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Psychosocial, sexual, reproductive and menopausal health in women with and without HIV in a high-income setting

RUNNING HEAD: Psychosocial and sexual health in women with HIV

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ABSTRACT

Objectives: To investigate psychosocial, sexual, reproductive and menopausal health in women with HIV (WWH) compared to women without HIV (WWOH) in Denmark.

Design: A nationwide cross-sectional study.

Methods: Data was retrieved from the *SHARE study*, a Danish nationwide cross-sectional survey examining psychosocial, sexual and reproductive health in people with HIV. Data from WWH, collected in 2021-2022, was matched 1:10 on age to a comparison group of WWOH from the nationally representative cohort study *Project SEXUS*. Associations between HIV status and psychosocial and sexual health outcomes were assessed by adjusted odds ratios (aOR) with 95% confidence intervals (95%CI) obtained in logistic regression analyses controlling for potential confounding variables. The severity of menopausal symptoms in WWH was compared to published reference norms.

Results: Among 144 WWH and 1,440 WWOH, recurrent loneliness was significantly more common among WWH (aOR 2.22 [95%CI: 1.25-3.96]), and WWH had significantly fewer

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children and close friends (aOR 0.52 [95%CI: 0.28-0.96] for 3-9 vs. 0-2 close friends). Symptoms of anxiety and depression did not differ between groups. Lack of sexual desire (aOR 2.90 [95%CI: 1.29-6.50]), low FSFI-6 score indicating sexual dysfunction (aOR 3.40 [95%CI: 1.33-8.69]), lubrication dysfunction (aOR 8.24 [95%CI: 2.83-24.00]) and genital pain dysfunction (aOR 5.13 [95%CI: 1.26-20.86]) were significantly more common in WWH compared to WWOH. No differences were seen in menopausal characteristics.

Conclusions: WWH in Denmark have fewer children and close friends, and more often report recurrent loneliness, lacking sexual desire and sexual dysfunction compared to WWOH. No differences were evident in menopausal characteristics.

KEYWORDS: HIV, women, sexual health, mental health, menopause, loneliness, cross-sectional

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INTRODUCTION

Women with HIV (WWH) have been found to report worse physical and mental health outcomes when compared to both men with HIV (MWH) and women without HIV (WWOH) [1–3]. With respect to sexual health, WWH show lower sexual activity levels and higher rates of sexual problems and dysfunction when compared to WWOH [4,5]. As poor sexual health is linked with lower health-related quality of life and risk of mental health problems [6–9], this is a relevant clinical concern. Sexual health research in WWH has often operated in a 'risk' paradigm focusing on lowering transmission rates. In light of 'undetectable equals untransmittable' (U=U) [10], it is time to broaden the focus to include other aspects of sexual health, such as desire and sexual quality of life, to ensure optimal sexual health in WWH.

A unique aspect of women's health, the menopausal transition, has long been associated with negative effects on physical and mental health [11–13]. In WWH, concerns have been raised that menopause might occur at an earlier age [14] and may be associated with worse symptomology when compared to WWOH [15,16].

Research exploring sexual health in WWH has often been conducted in non-European settings where the social contexts differ from those of WWH living in high-income settings in terms of access to health care and socioeconomic circumstances. Psychosocial, sexual, reproductive and menopausal health in WWH has not previously been explored among the approximately 1,600 WWH living in Denmark [17].

Aim

The aim of this study was to investigate psychosocial, sexual, reproductive and menopausal health in WWH in comparison to WWOH in Denmark.

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METHODS

Study population

The present study utilised data collected in the nationwide cross-sectional survey *Perception of psychosocial, sexual, and reproductive health among people living with and without HIV in Denmark - the SHARE study*. The *SHARE study* aimed to examine psychosocial, sexual and reproductive health in all adult people with HIV in Denmark. Its recruitment period ran from March 1st, 2021, to February 28th, 2022. A total of 1,000 people with HIV consented to participate. HIV treatment in Denmark is centralised at university hospital clinics in Copenhagen, Aalborg, Aarhus and Odense. Eligible *SHARE study* participants were recruited by healthcare professionals during routine appointments. For the present study, we included cis-gendered WWH, aged ≥18 years who were able to read Danish or English. The comparison group of WWOH were sampled from *Project SEXUS*, a nationally representative, individual-based, prospective cohort study on sexual health with 62,675 Danish citizens, aged 15 to 89 years, as participants [18].

Questionnaire

The *SHARE study* questionnaire was available in Danish and English and consisted of several validated patient-reported outcome measures (PROM) and individual items, several of which were derived from the *Project SEXUS* questionnaire [18]. Specifically, WWH and WWOH were queried about psychosocial health (i.e., anxiety (GAD-7), depression (PHQ-2), loneliness and number of close friends) and sexual health (i.e., sexual quality of life, sexual desire, overall sexual function (FSFI-6) and individual sexual dysfunctions). For WWH, the severity of menopausal symptoms (MRS) was reported. Further details on the *Project SEXUS* questionnaire, the PROM used in this study, and the clinical HIV data collected from WWH, are provided in the Supplemental Digital Content 1, http://links.lww.com/QAD/C846.

Statistical analysis

Categorical variables were summarised with count and proportion (n, %) and continuous variables with median value and interquartile range (IQR) or mean value with standard deviation (SD).

The sociodemographic, physical health, lifestyle, reproductive and menopausal health-related characteristics of WWH and WWOH were summarised. Group differences were examined with Pearson's Chi-squared test. HIV characteristics were summarised for WWH. MRS scores were compared to published European reference norms [19] using Pearson's Chi-squared test.

Unconditional binomial logistic regression analyses provided odds ratios (ORs) for associations between HIV status and measures of psychosocial and sexual health, presented as ORs with adjustment only for age, and as fully adjusted ORs (aORs) with adjustment for age, ethnicity, relationship status, financial situation, BMI, physical health status, mental health status, current smoker status, weekly alcohol intake and recreational drug use, as detailed in

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the footnote of *Table 2*. All *p*-values are two-sided with a significance level of 0.05. Statistical analyses were performed in *R* version 4.0.2.

Ethics

The *SHARE study* has been approved by the Danish Data Protection Agency (approval no. P2021-167). According to Danish law, questionnaire-based studies do not require further ethical approval.

RESULTS

In total, 152 WWH agreed to participate in the *SHARE study*. Incomplete data from eight women were excluded, leaving 144 women in our study population. After frequency-matching 1:10 on age, 1,440 WWOH from *Project SEXUS* were included as comparison group.

Sociodemographic, physical, lifestyle, reproductive and menopausal characteristics

Significantly higher proportions of WWH compared to WWOH were single (37% vs. 18%), had unplaceable or undecided sexual identities (12% vs. 4%), were on long-term sick leave or in disability-related early retirement (12% vs. 7%), had a short formal education (20% vs. 7%), had parents of non-Danish origin (49% vs. 3%), reported past recreational drug use (17% vs. 9%) and had 0-1 children (58% vs. 31%) (*Table 1*). There were no differences between WWH and WWOH in menopausal status or age at menopausal onset. The severity of menopausal symptoms among WWH was compared to published European reference means and did not demonstrate a statistically significant difference ($p>0.10$), as can be seen Figure S1 in Supplemental Digital Content 2, http://links.lww.com/QAD/C847

HIV-related characteristics of WWH are shown in Table S1 in Supplemental Digital Content 3, http://links.lww.com/QAD/C848

Psychosocial and sexual health outcomes

While HIV status was not associated with current symptoms of anxiety or depression, WWH significantly more often reported recurrent loneliness (aOR 2.22 [95%CI: 1.25-3.96]) and fewer close friends (aOR: 0.52 [95%CI: 0.28-0.96] of having 3-9 vs. 0-2 close friends) compared to WWOH (*Table 2*). Measures of sexual quality of life did not differ significantly between WWH and WWOH. In age-adjusted analyses, experiences of sexual violence and low levels of sexual activity were more common among WWH, but these associations lost significance in the fully adjusted model. However, more WWH than WWOH (26% vs. 8%) had not felt any sexual desire in the last year (aOR 2.90 [95%CI: 1.29-6.50]), and HIV status was significantly associated with sexual dysfunction as measured by the FSFI-6 instrument (aOR 3.40 [95%CI: 1.33-8.69]), lubrication dysfunction (aOR 8.24 [95%CI: 2.83-24.00]) and genital pain dysfunction (aOR 5.13 [95%CI: 1.26-20.86]).

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DISCUSSION

Our finding of no differences in mental health problems, assessed by recent symptoms and in reports of prior treatment for mental health issues, contrasts evidence from other countries where rates of anxiety and depression were found to be higher among WWH when compared to both MWH and WWOH [20,21]. Most studies have however been conducted in societal settings that are considerably different from that in Denmark, which might at least in part explain the lower frequencies of mental health challenges reported in our population.

Our results demonstrated differences in loneliness and number of close friends. Loneliness has been identified as a predictor of early mortality [22] and has long been closely associated with HIV status [21,23]. However, our findings may to some extent have been influenced by the enforced periods of social isolation during the COVID-19 pandemic, as *SHARE study* data were collected at the end of, and immediately after, the pandemic, in contrast to the *Project SEXUS* control data, which were collected in 2017-2018.

The measures used to capture sexual quality of life revealed no significant differences between WWH and WWOH. However, a larger proportion of WWH than WWOH reported a lack of sexual desire which is in accordance with other studies [5,24]. Our results also showed decreased overall sexual function and increased rates of lubrication dysfunction and genital pain dysfunction among WWH. Given the concurrent lower levels of sexual desire, these dysfunctions could well be interrelated. Much of the available literature on sexual dysfunction among WWH support our results [25,26]. In our sample of WWH, the associations did not appear to be explained by a history of sexual victimisation or by poor physical or mental health; factors otherwise known to be strongly associated with sexual problems [6,7,27]. However, as HIV is predominately transmitted via sex, sexual problems and their causes may be difficult to separate in contrast to most other chronic illnesses. For instance, low sexual desire levels are found to be particularly prevalent in women who associated sex with the way in which they acquired HIV [28]. This fits the characteristic of our study population, where the vast majority of WWH had acquired HIV through sexual transmission and may therefore offer a plausible explanation for our findings.

WWH had significantly fewer children than WWOH. As the majority of WWH had lived with HIV for many years, this finding likely reflects a time when vertical HIV transmission posed a great concern in regard to family planning. Menopausal health has previously been highlighted as an under-explored area of research in WWH with concerns that WWH may suffer worse health during this phase of life compared to WWOH [14]. In our study, however, we observed no differences in age at menopause onset or in the severity of menopausal symptoms.

Strengths and limitations

A main strength of this study was the inclusion of a comparison group of WWOH from a nationally representative cohort study. Of limitations, our findings are based on cross-sectional,

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self-reported data. The study population consisted of a relatively small number of WWH which rendered some associations statistically unstable as reflected by wide confidence intervals around their OR estimates. Also, caution is required in regard to external validity, as we had no information to assess how representative our WWH participants were of the total WWH population in Denmark. There may also have been some residual confounding present due to ethnic differences between WWH and WWOH in our study. Lastly, while data from the comparison group of WWOH were collected in pre-pandemic years, data from our WWH participants were collected at the end of the COVID-19 pandemic, which may have affected some outcomes.

Implications

There are several ways to utilise the findings of the present study. On an interpersonal level, healthcare professionals need to initiate conversations on issues such as loneliness and sexual health in their routine care of WWH. At a societal level, these problems also require attention, as HIV stigma may still play a role in the sexual and psychosocial health inequalities identified between WWH and WWOH in our study. Qualitative research could be a suitable method to further explore this.

Conclusion

Mental and menopausal health outcomes appear not to differ markedly between WWH and WWOH in Denmark. However, our study reveals that WWH have fewer children, fewer close friends and significantly more often report recurrent loneliness, lack of sexual desire and sexual dysfunctions compared to WWOH.

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All authors contributed to the study design/conception, or to the acquisition, analysis or interpretation of the data for the work. N.W., M.S., G.P., I.S.J., T.L.K. and E.M. participated in the data collection. D.S. drafted the manuscript. M.A. and D.S. conducted the statistical analyses.

E.M., M.F. and N.W. participated in the analysis process and manuscript development. All listed authors critically revised, commented and approved the final manuscript before submission.

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role in the study design, data collection, data analysis, data interpretation or in writing of the manuscript. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

CONFLICTS OF INTEREST

E.M. reports unrestricted grants from the Novo Nordisk Foundation and Gilead Sciences, outside of the submitted work, and personal fees from Gilead and Bristol Myers Squibb, outside of the submitted work: honorarium paid to her institution. N.W. has been clinical investigator for Abbvie and Merck Sharp Dohme: honorarium paid to her institution. T.L.K. reports personal fees and grants from ViiV/Glaxo Smith Kline, Gilead, CLS Behring, and Baxalta, outside of the submitted work. The remaining authors D.S., M.F., M.A., M.S., G.P., I.S.J. and C.G. declare no conflicts of interest.

Preliminary data from this study was presented as a poster at the Nordic HIV & Virology Conference in Stockholm, Sweden, September 2022.

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Table 1: Sociodemographic, physical health, lifestyle, reproductive and menopausal characteristics among 144 women with HIV (WWH) and 1,440 women without HIV (WWOH) in Denmark

	WWH	WWOH	*p*-value
Sociodemographic characteristics	n (%)	n (%)	
Age			1.00
Age, years [median, IQR]	49 [42;55]	49 [42;55]	
18-39	26 (18.0)	260 (18.0)	
40-59	95 (66.0)	950 (66.0)	
≥60	23 (16.0)	230 (16.0)	
Ethnicity			<0.001
Parents of Danish origin	74 (51.4)	1,404 (97.5)	
Parents of non-Danish origin	70 (48.6)	36 (2.5)	
Relationship status			<0.001
Married/steady relationship	90 (63.4)	1,174 (81.9)	
Single	52 (36.6)	260 (18.1)	
Sexual identity			<0.001
Heterosexual	118 (82.5)	1,304 (90.6)	
Non-heterosexual[a]	8 (5.6)	77 (5.3)	
Unplaceable/undecided or do not know	17 (11.9)	59 (4.1)	
Employment status			0.03
Employed/full-time student	106 (73.6)	1,118 (77.7)	
Unemployed	8 (5.6)	46 (3.2)	
Long-term sick leave/disability-related early retirement	17 (11.8)	93 (6.5)	
Other[b]	13 (9.0)	182 (12.6)	
Formal education			<0.001
Short (≤10 years)	28 (19.6)	96 (6.7)	
Medium (11-14 years)	94 (65.7)	1,106 (76.9)	
Long (≥15 years)	21 (14.7)	236 (16.4)	
Financial situation			0.60
Difficulties paying bills in the last year			
No	121 (84.0)	1,228 (85.6)	
Yes	23 (16.0)	206 (14.4)	
Physical health-related characteristics			
Body Mass Index (kg/m²)			0.42
Median [IQR]	25.6 [21.3-28.7]	24.8 [22.0-29.1]	
<25	69 (47.9)	739 (51.4)	
≥25	75 (52.1)	698 (48.6)	
Self-rated health			0.30
Very good or good	105 (72.9)	1,115 (77.4)	
Neither good nor bad	30 (20.8)	228 (15.8)	

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Bad or very bad	9 (6.3)	97 (6.8)	
History of physical health problems[c]			0.86
No	97 (69.3)	991 (70.0)	
Yes	43 (30.7)	425 (30.0)	
Lifestyle-related characteristics			
Physical activity - moderate to hard			0.51
>30 mins per week	108 (75.0)	1,115 (77.4)	
0-30 mins per week	36 (25.0)	325 (22.6)	
Substance use			
Current smoker			0.99
No	121 (84.0)	1,208 (84.0)	
Yes	23 (16.0)	230 (16.0)	
Alcohol intake - weekly			0.16
≤7 units	124 (90.5)	1,233 (86.2)	
>7 units	13 (9.5)	197 (13.8)	
Recreational drug use[d]			0.02
Never	99 (80.5)	954 (88.0)	
1-12 months ago	3 (2.4)	31 (2.9)	
>12 months ago	21 (17.1)	99 (9.1)	
Reproductive and menopausal characteristics			
Parity[e]			<0.001
No children	36 (26.1)	240 (16.7)	
1 child	44 (31.9)	204 (14.2)	
2-3 children	53 (38.4)	926 (64.3)	
≥4 children	5 (3.6)	70 (4.9)	
Menstrual cessation[f]			0.29
No	39 (41.9)	473 (47.6)	
Yes	54 (58.1)	520 (52.4)	
Age at menopause, years[g]			0.08
Median [IQR]	49 [45;50]	50 [46;52]	
≥40	57 (86.4)	599 (92.6)	
<40	9 (13.6)	48 (7.4)	

Note: P-values are based on the $\chi2$-test; Numbers do not always sum up to 144 for WWH or 1,440 for WWOH as not all items were presented to all participants (due to filtering from previous responses), and those who responded "I do not know", were excluded.

[a] Including homosexual, bisexual and asexual.

[b] Including parental leave, early retirement, retired or other.

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[c] Answers to the question: "Have you ever been treated by a doctor for a long-lasting or severe physical disease other than HIV?"

[d] Including cannabis, euphoriant or hallucinogenic drugs.

[e] Answered by WWH (n=138) and WWOH (n=1,440) who reported ever having been pregnant.

[f] Answered by WWH (n=101) and WWOH (n=1,039), aged ≥40-64 years, who reported ever having had a menstrual period.

[g] Answered by WWH (n=54) and WWOH (n=520) who reported menstrual cessation, and WWH (n=12) and WWOH (n=127) aged ≥65 years.

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Table 2: Prevalence and odd ratios (95% confidence intervals) of psychosocial and sexual health outcomes according to HIV status among 144 women with HIV (WWH) and 1,440 women without HIV (WWOH) in Denmark

	WWH	**WWOH**	**OR[a][95% CI]**	**aOR[b][95%CI]**
Psychosocial health	n (%)	n (%)		
History of mental health problems[c]				
No	91 (64.5)	833 (58.1)	1 [REF]	1 [REF]
Yes	50 (35.5)	601 (41.9)	0.75 [0.52-1.08]	1.14 [0.63-2.06]
Symptoms of anxiety in the last two weeks				
GAD-7 score, mean (SD)	3.76 (4.98)	3.35 (3.98)		
Symptoms not present (score <5)	97 (67.4)	1,017 (70.6)	1 [REF]	1 [REF]
Symptoms present (score ≥5)	47 (32.6)	423 (29.4)	1.17 [0.81-1.70]	0.70 [0.37-1.31]
Symptoms of depression the last two weeks				
PHQ-2 score, mean (SD)	1.21 (1.48)	1.02 (1.36)		
Symptoms not present (score <3)	117 (81.2)	1,228 (85.3)	1 [REF]	1 [REF]
Symptoms present (score ≥3)	27 (18.8)	212 (14.7)	1.35 [0.86-2.11]	0.67 [0.31-1.42]
Loneliness				
Never or rarely feel lonely	80 (55.9)	997 (69.4)	1 [REF]	1 [REF]
Sometimes feel lonely	53 (37.1)	349 (24.3)	1.96 [1.35-2.86]	2.22 [1.25-3.96]
Often or always feel lonely	10 (7.0)	90 (6.3)	1.41 [0.70-2.87]	0.94 [0.27-3.27]
Social network size				
0-2 close friends	45 (32.6)	333 (23.4)	1 [REF]	1 [REF]
3-9 close friends	78 (56.5)	943 (66.2)	0.60 [0.41-0.89]	0.52 [0.28-0.96]

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≥10 close friends	15 (10.9)	149 (10.5)	0.74 [0.39-1.39]	0.45 [0.16-1.24]
Sexual health				
Sexual quality of life				
Importance of having a good sex life				
Extremely important, very important or important	95 (72.0)	1,101 (77.4)	1 [REF]	1 [REF]
Not very important or not at all important	37 (28.0)	322 (22.6)	1.41 [0.93-2.16]	0.95 [0.50-1.80]
Self-rated sex life in the last year				
Very good or good	58 (42.3)	702 (49.1)	1 [REF]	1 [REF]
Neither good nor bad, bad or very bad	42 (30.7)	538 (37.7)	0.97 [0.64-1.47]	0.88 [0.46-1.66]
No sex life in the last year	37 (27.0)	188 (13.2)	2.64 [1.65-4.23]	1.44 [0.65-3.21]
Sexual needs fulfillment in the last year				
To a very high extent, to a high extent or to some extent	79 (58.1)	1,010 (71.4)	1 [REF]	1 [REF]
To a low extent or not at all	35 (25.7)	302 (21.3)	1.52 [0.99-2.33]	1.09 [0.53-2.23]
No sexual needs in the last year	22 (16.2)	103 (7.3)	3.14 [1.81-5.46]	1.71 [0.70-4.17]
Sexual activity				
Time since last vaginal intercourse[d]				
<1 month ago	53 (48.6)	874 (63.9)	1 [REF]	1 [REF]
1-12 months ago	12 (11.0)	184 (13.5)	1.03 [0.53-1.99]	1.00 [0.39-2.61]
≥12 months ago	44 (40.4)	309 (22.6)	2.62 [1.66-4.14]	1.61 [0.77-3.39]
Sexual desire				
Frequency of desire to have sex (with or without a partner) in the last year				
At least once a month	69 (56.6)	1,107 (79.5)	1 [REF]	1 [REF]
Less than once a month	21 (17.2)	172 (12.3)	2.22 [1.30-3.81]	1.81 [0.80-4.09]
Not at all in the last year	32 (26.2)	114 (8.2)	5.93 [3.51-10.01]	2.90 [1.29-6.50]
Sexual dysfunctions				
The 6-item Female Sexual Function Index (FSFI-6)[e]				
Total score, mean (SD)	21.78 (5.38)	23.50 (4.70)		
Normal sexual function (FSFI-6 score 20-30)	46 (66.7)	803 (83.0)	1 [REF]	1 [REF]
Sexual dysfunction (FSFI-6 score 6-19)	23 (33.3)	165 (17.0)	3.09 [1.74-5.49]	3.40 [1.33-8.69]
Lubrication dysfunction[f, g]				
No	62 (76.5)	1,010 (88.1)	1 [REF]	1 [REF]
Yes	14 (17.3)	93 (8.1)	3.15 [1.61-6.16]	8.24 [2.83-24.00]

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Orgasmic dysfunction[f, h]				
No	62 (79.5)	955 (83.1)	1 [REF]	1 [REF]
Yes	6 (7.7)	105 (9.1)	0.83 [0.34-2.02]	0.63 [0.15-2.70]
Genital pain dysfunction[f, i]				
No	74 (88.1)	1,099 (95.7)	1 [REF]	1 [REF]
Yes	9 (10.7)	43 (3.7)	4.01 [1.79-8.99]	5.13 [1.26-20.86]
Sexual violence				
Victim of a sexual assault[j]				
No	102 (75.6)	1,250 (87.5)	1 [REF]	1 [REF]
Yes	33 (24.4)	178 (12.5)	2.43 [1.52-3.60]	1.73 [0.84-3.57]

Note: Odds ratio (OR); Confidence intervals (CI); Reference category (REF).

[a] Adjusted for age (1-year age groups).

[b] Adjusted for age (1-year age groups), ethnicity (both parents born and raised in Denmark – yes/no), relationship status (married or in a steady relationship – yes/no), financial situation (difficulties paying bills in the last year – yes/no), BMI (<25 or ≥ 25 kg/m^2), physical health status (ever treated by a doctor for a long-lasting or severe physical disease other than HIV – yes/no), mental health status (ever treated by a doctor, psychologist or similar professional for a mental health problem – yes/no), current smoker status (yes/no), weekly alcohol intake (≤ 7 or >7 units) and recreational drug use (never, 1-12 months ago, ≥12 months ago).

[c] Answers to the question "Have you ever received treatment by a doctor, psychologist or similar professional for a mental health problem?"

[d] Answered by WWH (n=109) and WWOH (n= 1,367) who reported at least once having had vaginal intercourse with a man.

[e] Answered by WWH (n= 69) and WWOH (n= 968), either married or in a steady relationship, who reported having had vaginal intercourse in the last four weeks.

[f] Sexual dysfunctions are defined as having experienced the particular sexual difficulty 'often' or 'every time' during sexual activity with another person in the last year and found it to be problematic. The category of respondents who had experienced the difficulty, but not found it to be problematic, is not shown.

[g] Answered by WWH (n=76) and WWOH (n= 1,103) who reported having had sex with a man in the last year.

[h] Answered by WWH (n=68) and WWOH (n= 1,060) who reported having had sex with a man in the last year.

[i] Answered by WWH (n=83) and WWOH (n= 1,142) who reported having had sex with a man in the last year.

[j] Sexual assault defined as sexual experiences in which someone threatened, forced or used violence to involve the respondent into sexual acts against her will.

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