Sex-Specific Association Between Antidepressant Use and Body Weight in a Population-Based Study in Older Adults

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ABSTRACT

Objective: To investigate the association between antidepressant use and body weight in a population-based study in older adults.

Method: All participant records (N = 7,269) from the prospective Rotterdam Study with data on anthropometrics and current depressive symptoms were studied post hoc (data were collected between September 1993 and December 2011). The association between antidepressant use, derived from pharmacy records, and change in body mass index (BMI) between repeated examination rounds was analyzed. Current depressive symptoms (assessed by questionnaire) and baseline BMI (for the change in BMI analysis only) were deemed important covariates. Additional analyses were stratified by sex and restricted to long-term use (≥ 90 days) and by level of binding affinity to the serotonin reuptake transporter (denoted as hSERT antidepressants).

Results: Participants who used selective serotonin reuptake inhibitors (SSRIs, n = 198) had a larger increase in BMI compared to nonusers (+0.74 and +0.23 kg/m^2, respectively, $P < .001$) between repeated examination rounds. No change in BMI was observed for users of tricyclic antidepressants (n = 146) and other antidepressants (n = 57) compared to nonusers. Weight gain was observed only in women who were treated for ≥ 90 days with hSERT antidepressants or SSRIs, and not in men (*P* value for interaction = .002).

Conclusions: Within our study of older adults, hSERT antidepressants were associated with an increased body weight in women, which is supported by the biological function of serotonin in weight control and the differences in serotonergic signaling between males and females.

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In the biology and treatment of psychiatric diseases, such as depression, the neurotransmitter serotonin is of great interest. The transmission of serotonin across neurons in the central nervous system, but more specifically in the prefrontal cortex, plays an important role in experiencing emotion. Besides being a treatment target for depression, the transmission of serotonin across neurons also has an important role in energy metabolism and weight control.[1] The involvement of serotonin in mechanisms other than emotion was clearly shown in genetic studies. For example, genetic variation in the serotonin receptor and the serotonin reuptake transporter and availability of serotonin receptors on the membrane of neurons are associated with body weight.[1–4] Also, the efficiency of serotonergic signaling across the membrane of neurons is different for males and females. Serotonin (5-HT) has a higher level of binding potential to the postsynaptic 5-HT$_{1A}$ receptor and a lower level of binding potential to the serotonin reuptake transporter in females as compared to males.[5,6] This difference might partly explain the already observed difference between males and females in antidepressant treatment response.[7–10] Taken together, these studies suggest not only that drugs (including antidepressants and other psychotropic drugs) that affect the bioavailability of serotonin in neurons might be able to increase body weight, but also that the increase in body weight is different for males and females.

Several studies[11–14] aimed to examine the effect of antidepressant use on body weight. However, a limited sample size might explain why results were often contradictory between these studies. Results of a meta-analysis showed that the use of paroxetine and amitriptyline for a duration of at least 4 months was associated with an increased body weight.[12] These studies included patients who were diagnosed with a major depressive disorder, treated with antidepressants, and followed over time. As depressive symptoms are often accompanied by a reduction in appetite, these studies were unable to disentangle whether the observed weight gain was caused by relief in depressive symptoms (and therefore an increase in appetite) or by the antidepressant drug itself.

Based on biological findings, antidepressants with a high binding affinity to the serotonin transporter, like selective serotonin reuptake inhibitors (SSRIs), can be hypothesized to increase body weight. Because of the limitations of previously conducted studies, we performed a population-based study comprising older adults with body weight and current depressive symptoms being measured at repeated examination rounds. Within this study population, we examined the association between antidepressants, by drug class and level of binding affinity to the serotonin transporter, and body mass index (BMI), stratified by sex and treatment duration.

METHOD

Research Setting

For the current post hoc study, we used data from the prospective Rotterdam Study, which aims to investigate the incidence of, and risk factors for, several age-related diseases. A more detailed description of the design and rationale of the study is published elsewhere.[15,16] Data were collected between September 1993 and December 2011. The cohort represents inhabitants aged 55 years and older at the date of inclusion from a district (Ommoord) located in Rotterdam,

Clinical Points

- Whether antidepressant use in daily practice increases body weight is unclear.
- The current study suggests that use of selective serotonin reuptake inhibitors (SSRIs) increases body weight in women.
- Clinicians should be aware that women are at risk to gain weight when using SSRIs.

the Netherlands. From 1990 to 1993, participants were asked to participate in the original study (denoted hereafter as RS-I). In total, 7,983 individuals agreed to participate (response rate 78%). An extension of the original cohort was initiated in 2000 (denoted hereafter as RS-II). Within this subcohort, all inhabitants from Ommoord aged 55 years and older, and not already participating in RS-I, were asked to participate in RS-II. In total, 3,011 individuals agreed to participate (response rate 67%). Follow-up examinations were conducted every 4–5 years after start at baseline. The Rotterdam Study has been approved by the medical ethics committee according to the Wet Bevolkingsonderzoek ERGO (Population Study Act Rotterdam Study), executed by the Ministry of Health, Welfare and Sport of the Netherlands, and written informed consent was obtained from all study participants.

Study Population

For the current study, we included all participants who had their height and weight measured and who had completed a depression questionnaire during the center visits. Participants from RS-I could at most have 4 measurements, while participants from RS-II had a maximum of 3 measurements.

Exposure

More than 99% of the participants have their drug prescriptions filled at 1 of the 7 regional pharmacies, which are fully computerized. From January 1, 1991, onward, complete prescription data are available and include the Anatomic Therapeutical Chemical (ATC) code,[17] the dispensing date, the total amount of drug units per prescription, the prescribed daily number of units, and the product name of the drug. Exposure to an antidepressant drug was defined as current if the center visit date fell within a prescription episode, calculated by dividing the total number of filled tablets/capsules by the daily prescribed number. Antidepressant use was subdivided into tricyclic antidepressants (TCAs) (N06AA) SSRIs (N06AB), and other antidepressants (N06AX). Participants without an antidepressant drug prescription at a center visit were considered to be nonusers and were used as the reference population. We also defined an antidepressant exposure category based on a low dissociation constant to the serotonin reuptake transporter (0–1 nmol/L), and thus antidepressants with a high level of binding affinity (denoted as hSERT antidepressants). With this reclassification of antidepressants, the specific role of serotonin modulation by antidepressants could be best studied.[18] This category included the antidepressants clomipramine, fluoxetine, paroxetine, and sertraline.[19,20] The duration of treatment at the time of the study center visit was computed by calculating the cumulative number of prescription days. Long-term exposure was defined as the cumulative use of any antidepressant for more than 90 days. The prescribed dose was calculated relative to the defined daily dose.[17]

Outcome Definition

For the current study, we defined the following outcomes: BMI, waist-to-hip ratio (WHR), height, and weight for cross-sectional analyses, and the change in BMI between repeated examination rounds for the longitudinal analyses. Height (in centimeters) and weight (in kilograms) were measured by research nurses during all follow-up visits. WHR was measured (in centimeters) by research nurses at all follow-up visits except the second center visit of RS-I. BMI was calculated by dividing the weight (in kilograms) by the height (in meters) squared. For the longitudinal analysis, we calculated the difference in BMI between the repeated examination rounds.

Covariables

For the current study, we considered age, sex, current smoking status, use of alcohol, depressive symptoms, and concomitant use of antipsychotics as potential confounding factors. For the analyses on weight, height was also considered as a potentially confounding factor, as antidepressants, and mainly SSRIs, are suspected to decrease bone mineral density and might therefore ultimately decrease height and lead to increased BMI.[21] Current smoking status (yes/no) and alcohol use were obtained using interview questionnaires. As different questionnaires were used to assess habitual alcohol intake for every examination round, the median intake per round was used to define low and high alcohol use. Antipsychotic treatment (yes/no) at the examination round was determined using pharmacy records (ATC code: N05A). Depressive symptoms were screened with a Dutch version of the Center for Epidemiologic Studies Depression Scale (CES-D).[22,23] The questionnaire gives a score, ranging from 0 to 60, with higher scores indicative of more depressed feelings. A score above 16 was considered to be an indicator for a potential depression.[22,23] For the analyses on the change in BMI, the baseline BMI was also considered.

Statistical Analyses

As we had multiple measurements of the study outcomes from most study participants, analyses were performed using repeated measurement analyses (generalized equation estimation). Covariables, as described above, were included in the analysis only when they reached statistical significance ($P < .05$) in a multivariable analysis with BMI. For the analysis on weight, we included height (in meters) squared in the model to assess whether a difference in BMI was independent from height. We used pairwise comparisons to assess the associations between nonuse and the different antidepressant drug classes (TCAs, SSRIs, and others) and BMI, and change

in BMI between repeated examination rounds. These analyses were also stratified by treatment (short- and long-term treatment) and by the presence or absence of clinically relevant depressive symptoms (CES-D score > 16). Within the nontreated population, the difference in BMI was also compared between depressed and nondepressed participants.

The analyses of BMI and change in BMI between repeated examination rounds were additionally stratified by sex for SSRIs, TCAs, and hSERT antidepressants. Other antidepressants were not taken into account due to a limited number of participants. All analyses were additionally restricted to long-term drug exposure. Statistical interaction between sex and drug exposure on BMI or change in BMI was assessed by including an interaction term between them in the multivariate model.

All statistical analyses were performed using SPSS (version 20.0, IBM, Armonk, New York). *P* values below .05 were considered statistically significant.

RESULTS

Baseline Characteristics

In total, 7,269 participants (16,331 measurements) from both RS cohorts had complete data included from at least 1 BMI measurement taken at the center visits (Table 1). Time intervals between examination rounds were on average 5.1 years (SD = 1.1). The study population had a mean age of 68.9 years (SD = 8.1) and comprised 57% women. The mean BMI was 27.0 kg/m^2 (SD = 4.0) with 19.5% being obese (BMI > 30 kg/m^2). At baseline, TCAs were used by 1.1%, SSRIs by 1.7%, and other antidepressants by 0.3% of the participants.

Among nonusers, BMI was 0.17 kg/m^2 (95% CI, 0.06–0.29; *P* = .002) lower in participants with clinically relevant depressive symptoms compared to nondepressed participants.

Table 1. First Visit Characteristics of the Study Population[a]

Characteristic	Study Population (N = 7,269)	
Age, y, mean (SD)	68.9	(8.1)
Women, n (%)	4,142	(57.0)
Body mass index (kg/m^2), mean (SD)	27.0	(4.0)
Length (centimeters), mean (SD)	167.3	(9.3)
Weight (kilograms), mean (SD)	75.5	(12.9)
Body mass index > 30 kg/m^2, n (%)	1,420	(19.5)
Waist-to-hip ratio, mean (SD)	0.92	(0.10)
Depression (CES-D > 16), n (%)	662	(9.1)
Current smoking (yes/no), n (%)	1,492	(20.5)
High alcohol use (yes/no),[b] n (%)	3,525	(48.5)
Medication use, n (%)		
Tricyclic antidepressants (N06AA)	80	(1.1)
Selective serotonin reuptake inhibitors (N06AB)	120	(1.7)
Other antidepressants (N06AX)	20	(0.3)
Antipsychotic drugs (N05A)	30	(0.4)

[a]Data presented as the means or percentages of the different variables at the first examination round that was included in this study.
[b]High alcohol use was defined as having an alcohol use level above the median of the study population.
Abbreviation: CES-D = Center for Epidemiologic Studies Depression scale.

Association Between Antidepressant Drug Use and Anthropometric Measures

Participants treated with SSRIs (n = 288) had a higher BMI compared to control participants (28.4 and 27.9 kg/m^2, respectively, *P* = .017; Table 2). A similar result was obtained when this analysis was repeated with weight (79.3 and 78.1 kg, respectively, for SSRI users and controls, *P* = .017). When we stratified for treatment duration, a higher BMI in SSRI users was observed only in participants who used SSRIs for a period of at least 90 days (28.5 and 27.9 kg/m^2, respectively, *P* = .005), whereas no association was observed for the participants who used SSRIs for a period less than 90 days (27.7 and 27.9 kg/m^2, respectively, *P* = .68). BMI was similar for participants using a TCA compared to nonusers (28.0 and 27.9 kg/m^2, respectively, *P* = .66). The difference between TCA use and nonuse did not materially change when we stratified by treatment duration. The use of other antidepressants was also not associated with BMI or weight. WHR was significantly lower in users of other antidepressants for a period less than 90 days, but sample size of this group was small (n = 9). For all antidepressant drugs, no association was observed with height. In addition, the estimates for SSRIs did not differ when the analyses were stratified for the presence or absence of clinically relevant depressive symptoms (results not shown).

Association Between Antidepressant Drug Classes and Change in BMI Between Repeated Examination Rounds

Between repeated examination rounds, participants who used an SSRI had a larger increase in BMI as compared to participants who did not use an antidepressant (+0.74 and +0.23, respectively, *P* < .001; Table 3). In addition, an increase in BMI for treatment durations that lasted longer than 90 days was also observed at the consecutive visits (+0.74 and +0.24, respectively, *P* < .001). There was no difference in BMI between users of TCAs and other antidepressants compared to nonuse. Participants treated with other antidepressants for fewer than 90 days had a decreased BMI (−1.38 and +0.24, respectively, *P* = .014, n = 6). No difference in change in BMI was observed for both TCA treatment duration categories and long-term use of other antidepressants.

Sex-Stratified Analyses

In female participants, the use of SSRIs (Figure 1) was associated with a significantly larger increase in BMI between repeated examination rounds compared to participants who did not use antidepressants (+0.685 kg/m^2). No increase in BMI was observed in male SSRI users (−0.144 kg/m^2, *P* value for interaction between sex and SSRI use on BMI = .002). A similar result was observed when restricting to participants who used an SSRI for at least 90 days (*P* value for interaction = .006). Although women tended to have a larger increase in BMI when using a TCA compared to controls, this difference was not statistically significant, nor was it significantly different from men (*P* value for interaction = .13). This result was similar when the analysis was restricted to a treatment duration of at least 90 days. Similar to SSRIs, hSERT antidepressants were associated with increased BMI in women only. The difference in association

Table 2. Association Between Different Antidepressant Drug Classes and Anthropometric Measurements[a,b]

	Nonuse[c] (ref)		SSRI			TCA			Others		
Measurement	Mean	95% CI	Mean	95% CI	*P* Value	Mean	95% CI	*P* Value	Mean	95% CI	*P* Value
Overall											
No. of measurements	15,782		288			193			68		
Dosage[d]	NA		1.03			0.52			0.78		
BMI (kg/m^2)	27.9	26.9–29.0	28.4	27.3–29.4	**.017**	28.0	27.0–29.1	.59	27.7	26.6–28.9	.58
Weight (kg)	78.1	73.2–82.9	79.3	75.4–83.2	**.017**	78.4	74.7–82.0	.65	77.3	73.9–80.8	.49
Height (cm)	167.9	167.3–168.6	167.9	167.0–168.7	.52	167.7	166.8–168.7	.84	167.3	166.0–168.6	.29
Waist-to-hip ratio	0.92	0.91–0.94	0.92	0.91–0.94	.70	0.93	0.91–0.94	.60	0.91	0.88–0.93	.095
< 90 days of treatment											
No. of measurements	15,782		36			25			9		
Dosage[d]	NA		0.90			0.39			0.71		
BMI (kg/m^2)	27.9	26.9–28.9	27.7	26.5–29.0	.68	28.1	26.8–29.4	.70	26.8	25.0–28.7	.21
Weight (kg)	78.1	73.8–82.4	77.7	74.3–81.2	.76	78.7	75.0–82.4	.69	74.5	69.5–79.6	.13
Height (cm)	168.2	167.5–168.8	168.7	167.5–170.0	.32	167.2	165.8–168.7	.17	167.7	165–170.0	.67
Waist-to-hip ratio	0.92	0.91–0.94	0.92	0.89–0.95	.79	0.93	0.90–0.96	.53	0.86	0.81–0.90	**.002**
≥ 90 days of treatment											
No. of measurements	15,782		252			168			59		
Dosage[d]	NA		1.05			0.54			0.79		
BMI (kg/m^2)	27.9	26.9–28.9	28.5	27.5–29.5	**.005**	28.0	27.0–29.1	.66	28.0	26.8–29.1	.91
Weight (kg)	78.1	73.8–82.4	79.7	76.1–83.2	**.005**	78.4	75.1–81.7	.68	77.9	74.5–81.3	.86
Height (cm)	167.8	167.5–168.2	167.9	167.5–168.4	.59	167.9	167.4–168.4	.63	167.5	166.8–168.2	.27
Waist-to-hip ratio	0.92	0.91–0.94	0.93	0.91–0.94	.79	0.92	0.90–0.94	.89	0.92	0.89–0.94	.60

[a]Data presented as the estimated means with 95% confidence interval. Analyses were adjusted for age, gender, depression (CES-D score above 16), concomitant use of antipsychotics, smoking (yes/no), and alcohol use (low/high). Weight was additionally adjusted for the height squared to assess which component in BMI was responsible for the association.
[b]Values in boldface type are significant.
[c]Reference population.
[d]Calculated by dividing the prescribed daily dosage with the defined daily dosage.
Abbreviations: BMI = body mass index, NA = not applicable, SSRI = selective serotonin reuptake inhibitor, TCA = tricyclic antidepressant.

Table 3. Association Between Different Antidepressant Drug Classes and Change in BMI in a Longitudinal Analysis[a,b]

	Nonuse[c]		SSRI			TCA			Others		
Measurement	Mean	95% CI	Mean	95% CI	*P* Value	Mean	95% CI	*P* Value	Mean	95% CI	*P* Value
Overall											
No. of measurements	12,593		198			146			57		
Mean defined daily dosage	NA		1.02			0.50			0.74		
BMI change (kg/m^2)	0.23	−0.18 to 0.63	0.74	0.28 to 1.20	**<.001**	0.32	−0.16 to 0.80	.52	+0.11	−0.47 to 0.70	.60
< 90 days of treatment											
No. of measurements	12,593		25			22			6		
Mean defined daily dosage	NA		0.88			0.38			0.54		
BMI change (kg/m^2)	0.24	−0.11 to 0.59	0.78	0.07 to 1.50	.091	0.13	−0.61 to 0.87	.75	−1.38	−2.70 to −0.07	**.014**
≥ 90 days of treatment											
No. of measurements	12,593		173			124			51		
Mean defined daily dosage	NA		1.03			0.52			0.76		
BMI change (kg/m^2)	0.24	−0.11 to 0.59	0.74	0.32 to 1.16	**<.001**	0.38	−0.06 to 0.83	.33	+0.34	−0.22 to 0.90	.66

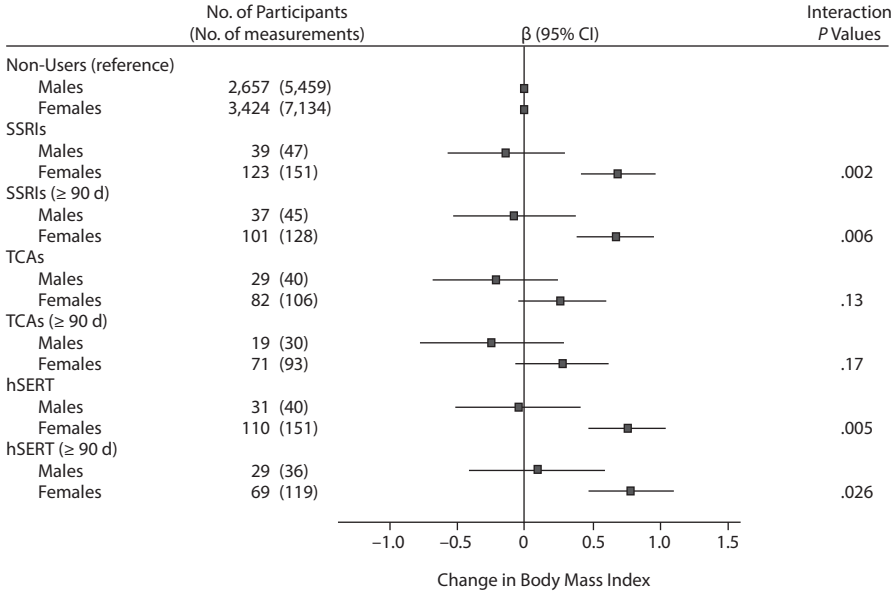
[a]Data presented as the estimated means with 95% confidence interval. Analyses were adjusted for age, gender, depression (CES-D score above 16), concomitant use of antipsychotics, smoking (yes/no), and alcohol use (low/high). Weight was additionally adjusted for the height squared to assess which component in BMI was responsible for the association.
[b]Values in boldface type are significant.
[c]Reference population.
Abbreviations: BMI = body mass index, NA = not applicable, SSRI = selective serotonin reuptake inhibitor, TCA = tricyclic antidepressants.

between hSERT antidepressants and BMI between men and women was statistically significant (−0.054 and +0.757 kg/m^2, respectively, *P* value for interaction = .005). When we restricted for treatment duration that lasted for more than 90 days, the *P* value for interaction was .026 comparing men to women. Similar results were obtained for BMI (results not shown).

DISCUSSION

In this population-based study, we observed that SSRI use was associated with approximately 0.5 kg/m^2 higher BMI compared to nonuse. This observation, which was independent of the baseline BMI, was also reflected in a larger increase in BMI (0.5 kg/m^2) between repeated examination rounds. The increase in BMI was observed only when participants were using SSRIs for a period of at least 90 days. When we performed this analysis on weight, the use of SSRIs was associated with a 1.2-kg higher weight compared to nonusers, independent of height. In addition, use of SSRIs was not significantly associated with height. These associations were not observed in participants who used TCAs or other antidepressants, which would suggest that TCAs and other antidepressants do not cause weight gain or that the prescribed dosage is too low to observe a significant effect. However, in both cases this would mean that, at least in an older population, TCA and other antidepressant use

Figure 1. Association Between Antidepressants and Change in Body Mass Index (BMI) Stratified by Sex[a]



[a]Analyses performed in all treatment durations and restricted to treatments ≥90 days. Analyses were adjusted for age, gender, depression (CES-D score above 16), concomitant use of antipsychotics, smoking (yes/no), alcohol use (low/high), and the baseline BMI. All data presented as the mean difference in change in BMI between users of antidepressants and nonusers.

Abbreviations: CI = confidence interval, hSERT = high affinity to the serotonin reuptake transporter (namely: clomipramine, fluoxetine, paroxetine and sertraline), SSRIs = selective serotonin reuptake inhibitors, TCAs = tricyclic antidepressants.

in daily practice does not lead to weight gain. When the analyses were stratified by sex, an increased BMI in SSRI and hSERT users was observed only in women and not in men.

Most of the previously published studies were clinical trials in which depressive patients were followed from start of antidepressant therapy to the end of the study.[11–14] The main limitation of these studies is that they were not able to disentangle weight gain induced by the drug from weight gain induced by the relief in depressive symptoms. To our knowledge, only 1 population-based study[24] has investigated the association between the use of SSRIs and obesity. Similar to our study, the authors showed that the use of SSRIs and use of SSRIs with a high affinity to the serotonin reuptake transporter (paroxetine and sertraline) were associated with an increased risk of obesity. Although the authors adjusted for depression and anxiety, the chance that these results were caused by confounding by indication cannot be ruled out, as there might, for example, be a preference to prescribe SSRIs to people with a higher BMI. Confounding by indication is therefore also a risk in our cross-sectional analyses. However, compared with the previous population-based study,[24] we were able to take into account the treatment duration. As the effect was observed only with a treatment duration of more than 90 days, the increase was more likely due to the drug instead of the underlying indication. In addition, the risk of confounding by indication was further minimized by our longitudinal study design, in which we studied the change in BMI between repeated examination rounds. Other differences between our study and the previously reported clinical trials include the usage of antidepressants for indications other than depression (which are not associated with weight), the ability to adjust for depressive symptoms, and the inclusion of participants with depression but who were not treated with antidepressant drugs. In addition, the findings of our study are in line with findings on the biological role of serotonin in energy metabolism and weight control.[1] Genetic polymorphisms in the serotonin reuptake transporter gene[3,4] and the postsynaptic serotonin receptor,[2] which affect the efficiency of serotonergic signaling, are associated with an increased risk of obesity.

To our knowledge, so far, only 1 study[25] observed that females had a larger gain in weight compared to males when using SSRIs. However, as the data of the study outcomes were self-reported, the authors suggested that this difference might be due to bias. The observed difference between men and women within our study might be caused by factors that affect the bioavailability of serotonin in neurons.[5,6] Influencing this pathway by use of SSRIs or hSERT antidepressants might result in a more enhanced signaling in females compared to males. However, these studies were performed in a much younger population, in which females were still premenopausal.[5,6] Translating these results to our aging population, and thus postmenopausal population, should therefore be done with caution. A second biological explanation might include leptin and the leptin receptor, which are key players in the central regulation of energy metabolism.[26] Genetic variations in genes encoding for leptin and the leptin receptor were associated with BMI only in females, and not in males.[27–31] These genetic variations were also associated with the antidepressant drug response,[32]

although this study did not stratify on sex. Future research should be performed to disentangle the exact mechanism that gives a different SSRI-induced increase in weight between males and females.

Main strengths of the present study include the longitudinal design of part of the analyses, the use of pharmacy records instead of drug exposure defined by interview, and the availability of data on depressive symptoms. Using the longitudinal design with the adjustment for the baseline BMI and adjustment for current depression, we were able to reduce a possible effect of confounding by indication in our results. This strategy allowed us to disentangle weight gain by relief in depressive symptoms from a drug-induced effect. Using the pharmacy records to define drug exposure, we were able to calculate the duration of exposure and to rule out recall bias and information bias. Also, our study did not suffer from selection bias, as participants of the Rotterdam Study were included regardless of their health status. This study, however, had a limited number of participants on short-term antidepressant exposure. However, because no trend of an effect was observed for short-term treatment, the effect of long-term treatment with SSRIs and hSERT antidepressants is likely to be causal. With this limited number, we were not able to study the effect of antidepressant drug dosage on weight gain. Also, the time period between 2 examination rounds (4–5 years) in which we calculated the change in BMI is rather long. However, this time period is similar for the treated and untreated group, and potential misclassification would be nondifferential. In addition, because of the nonrandomized design of the study, residual confounding might still be present. One possible confounding factor, which we did not take into account, might be food intake. However, because serotonin increases appetite, dietary intake is most probably an intermediate rather than a confounding factor.

In conclusion, the data from the current study showed that, in older adults, the use of SSRIs and hSERT antidepressants for a longer period was associated with a higher BMI and a larger increase in BMI between repeated examination rounds, notably in women only. The difference in SSRI-induced higher BMI between males and females might be explained by the difference in serotonergic signaling. Future studies should focus on disentangling the mechanism explaining SSRI- and hSERT-induced weight gain in females.

Drug names: clomipramine (Anafranil and others), fluoxetine (Prozac and others), paroxetine (Paxil, Pexeva, and others), sertraline (Zoloft and others).

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Additional information: Data can be obtained upon request. Requests should be directed toward the management team of the Rotterdam Study (secretariat.epi@erasmusmc.nl), which has a protocol for approving data requests. Because of restrictions based on privacy regulations and informed consent of the participants, data cannot be made freely available in a public repository.

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