ORIGINAL ARTICLE

Impact of Anti-hypertensive Therapy in the Sexual Health of Men and Women: An Analysis From the SPRINT Trial

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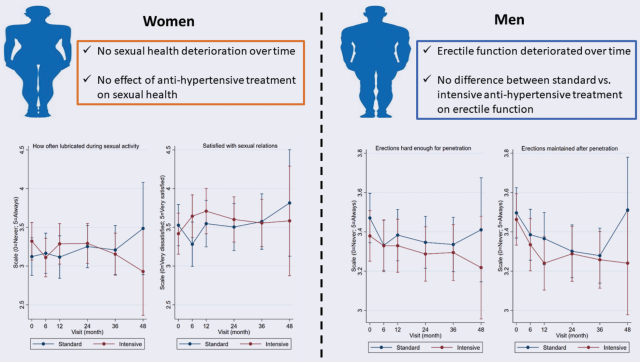
BACKGROUND
Pharmacologic anti-hypertensive (HT) treatment reduces cardiovascular risk. However, many patients are nonadherent due to perceived or real concern about sexual-related side effects.

METHODS
In a subset of the SPRINT (a randomized trial of intensive vs. standard blood-pressure control) trial, we sought to investigate the impact of anti-HT treatment on sexual activities of men and women over time, and whether this impact varied with a more or less intensive anti-HT therapy. Random-effects models for panel/longitudinal data.

RESULTS
Among the 1,268 men and 613 women included in this substudy, 862 (68%) men and 178 (29%) women declared to be engaged in sexual activity of any kind. Compared with women and men not engaged in sexual activity, those engaged were younger (64 vs. 69 years for women and 65 vs. 75 years for men). Women had an overall low satisfaction with their sexual life but their sexual health was not affected by anti-HT therapy over time nor modified by an intensive treatment. Men's erections were slightly deteriorated over time (−0.1 to −0.2 points on a scale of 1 (worse) to 5 (best); $P < 0.05$), but were not aggravated by intensive anti-HT therapy ($P > 0.05$ for all).

CONCLUSIONS
Self-declared women's sexual health was not affected by an intensive anti-HT therapy. Men reported a slight deterioration in the quality of their erections, irrespective of standard or intensive therapy. These findings may help reassuring patients about the sexual safety of intensive anti-HT therapy, therefore, potentially improving adherence to intensive therapy strategy.

GRAPHICAL ABSTRACT



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Arterial hypertension (HT) affects more than 25% of the adult population worldwide regardless of sex.[1] Pharmacologic treatment of HT is key to reduce the cardiovascular risk associated with uncontrolled blood pressure (BP). However, many patients are not willing to take their anti-HT drugs due to concern about side effects.[2] Long-term treatment nonadherence is one of the major causes for uncontrolled BP and, consequently, increasing the morbidity and mortality risk (e.g., stroke, myocardial infarction, renal insufficiency, and death).[3]

In clinical practice, sexual side effects are frequently evoked as an important reason for not taking the anti-HT treatment. Particularly younger, sexually active men often complain of erectile dysfunction; whereas women report less sexual side effects.[4] Moreover, sexual side effects may be underrecognized, and underreported because of difficulties in approaching the problem both by the patient and the clinician.[5] HT itself can also cause sexual dysfunction in the long term which might be seen by patients as a far away, unlikely future; however, the treatment side effects occur and are felt in the present, leading to poor treatment adherence and discontinuation—a "so-called" present-self vs. future-self conflict.[6]

In a subset of the SPRINT (a randomized trial of intensive vs. standard blood-pressure control) trial,[7] patients were questioned about their sexual activities at baseline and throughout the follow-up using validated sexual health

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questionnaires. This study sought to investigate the impact of anti-HT treatment on self-declared sexual activities over time, and whether this impact could vary with a more or less intensive anti-HT therapy in men and women.

METHODS

Trial oversight

SPRINT was sponsored by the National Heart, Lung, and Blood Institute (NHLBI), with cosponsorship by the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute of Neurological Disorders and Stroke, and the National Institute on Aging. The rationale and protocol for the trial have been previously published and are publicly available.[7,8] All participants provided written informed consent to participate in the study. The authors of this manuscript had authorization from the National Institutes of Health (NIH)/NHLBI to perform the present analysis under the coordination of the Biologic Specimen and Data Repository Information Coordinating Center (BioLINCC; request #7509).

To be enrolled in the SPRINT trial, participants were required to meet all the following criteria: an age of at least 50 years, a systolic BP of 130–180 mm Hg, and an increased risk of cardiovascular events (defined by one or more of the following: clinical or subclinical cardiovascular disease other than stroke; chronic kidney disease with an estimated glomerular filtration rate of 20–60 ml/min/1.73 m^2 calculated with the use of the 4-variable Modification of Diet in Renal Disease Equation[9]; a 10-year risk of cardiovascular disease ≥15% on the basis of the Framingham risk score; or an age ≥75 years). Patients with diabetes mellitus or prior stroke were excluded. Participants and study personnel were aware of the study-group assignments, but outcome adjudicators were not. The protocol encouraged, but did not mandate, the use of drug classes with the strongest evidence for reduction in cardiovascular outcomes.[10] BP was considered as the mean of 3 BP measurements at an office visit while the patient was seated after 5 minutes of quiet rest; the measurements were made with the use of an automated measurement system (Model 907, Omron Healthcare). The preferred method was the automated device as it offers reduced potential for observer biases and decreased demand on staff in terms of training and effort in data collection. Medical records and electrocardiograms were obtained for documentation of events. Whenever clinical site staff became aware of a death, a standard protocol was used to obtain information on the event. A total of 9,361 participants were randomized. The trial was stopped earlier than expected after analyses of the primary outcome exceeded the monitoring boundaries at 2 consecutive time-points. The median follow-up time was 3.26 years. The primary outcome was a composite of myocardial infarction, other acute coronary syndromes, stroke, heart failure, or cardiovascular death. Compared with a standard systolic BP target of <140 mm Hg and intensive strategy with a <120 mm Hg, reduced the primary outcome (6.8% vs. 5.2%; 1.65% per year vs. 2.19% per year; hazard ratio with intensive treatment, 0.75; 95% confidence interval, 0.64–0.89; $P < 0.001$).[7]

Sexual health questionnaires

Sexual health questionnaires were obtained in a subset of the SPRINT trial population (n = 1,881; 20% of the overall trial population), where 1,268 were men and 613 women. The characteristics of these patients were similar to those of the overall trial population (Supplementary Table S1 online). Throughout the trial, the most frequently prescribed anti-HT drugs were angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEi/ARBs) and thiazides, followed by calcium-channel blockers and beta-blockers (Supplementary Table S2 online).

For those engaged in sexual activities of any kind and who agreed to reply to the questionnaires (178 women and 862 men), the sexual health questions included an overall sexual life satisfaction question for both sexes, ranging from 1 (very dissatisfied) to 5 (very satisfied). Sexual health questionnaire for women was performed using a modified version of the Female Sexual Function Inventory (FSFI),[11] and included questions about their sexual desire or interest, sexual arousal, vaginal lubrication during sexual activity, orgasm frequency, satisfaction with sexual relationship, and emotional closeness with partner. These questions were classified from 1 (almost never satisfied or very dissatisfied) to 5 (almost always or very satisfied). We have also dichotomized these variables in half of the times or more (≥3 points) and less than half of the times (<3 points).

For men the questionnaires were performed using the 5-item version of International Index of Erectile Function (IIEF-5) questionnaire,[12] and included questions about confidence to get and keep an erection, if the erections were hard enough for penetration, and whether the erections could be maintained after penetration. These questions were also classified from 1 (almost never or very dissatisfied) to 5 (almost always or very satisfied) and we have also dichotomized these variables in half of the times or more (≥3 points) and less than half of the times (<3 points).

These questionnaires are detailed in Supplementary Material online.

Statistical analysis

In descriptive analyses, continuous variables are expressed as mean ± SD or median (percentile$_{25-75}$) based on their histogram distribution. Categorical variables are expressed as frequencies and proportions (%). Population description and comparison of men vs. women were performed using independent samples t-test for normally distributed continuous variables, Mann–Whitney test for skewed variables, and chi-square test for categorical variables. As the aim of our study was to assess the impact on anti-HT therapy on the sexual function of men and women throughout the follow-up, the evolution of the sexual scores over time, was performed using linear (for continuous) and logistic (for binary) random-effects models for panel data i.e., data with

multiple observations per patient over time (study visits: 0, 6, 12, 24, 36, and 48 months). The sexual scores were set as dependent variables and visit time as independent variable. To assess the effect of treatment (intensive vs. standard) a treatment-by-time interaction was included in the model. The individual anti-HT drugs used during the follow-up were retrieved from "free text" forms. To assess the impact of comorbidities on the sexual function scores, age, race, systolic BP, body mass index, smoking history, number of anti-HT agents, estimated glomerular filtration rate, presence of clinical or subclinical cardiovascular disease, total cholesterol levels, glucose levels, and urinary albumin-to-creatinine ratio were added to the panel data models in a multivariable fashion, retaining only the variables significantly associated with each individual sexual score in a stepwise backward fashion. Time-updated Cox models were used to study the association of erectile function and the study primary outcome adjusted on age, body mass index, chronic kidney disease, and history of clinical or subclinical cardiovascular disease. All analyses were performed with the Stata software (StataCorp., 2019, Stata Statistical Software: Release 16, College Station, TX: StataCorp LLC).

RESULTS

Baseline patients' characteristics by sex

Among the 1,268 men and 613 women included in this substudy, 862 (68%) men and 178 (29%) women declared to be engaged in sexual activity of any kind. Compared with women declaring not to be engaged in sexual activity of any kind, those who declared to be engaged in sexual activity were younger (64 vs. 69 years), more often current smokers, and with better renal function (Table 1). Compared with men not engaged in sexual activity of any kind, those who declared to be engaged in sexual activity were younger (65 vs. 71 years), more often black, with slightly higher body mass index, and with better renal function (Table 1). Comparing men and women with sexual activity of any kind, women

Table 1. Baseline characteristics of men and women by sex activity patterns

Characteristic	Women			Men			With sex activity		
Sex activity	No	Yes	*P* value	No	Yes	*P* value	Women	Men	*P* value
N.	426	178		399	862		178	862	
Intensive	218 (51.2%)	88 (49.4%)	0.70	192 (48.1%)	429 (49.8%)	0.59	88 (49.4%)	429 (49.8%)	0.94
Age, year	68.8 ± 9.8	63.5 ± 9.1	<0.001	70.9 ± 9.9	65.0 ± 8.9	<0.001	63.5 ± 9.1	65.0 ± 8.9	0.049
Race									
Black	167 (39.2%)	68 (38.2%)	0.043	83 (20.8%)	266 (30.9%)	0.003	68 (38.2%)	266 (30.9%)	0.001
Hispanic	68 (16.0%)	29 (16.3%)		51 (12.8%)	88 (10.2%)		29 (16.3%)	88 (10.2%)	
Other	2 (0.5%)	6 (3.4%)		7 (1.8%)	14 (1.6%)		6 (3.4%)	14 (1.6%)	
White	189 (44.4%)	75 (42.1%)		258 (64.7%)	494 (57.3%)		75 (42.1%)	494 (57.3%)	
BMI, kg/m^2	30.0 ± 6.9	30.8 ± 6.3	0.18	29.3 ± 5.2	30.2 ± 5.6	0.007	30.8 ± 6.3	30.2 ± 5.6	0.20
SBP, mm Hg	142.2 ± 16.8	140.8 ± 16.8	0.35	139.8 ± 15.1	138.6 ± 14.8	0.19	140.8 ± 16.8	138.6 ± 14.8	0.070
DBP, mm Hg	77.9 ± 11.6	81.2 ± 12.9	0.002	76.3 ± 11.6	80.0 ± 11.6	<0.001	81.2 ± 12.9	80.0 ± 11.6	0.19
Smoking									
Never	241 (56.6%)	81 (45.5%)	0.002	161 (40.4%)	314 (36.4%)	0.40	81 (45.5%)	314 (36.4%)	<0.001
Former	133 (31.2%)	56 (31.5%)		184 (46.1%)	412 (47.8%)		56 (31.5%)	412 (47.8%)	
Current	52 (12.2%)	41 (23.0%)		54 (13.5%)	134 (15.5%)		41 (23.0%)	134 (15.5%)	
eGFR, ml/min	70.2 ± 22.8	73.8 ± 20.0	0.068	70.3 ± 21.5	75.9 ± 20.0	<0.001	73.8 ± 20.0	75.9 ± 20.0	0.21
eGFR <60	148 (34.7%)	41 (23.0%)	0.005	136 (34.1%)	171 (19.8%)	<0.001	41 (23.0%)	171 (19.8%)	0.34
HDL-c, mg/dl	60.2 ± 16.6	56.6 ± 14.6	0.011	48.3 ± 12.5	49.1 ± 12.0	0.26	56.6 ± 14.6	49.1 ± 12.0	<0.001
Triglycerides, mg/dl	124.7 ± 90.5	137.2 ± 66.1	0.097	137.1 ± 193.3	134.2 ± 99.6	0.73	137.2 ± 66.1	134.2 ± 99.6	0.71
UACR, mg/gCr	11.3 (6.7, 27.6)	8.4 (5.6, 15.3)	<0.001	9.5 (5.4, 22.8)	8.5 (5.0, 19.2)	0.073	8.4 (5.6, 15.3)	8.5 (5.0, 19.2)	0.71
Subclinical CVD	21 (4.9%)	7 (3.9%)	0.60	25 (6.3%)	44 (5.1%)	0.40	7 (3.9%)	44 (5.1%)	0.51
N. anti-HT drugs									
0	27 (6.3%)	18 (10.1%)	0.12	30 (7.5%)	90 (10.4%)	0.51	18 (10.1%)	90 (10.4%)	0.78
1	129 (30.3%)	50 (28.1%)		123 (30.8%)	250 (29.0%)		50 (28.1%)	250 (29.0%)	
2	152 (35.7%)	68 (38.2%)		141 (35.3%)	310 (36.0%)		68 (38.2%)	310 (36.0%)	
3+	118 (27.8%)	42 (23.5%)		104 (26.1%)	211 (24.5%)		42 (23.5%)	211 (24.5%)	
Statin use	167 (39.5%)	52 (29.5%)	0.021	208 (52.1%)	395 (45.9%)	0.039	52 (29.5%)	395 (45.9%)	<0.001

Abbreviations: BMI, body mass index; CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HDL-c, high densisty lipoprotein cholesterol; HT, hypertensive; SBP, systolic blood pressure; UACR, urinary albumin-to-creatinine ratio.

were slightly younger, more often black, more often current smokers, with higher HDL-cholesterol and less likely to be on a statin (Table 1).

Baseline sexual health

The main description of the questionnaires by sex is depicted in Table 2. Women declared having an overall low satisfaction with their sexual life. Less than 50% of women declared to feel sexual desire or interest on at least half of the occasions and 30% said that they would almost never/never feel sexual desire; however, most declared to feel sexual arousal, become lubricated, and reach orgasm in at least half of the occasions they had sexual intercourse, most women were also satisfied with their relationship and emotional closeness during sexual activity (Table 2).

Most men said they felt at least moderately confident that they could get and keep an erection that the erections would be hard for penetration and maintained after penetration in most occasions (Table 2).

Sexual health over time by sex and treatment allocation

Women's sexual satisfaction, desire, arousal, lubrication, orgasm, and emotional closeness did not significantly change over time, neither did they differ by treatment allocation (i.e., they were not aggravated by intensive therapy) (Table 3 and Figure 1).

Men's overall sexual satisfaction was maintained over time and did not differ by treatment group. However, they declared that their erections (particularly hard erections and their maintenance during intercourse) were slightly deteriorated over time (−0.1 to −0.2 points; $P < 0.05$), but they were not aggravated by intensive anti-HT therapy ($P > 0.05$ for all) (Table 4 and Figure 2). All therapeutic regimens could have had a negative impact on the quality of the erections, but those without thiazides and/or beta-blockers could have been less impactful (Supplementary Table S3 online).

Association with clinical features and comorbid conditions

In men, older age (>65 years) and a body mass index above 30 kg/m^2, were associated with lower overall sexual satisfaction and lower quality of erections. Patients with clinical or subclinical cardiovascular disease and those with impaired renal function had more difficulty in maintaining erections (Supplementary Table S4 online). Women taking a higher number of anti-HT drugs were less satisfied with their sexual life, and older women (>65 years) had less sexual desire and became less often lubricated during sexual activity (Supplementary Table S4 online).

Outcome associations

Among men, 117 primary outcome events occurred. In adjusted models, the sexual/erectile function was not significantly associated with the study primary outcome (Supplementary Table S5 online). Among women, 31 primary outcome events occurred. Feeling sexual desire or interest more often was independently associated with a lower rate of the study primary outcome (hazard ratio [95% confidence interval] = 0.62 [0.41–0.94], $P = 0.025$), but the other sex-related questions were not (Supplementary Table S5 online).

DISCUSSION

This study shows that in a population with arterial HT and a moderate-to-high cardiovascular risk (but without diabetes or prior stroke), most women declared that they were not engaged in any sexual activity while most men declared they were. Women's sexual desire was low but once they were engaged in sexual activities their sexual satisfaction was at least moderate in most occasions and was not deteriorated with intensive anti-HT therapy over time. Most men were confident that they could get and keep an erection, but the maintenance of hard erections was slightly diminished throughout the trial, albeit not aggravated by intensive therapy, suggesting that anti-HT treatment may impair the quality of erections but that is not dependent on the intensity of the anti-HT treatment.

Sexual dysfunction might be more prevalent in women than in men and is associated with poor physical and emotional health as well as poor overall well-being.[13] Although the sexual problems tend to increase with age, these seem to affect men in particular, still lubrication problems may also be aggravated with women's age.[14] This study included mostly elderly people (mean age 67 years for women and 68 years for men) with moderate–high cardiovascular risk and HT, which is a population with a particularly high risk for experiencing sexual dysfunction.[14] While most women declared that they were not engaged in any sexual activity, most men declared they were. The lack of sexual interest in older women has been reported, while most men could have stated to have more sexual interest due to fear of judgments about their "masculinity."[14,15] Interestingly, women that stated to have a sexual activity of any kind reported to have an overall (at least) moderate sexual satisfaction. In a report using the baseline data of SPRINT, BP was not associated with sexual activity in women, which was more related to psychosocial factors,[16] and, at baseline, no single class of anti-HT medication was associated with sexual dysfunction in women.[17] Furthermore, our study shows that women did not experience any deterioration of their sexual health during the follow-up nor their sexual health was influenced by the allocation to an intensive anti-HT therapy regimen. These findings have clinical relevance, because they suggest that regardless of the baseline sexual health in women (that may be related to many other factors rather than BP) this is unlikely to be deteriorated with an intensive treatment and should not preclude clinicians to try a systolic BP goal of 120 mm Hg.

Men were overall confident of their sexual performance, but many reported to have erectile problems at baseline and to have difficulties in maintaining an erection during sexual intercourse. These findings are compatible with other reports, stating that erectile dysfunction is common in men in their 60s and even more in men aged 70 and older,

Table 2. Baseline sexual health questionnaires in men and women

Variable	Men	Women	*P* value
N.	1,296	655	
How satisfied with your overall sexual life?			
Very dissatisfied	73 (8.5%)	104 (19.7%)	<0.001
Moderately dissatisfied	76 (8.9%)	55 (10.4%)	
Equally satisfied and dissatisfied	107 (12.5%)	134 (25.4%)	
Moderately satisfied	232 (27.2%)	104 (19.7%)	
Very satisfied	361 (42.3%)	101 (19.2%)	
Half of times or more	700 (82.4%)	339 (68.1%)	<0.001
Sexual health questions (women)			
How often do you feel sexual desire or interest?			
Not answered	NA	27 (4.9%)	
Almost never/never	NA	162 (29.6%)	
A few times (less than half)	NA	115 (21.0%)	
Sometimes (about half)	NA	128 (23.4%)	
Most times	NA	78 (14.3%)	
Almost always/always	NA	37 (6.8%)	
Half of times or more	NA	243 (46.7%)	
How often do you feel sexually aroused during sexual activity?			
Not answered	NA	4 (2.2%)	
Almost never/never	NA	17 (9.2%)	
A few times (less than half)	NA	35 (19.0%)	
Sometimes (about half)	NA	38 (20.7%)	
Most times	NA	53 (28.8%)	
Almost always/always	NA	37 (20.1%)	
Half of times or more	NA	128 (71.1%)	
How often do you become lubricated during sexual activity?			
Not answered	NA	3 (1.6%)	
Almost never/never	NA	23 (12.6%)	
A few times (less than half)	NA	24 (13.1%)	
Sometimes (about half)	NA	44 (24.0%)	
Most times	NA	53 (29.0%)	
Almost always/always	NA	36 (19.7%)	
Half of times or more	NA	133 (73.9%)	
How often do you reach orgasm?			
Not answered	NA	3 (1.6%)	
Almost never/never	NA	19 (10.3%)	
A few times (less than half)	NA	28 (15.1%)	
Sometimes (about half)	NA	35 (18.9%)	
Most times	NA	55 (29.7%)	
Almost always/always	NA	45 (24.3%)	
Half of times or more	NA	135 (74.2%)	
Satisfied with sexual relationship with partner?			
Not answered	NA	4 (2.2%)	
Very dissatisfied	NA	18 (10.0%)	

Table 2. Continued

Variable	Men	Women	*P* value
Moderately dissatisfied	NA	25 (13.9%)	
Equally satisfied and dissatisfied	NA	34 (18.9%)	
Moderately satisfied	NA	46 (25.6%)	
Very satisfied	NA	53 (29.4%)	
Half of times or more	NA	133 (75.6%)	
Satisfied with emotional closeness during sexual activity?			
Not answered	NA	4 (2.6%)	
Very dissatisfied	NA	14 (9.0%)	
Moderately dissatisfied	NA	15 (9.6%)	
Equally satisfied and dissatisfied	NA	23 (14.7%)	
Moderately satisfied	NA	42 (26.9%)	
Very satisfied	NA	58 (37.2%)	
Half of times or more	NA	123 (80.9%)	
Sexual activity questions (men)			
Confidence that you could get and keep an erection?			
Not answered	4 (0.5%)	NA	
Very low	113 (12.9%)	NA	
Low	150 (17.1%)	NA	
Moderate	301 (34.4%)	NA	
High	182 (20.8%)	NA	
Very high	125 (14.3%)	NA	
Moderate or higher	608 (69.8%)	NA	
Erections hard enough for penetration?			
Not answered	7 (0.8%)	NA	
Almost never/never	92 (10.6%)	NA	
A few times (less than half)	134 (15.5%)	NA	
Sometimes (about half)	140 (16.1%)	NA	
Most times	194 (22.4%)	NA	
Almost always/always	300 (34.6%)	NA	
Half of times or more	634 (73.7%)	NA	
Erections maintained after penetration?			
Not answered	6 (0.7%)	NA	
Almost never/never	96 (11.3%)	NA	
A few times (less than half)	113 (13.2%)	NA	
Sometimes (about half)	131 (15.4%)	NA	
Most times	209 (24.5%)	NA	
Almost always/always	298 (34.9%)	NA	
Half of times or more	638 (75.3%)	NA	

affecting more than 50% of men in these age ranges.[18,19] In patients with HT, erectile dysfunction has been independently associated with adverse cardiovascular outcomes.[20] In our report, the associations between erectile dysfunction and the study primary outcome did not reach statistical significance; probably due to the small size and few events in this subsample. In a report from SPRINT, baseline BP was not associated with sexual activity in men either.[21] Our study suggests that erectile function (hard and sustained erections, in particular) may be aggravated with anti-HT treatment over time; however, erectile dysfunction was not furtherly deteriorated with intensive anti-heart failure treatment for a systolic BP goal of 120 mm Hg, which suggests that erectile dysfunction is not dependent on the intensity of the anti-HT

Table 3. Women: changes in sexual health questionnaires over time and by treatment allocation (standard vs. intensive)

Women	Coef.	LCI	UCI	*P*		Coef.	LCI	UCI	*P*
Sexual health change over time (months): 0 (randomization) to 48 months									
Sexual activity questions	**Continuous**					**Categorical**			
How satisfied with your overall sexual life?					Half of times or more				
0	Ref.					Ref.			
6	0.09	−0.07	0.25	0.26		0.04	−0.27	0.36	0.78
12	−0.03	−0.19	0.13	0.73		−0.19	−0.51	0.12	0.22
24	0.03	−0.13	0.19	0.67		−0.07	−0.39	0.25	0.65
36	0.15	−0.01	0.32	0.066		0.13	−0.21	0.46	0.46
48	−0.06	−0.37	0.24	0.69		−0.24	−0.83	0.36	0.43
How often do you feel sexual desire or interest?					Half of times or more				
0	Ref.					Ref.			
6	0.02	−0.08	0.13	0.69		0.32	−0.03	0.67	0.071
12	−0.11	−0.22	0	0.047		−0.16	−0.52	0.2	0.37
24	−0.09	−0.2	0.02	0.10		0	−0.36	0.36	0.99
36	−0.09	−0.2	0.02	0.12		−0.17	−0.54	0.21	0.38
48	0.03	−0.19	0.24	0.81		0.43	−0.29	1.15	0.24
How often do you feel sexually aroused during sexual activity?					Half of times or more				
0	Ref.					Ref.			
6	0.02	−0.16	0.21	0.80		0.6	−0.2	1.4	0.14
12	−0.02	−0.21	0.18	0.86		0.3	−0.52	1.13	0.47
24	0.06	−0.14	0.25	0.55		0.86	−0.01	1.72	0.052
36	0.16	−0.05	0.37	0.12		0.67	−0.24	1.58	0.15
48	0.14	−0.26	0.55	0.48		0.83	−0.8	2.47	0.31
How often do you become lubricated during sexual activity?					Half of times or more				
0	Ref.					Ref.			
6	−0.09	−0.28	0.1	0.37		−0.17	−0.86	0.52	0.62
12	−0.02	−0.22	0.18	0.85		0.11	−0.63	0.85	0.77
24	0.05	−0.15	0.25	0.63		0.25	−0.5	1	0.51
36	−0.05	−0.27	0.16	0.62		−0.19	−0.98	0.61	0.64
48	−0.03	−0.44	0.39	0.89		1.12	−0.84	3.09	0.26
48	−0.16	−0.59	0.28	0.47		−0.64	−2.16	0.88	0.41
When you had sexual stimulation/ intercourse, how often do you reach orgasm?					Half of times or more				
0	Ref.					Ref.			
6	−0.07	−0.24	0.1	0.44		−0.29	−1.07	0.48	0.46
12	−0.02	−0.2	0.16	0.84		−0.08	−0.89	0.72	0.83
24	0.07	−0.11	0.25	0.45		0.45	−0.39	1.3	0.29
36	0.02	−0.18	0.21	0.86		−0.06	−0.97	0.84	0.88
48	0.02	−0.36	0.4	0.91		−0.24	−2.17	1.69	0.80
Satisfied with sexual relationship with partner?					Half of times or more				
0	Ref.					Ref.			

Table 3. Continued

Women	Coef.	LCI	UCI	*P*		Coef.	LCI	UCI	*P*
Sexual health change over time (months): 0 (randomization) to 48 months									
6	0	−0.23	0.22	0.99		0.13	−0.54	0.79	0.71
12	0.16	−0.07	0.4	0.17		0.41	−0.3	1.12	0.25
24	0.08	−0.16	0.32	0.50		0.06	−0.63	0.76	0.85
36	0.09	−0.17	0.34	0.51		0.23	−0.52	0.99	0.54
48	0.24	−0.27	0.74	0.35		1.09	−0.68	2.87	0.22
Satisfied with emotional closeness during sexual activity?					Half of times or more				
0	Ref.					Ref.			
6	−0.13	−0.38	0.11	0.28		−0.33	−1.05	0.38	0.35
12	−0.12	−0.37	0.14	0.36		0.03	−0.72	0.79	0.93
24	0.06	−0.19	0.32	0.63		0.11	−0.65	0.88	0.77
36	0.14	−0.13	0.41	0.30		0.23	−0.6	1.06	0.58
48	0.25	−0.28	0.78	0.35		1.14	−0.81	3.09	0.25
Sexual health change by treatment: comparison of intensive vs. standard anti-hypertensive treatment									
Sexual activity questions	Continuous				Categorical				
How satisfied with your overall sexual life?	−0.14	−0.3	0.02	0.092	Half of times or more	−0.08	−0.38	0.21	0.58
How often do you feel sexual desire or interest?	0.0	−0.17	0.16	0.95	Half of times or more	−0.07	−0.54	0.4	0.76
How often do you feel sexually aroused?	0.0	−0.27	0.27	0.99	Half of times or more	−0.02	−1.02	0.97	0.96
How often do you become lubricated during sexual activity?	0.06	−0.21	0.32	0.67	Half of times or more	0.07	−0.72	0.87	0.85
When you had sexual stimulation/ intercourse, how difficult was it to reach orgasm?	0.03	−0.2	0.26	0.81	Difficult or worse	−0.66	−1.64	0.31	0.18
Satisfied with sexual relationship with partner?	0.09	−0.18	0.36	0.51	Half of times or more	0.33	−0.34	1	0.33
Satisfied with emotional closeness during sexual activity?	0.10	−0.18	0.39	0.46	Half of times or more	0.14	−0.54	0.83	0.68

Abbreviations: LCI, lower bound of the 95% confidence interval; *P*, *P* value; UCI, upper bound of the 95% confidence interval.

therapy. In a report from SPRINT, the erectile dysfunction induced by a more intensive BP lowering strategy was found to be more marked in non-Hispanic blacks compared with non-Hispanic whites, differences that disappeared in the adjusted models.[22] In our report, race was not independently associated with any sexual/erection question in the fully adjusted models.

In SPRINT (overall and in this subpopulation) the most commonly used anti-HT drug was ACEi/ARBs (in over 70% of the participant episodes), followed by thiazide-type diuretics (over 50%), calcium-channel blockers (in almost 50%), and beta-blockers (up to 40%). The combination of ACEi/ARBs plus thiazides was used in 53% of the observations in men. Other anti-HT agents such as mineralocorticoid receptor antagonists and central-acting drugs were used in a much lower frequency (<10%). The use of ACEi/ARBs and calcium-channel blockers has been reported as not being associated with erectile dysfunction, with many reports showing a "neutral" effect of these agents in erectile function[23–25]; ARBs in particular by blocking the vasoconstrictive action of angiotensin II may positively affect erectile function and are thus regarded as a first-line treatment in HT patients with erectile dysfunction.[26–29] On the other hand, thiazides, beta-blockers (with the possible exception of nebivolol),[30] mineralocorticoid receptor antagonists, and central-acting anti-HT agents may impair erectile function.[31–35] Unfortunately, for an adequate BP control one often requires anti-HT drug combinations, which often include a diuretic to increase sodium excretion.[36] In SPRINT this was no exception with more than half of men having a thiazide diuretic prescribed in association with other drugs, most frequently an ACEi/ARB. Nonetheless, consistently with prior studies, our observational data suggest that anti-HT regimens without beta-blockers or thiazides may be less impactful on erectile function.

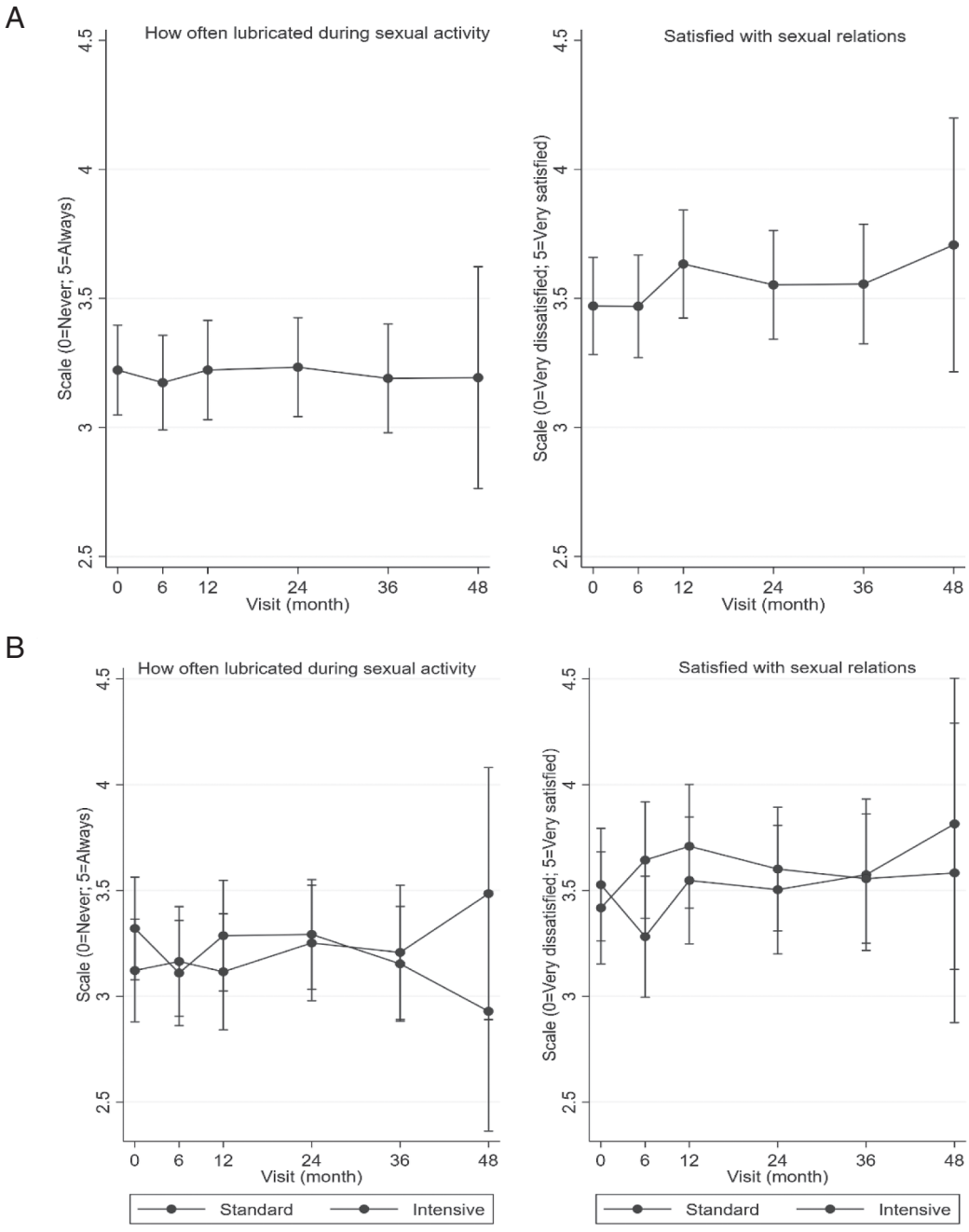

Figure 1. Women: change in lubrication and satisfaction during sexual intercourse over time and by treatment (intensive vs. standard). (**a**) Change over time. (**b**) Change by treatment. No significant differences observed (all $P > 0.05$).

Limitations

The impact of each individual drug on erectile function is hard to ascertain, because most patients take several medications that change over time and the individual effects of each drug cannot be assessed in a reliable fashion. However, the observation that an intensive anti-HT therapy does not furtherly deteriorate erectile function is reassuring and may help clinicians guiding their treatment strategies i.e., intensifying anti-HT treatment can improve outcomes and does not seem to further impact erectile function. The use of other medications (e.g., over the counter phosphodiesterase-5 inhibitors) could not be accounted for because was not systematically recorded in the dataset; however, it is expected that the use of other (non anti-HT) medications that could impact sexual function was used similarly (i.e., at random)

Table 4. Men: changes in sexual health questionnaires over time and by treatment allocation (standard vs. intensive)

Men	Coef.	LCI	UCI	*P*		Coef.	LCI	UCI	*P*
Sexual health change over time (months): 0 (randomization) to 48 months									
Sexual activity questions	**Continuous**					**Categorical**			
How satisfied with your overall sexual life?					Half of times or more				
0	Ref.					Ref.			
6	-0.08	−0.16	0	0.054		−0.34	−0.7	0.02	0.061
12	−0.08	−0.17	0	0.047		−0.36	−0.73	0.01	0.054
24	−0.06	−0.14	0.03	0.17		−0.23	−0.62	0.15	0.23
36	−0.06	−0.15	0.03	0.16		−0.23	−0.63	0.17	0.26
48	−0.03	−0.21	0.15	0.73		−0.28	−1.07	0.51	0.48
Confidence that you could get and keep an erection?					Moderate or higher				
0	Ref.					Ref.			
6	−0.08	−0.14	−0.01	0.026		−0.26	−0.59	0.07	0.11
12	−0.06	−0.13	0.01	0.10		0.1	−0.24	0.45	0.54
24	−0.08	−0.15	0	0.038		−0.22	−0.57	0.13	0.21
36	−0.13	−0.21	−0.06	0.001		−0.31	−0.67	0.05	0.091
48	−0.15	−0.3	0	0.051		−0.43	−1.13	0.28	0.23
Erections hard enough for penetration?					Half of times or more				
0	Ref.					Ref.			
6	−0.1	−0.18	−0.02	0.019		−0.13	−0.44	0.19	0.43
12	−0.07	−0.15	0.01	0.095		−0.02	−0.34	0.31	0.92
24	−0.11	−0.19	−0.03	0.010		−0.11	−0.45	0.22	0.50
36	−0.12	−0.21	−0.03	0.008		−0.11	−0.46	0.23	0.52
48	−0.12	−0.29	0.06	0.20		0.2	−0.52	0.92	0.59
Erections maintained after penetration?					Half of times or more				
0	Ref.					Ref.			
6	−0.12	−0.2	−0.04	0.004		−0.43	−0.76	−0.1	0.011
12	−0.17	−0.26	−0.09	<0.001		−0.43	−0.77	−0.09	0.013
24	−0.19	−0.27	−0.1	<0.001		−0.57	−0.92	−0.22	0.001
36	−0.21	−0.3	−0.12	<0.001		−0.53	−0.89	−0.17	0.004
48	−0.11	−0.29	0.07	0.24		0.01	−0.77	0.79	0.97
Erection maintained to completion of intercourse?									
0	Ref.					Ref.			
6	−0.09	−0.16	−0.02	0.01		−0.49	−0.9	−0.08	0.02
12	−0.07	−0.14	0	0.065		−0.53	−0.96	−0.11	0.013
24	−0.1	−0.18	−0.03	0.008		−0.62	−1.05	−0.18	0.005
36	−0.12	−0.2	−0.04	0.003		−0.58	−1.04	−0.13	0.012
48	−0.04	−0.2	0.11	0.58		−0.82	−1.68	0.05	0.06
Sexual health change by treatment: comparison of intensive vs. standard anti-hypertensive treatment									
Sexual activity questions	Continuous					Categorical			
How satisfied with your overall sexual life?	−0.08	−0.23	0.07	0.28	Half of times or more	−0.33	−0.79	0.13	0.16
Confidence that you could get and keep an erection?	−0.07	−0.2	0.06	0.32	Moderate or higher	−0.09	−0.58	0.4	0.72
Erections hard enough for penetration?	−0.06	−0.21	0.09	0.43	Half of times or more	−0.18	−0.6	0.25	0.41
Erections maintained after penetration?	−0.05	−0.21	0.11	0.52	Half of times or more	−0.01	−0.45	0.44	0.97
Erection maintained to completion of intercourse?	−0.08	−0.24	0.07	0.29	Half of times or more	−0.32	−0.86	0.23	0.26
Total score (continuous: min. 5 to 25 max.) at each time-point (months)					Score ≤21 (categorical)				
0	−0.27	−1.32	0.78	0.62		0.17	−0.1	0.43	0.22
6	−0.12	−1.16	0.92	0.82		0.1	−0.18	0.38	0.48
12	−0.38	−1.44	0.68	0.48		0	−0.28	0.29	1.00

Table 4. Continued

Men	Coef.	LCI	UCI	*P*	Coef.	LCI	UCI	*P*
Sexual health change over time (months): 0 (randomization) to 48 months								
Sexual activity questions	**Continuous**				**Categorical**			
24	−0.73	−1.79	0.33	0.18	0.25	−0.04	0.54	0.09
36	−0.17	−1.21	0.87	0.75	0.15	−0.16	0.46	0.34
48	0.11	−0.44	0.65	0.70	−0.11	−0.82	0.6	0.77

Abbreviations: LCI, lower bound of the 95% confidence interval; *P*, *P* value; UCI, upper bound of the 95% confidence interval.

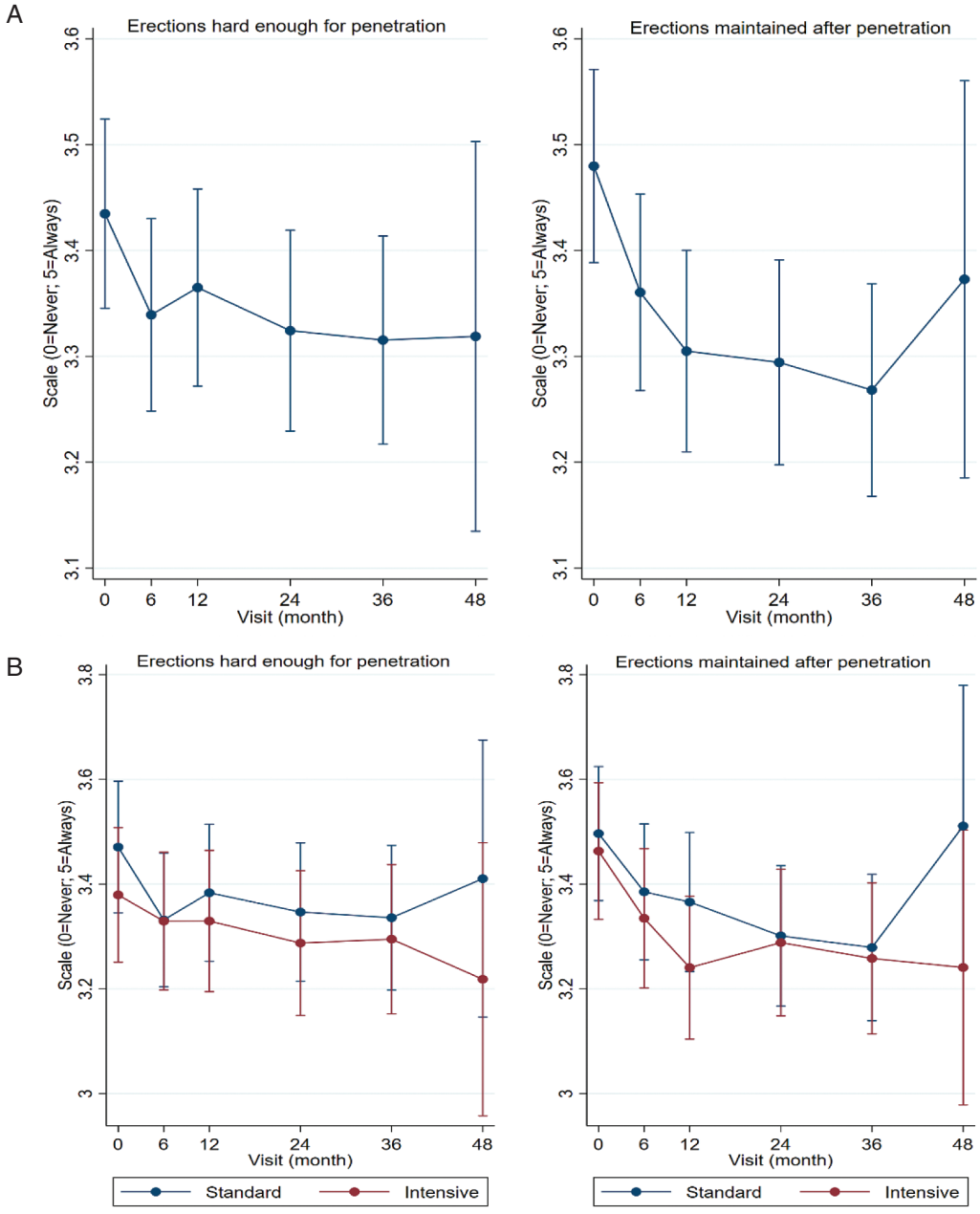

Figure 2. Men: change in the quality of erections during sexual intercourse over time and by treatment (intensive vs. standard). (**a**) Change over time. (**b**) Change with treatment. Slight decrease in the quality of erections over time ($P < 0.05$ for all time-points, except 48 months were the estimates are imprecise due to low number of patients) but not by intensive treatment (vs. standard) ($P > 0.05$ for all comparisons).

between the intensive and standard anti-HT therapy groups, and therefore does not impact our findings comparing the effect of intensive vs. standard anti-HT therapy on sexual function. The small number of events in this sexual questionnaire subsample (furtherly subdivided in men and women) likely lacked enough power to study the associations between sexual function and outcomes in a more robust fashion.

In SPRINT, women's sexual health was maintained over time and was not affected by intensive anti-HT therapy. Men, declared having a slight deterioration in the quality of their erections over time, without further aggravation by intensive anti-HT therapy. These findings may help reassuring patients about the sexual safety of intensive anti-HT therapy, therefore, potentially improving adherence to intensive therapy strategy.

Clinical perspectives

Women had an overall low satisfaction with their sexual life but their sexual health was not affected by anti-HT therapy over time nor modified by an intensive treatment.

Men's erections were slightly deteriorated over time but were not aggravated by an intensive anti-HT therapy.

These findings may help reassuring patients about the sexual safety of intensive anti-HT therapy and improve treatment adherence.

SUPPLEMENTARY MATERIAL

Supplementary data are available at *American Journal of Hypertension* online.

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DISCLOSURE

The content of this manuscript is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health (NIH), the Department of Veterans Affairs, or the U.S. Government.

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