than 1 complication.

Hysteroscopic sterilization was associated with a significantly higher risk of a women undergoing a second sterilization procedure at 1 year than was laparoscopic sterilization (4.10% vs 0.16%; adjusted HR, 25.99; 95% CI, 17.84-37.86; adjusted RD, 4.11 per 100 person-years; 95% CI, 2.77-6.07). Among 2955 women in the hysteroscopic group who underwent a second sterilization, 65.4% had a laparoscopic sterilization and 35.5% another hysteroscopic sterilization for their second procedure; among 56 women in the laparoscopic group who underwent a second sterilization, 84% had a laparocopic sterilization, 9% hysteroscopic sterilization, and 7% minilaparotomy (Table 4).

Hysteroscopic sterilization was associated with a significantly lower risk of pregnancy at 1 year than was laparoscopic sterilization (0.24% vs 0.41%; adjusted HR, 0.70; 95% CI, 0.53 to 0.92; adjusted RD, −0.12 per 100 person-years; 95% CI, −0.19 to −0.03). However, this difference was no longer significant at 3 years (0.48% vs 0.57%; adjusted HR, 1.04; 95% CI, 0.83 to 1.30; adjusted RD, 0.001 per 100 person-years; 95% CI, −0.04 to 0.07). In the hysteroscopic group, women who did not complete a confirmation test compared with those who did were more likely to be pregnant at the 1-year follow-up (0.28% vs 0.16%; adjusted HR, 1.49; 95% CI, 1.01 to 2.19; adjusted RD, 0.08 per 100 person-years; 95% CI, 0.002 to 0.19) (eTable 10 in the Supplement); and, women whose practitioners performed fewer than 12 procedures in the preceding year than practitioners who performed 12 or more were more likely to be pregnant at the 1-year follow-up (eTable 11 in the Supplement).

Hysteroscopic sterilization was associated with a significantly higher risk of sterilization failure after 1 year (4.83% vs 0.69%; adjusted HR, 7.11; 95% CI, 5.92 to 8.54; adjusted RD, 4.23 per 100 person-years; 95% CI, 3.40 to 5.22) and after 3 years than was laparoscopic sterilization (5.75% vs 1.29%; adjusted HR, 4.66; 95% CI, 4.06 to 5.34; adjusted RD, 1.87 per 100 person-years; 95% CI, 1.56 to 2.22). This was also the case with the risk of reoperation after 1 and 3 years (Table 4). When salpingectomy was removed from these composite outcomes, adjusted HRs at 1 year of follow-up increased from 7.11 to 8.57 (95% CI, 6.93 to 10.61; adjusted RD, 3.86 per 100 person-years; 95% CI, 3.02 to 4.90) for sterilization failure and from 3.26 to 3.28 (95% CI, 2.90 to 3.71; adjusted RD, 3.68 per 100 person-years; 95% CI, 3.07 to 4.38) for reoperation.

Medical Outcomes

Hysteroscopic sterilization compared with laparoscopic sterilization did not significantly differ in the risks of autoimmune diseases (overall and by type) and in thyroid disorders at both time points (**Table 5**). Details of autoimmune diseases are provided in eTable 12 in the Supplement.

Hysteroscopic compared with laparoscopic sterilization did not nonsignificantly differ in the risk of allergy at either the 1 year or 3 year follow-up (Table 5). However, results

Table 4. One-Year and 3-Year Gynecologic Outcomes After Hysteroscopic and Laparoscopic Sterilization, 2010-2014, France

Gynecologic Disorder	Hysteroscopic Sterilization (n = 71 303)			Laparoscopic Sterilization (n = 34 054)			Adjusted Risk Difference per 100 Person-Years (95% CI)[a]	Adjusted Hazard Ratio (95% CI)[a,b]	*P* Value[c]
	No. (%) of Women	No. of Person-Years	Unadjusted Incidence per 100 Person-Years	No. (%) of Women	No. of Person-Years	Unadjusted Incidence per 100 Person-Years			
One-Year Follow-up									
Fallopian tubal disorder or surgery	500 (0.70)	71 002	0.70	80 (0.23)	34 010	0.24	0.47 (0.28 to 0.73)	2.98 (2.17 to 4.10)	<.001
Complications of genitourinary prosthetic devices, implants, and grafts	75 (0.11)	71 242	0.11	0	34 049	0			
Salpingectomy	441 (0.62)	71 041	0.62	80 (0.23)	34 010	0.24	0.39 (0.22 to 0.62)	2.65 (1.92 to 3.65)	<.001
Uterine disorder	914 (1.28)	70 859	1.29	510 (1.50)	33 835	1.51	−0.23 (−0.39 to −0.03)	0.85 (0.74 to 0.98)	.02
Hysterectomy	308 (0.43)	71 171	0.43	275 (0.81)	33 938	0.81	−0.37 (−0.45 to −0.28)	0.54 (0.44 to 0.66)	<.001
Abnormal vaginal bleeding	164 (0.23)	71 216	0.23	112 (0.33)	34 001	0.33	−0.09 (−0.16 to −0.01)	0.71 (0.52 to 0.96)	.03
Endometrectomy or curettage[d]	508 (0.71)	71 048	0.72	215 (0.63)	33 956	0.63	0.09 (−0.04 to 0.25)	1.14 (0.93 to 1.40)	.22
Myomectomy[d]	157 (0.22)	71 206	0.22	32 (0.09)	34 038	0.09	0.11 (0.03 to 0.24)	2.14 (1.28 to 3.59)	.004
Second sterilization procedure	2955 (4.10)	69 290	4.26	56 (0.16)	34 015	0.16	4.11 (2.77 to 6.07)	25.99 (17.84 to 37.86)	<.001
Pregnancy[e]	168 (0.24)	71 213	0.24	138 (0.41)	33 968	0.41	−0.12 (−0.19 to −0.03)	0.70 (0.53 to 0.92)	.02
Sterilization failure[f]	3446 (4.83)	69 017	4.99	235 (0.69)	33 912	0.69	4.23 (3.40 to 5.22)	7.11 (5.92 to 8.54)	<.001
Reoperation[g]	4032 (5.65)	68 775	5.86	601 (1.76)	33 784	1.78	4.63 (3.38 to 4.75)	3.26 (2.90 to 3.67)	<.001
Three-Year Follow-up									
Fallopian tubal disorder or surgery	834 (1.17)	177 986	0.47	233 (0.68)	86 187	0.27	0.21 (0.13 to 0.32)	1.79 (1.47 to 2.17)	<.001
Complications of genitourinary prosthetic devices, implants, and grafts	86 (0.12)	179 076	0.05	3 (0.01)	86 474	0.003	0.04 (0.001 to 0.22)	13.12 (2.70 to 63.20)	.001
Salpingectomy	772 (1.10)	178 111	0.43	231 (0.68)	86 190	0.27	0.18 (0.10 to 0.28)	1.68 (1.38 to 2.04)	<.001
Uterine disorder	3028 (4.25)	175 645	1.72	1792 (5.26)	84 361	2.12	−0.38 (−0.51 to −0.25)	0.82 (0.76 to 0.88)	<.001
Hysterectomy	1339 (1.90)	177 794	0.75	992 (2.90)	85 326	1.16	−0.40 (−0.48 to −0.31)	0.66 (0.59 to 0.73)	<.001
Abnormal vaginal bleeding	613 (0.86)	178 541	0.34	364 (1.10)	86 038	0.42	−0.07 (−0.13 to −0.01)	0.83 (0.70 to 0.97)	.02
Endometrectomy or curettage[d]	1661 (2.30)	177 287	0.94	860 (2.50)	85 489	1.01	−0.06 (−0.15 to 0.05)	0.94 (0.85 to 1.05)	.29
Myomectomy[d]	334 (0.47)	178 781	0.19	117 (0.34)	86 356	0.14	0.04 (0.0 to 0.09)	1.29 (0.98 to 1.70)	.08
Second sterilization procedure	3230 (4.50)	172 485	1.87	97 (0.28)	86 311	0.11	1.76 (1.29 to 2.38)	16.63 (12.50 to 22.20)	<.001
Pregnancy[e]	343 (0.48)	178 721	0.19	194 (0.57)	86 118	0.23	0.001 (−0.04 to 0.07)	1.04 (0.83 to 1.30)	.74
Sterilization failure[f]	4098 (5.75)	171 190	2.39	438 (1.29)	85 796	0.51	1.87 (1.56 to 2.22)	4.66 (4.06 to 5.34)	<.001
Reoperation[g]	6444 (9.04)	168 555	3.82	1979 (5.81)	84 067	2.35	1.46 (1.20 to 1.72)	1.62 (1.51 to 1.73)	<.001

[a] Adjusted for age, propensity score for socioeconomic characteristics, medicines use, and medical, surgical, gynecological history.

[b] Laparoscopic group is the reference group for comparisons

[c] Wald χ^2 statistic was used to calculate *P* values.

[d] Not concomitant to salpingectomy or second sterilization procedure.

[e] Pregnancy occurring subsequent to a second sterilization procedure or to a poststerilization regret (fertility treatment or surgical reanastomosis of the fallopian tubes) was not considered. For further details on the definition of poststerilization regret, see eTable 3 in the Supplement.

[f] Sterilization failure includes salpingectomy, second sterilization procedure, or pregnancy.

[g] Reoperation includes salpingectomy, hysterectomy, endometrectomy or curettage, myomectomy, or second sterilization procedure.

Table 5. One-Year and 3-Year Medical Outcomes After Hysteroscopic and Laparoscopic Sterilization, 2010-2014, France

	Hysteroscopic Sterilization (n = 71 303)			Laparoscopic Sterilization (n = 34 054)			Adjusted Risk Difference per 100 Person-Years (95% CI)[a]	Adjusted HR (95% CI)[a,b]	*P* Value[c]
	No. (%) of Women	No. of Person-Years	Unadjusted Incidence per 100 Person-Years	No. (%) of Women	No. of Person-Years	Unadjusted Incidence per 100 Person-Years			
One-Year Follow-up									
Autoimmune disease	393 (0.55)	71 054	0.55	198 (0.58)	33 931	0.58	0.00 (−0.12 to 0.15)	1.00 (0.80 to 1.25)	.98
Thyroid disorder	4789 (6.72)	66 962	7.15	2200 (6.46)	32 066	6.86	0.00 (−0.48 to 0.41)	1.00 (0.93 to 1.06)	.92
Allergy	9373 (13.15)	64 435	14.55	4691 (13.78)	30 625	15.32	0.31 (−0.31 to 1.07)	1.02 (0.98 to 1.07)	.33
Analgesics[d]	38 434 (53.90)	44 288	86.78	19 096 (56.08)	20 676	92.36	−2.77 (−4.62 to −0.92)	0.97 (0.95 to 0.99)	.004
Antimigraines[e]	2665 (3.74)	69 343	3.84	1299 (3.81)	33 104	3.92	0.35 (0.00 to 0.74)	1.09 (1.00 to 1.19)	.04
Antidepressants[e]	7583 (10.63)	65 680	11.54	4039 (11.86)	31 093	12.99	−0.52 (−1.04 to 0.13)	0.96 (0.92 to 1.01)	.11
Benzodiazepines[e]	8378 (11.75)	65 361	12.82	4557 (13.38)	30 820	14.79	−1.03 (−1.63 to −0.44)	0.93 (0.89 to 0.97)	.002
Suicide attempt	144 (0.20)	71 222	0.20	99 (0.29)	33 998	0.29	−0.06 (−0.12 to 0.03)	0.81 (0.59 to 1.11)	.18
Death	24 (0.03)	71 291	0.03	10 (0.03)	34 049	0.03	0.01 (−0.02 to 0.07)	1.28 (0.48 to 3.41)	.62
Three-Year Follow-up									
Autoimmune disease	704 (0.99)	178 118	0.40	378 (1.10)	85 884	0.44	−0.03 (−0.09 to 0.05)	0.94 (0.80 to 1.11)	.48
Thyroid disorder	5492 (7.70)	166 736	3.29	2591 (7.61)	80 639	3.21	−0.06 (−0.26 to 0.13)	0.98 (0.92 to 1.04)	.56
Allergy	7203 (10.10)	164 175	4.39	3555 (10.44)	78 956	4.50	0.18 (−0.05 to 0.45)	1.04 (0.99 to 1.10)	.12
Analgesics[d]	33 228 (46.60)	103 852	32.0	17 379 (51.03)	46 705	37.20	−3.35 (−4.09 to −2.60)	0.91 (0.89 to 0.93)	<.001
Antimigraines[e]	4251 (5.96)	170 564	2.49	2214 (6.50)	81 955	2.70	0.00 (−0.19 to 0.19)	1.00 (0.93 to 1.07)	.97
Antidepressants[e]	11560 (16.21)	156 969	7.36	6272 (18.42)	74 304	8.44	−0.68 (−1.01 to −0.34)	0.92 (0.88 to 0.96)	<.001
Benzodiazepines[e]	15 094 (21.17)	148 916	10.14	8236 (24.19)	69 860	11.79	−1.18 (−1.53 to −0.83)	0.90 (0.87 to 0.93)	<.001
Suicide attempt	392 (0.55)	178 716	0.22	270 (0.79)	86 104	0.31	−0.06 (−0.11 to −0.01)	0.80 (0.66 to 0.97)	.03
Death	77 (0.11)	179 246	0.04	34 (0.10)	86 478	0.04	0.01 (−0.01 to 0.04)	1.12 (0.66 to 1.90)	.67

[a] Laparoscopic group is the reference group for comparisons.

[b] Adjusted for age, propensity score for socioeconomic characteristics, medicines use, and medical, surgical, gynecological history.

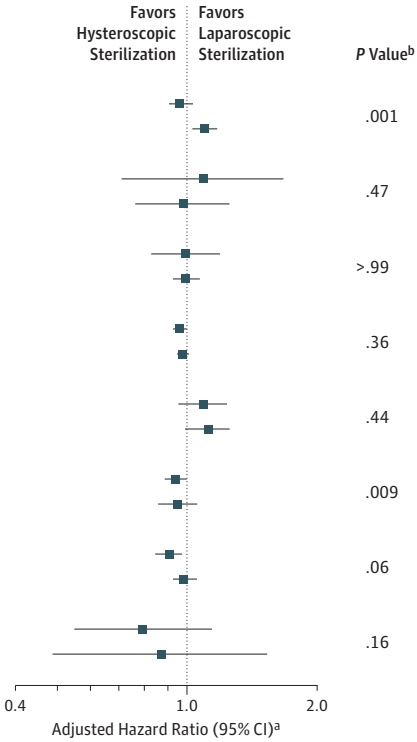
[c] Wald χ^2 statistic was used to calculate *P* values.

[d] Having at least 2 reimbursements of antalgics within first year of follow-up and 6 reimbursements within 3 years of follow-up. Reimbursements occurring during the first month of follow-up were not taken into account. Duration of follow-up was estimated between 1 month after the hospital discharge date for sterilization and the date of the first reimbursement.

[e] Having at least 2 reimbursements. Duration of follow-up was estimated between the hospital discharge date for sterilization and the date of the first reimbursement.

Figure. One-Year Medical Outcomes by Prior History of Each Outcome After Hysteroscopic and Laparoscopic Sterilization, 2010-2014, France

Medical Outcome	Hysteroscopic Sterilization No. With Outcome/Total (%)	Laparoscopic Sterilization No. With Outcome/Total (%)	Adjusted Hazard Ratio (95% CI)[a]	P Value[b]
Allergy				
No history	5068/61 333 (8.3)	2492/28 561 (8.7)	0.96 (0.91-1.03)	.001
History	4305/9970 (43.2)	2199/5493 (40.0)	1.10 (1.03-1.17)	
Autoimmune disease				
No history	116/69 678 (0.2)	50/33 220 (0.2)	1.09 (0.71-1.67)	.47
History	277/1625 (17.0)	148/834 (17.7)	0.98 (0.76-1.25)	
Thyroid disorder				
No history	587/66 930 (0.9)	290/32 068 (0.9)	0.99 (0.83-1.19)	>.99
History	4202/4373 (96.1)	1910/1986 (96.2)	0.99 (0.93-1.07)	
Analgesic use				
No history	19 415/46 129 (42.1)	9578/21 680 (44.2)	0.96 (0.93-0.99)	.36
History	19 019/25 174 (75.6)	9518/12 374 (76.9)	0.98 (0.95-1.01)	
Antimigraine use				
No history	1281/69 466 (1.8)	578/33 031 (1.7)	1.09 (0.96-1.23)	.44
History	1384/1837 (75.3)	721/1023 (70.5)	1.12 (0.99-1.25)	
Antidepressant use				
No history	2857/66 295 (4.4)	1502/30 818 (4.9)	0.94 (0.89-1.00)	.009
History	4726/6008 (78.7)	2537/3236 (78.4)	0.95 (0.86-1.05)	
Benzodiazepine use				
No history	4569/66 899 (6.9)	2342/30 910 (7.6)	0.91 (0.85-0.97)	.06
History	3809/5404 (70.5)	2215/3144 (70.5)	0.98 (0.93-1.05)	
Suicide attempt				
No history	115/70 736 (0.2)	75/33 632 (0.2)	0.79 (0.55-1.14)	.16
History	29/567 (5.1)	24/422 (5.7)	0.87 (0.49-1.53)	



[a] Laparoscopic group is the reference group for comparisons. Adjusted for age, propensity score for socioeconomic characteristics, medicines use, and medical, surgical, gynecological history.

[b] *P* value for interaction.

differed according to allergy history (*P* value for interaction = .001): in women who had prior allergies, hysteroscopic sterilization was associated with a significantly higher risk of developing an allergic reaction during follow-up than laparoscopic sterilization (43.20% vs 40.00%; adjusted HR, 1.10; 95% CI, 1.03 to 1.17; adjusted RD, 5.86 per 100 person-years; 95% CI, 1.76 to 9.96 at 1 year; and 37.70% vs 34.60%; adjusted HR, 1.10; 95%CI, 1.03 to 1.18; adjusted RD, 2.00 per 100 person-years; 95% CI, 0.60 to 3.59 at 3 years) whereas risk of allergies among women who did not have prior allergies did not differ (eTable 13 in the Supplement).

Hysteroscopic sterilization was associated with lower use of analgesics, antidepressants, and benzodiazepines at 1 year than was laparoscopic sterilization (Table 5). This lower risk was slightly more pronounced at 3 years. Hysteroscopic sterilization was associated with a higher risk of using antimigraines at 1 year than was laparoscopic sterilization, but this difference was no longer significant at 3 years (Table 5).

Hysteroscopic compared with laparoscopic sterilization did not differ significantly in the risk of attempted suicide at 1 year (0.20% vs 0.29%; adjusted HR, 0.81; 95% CI, 0.59 to 1.11; adjusted RD, −0.06 per 100 person-years; 95% CI, −0.12 to 0.03) but had a lower risk at 3 years (0.55% vs 0.79%; adjusted HR, 0.80; 95% CI, 0.66 to 0.97; adjusted RD, −0.06 per 100 person-years; 95% CI, −0.11 to −0.01). The risk of death was not significantly different between these groups whatever the length of follow-up (Table 5).

Hysteroscopic sterilization had a lower mean number of physician office or outpatient visits than laparoscopic sterilization at 1 year (8.63 vs 9.11; mean difference, −0.48; 95% CI, −0.58 to −0.38; *P* value <.001) and 3 years (20.74 vs 22.39; mean difference, −1.65; 95% CI, −1.90 to −1.40; *P* value <.001) and fewer number of sick days (5.90 vs 6.50 at the 1-year follow-up; mean difference, −0.60; 95% CI, −0.93 to −0.27; *P* value <.001; and, 28.3 vs 32.3 at the 3-year follow-up, mean difference, −4.00; 95% CI, −5.21 to −2.79; *P* value <.001) (eTable 14 in the Supplement).

Subgroups Analyses

A significant interaction with allergy history was found and the results of subgroup analysis are described above. Other interaction terms were not significant and results of subgroup analyses are presented in the **Figure** and in eTables 15 through 17 and the eFigure in the Supplement.

Discussion

Among women undergoing their first sterilization, the use of hysteroscopic vs laparoscopic sterilization was associated with lower risk of procedural (surgical and medical) complications and higher risk of gynecological complications over

1 or 3 years. In absolute terms, RDs were very small for procedural complications (−0.64% and −0.05% for surgical and medical complications, respectively) and more important for gynecological complications with 4.23 and 1.87 per 100 person-years' excess sterilization failure and 4.63 and 1.46 per 100 person-years' excess gynecological reoperation over 1 and 3 years, respectively. Risks of a wide range of medical outcomes were not significantly increased over 1 or 3 years.

Four studies comparing women with hysteroscopic vs laparoscopic sterilization were published between 2014 and 2017.[7-10] The present results regarding procedural (surgical and medical) complications[8] and gynecological outcomes[7-10] are consistent with these studies. Regarding the risk of pregnancy, these studies provided inconsistent results when hysteroscopic sterilization was compared with laparoscopic sterilization: Perkins et al[9] reported a higher pregnancy risk, Fernandez et al[7] a lower risk, and Mao et al[8] a not significantly different risk with the pregnancy rate at 1 year varying between 0.2% to 2.0%. In the present study, the frequency of pregnancy following hysteroscopic sterilization was lower within the first year following sterilization (potentially in relation with the recommendation of maintaining contraception during the first 3 months after hysteroscopic sterilization, until the occlusive fibrosis is obtained), this difference was no longer significant over 3 years. A second sterilization procedure following hysteroscopic sterilization is a well-identified risk already described in phase 2[28] and 3[29] studies, in which the risk varied between 4.0% and 4.5%. In the present study, this risk was 4.1% at the 1-year follow-up, comparable with that reported in previous studies conducted in real-life conditions in patients who received care in public or private hospitals[8,9,30-33] and much higher than after laparoscopic sterilization.

Consistent with Perkins et al,[9] hysteroscopic sterilization was associated with a lower risk of hysterectomy than was laparoscopic sterilization after adjustment for known risk factors for hysterectomy (history of leiomyoma of uterus, genital bleeding, pelvic inflammatory disease, noninflammatory pelvic disorder). Chronic pelvic pain is also an important risk factor to consider.[34] To approximate this, in addition to the adjusted risk factors mentioned above, a proxy variable such as analgesics (opioids, nonsteroidal anti-inflammatory drugs, or others) use was also taken into account. In addition, an increased risk of hysterectomy in women with laparoscopic sterilization compared with women of same age but who had not undergone sterilization has been reported as well.[35-38]

To our knowledge, this is the first study aiming at comparing medical outcomes in addition to gynecological outcomes between hysteroscopic and laparoscopic sterilization. Thanks to the multiple information provided by health care databases (causes of hospitalization, reimbursed drugs, medical or surgical acts, physician visits, days of sickness absence), a wide range of outcomes corresponding to the heterogeneous nature of notified complaints could be examined.

To evaluate the safety and effectiveness of hysteroscopic sterilization, the FDA has ordered the manufacturer to conduct a study comparing outcomes between women receiving hysteroscopic and laparoscopic sterilization. The results of an open-label, nonrandomized, prospective cohort of 2800 (1400 per group) women are expected in 2023.[39] Overall, our study was able to timely respond to issues raised by the FDA and by others who have debated hysteroscopic sterilization.

Limitations

This observational study has several limitations. First, to investigate a possible role of hysteroscopic sterilization in notified complaints, administrative databases were used. Therefore, all individual disorders reported by patients or physicians and collected into medical device vigilance databases could not be examined. To take into account the different nature of complaints, both specific (gynecological events, allergy, autoimmune diseases, thyroid disorders, suicide attempts, death) and unspecific (use of analgesics, antimigraines, antidepressants, and benzodiazepines; physician visits; sick day absences) outcomes were studied. Despite the examination of numerous and heterogeneous outcomes, the present findings do not support the concern that increased medical risks are associated with hysteroscopic sterilization. However, the upper limits of the 95% CIs around the adjusted RDs for the nonstatistically significant associations varied between −0.48 and 1.07 per 100 person-years (Table 4 and Table 5). If a clinically important difference is not considered to be included within these values, power should not be a concern.

Although a subgroup analysis found a significantly increased allergy risk in the subgroup of women who had allergies, the combination of a null overall effect and large number of tested interactions makes this finding very tenuous; it should be considered only hypothesis generating.

Second, the risk of salpingectomy may have been underestimated in the laparoscopic group because salpingectomy could have been performed during the first sterilization. However, this may not be the case because opportunistic salpingectomy for ovarian cancer prevention in France was rarely conducted during the period of inclusion (2010-2014).[40] In addition, the overall conclusion on gynecological outcomes did not change when composite outcomes were examined without salpingectomy: adjusted HR at the 1-year follow-up increased from 7.11 to 8.57 for sterilization failure and from 3.26 to 3.28 for reoperation, confirming that gynecological outcomes were still worse with hysteroscopic than with laparoscopic sterilization.

Third, in this study, it was not possible to assess the formal validity of the *ICD-10* diagnoses for outcomes of the PMSI database compared with a medical review and adjudication. Although it is not available, information on hospital stay such as causes of hospitalization is accurate and precise because such data are used to allocate the budgets to both public and private hospitals; therefore, the quality of diagnostic codes from these data are regularly checked against patients' medical records. Moreover, when comparative results exist in the literature, the present findings were consistent with those found in the previous studies as dis-

cussed above: similar incidence of pregnancy to that found by Fernandez et al,[7] comparative baseline characteristics between hysteroscopic and laparoscopic groups close to that in the study by Perkins et al,[9] and most importantly same direction of association for procedural and gynecological outcomes.[7-10]

Fourth, only women with the general insurance coverage were included. This may question generalizability of the present results. However, because this covers 75% of the French population, these findings are likely to be generalizable, and it is unlikely that the present findings were affected by selection bias, in particular by geographic variability, which was also considered for these analyses. In addition, to further avoid selection bias and to render baseline characteristics more comparable between comparison groups, exclusion criteria had been applied (n = 4942; 4.5% of initial population) and the inverse probability of treatment weighting using the propensity score was performed making comparison groups well balanced. However, residual selection bias and confounding effect of unmeasured or unknown factors cannot be ruled out.

Conclusions

Among women undergoing first sterilization, the use of hysteroscopic sterilization was significantly associated with higher risk of gynecological complications over 1 year and over 3 years than was laparoscopic sterilization. Risk of medical outcomes was not significantly increased over 1 year or over 3 years. These findings do not support increased medical risks associated with hysteroscopic sterilization.

ARTICLE INFORMATION

Accepted for Publication: December 18, 2017.

Author Contributions: Dr Bouillon and Ms Bertrand had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Drs Bouillon and Zureik are its guarantors.
Concept and design: Bouillon, Dray-Spira, Zureik.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Bouillon, Zureik.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Bouillon, Bertrand.
Administrative, technical, or material support: Bouillon, Bertrand, Dray-Spira, Zureik.
Supervision: Dray-Spira, Zureik.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Lucot reported receiving personal fees from Boston Scientific. No other disclosures were reported.

REFERENCES

1. McCarthy M. US to require safety warnings for Essure sterilization device. *BMJ*. 2016;352:i1283.

2. Dhruva SS, Ross JS, Gariepy AM. Revisiting Essure—toward safe and effective sterilization. *N Engl J Med*. 2015;373(15):e17. doi:10.1056/NEJMp1510514

3. US Food and Drug Administration. FDA activities: Essure. https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/EssurePermanentBirthControl/ucm452254.htm. Accessed May 10, 2017.

4. Summary safety review—ESSURE permanent birth control system—assessing the risk of complications and the potential need for device removal. https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/safety-reviews/summary-safety-review-essure-permanent-birth-control-system-assessing-risk.html. Published May 25, 2016. Accessed January 4, 2018.

5. Van Drongelen AW, van Elk M, Moltó-Puigmartí C. Janssen SWJ. Analysis of complaints in the Netherlands on Essure. http://www.rivm.nl/Documenten_en_publicaties/Wetenschappelijk/Rapporten/2016/september/Analysis_of_complaints_in_the_Netherlands_on_Essure_Health_problems_following_a_non_surgical_sterilization_procedure_for_women. Accessed May 10, 2017.

6. French National Agency for Medicines and Health Products Safety. Temporary Specialist Scientific Committee for permanent sterilization device Essure. http://ansm.sante.fr/L-ANSM/Comites-scientifiques-specialises-temporaires/Comites-scientifiques-specialises-temporaires/Comites-scientifiques-specialises-temporaires/CSST-Dispositif-de-sterilisation-definitive-Essure. Accessed January 4, 2018.

7. Fernandez H, Legendre G, Blein C, Lamarsalle L, Panel P. Tubal sterilization: pregnancy rates after hysteroscopic versus laparoscopic sterilization in France, 2006-2010. *Eur J Obstet Gynecol Reprod Biol*. 2014;180:133-137.

8. Mao J, Pfeifer S, Schlegel P, Sedrakyan A. Safety and efficacy of hysteroscopic sterilization compared with laparoscopic sterilization: an observational cohort study. *BMJ*. 2015;351:h5162.

9. Perkins RB, Morgan JR, Awosogba TP, Ramanadhan S, Paasche-Orlow MK. Gynecologic outcomes after hysteroscopic and laparoscopic sterilization procedures. *Obstet Gynecol*. 2016;128(4):843-852.

10. Antoun L, Smith P, Gupta JK, Clark TJ. The feasibility, safety, and effectiveness of hysteroscopic sterilization compared with laparoscopic sterilization. *Am J Obstet Gynecol*. 2017;217(5):570.e1-570.e6.

11. Beziz D, Colas S, Collin C, Dray-Spira R, Zureik M. Association between exposure to benzodiazepines and related drugs and survivorship of total hip replacement in arthritis: a population-based cohort study of 246,940 patients. *PLoS One*. 2016;11(5):e0155783.

12. Bouillon K, Bertrand M, Maura G, Blotière PO, Ricordeau P, Zureik M. Risk of bleeding and arterial thromboembolism in patients with non-valvular atrial fibrillation either maintained on a vitamin K antagonist or switched to a non-vitamin K-antagonist oral anticoagulant: a retrospective, matched-cohort study. *Lancet Haematol*. 2015;2(4):e150-e159.

13. Bouillon K, Bertrand M, Boudali L, Ducimetière P, Dray-Spira R, Zureik M. Short-term risk of bleeding during heparin bridging at initiation of vitamin k antagonist therapy in more than 90 000 patients with nonvalvular atrial fibrillation managed in outpatient care. *J Am Heart Assoc*. 2016;5(11):e004065.

14. Colas S, Collin C, Piriou P, Zureik M. Association between total hip replacement characteristics and 3-year prosthetic survivorship: a population-based study. *JAMA Surg*. 2015;150(10):979-988.

15. Colas S, Allalou A, Poichotte A, Piriou P, Dray-Spira R, Zureik M. Exchangeable femoral neck (dual-modular) THA prostheses have poorer survivorship than other designs: a nationwide cohort of 324,108 patients. *Clin Orthop Relat Res*. 2017;475(8):2046-2059.

16. Kirchgesner J, Lemaitre M, Rudnichi A, et al. Therapeutic management of inflammatory bowel disease in real-life practice in the current era of anti-TNF agents: analysis of the French administrative health databases 2009-2014. *Aliment Pharmacol Ther*. 2017;45(1):37-49.

17. Maura G, Blotière P-O, Bouillon K, et al. Comparison of the short-term risk of bleeding and arterial thromboembolic events in nonvalvular atrial fibrillation patients newly treated with dabigatran or rivaroxaban versus vitamin K antagonists: a French nationwide propensity-matched cohort study. *Circulation*. 2015;132(13):1252-1260.

18. Raguideau F, Mezzarobba M, Zureik M, Weill A, Ricordeau P, Alla F. Compliance with pregnancy prevention plan recommendations in 8672 French women of childbearing potential exposed to acitretin. *Pharmacoepidemiol Drug Saf*. 2015;24(5):526-533.

19. Raguideau F, Lemaitre M, Dray-Spira R, Zureik M. Association between oral fluoroquinolone use and retinal detachment. *JAMA Ophtalmol*. 2016;134(4):415-21.

20. Tricotel A, Collin C, Zureik M. Impact of the sharp changes in the use of contraception in 2013 on the risk of pulmonary embolism in France. *J Thromb Haemost*. 2015;13(9):1576-1580.

21. Weill A, Païta M, Tuppin P, et al. Benfluorex and valvular heart disease: a cohort study of a million people with diabetes mellitus. *Pharmacoepidemiol Drug Saf*. 2010;19(12):1256-1262.

22. Weill A, Dalichampt M, Raguideau F, et al. Low dose oestrogen combined oral contraception and risk of pulmonary embolism, stroke, and myocardial infarction in five million French women: cohort study. *BMJ*. 2016;353:i2002.

23. Lemaitre M, Kirchgesner J, Rudnichi A, et al. Association between use of thiopurines or tumor necrosis factor antagonists alone or in combination and risk of lymphoma in patients with inflammatory bowel disease. *JAMA*. 2017;318(17):1679-1686.

24. Rey G, Jougla E, Fouillet A, Hémon D. Ecological association between a deprivation index and mortality in France over the period 1997-2001: variations with spatial scale, degree of urbanicity, age, gender and cause of death. *BMC Public Health*. 2009;9:33.

25. Austin PC, Stuart EA. Moving towards best practice when using inverse probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies. *Stat Med*. 2015;34(28):3661-3679.

26. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. Hillsdale, New Jersey: Lawrence Erlbaum Associates; 1988.

27. Powell CB, Alabaster A, Simmons S, et al. Salpingectomy for sterilization: change in practice in a large integrated health care system, 2011-2016. *Obstet Gynecol*. 2017;130(5):961-967.

28. Kerin JF, Cooper JM, Price T, et al. Hysteroscopic sterilization using a micro-insert device: results of a multicentre phase II study. *Hum Reprod*. 2003;18(6):1223-1230.

29. Cooper JM, Carignan CS, Cher D, Kerin JF; Selective Tubal Occlusion Procedure 2000 Investigators Group. Microinsert nonincisional hysteroscopic sterilization. *Obstet Gynecol*. 2003;102(1):59-67.

30. Miño M, Arjona JE, Cordón J, Pelegrin B, Povedano B, Chacon E. Success rate and patient satisfaction with the Essure sterilisation in an outpatient setting: a prospective study of 857 women. *BJOG*. 2007;114(6):763-766.

31. Grosdemouge I, Engrand J-B, Dhainault C, et al. Essure implants for tubal sterilisation in France. *Gynecol Obstet Fertil*. 2009;37(5):389-395.

32. Povedano B, Arjona JE, Velasco E, Monserrat JA, Lorente J, Castelo-Branco C. Complications of hysteroscopic Essure(®) sterilisation: report on 4306 procedures performed in a single centre. *BJOG*. 2012;119(7):795-799.

33. Ríos-Castillo JE, Velasco E, Arjona-Berral JE, Monserrat Jordán JA, Povedano-Cañizares B, Castelo-Branco C. Efficacy of Essure hysteroscopic sterilization—5 years follow up of 1200 women. *Gynecol Endocrinol*. 2013;29(6):580-582.

34. Lamvu G. Role of hysterectomy in the treatment of chronic pelvic pain. *Obstet Gynecol*. 2011;117(5):1175-1178.

35. Templeton AA, Cole S. Hysterectomy following sterilization. *Br J Obstet Gynaecol*. 1982;89(10):845-848.

36. Kjer JJ, Knudsen L. Hysterectomy subsequent to laparoscopic sterilization. *Eur J Obstet Gynecol Reprod Biol*. 1990;35(1):63-68.

37. Stergachis A, Shy KK, Grothaus LC, et al. Tubal sterilization and the long-term risk of hysterectomy. *JAMA*. 1990;264(22):2893-2898.

38. Goldhaber MK, Armstrong MA, Golditch IM, Sheehe PR, Petitti DB, Friedman GD. Long-term risk of hysterectomy among 80,007 sterilized and comparison women at Kaiser Permanente, 1971-1987. *Am J Epidemiol*. 1993;138(7):508-521.

39. US Food and Drug Administration. Postmarket surveillance studies. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pss.cfm?t_id=356&c_id=3854. Accessed November 7, 2017.

40. Chene G, de Rochambeau B, Le Bail-Carval K, et al. Current surgical practice of prophylactic and opportunistic salpingectomy in France. *Gynecol Obstet Fertil*. 2016;44(7-8):377-384.