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Prevalence of sexual dysfunction after breast cancer compared to controls, a study from CONSTANCES cohort

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Abstract

Purpose Sexuality, a substantial factor in quality of life, may be altered after breast cancer (BC) treatments as they intimately afflict femininity. This study aimed to assess the prevalence of sexual dysfunction in women with a history of BC and to compare it with women without a BC history.

Methods The French general epidemiological cohort CONSTANCES includes more than 200,000 adults. All inclusion questionnaires from CONSTANCES non-virgin adult female participants were analyzed. Women reporting a history of BC were compared to controls in univariate analysis. Multivariate analysis was performed to highlight any demographic risk factor for sexual dysfunction.

Results Among the 2,680 participants who had a history of BC, 34% did not engage in sexual intercourse (SI) in the month preceding the completion of the questionnaire (n = 911), 34% had pain during SI (n = 901) and 30% were not satisfied with their sex life (n = 803). Sexual dysfunction was significantly more frequent in women who had a history of BC: they had less sexual interest (OR 1.79 [1.65;1.94], $p < 0.001$), experienced more pain during SI (OR 1.10 [1.02;1.19], $p < 0.001$) and were more dissatisfied with their sex life (OR 1.58 [1.47;1.71], $p < 0.001$). This stayed true after adjustment on multiple demographic factors such as age, menopausal status, body mass index and depression.

Conclusions Overall, in this real-life study in a large national cohort, history of BC appeared to be a risk factor for sexual disorders.

Implications for cancer survivors Efforts to detect sexual disorders in BC survivors and offer quality support must be pursued.

Keywords Breast cancer · survivorship · sexuality · sexual function · supportive care · national cohort

Highlights
- 1 in 3 breast cancer female survivor does not have regular sexual intercourse.
- 1 in 3 breast cancer female survivor experiences pain during sexual intercourse.
- 1 in 3 breast cancer female survivor is not satisfied with her sexual life.
- Sexual dysfunction is more frequent in breast cancer female survivors than in controls.
- This stays true independently of age and menopause status.

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Introduction

With more than 2.3 million new cases worldwide each year, it is now considered that one in eight women will be affected by BC in her lifetime [1–3]. Treatment generally consists of

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surgery, radiation therapy and/or systemic therapy (endocrine therapy, chemotherapy and in some cases targeted biologic therapy) [1]. Supportive care is of important significance to help patients deal with potential expected changes due to cancer and its treatments. One of the major [4–6] but less addressed [7–10] impact is on their *sexuality*, although survivors see it as a priority [11].

Prevalence of sexual dysfunction, defined as persistent problems with sexual response or pleasure that cause clinically significant distress [12], is difficult to evaluate because of the imprecision of its current diagnostic system [13, 14], a lack of concern and knowledge from clinicians [15–17] and crucial socio-cultural disparities [18–21]. In the literature, the prevalence of sexual dysfunction in cancer-free women fluctuates between 20 and 40% [22–24] compared to 40 to 70% for women with a history of BC [7, 25–30]. In one study, after BC treatments, women had four to six times higher odds of presenting a sexual disorder compared to women who did not have cancer [31]. The largest French survivors' quality of life VICAN study [32, 33] included 1,955 sexually active male and female survivors from all cancer sites [30]. Among the 750 women treated for BC, 28%, 42% and 14% reported a respectively weak, moderate or strong deterioration in their sexual health [32]. However, all previous studies took place in the cancer setting with limited retrospect from the diagnosis and leaves open the question of a long-term impact of BC on sexuality. Moreover, these studies involved limited sample size on BC as compared to what allows a large generalist cohort like CONSTANCES [34], which might reflect the daily reality of BC survivors with more hindsight.

The main objective of this study was to describe the sexual function of women who had a history of BC using the large-scale national CONSTANCES cohort. The secondary objective was to evaluate the impact of BC on sexuality by comparing to an unexposed population.

Methods

Population and design

This study used data available at inclusion from the CONSTANCES cohort. The CONSTANCES cohort is a large-scale national generalist prospective cohort intended to contribute to the development of epidemiological research [34, 35]. It was designed as a representative sample of the population covered by the National Health Insurance Fund, and included 220 000 volunteers aged between 18 and 69 at inclusion. The volunteers benefit from a health examination in one of the 22 selected Social Security Health Examination Centers on entry and then every 4 years, and answer an annual questionnaire. All female CONSTANCES participants aged 18 to 75 and reporting a history of sexual intercourse (SI) were analyzed.

Data

The CONSTANCES questionnaires content were previously published [34] and included data on socio-demographics, lifestyle, medical history, gynecological, reproductive and sexual health. All data for this study came from the participants self-administered questionnaires and from the medical questionnaire filled by the doctor during the initial medical exam, at time of inclusion in the CONSTANCES cohort.

Exposure and outcome definition

The exposed population involved participants whose medical questionnaire (completed by a doctor) mentioned a history of BC. The unexposed population was defined as participants who did not have a history of BC.

Sexual function was defined using three binary variables reported in a self-questionnaire at inclusion: lack of sexual interest (absence of SI within the month of the questionnaire being submitted) (binary variable), pain during SI and sexual dissatisfaction (both categorical variables binarized). Lack of sexual interest describes if the participant reported the absence of SI in the month before filling the questionnaire. Pain during SI is assessed from a four-item answer ("never or exceptionally", "sometimes", "often" and "always") and is considered absent if the participant answers "never or exceptionally" and present otherwise. Sexual dissatisfaction is assessed from a four-item answer ("not at all satisfactory", "not very satisfactory", "satisfactory" and "very satisfactory"). Dissatisfaction was considered present if the answer was "not at all satisfactory" or "not very satisfactory" and absent otherwise.

Regarding covariates, *age* is calculated as the subtraction of the date the questionnaire was completed minus the date of birth. *Menopausal* and s*moking status* were assessed from three-item answers (respectively "yes", "no", "do not know" and "yes, actual smoker", "yes, past smoker", "no, never smoked", the latter was considered present if the answer were yes, actual and past). *Depression* and *diabetes (types 1 and 2)* were considered present if checked in the medical questionnaire filled during the initial medical examination. *Body mass index (BMI)* was measured in kg/m^2 during the initial medical examination.

Statistical analysis

Analyzes were performed using R version 4.1.1. All statistical tests were two-sided and carried out at the α risk of 5%.

Descriptive analysis

A descriptive analysis was carried out for the overall population and the exposed (BC) and non-exposed groups. This description covered socio-demographic data, medical history (including body mass index, depression, oncology, gynecology and obstetrics) and lifestyle (physical activity, smoking status and perceived state of health). The qualitative or binary variables were characterized by their counts and percentages. The quantitative variables were described by an estimation of their median and quartiles. A graphical representation for certain variables is provided in the appendix (histograms for quantitative variables, and bar charts for qualitative variables).

Missing data

In all questionnaires, the modality "Do not wish to answer" was considered a missing data for carrying out statistical tests (not for descriptive analysis). Multivariate imputation by chained equations was performed using the MICE function in R.

Univariate analysis

Socio-demographic variables were compared between exposure groups using Chi-square test, Fisher test or Student t-test. Univariate association between exposure and outcome was assessed with logistic regression and odd-ratio (OR), 95% confidence interval ($_{95\%}$CI) and *p*-value (*p*) were reported.

Multivariate analysis

Multivariate analysis by multiple logistic regression was performed. Variables included in the model were selected based on their clinical significance in the previous literature and on statistical significance in the univariate analysis.

Ethics

This study was reviewed and approved by our local ethical committee (DATA220042). CONSTANCES was approved by French national committees regarding ethics and data protection. No opinion from the *Committee for the Protection of Persons* (CPP) was required for this study according to French regulations.

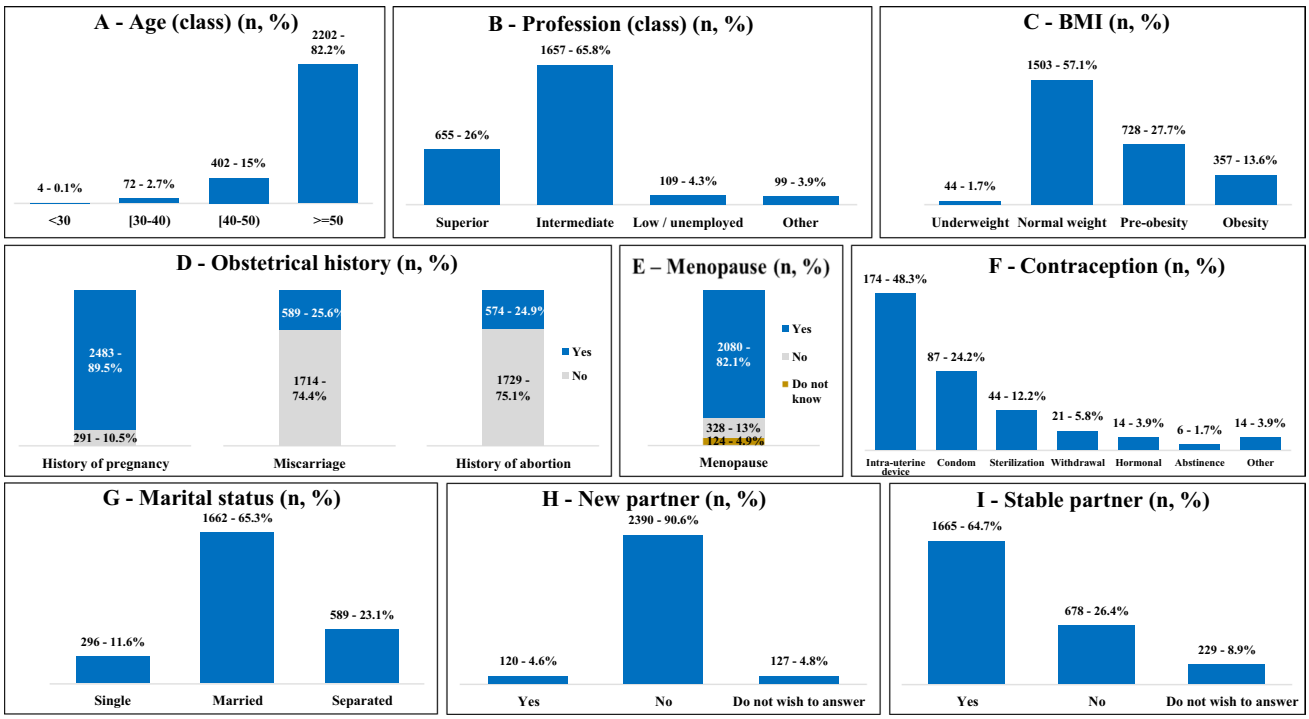

Fig. 1 Socio-demographics of the CONSTANCES Cohort female participants with a history of BC. (**A**) Age was over 50 years old in 4 out of 5 women with a history of BC, (**B**) women with a history of BC mostly held mid-level or superior professional positions, (**C**) BMI was mostly normal, 1 in 4 women was overweight, (**D**) 9 in 10 had been pregnant in her life and 1 in 4 suffered a miscarriage or abortion, (**E**) BC population was mainly menopaused, (**F**) contraception was mainly non-hormonal as recommended after BC, nonetheless 3.9% of the 360 non-menopaused BC survivors declared using a hormonal birth control method, (G, H, I) they were mostly in a stable relationship or married. Abbreviation: Body Mass Index (BMI)

Table 1 Sexual function of the CONSTANCES Cohort female participants overall and by exposure

Variable	Class	Overall	Women with history of BC	Women with no history of BC	*p*
n =		101,629	2680	98,727	
Stable partner (n, %)					< 0.001
	No	19,785 (19.5)	678 (25.3)	19,063 (19.3)	
	Yes	74,804 (73.6)	1665 (62.1)	73,004 (73.9)	
	Do not want to answer	4621 (4.5)	229 (8.5)	4364 (4.4)	
Sexual intercourse in the last month (n, %)					< 0.001
	No	24,172 (23.8)	911 (34.0)	23,204 (23.5)	
	Yes	70,160 (69.0)	1442 (53.8)	68,598 (69.5)	
	Do not want to answer	6203 (6.1)	286 (10.7)	5880 (6.0)	
Frequence of sexual intercourse (n, %)					< 0.001
	< once per month	370 (0.4)	16 (0.6)	354 (0.4)	
	1 to 3 times per month	28,115 (27.7)	717 (26.7)	27,709 (28.1)	
	1 to 2 times per week	27,941 (27.5)	522 (19.5)	27,473 (27.8)	
	3 to 6 times per week	8216 (8.1)	98 (3.7)	8202 (8.3)	
	Once a day or more	484 (0.5)	5 (0.2)	489 (0.5)	
	Do not want to answer	227 (0.2)	3 (0.1)	224 (0.2)	
Pain during intercourse (n, %)					< 0.001
	Never or exceptionnally	56,407 (55.5)	1203 (44.9)	55,107 (55.8)	
	Sometimes	26,234 (25.8)	586 (21.9)	25,595 (25.9)	
	Often	5961 (5.9)	210 (7.8)	5746 (5.8)	
	Always	2131 (2.1)	105 (3.9)	2021 (2.0)	
	Do not want to answer	4847 (4.8)	262 (9.8)	4551 (4.6)	
Consequence of dyspareunia (n, %)					< 0.001
	No consequence	19,900 (19.6)	377 (14.1)	19,485 (19.7)	
	Slight inconvenience	19,246 (18.9)	460 (17.2)	18,753 (19.0)	
	Necessity of interrupting sexual intercourse	6547 (6.4)	161 (6.0)	6377 (6.5)	
	Impossibility of having sexual intercourse	1111 (1.1)	76 (2.8)	1033 (1.0)	
	Do not want to answer	6120 (6.0)	307 (11.5)	5772 (5.8)	
Satisfaction with sexual life (n, %)					< 0.001
	Not at all satisfying	9347 (9.2)	295 (11.0)	9037 (9.2)	
	Not very satisfying	18,638 (18.3	508 (19.0)	18,104 (18.3)	
	Satisfying	41,142 (40.5)	958 (35.7)	40,125 (40.6)	
	Very satisfying	16,373 (16.1)	233 (8.7)	16,107 (16.3)	
	Do not want to answer	10,602 (10.4)	464 (17.3)	10,076 (10.2)	
Satisfaction with couple life (n, %)					< 0.001
	Not at all satisfying	3527 (3.5)	90 (3.4)	3429 (3.5)	
	Not very satisfying	8708 (8.6)	204 (7.6)	8491 (8.6)	
	Satisfying	34,532 (34.0)	963 (35.9)	33,512 (33.9)	
	Very satisfying	31,744 (31.2)	620 (23.1)	31,070 (31.5)	
	Do not want to answer	4907 (4.8)	219 (8.2)	4665 (4.7)	
	Do not apply	12,115 (11.9)	330 (12.3)	11,748 (11.9)	

BC Breast Cancer, *p* P-value

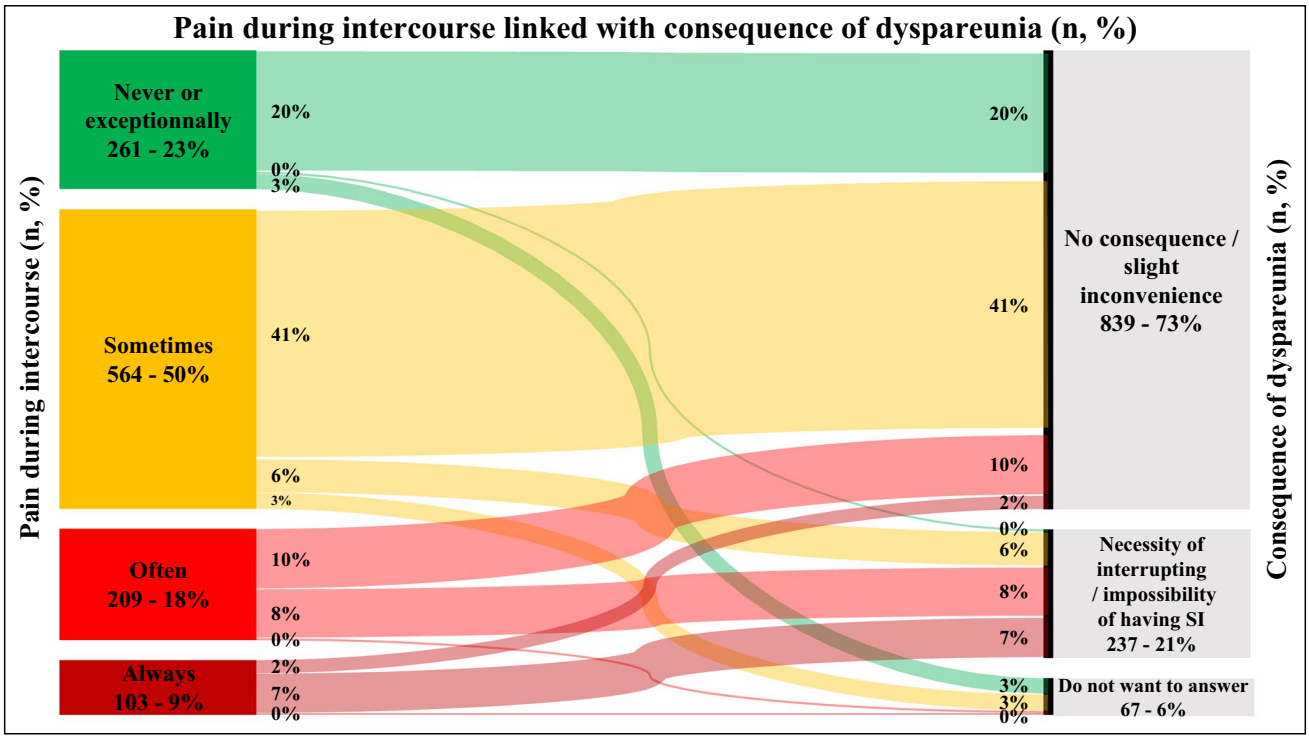

Fig. 2 Pain during sexual intercourse and its consequences within participants with a history of BC. Abbreviation: Sexual intercourse (SI)

Results

Socio-cultural demographics

After selection on sex and history of SI in their life, 101,629 participants were included. Median age was 46.0 years [36.0; 57.5]. The participants had mostly reached university level (n = 64,138; 63,1%) and occupied an intermediate profession (n = 62,093; 61.1%). Most participants were in a couple (n = 58,286; 57.4%) (see Supplementary Table A). Two-thousand six-hundred eighty had a history of BC (2.6%) (data available for 101,407 participants). The median of time between the reported age at BC diagnosis and inclusion in the study was 7.5 years [4.0; 13.5]. Socio-demographics of participants with a history of BC are illustrated in Fig. 1.

Sexual function and consequence in the BC population

Among participants who had a history of BC, 34.0% did not engage in SI in the month preceding the completion of the questionnaire (n = 911), 33.6% experienced pain during SI (n = 901) and 30.0% did not find their sex life satisfactory (n = 803) (see Table 1).

As a result of pain during SI, 8.8% of participants affected by BC had to interrupt or even avoid SI (n = 237) (see Fig. 2). Satisfaction with couple life was high (satisfied n = 963, 35.9%; very satisfied 620, 23.1%) (see Table 1).

Difference of sexual function between BC and non-BC populations

In univariate analysis, participants with a history of BC were significantly less likely to have had sex in the last month (OR 1.79 [1.65;1.94], $p < 0.001$). They were more likely to report pain during SI (OR 1.10 [1.02;1.19], $p < 0.001$). Finally, they were significantly less satisfied with their sex life (OR 1.58 [1.47;1.71], $p < 0.001$) (see Table 2).

In multivariate analysis, when adjusted on age, BC remained an independent risk factor for lack of sexual interest (OR 1.11 [1.02;1.20], $p = 0.013$), pain during SI (OR 1.38 [1.28;1.50], $p < 0.001$) and sexual dissatisfaction (OR 1.24 [1.15;1.34], $p < 0.001$) (see Table 2). BC was an independent risk factor for the 3 variables after adjustment on BMI, menopausal and smoking status, history of depression and diabetes (see Table 2).

Discussion

This study, which focused on the sexuality of 2,680 women after BC, showed that 1 in 3 does not have a regular sexual activity, experiences dyspareunia and is dissatisfied with her

Table 2 Uni- and multivariate analysis by multiple logistic regressions on imputed data of the impact of a history of BC on sexual function, adjusted on potential confounding factors

	Lack of sexual interest				Pain during SI				Sexual dissatisfaction			
	Interest	No interest	OR [95%CI]	*p*	No pain	Pain	OR [95%CI]	*p*	Satisfied	Dissatisfied	OR [95%CI]	*p*
Overall	75,100 (73.9)	26,529 (26.1)			65,219 (64.2)	36,410 (35.8)			60,124 (59.2)	41,505 (40.8)		
History of BC (binary)	1666 (62.2)	1014 (37.8)	1.79 [1.65;1.94]	< 0.001	1674 (62.5)	1006 (37.5)	1.10 [1.02;1.19]	< 0.001	1299 (48.5)	1381 (51.5)	1.58 [1.47;1.71]	< 0.001
Age (years, continuous) (median [Q1;Q3])	59.5 [53.0;65.5]		1.11 [1.02;1.20]	0.013	59.5 [53.0;65.5]		1.38 [1.28;1.50]	< 0.001	59.5 [53.0;65.5]		1.24 [1.15;1.34]	< 0.001
BMI (kg/m^2, continuous)	23.9 [21.6;27.3]		1.76 [1.62;1.90]	< 0.001	23.9 [21.6;27.3]		1.12 [1.04;1.21]	0.005	23.9 [21.6;27.3]		1.56 [1.45;1.69]	< 0.001
Menopause (binary) (n, %)	884 (60.1)	588 (39.9)	1.60 [1.48;1.73]	< 0.001	872 (59.2)	600 (40.8)	1.12 [1.04;1.22]	0.004	682 (46.3)	790 (53.7)	1.49 [1.38;1.61]	< 0.001
History of depression (binary)	380 (55.4)	306 (44.6)	1.74 [1.61;1.88]	< 0.001	381 (55.5)	305 (44.5)	1.08 [1.00;1.17]	0.045	267 (38.9)	419 (61.1)	1.54 [1.42;1.66]	< 0.001
Smoker (binary)	795 (58.9)	554 (41.1)	1.79 [1.65;1.94]	< 0.001	836 (62.0)	513 (38.0)	1.10 [1.02;1.19]	0.016	613 (45.4)	736 (54.6)	1.58 [1.47;1.71]	< 0.001
Diabetes (binary)	40 (52.6)	36 (47.4)	1.77 [1.63;1.91]	< 0.001	55 (72.4)	21 (27.6)	1.11 [1.02;1.20]	0.012	37 (48.7)	39 (51.3)	1.57 [1.46;1.70]	< 0.001

BMI Body Mass Index, *BC* Breast Cancer, *CI* Confidence Interval, *OR* Odd-ratio, *p* p-value.

sex life. The prevalence of these disorders was significantly higher than in women without a history of BC.

The population of the CONSTANCES cohort, whose recruitment is done from the National Social Security System, has the advantage of being real-life data, as opposed to a hospital or cancer-center based cohort, which might select for affective biases (distortion of judgment driven by the influence of affective states in relation to the temporal and geographical proximity of cancer treatment memories). However, it has the limitation of selecting a population of high socio-professional category, more inclined to participate in a study on questionnaires with annual follow-up, and in better health. It is representative of the prevalence of BC in French women. Indeed, in 2017 the National Cancer Institute estimates a prevalence of 913,089 cases of BC [36] for 34,48 million women identified in France the same year [37, 38], *i.e.* 2.6% (in this study there were 2,680 BC cases, *i.e.* 2.7% of the female cohort). The history of BC was reported by the patients (n = 2,909) and validated by a medical questionnaire completed by a doctor (n = 3,002) as part of the study. These data do not coincide perfectly. We made the choice to select the participants for whom the history had been retained by the doctor. Furthermore, the only information on BC available in the CONSTANCES data is the age at diagnosis, which calls on the patient's memory and exposes to understanding and memory bias. Based on this data, median of time between the diagnosis and inclusion in the study is 7.5 years [4.0; 13.5], which is longer than previous studies.

The study of sexuality remains a taboo subject to this day [39, 40] and leads to a high number of non-responses [41, 42]. It is particularly true in the BC survivors' group (see Table 1) and can be related to psychological factors such as depressive symptoms, body image alteration and femininity violation caused by BC treatments which may add to the discomfort of addressing such an intimate topic. Our imputation strategy made it possible to overcome this limitation on the assumption that the data missing is only associated with observed variables (*e.g.* socio-demographic), however more complex mechanisms (*e.g.* the probability of missing also depends on the unknown value of the variable) are possible. Furthermore, specific analysis on non-respondents to identify potential patterns are currently ongoing.

This study was not carried out on validated sexuality questionnaires such as the Female Sexual Function Index [43], and the choice was made to retain the three variables of interest "SI in the last month" to represent frequency, "pain during sex" and "satisfaction with sex life". These three variables seemed to be both easily exploitable and to represent sexual function as broadly and faithfully as possible based on the data available in CONSTANCES. However, they have their limits as they are automatically boosted in coupled-up participants who will more likely report more frequent and satisfying SI.

In conclusion, our study, which to our knowledge for the first time compared the sexual life of women with a history of BC to women without BC in real life, has shown an impairment of the sexual life of women receiving BC treatments, independently of age.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11764-023-01407-z.

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Access to some confidential data, on which this work is based, was made possible within a secure environment provided by the *Centre d'accès sécurisé aux données* (CASD) (Ref. https://doi.org/10.34724/CASD).

Authors contribution All authors contributed to the study conception and design. Material preparation and data collection were performed by M.C-P, M.G and M.Z. Analysis was performed by M.M-V and C.B. The first draft of the manuscript was written by M.M-V and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability Access to sensitive and personal data, such as those of the CONSTANCES cohort, is restricted by French law. The CONSTANCES coordination team makes the data available, upon request, to qualified researchers who have obtained prior authorization from the French national data protection authority (Commission nationale de l'informatique et des libertés, CNIL). Information for applicants to CONSTANCES data is available on the website: https://www.constances.fr/CFP.pdf. CONSTANCES investigators may be contacted at the following address: contact@constances.fr.

Declarations

Competing interests Authors have nothing to declare.

Ethics approval and consent to participate The authors assert that all procedures contributing to this work comply with the ethical standards of the national and institutional committees on human experimentation and with the Helsinki Declaration, as revised in 2008. All procedures were approved by the Institutional Review Board of the French Institute of Health Research (INSERM). The CONSTANCES cohort was also approved by the French Data Protection Agency (CNIL). All participants provided written informed consent.

Consent for publication Not applicable.

Conflict of interest We have no conflicts of interest to declare.

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