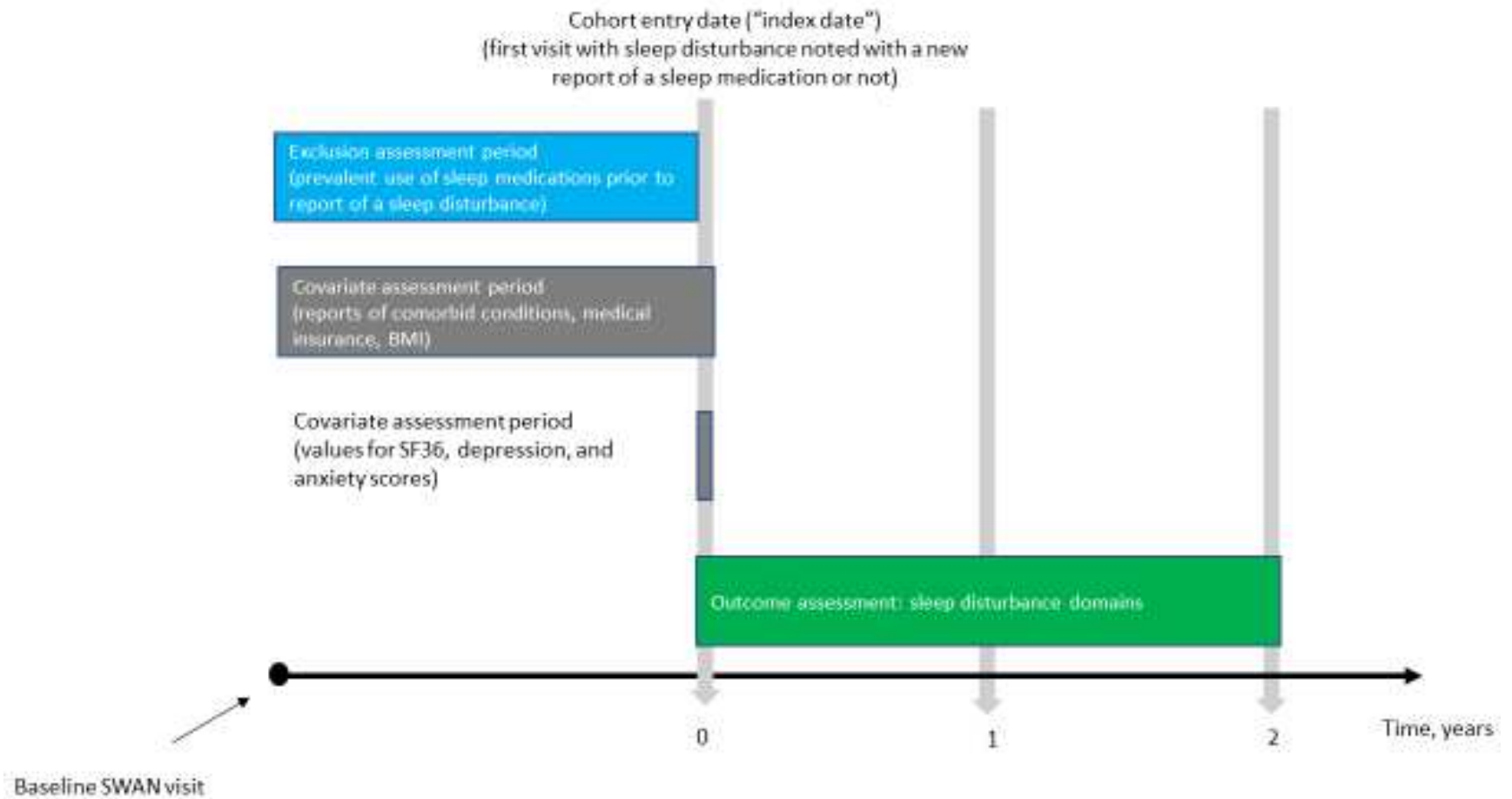**SUPPLEMENTARY TABLES AND FIGURES**

Supplementary Table 1: Design of the Target Trial and the Observational Corollary

Protocol component	Target Trial	Observational Corollary*
Study question	Are sleep medications effective over one year?	Same
Eligible criteria	Adult men and women reporting a sleep disturbance	Women in the SWAN cohort reporting a sleep disturbance
Other selection criteria	No use of sleep medications at baseline (or a sufficient washout period); no obstructive sleep apnea	No use of sleep medications at entry into SWAN; one-year follow-up data
Treatment strategies	Specific medication for sleep at a known effective dosage versus placebo	All known sleep medications at a variety of dosages versus no use of a sleep medication
Treatment assignment procedures	Randomization	Based on clinical evaluation during routine medical visits
Outcome	Sleep disturbance, self-reported and measured; assessed monthly	Self-reported sleep disturbances assessed one- and two-years after baseline
Balancing method	Randomization	Propensity score matching
Causal contrasts of interest	Intention to treat	Same

*Current study. SWAN, Study of Women Across the Nation.

Based on Hernan and Robins, Am J Epidemiology, 2016;183:758.

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

BMJ Open

Supplementary Figure 1: Study Design

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

BMJ Open

Supplementary Table 2: Baseline Demographics of Women in SWAN Examined in the Primary Cohort

	Total N=1528	No Sleep Medication n=1268	Sleep Medication User n=260	SMD
	N (%) unless noted			
Age, mean (SD)	49.8 (8.4)	49.9 (8.5)	49.3 (7.6)	0.08
BMI, mean (SD)	28.8 (7.2)	28.7 (7.1)	29.2 (7.7)	0.07
Educational attainment				
High school or less	319 (20.9)	261 (20.6)	58 (22.3)	0.01
> high school	1201 (78.6)	999 (78.8)	202 (77.7)	
Ethnicity/race				
African American	406 (26.6)	345 (27.2)	61 (23.5)	0.09
White	782 (51.2)	634 (50.0)	148 (56.9)	0.14
Chinese	135 (8.8)	119 (9.4)	16 (6.2)	0.12
Hispanic	44 (2.9)	33 (2.6)	11 (4.2)	0.09
Japanese	161 (10.5)	137 (10.8)	24 (9.2)	0.05
Medical insurance	1438 (94.1)	1186 (93.5)	252 (96.9)	0.16
Marital status				
Single	194 (12.7)	155 (12.2)	39 (15.0)	0.06
Married	991 (64.9)	831 (65.6)	160 (61.5)	0.15
Separated	43 (2.8)	33 (2.6)	10 (3.9)	0.15
Widowed	67 (4.4)	54 (4.3)	13 (5.0)	0.08
Divorced	232 (15.2)	194 (15.3)	38 (14.6)	0.03
Tobacco use				
Never	895 (58.6)	761 (60.0)	113 (43.5)	0.17
Past/Current	629 (41.2)	504 (39.8)	125 (48.1)	
Alcohol use				0.05
None	733 (49.6)	621 (50.7)	112 (44.3)	0.13
<1 drink/week	373 (25.3)	321 (26.2)	52 (20.6)	0.13
1-7 drinks/week	252 (17.1)	190 (15.5)	62 (24.5)	0.23
>7 drinks/week	119 (8.1)	92 (7.5)	27 (10.7)	0.11
Depression (CES-D), mean (SD)	9.4 (9.4)	8.5 (8.6)	14.1 (11.4)	0.57
Anxiety score, mean (SD)	2.4 (2.4)	2.1 (2.2)	3.4 (2.8)	0.49
Body pain, mean (SD)	68.1 (22.4)	69.7 (21.7)	60.1 (24.0)	0.42
SF36-Mental, mean (SD)	49.1 (10.4)	49.9 (9.9)	45.0 (11.5)	0.45
SF36-Physical, mean (SD)	49.7 (9.9)	50.2 (9.5)	47.4 (11.5)	0.27
Menopausal Status				
Unknown	138 (9.0)	98 (7.7)	40 (15.4)	0.24
Pre-menopausal	113 (7.4)	102 (8.0)	11 (4.2)	0.16
Early/Late Peri-menopausal	597 (39.1)	508 (40.1)	89 (34.2)	0.12
Surgical menopause	54 (3.5)	42 (3.3)	12 (34.2)	0.07
Post-menopausal	625 (40.9)	517 (40.8)	108 (41.5)	0.02

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance
placed on this supplemental material which has been supplied by the author(s)

BMJ Open

Diabetes	152 (10.0)	123 (9.7)	29 (11.2)	0.05
Hypertension	616 (40.3)	488 (38.5)	128 (49.2)	0.22
Osteoarthritis	565 (37.0)	448 (35.3)	117 (45.0)	0.19
Cancer, current	26 (3.5)	12 (1.0)	14 (5.4)	0.16
Any antidepressant	28 (1.8)	11 (0.9)	17 (6.5)	0.30
Any analgesic	72 (4.7)	65 (5.1)	7 (2.7)	0.13

Supplementary Table 3: Baseline Demographics of Women in SWAN Who Were Included in the Current Analyses and Women Who Were Not

	Women Included in Study Cohort N=685	Women not Included in Study Cohort n=1846	SMD
	N (%) unless noted		
Age, mean (SD)	46.5 (2.7)	46.3 (2.7)	0.02
BMI, mean (SD)	28.2 (7.4)	28.5 (7.4)	0.03
Educational attainment			0.001
High school or less	141 (20.6)	443 (24.2)	
> high school	542 (79.4)	1387 (75.8)	
Ethnicity/race			0.001
African American	158 (23.1)	564 (30.6)	
White	394 (57.5)	867 (47.0)	
Chinese	45 (6.6)	145 (7.9)	
Hispanic	25 (3.7)	127 (6.9)	
Japanese	63 (9.2)	143 (7.8)	
Medical insurance	657 (95.9)	1696 (92.0)	0.06
Tobacco use			0.16
Never	347 (50.7)	1088 (59.0)	
Past/Current	337 (49.3)	756 (41.0)	
Alcohol use			0.16
None	294 (44.8)	877 (50.2)	
< 1 drink/week	60 (9.1)	179 (10.3)	
1-7 drinks/week	175 (26.6)	469 (28.9)	
>7 drinks/week	128 (19.5)	221 (12.7)	
Depression (CES-D), mean (SD)	12.3 (10.2)	10.7 (9.6)	0.31
Anxiety score, mean (SD)	3.1 (2.7)	2.5 (2.3)	0.30
Body pain, mean (SD)	65.3 (21.5)	68.8 (22.6)	0.27
Menopausal Status			0.05
Unknown	2 (0.3)	3 (0.2)	
Pre-menopausal	315 (46.3)	1023 (55.8)	
Early Peri-menopausal	364 (53.5)	808 (44.1)	
Diabetes	33 (4.8)	90 (4.9)	0.01
Hypertension	160 (23.5)	423 (23.1)	0.07
Osteoarthritis	150 (22.1)	312 (17.1)	0.02

Abbreviations: SMD, standardized mean difference; CES-D, Center for Epidemiologic Studies Depression Scale; BMI, Body Mass Index; SF36 Mental, Mental Component Score; and SF36 Physical, Physical Component Score.

Supplementary Table 4: Change in severity of sleep disturbances from baseline to year 1 for those propensity score matched at baseline minus 1 year
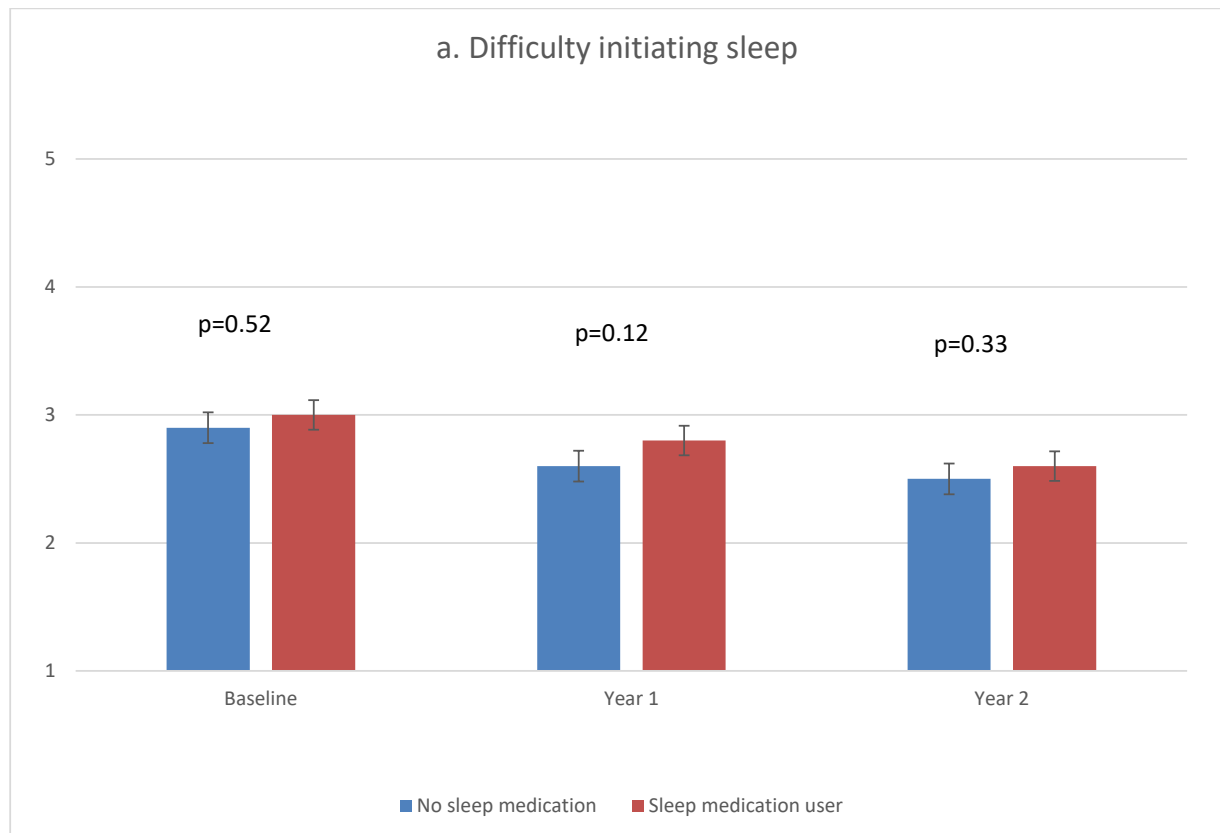
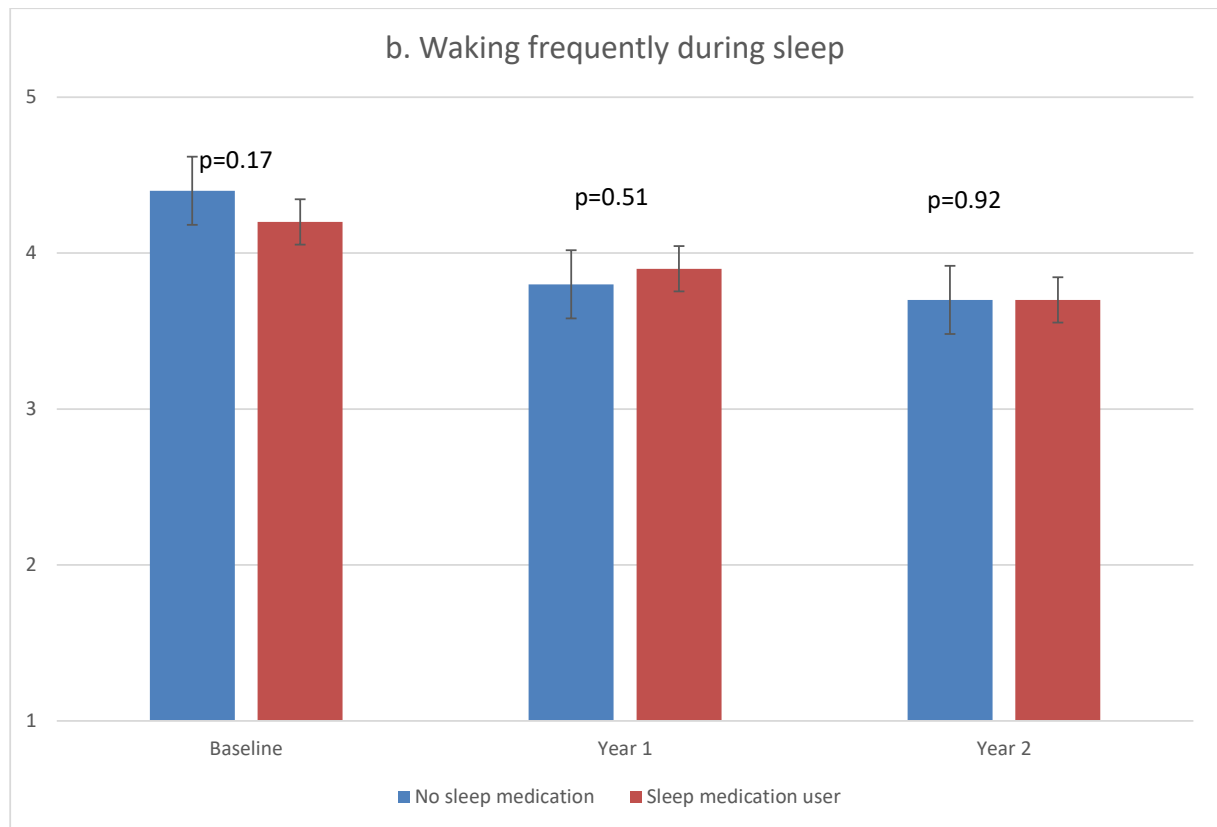|	Index Visit No Meds n=477		Index Visit Med Users n=253		Visit 1 year after No Meds n=477		Visit 1 year after Med Users n=253		Visit 2 year after No Meds n=361		Visit 2 year after Med Users n=197		P-value
	n	%	n	%	n	%	n	%	n	%	n	%	
Difficulty initiating sleep													0.17^{1} 0.11^{2} 0.83^{3}
1	188	39.4%	81	32.0%	199	41.7%	96	37.9%	150	41.6%	71	36.0%	
2	87	18.2%	31	12.3%	90	18.9%	31	12.3%	74	20.5%	34	17.3%	
3	98	20.5%	44	17.4%	90	18.9%	41	16.2%	72	19.9%	35	17.8%	
4	57	11.9%	42	16.6%	47	9.9%	38	15.0%	28	7.8%	18	9.1%	
5	47	9.9%	55	21.7%	51	10.7%	47	18.6%	37	10.2%	39	19.8%	
Waking frequently during sleep													0.55^{1} 0.14^{2} 0.31^{3}
1	58	12.2%	20	7.9%	78	16.4%	35	13.8%	60	16.6%	25	12.7%	
2	66	13.8%	23	9.1%	67	14.0%	27	10.7%	49	13.6%	25	12.7%	
3	102	21.4%	37	14.6%	96	20.1%	38	15.0%	75	20.8%	38	19.3%	
4	97	20.3%	73	28.9%	95	19.9%	52	20.6%	65	18.0%	41	20.8%	
5	154	32.3%	100	39.5%	141	29.6%	101	39.9%	112	31.0%	68	34.5%	
Early morning awakening													0.82^{1} 0.02^{2} 0.02^{3}
1	161	33.8%	69	27.3%	192	40.3%	77	30.4%	135	37.4%	73	37.1%	
2	105	22.0%	37	14.6%	94	19.7%	50	19.8%	75	20.8%	32	16.2%	
3	100	21.0%	53	20.9%	77	16.1%	37	14.6%	69	19.1%	37	18.8%	
4	66	13.8%	45	17.8%	62	13.0%	34	13.4%	39	10.8%	21	10.7%	
5	45	9.4%	49	19.4%	52	10.9%	55	21.7%	43	11.9%	34	17.3%	
Any Complaint of 3 or more times week													0.10^{1} 0.04^{2}
Yes	279	58.5%	198	78.3%	264	55.3%	172	68.0%	197	54.6%	128	65.0%	0.53^{3}

5-point Likert scale where 1 = no difficulties on any nights, 2 = difficulties on less <1 night/week, 3 = 1-2 nights per week, 4 = 3-4 nights per week, and 5 = 5-7 nights per week.

*p-values reflect change in severity of disturbances: [1]=baseline vs visit 1, [2]= baseline vs visit 2, [3]= visit 1 vs. visit 2.
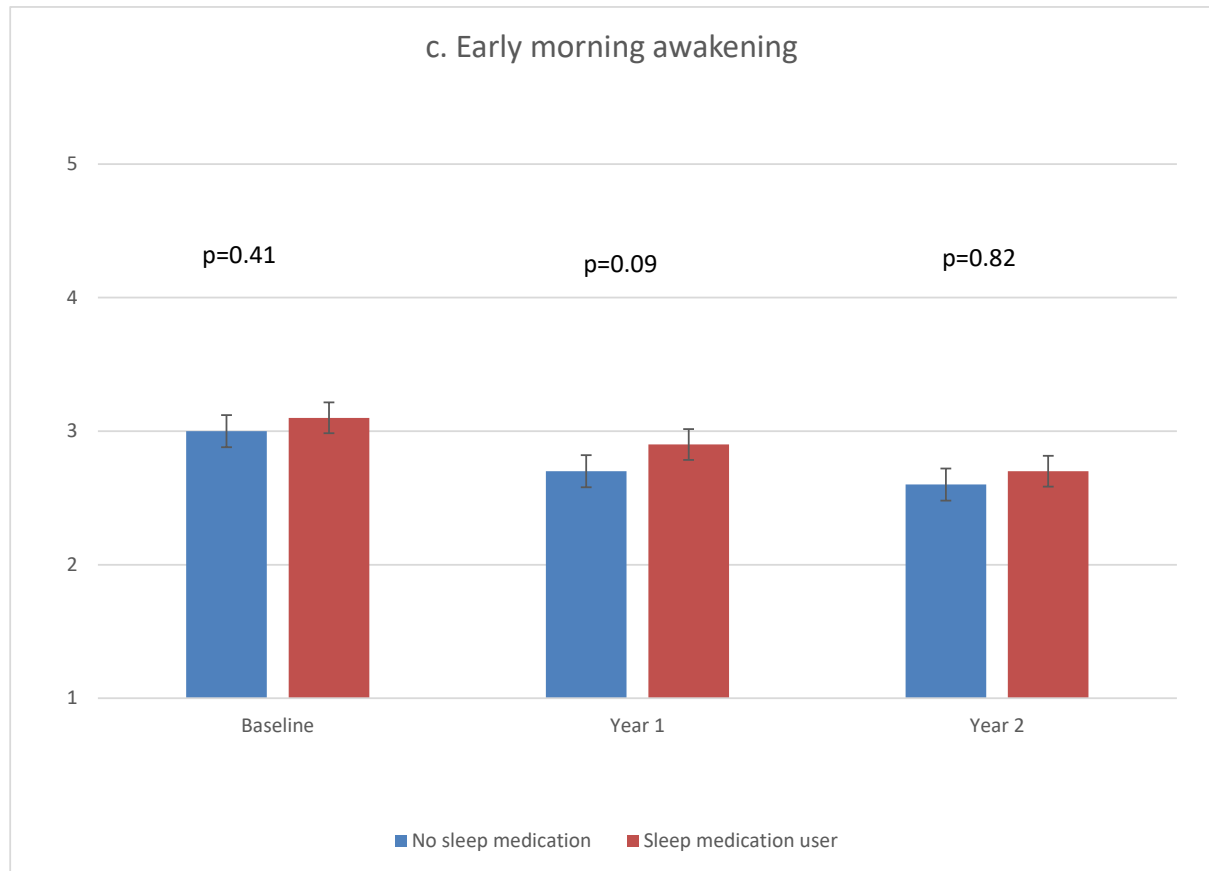
Supplementary Figure 2. Sleep Disturbance Ratings by Medication Exposure During Follow-up In women who reported a 4 or 5 on any severity scale
Legend: Means calculated based on 5-point Likert scale where 1 = no difficulties on any nights, 2 = difficulties on <1 night/week, 3 = 1-2 nights per week, 4 = 3-4 nights per week, and 5 = 5-7 nights per week . Error bars represent standard errors. P-values estimated from the Wilcoxon Rank Sum test.

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

BMJ Open

b. Waking frequently during sleep

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

BMJ Open

c. Early morning awakening

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance
placed on this supplemental material which has been supplied by the author(s)

BMJ Open

Supplementary Table 5: Change in severity of sleep disturbances from baseline to year 1 using a proportional odds analysis

	Year 0 versus Year 1	Year 1 versus Year 2	Year 0 versus Year 2
	Odds ratio (95% CI) comparing sleep medication users with non-users		
Difficulty initiating sleep	0.89 (0.58 – 1.30)	0.72 (0.42 – 1.30)	0.80 (0.61 – 1.00)
Waking frequently	0.92 (0.58 – 1.40)	1.44 (0.82 – 2.50)	1.20 (0.90 – 1.50)
Early morning awakening	0.75 (0.49 – 1.20)	1.20 (0.67 – 2.00)	0.94 (0.72 – 1.20)
Notes: The odds ratios represent the odds of a one level increase in the Likert scale, comparing sleep medication users to non-users.			

Supplementary Table 6: Original models additionally adjusted for site and estrogen use

	Year 0 vs Year 1		Year 0 vs Year 2		Year 1 vs Year 2	
	Estimate	P-value	Estimate	P-value	Estimate	P-value
Difficulty initiating sleep	-0.15	0.3	-0.18	0.04	-0.24	0.21
Waking Frequently	-0.03	0.83	0.11	0.22	0.21	0.02
Early morning awakening	-0.19	0.22	-0.12	0.17	-0.07	0.45
The significant p-value in Year 0 vs Year 2 shows that the non users decreased by .12 and the med users increased by .06. The significant p-value in Year 1 vs Year 2 shows that non users decreased by .004 and the med users decreased by .22.						