HHS Public Access

Author manuscript

Epidemiology. Author manuscript; available in PMC 2019 July 01.

Published in final edited form as:

Epidemiology. 2018 July ; 29(4): 547–555. doi:10.1097/EDE.0000000000000840.

Depressive Symptoms, Antidepressant Use, and Hypertension in Young Adulthood

Danielle M. Crookes[1], **Ryan T. Demmer**[1], **Katherine M. Keyes**[1], **Karestan C. Koenen**[2], and **Shakira F. Suglia**[1,3]

[1]Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY

[2]Department of Epidemiology, Harvard T.H. Chan School of Public Health, Harvard University, Boston, MA

[3]Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA

Abstract

Background—Among adults, depressive symptoms are associated with higher rates of cardiovascular disease; however, the evidence is mixed regarding the association between depressive symptoms and hypertension, especially among young adults. The deleterious effects of some antidepressant medications on blood pressure may contribute to mixed findings.

Methods—Adolescents enrolled in Add Health (N=11,183) (1994–2008) completed an abbreviated Center for Epidemiologic Studies Depression Scale at three waves (mean ages 16, 22, and 29). Antidepressant use was measured at age 22 and at age 29. Hypertension at age 29 was defined as measured systolic blood pressure of 140mmHg or greater, diastolic blood pressure of 90mmHg or greater, or staff-inventoried anti-hypertensive medication use.

Results—The prevalence of hypertension at age 29 was 20%. High depressive symptoms in adolescence or young adulthood were not associated with hypertension in young adulthood. Antidepressant use at age 29 was associated with increased prevalence of hypertension (Prevalence ratio (PR): 1.4, 95% CI: 1.2, 1.7) and an interaction with sex was observed (PR_{Men}: 1.6, 95% CI: 1.2, 2.0; PR_{Women}: 1.2, 95% CI: 0.89, 1.6, $p_{interaction}$ = 0.0227). Selective serotonin reuptake inhibitor (SSRI) and non-SSRI antidepressant use were associated with hypertension (PR_{SSRI}: 1.3, 95% CI: 1.0, 1.6; $PR_{non\text{-}SSRI}$: 1.6, 95% CI: 1.2, 2.1).

Corresponding author: Danielle M. Crookes, Mailman School of Public Health, Columbia University, 722 W. 168th Street, 7th Floor, New York, NY 10032; Phone: 404-727-3185; dac2179@cumc.columbia.edu.
R.T.D. is currently affiliated with the Division of Epidemiology and Community Health in the School of Public Health at the University of Minnesota.

Conflicts of interest: None declared.

Data and computing code: This research uses data from Add Health, a program project directed by Kathleen Mullan Harris and designed by J. Richard Udry, Peter S. Bearman, and Kathleen Mullan Harris at the University of North Carolina at Chapel Hill, and funded by grant P01-HD31921 from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, with cooperative funding from 23 other federal agencies and foundations. Special acknowledgment is due Ronald R. Rindfuss and Barbara Entwisle for assistance in the original design. Information on how to obtain the Add Health data files is available on the Add Health website (http://www.cpc.unc.edu/addhealth). No direct support was received from grant P01-HD31921 for this analysis.
Data for this analysis cannot be made available for replication because it utilizes restricted-access data from Add Health and SAS code would not be informative without the data.

Conclusions—In this sample, antidepressant use, but not depressive symptoms, was associated with hypertension in young adulthood. Further research is recommended to examine joint and independent relationships of depression and antidepressant use and hypertension among young adults.

Keywords

adolescents; antidepressants; depressive symptoms; hypertension; young adults

Introduction

The prevalence of hypertension among U.S. young adults aged 18–39 was estimated in 2011–2013 to be 7.3%.[1] Evidence suggests elevated blood pressure in young adulthood is associated with elevated blood pressure in adulthood and with impaired heart function and increased atherosclerosis later in life.[2,3] Psychosocial factors, such as depression, have been examined as potential determinants of hypertension. Results of studies looking at the effect of depressive symptoms on hypertension and blood pressure have been mixed,[4] including studies noting no association between depressive symptoms and blood pressure,[5] an association with lower blood pressure,[6] or an association with increased blood pressure[7] or hypertension.[8–10] Evidence is mixed for young adults as well as older adults. For example, among The Coronary Artery Risk Development in Young Adults Study (CARDIA) participants, diagnosis with high and moderate depressive symptoms at ages 23–35 was associated with increased risk of hypertension 5 years later (ages 27–40),[11] but no association was observed with incident hypertension 10 years later.[12]

Discrepancies among findings of the depression and hypertension association may be explained in part by differences in accounting for antidepressant use (e.g., including or excluding antidepressant use in analysis) in these studies. Some antidepressants may affect blood pressure,[4] heart disease, and cerebrovascular disease,[13] though not all studies examining the effects of antidepressant use account for depressive symptoms. Tricyclic antidepressants[4] (TCAs) and serotonine norepinephrine reuptake inhibitors[14] (SNRIs) have been linked to increased blood pressure;[4,14] however, selective serotonin reuptake inhibitors (SSRIs), which are more commonly prescribed to adolescents and young adults, have not been shown to have a substantial association with blood pressure or hypertension[15] outside of their risk for obesity and possibly glycemic control.[16] Most trials of antidepressants focus on children, adolescents,[15,17] or middle-aged adults in their 50s and 60s[18,19], but few studies[14] include young adults in substantial numbers. Few studies[20,21] have assessed sex differences in the relation between depression and hypertension, which could further explain discrepancies in findings of the depression and hypertension relation.

In this study, we examined the relationship between depressive symptoms, antidepressant use, and hypertension, within a nationally representative longitudinal cohort of adolescents followed through young adulthood. We hypothesized that depressive symptoms experienced in adolescence and early adulthood would increase risk for hypertension in early adulthood. We also aimed to explore if and in what direction there was an association between

antidepressant use and hypertension and whether sex differences were noted in the relation between depression, antidepressant use, and hypertension.

METHODS

Study Sample

The National Longitudinal Study of Adolescent to Adult Health (Add Health) is a nationally representative, longitudinal study that recruited adolescents in U.S. schools and followed them in school and at home through early adulthood. Four waves of in-home interviews were conducted (wave 1: 1994–1995, wave 2: 1996, wave 3: 2001–2002 and wave 4: 2008); a detailed description of study methods has been reported elsewhere.[22,23] Wave 1 in-home interviews were completed by 20,745 adolescents (ages 12 to 18 years). Follow-up interviews for wave 3 (2001–02; response rate 77.4%) and wave 4 (2008; response rate 80.3%) were conducted with individuals who had participated in wave 1. Of these, 12,288 participants had sampling weight information for waves 1, 3, and 4.

We excluded participants from the analysis if they reported pregnancy at wave 4 (n = 421) or if they reported ever being diagnosed with hypertension or were taking anti-hypertensive medications at wave 3 (n = 684), leaving 11,183 participants in the analytic sample. We used multiple imputation to impute missing data for systolic blood pressure (SBP) or diastolic blood pressure (DBP) (n = 329), depressive symptom scores at waves 1,3, or 4 (n = 116), or study covariates (race, sex, education, age, body mass index (BMI), smoking status, alcohol consumption, physical activity, fast-food consumption, and sugar sweetened beverage consumption) (n = 202). Imputation models included all variables in the final analytic models, as well as marijuana use, income, grand sampling weights, and region. While once controversial, inclusion of the outcome in the imputation models provides necessary information about missing values of predictors and covariates in multimple imputation.[24–26] Multiple imputation with deletion has been suggested when there is missing outcome and exposure data, but it is not recommended over standard multiple imputation techniques when auxiliary variables are included in the model, as we have done.[27] We pooled analyses of 20 imputed datasets using SAS-callable SUDAAN 11.0 (RTI International, Research Triangle Park, NC). The institutional review board (IRB) of the University of North Carolina, Chapel Hill approved the Add Health study and the IRB of Columbia University, New York, New York and Emory University, Atlanta, Georgia approved these analyses.

Main Exposures: Depressive symptoms and antidepressant use

We characterized depressive symptoms at waves 1, 3, and 4 using the Center for Epidemiologic Studies Depression Scale (CES-D).[28] Because different versions of the CES-D were used in Add Health follow-up waves, we characterized depressive symptoms using the nine items that were asked at all waves, as done in other studies.[29–31] Participants endorsed how often (never/rarely to most/all of the time) they experienced specific feelings (e.g., You were bothered by things that don't usually bother you) in the past week. For each wave, scores for the nine items were summed (max score = 27) and then dichotomized into high/low symptoms using a score of 11 or greater to signify high depressive symptoms.[32] The measure had good reliability (α = .79 (wave 1), α = .80 (wave 3), α = .81 (wave 4)).

Chronicity of high depressive symptoms was characterized by summing the presence of high depressive symptoms at each wave (range: 0 waves to 3 waves). For sensitivity analyses, depressive symptoms were dichotomized into high/low symptoms using a cut-off score of 10 or greater to indicate high depressive symptoms.[33]

We utilized self-reported antidepressant use at wave 3. Participants were asked if they had taken any prescription medications in the past 12 months. If respondents said “yes”, they were asked if they had taken prescription medications for specific conditions, including ‘depression or stress’.

Antidepressant use at wave 4 was assessed by in-home interviewers. Methods for medication assessment are detailed elsewhere.[34] Participants were asked if they had taken any prescription medications in the last four weeks. Those taking medications were asked to present their medication bottles to interviewers or to list medications from memory; 22% of participants taking medications reported these medications from memory. Self-reported antidepressant use has been shown to have good concordance with claims records data.[35] Interviewers recorded all medications and medications were later assigned to therapeutic classes using Multum Lexicon™. In this analysis, antidepressant use was defined as taking medications classified as selective serotonin reuptake inhibitors (SSRIs), Tricyclic antidepressants (TCAs), serotonin-norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase inhibitors (MAOIs), tetracyclic antidepressants, phenylpiperazine antidepressants, and non-specified antidepressants and psychotherapeutic agents. For both waves 3 and 4, we categorized participants by their antidepressant use and depressive symptoms (i.e., antidepressant use with concurrent high depressive symptoms, antidepressant use without concurrent high depressive symptoms, no antidepressant use and high depressive symptoms, and no antidepressant use and no high depressive symptoms).

Outcome: Blood pressure and hypertension

During the fourth wave of follow-up (2008, mean age 29), an in-home assessment was conducted and three SBP and DBP measurements were obtained with a Micro Life automated blood pressure monitor after the participant was seated for five minutes.[36] The last two measurements were averaged and hypertension was defined as having either a SBP of 140 mmHg or greater, DBP of 90 mmHg or greater, or taking anti-hypertensive medications at wave 4. Anti-hypertensive medication use was assessed in the same manner as described above for the assessment of antidepressant medications. Anti-hypertensive medications were identified from all medications provided by or self-reported by participants. Systolic blood pressure, diastolic blood pressure, and hypertension were analyzed as separate outcomes. In models for continuous blood pressure, SBP and DBP were corrected for medication use (i.e., for patients taking anti-hypertensive medication, 9 mmHg were added to SBP and 6 mmHg were added to DBP), as has been done in previous studies.[37,38] A brief description of the measures of the outcome and exposures is provided in eTable 1.

Covariates

Demographic covariates collected at wave 4 included race (Asian, black, Hispanic, white, or other race), sex, highest level of education completed (less than high school, high school graduate, some college, and college graduation or higher), and age. Health behavior-related covariates collected at wave 4 included BMI (weight (kg)/ height $(m)^2$; calculated from measured height and weight at wave 4), smoking status (current, former, and ever smoker, with current defined as smoking at least one cigarette per day for 30 days), alcohol consumption (dichotomized as drinking at least 3–5 days per week vs. 1–2 times/week or less over the past 12 months), fast-food consumption (eating at a fast food establishment at least seven times in the past week), sugar-sweetened beverage consumption (consuming sugar sweetened beverages at least seven times in the past week), physical activity level (engaging in physical activities such as walking for exercise, strength training, participation in strenuous team sports, or participation in individual sports at least five times in the past week).

Statistical Analyses

We calculated descriptive characteristics using grand sampling weights for waves 1, 3, and 4. We used multivariable regression models to estimate the association between the timing (at waves 1, 3, and 4, separately) or chronicity (chronic symptoms at one, two or all three waves) of high depressive symptoms and hypertension, without adjustment for antidepressant use. We estimated associations between antidepressant use at wave 3 and wave 4, separately, and hypertension, without adjustment for depressive symptoms. Next, the independent and joint effects of depressive symptoms and antidepressant use were estimated at wave 3 and wave 4 separately. Additional models further characterized antidepressant use by type (SSRI and non-SSRI antidepressant use). Similar models were conducted examining continuous measures of DBP and SBP. For cross-sectional models, we hypothesized that wave 4 high depressive symptoms and/or antidepressant use estimated the most proximal timing of these exposures.

All models were first adjusted for demographic variables (i.e., age, education, sex and race) (Model A) and then additionally adjusted for BMI, smoking, physical activity, alcohol consumption, fast food consumption, and sugar sweetened beverage consumption (Model B). We conducted sensitivity analyses to examine if characterization of high depressive symptoms using a CES-D score of 10 or higher changed associations with hypertension. Tests for interaction with sex were examined on multiplicative and additive scales given the common practice of examining multiplicative interaction and the public health relevance of examining departures from additivity.[39] If interactions were observed, models were further stratified by sex. All models utilized grand sampling weights and accounted for U.S. region and clustering at the school level. We conducted analyses in SAS version 9.3 (SAS Institute Inc., Cary, North Carolina) and SAS-callable SUDAAN 11.0 (RTI International, Research Triangle Park, NC), according to the guidelines specified for the analyses of Add Health Data.[40]

RESULTS

Demographics

Study participant characteristics are presented in Table 1. Overall, the sample was predominantly white (66%), approximately half were male (53%), and most had completed some college or had a college diploma at wave 4 (71%). The mean age was 29 years (SE: 0.12) and the mean BMI was 29 (SE: 0.15). The prevalence of antidepressant use at wave 3 for the sample was 5% and was 7% at wave 4. The incidence of hypertension at wave 4 in the sample was 20%. In bivariate analyses, participants classified as hypertensive at wave 4 were more likely than non-hypertensive participants to have lower levels of education, be male, have a higher BMI, have more frequent consumption of sugar sweetened beverages, and have more frequent consumption of alcohol. Participants who were hypertensive also were more likely to be using antidepressants at wave 4.

Multivariable Models

In models examining high depressive symptoms, regardless of antidepressant use, we observed no association between high depressive symptoms at wave 1, wave 3, or wave 4 and hypertension at wave 4 (Table 2). We also observed no association between chronicity of high depressive symptoms and hypertension. In models examining antidepressant use, without inclusion of depressive symptoms, confidence interverals and effect estimates suggest a longitudinal relationship between antidepressant use at wave 3 and hypertension at wave 4, as well a cross-sectional relationship between antidepressant use and hypertension at wave 4 (Table 3).

Table 4 details models that parse out the individual and joint associations of depressive symptoms and antidepressant use and hypertension. In longitudinal models characterizing participants by high depressive symptoms and antidepressant use at wave 3, the effect estimate and confidence interval (relative risk $(RR)_{\text{fully adjusted}}$: 1.2, 95% confidence interval (CI): 0.96, 1.6) indicate possible increased risk for incident hypertension among those taking antidepressants. We observed no differences by sex.

In cross-sectional models (wave 4), antidepressant use (without concurrent high depressive symptoms) was associated with hypertension in both demographic-adjusted models and fully adjusted models ($PR_{\text{fully adjusted}}$: 1.4, 95% CI: 1.2, 1.7). In the absence of high depressive symptoms, men taking antidepressants were more likely to be hypertensive than men not taking antidepressants ($PR_{\text{fully adjusted}}$: 1.6, 95% CI: 1.2, 2.0) (data not shown in table). There was no association between antidepressant use and hypertension among women ($PR_{\text{fully adjusted}}$: 1.2, 95% CI: 0.89, 1.6). Further examining antidepressant use by SSRI type, both SSRI use and non-SSRI antidepressant use were associated with hypertension (PR_{SSRI}: 1.3, 95% CI: 1.0, 1.6; $PR_{\text{non-SSRI}}$: 1.6, 95% CI: 1.2, 2.1). Differences by sex were only observed for SSRI use ($PR_{\text{fully adjusted for men}}$: 1.6, 95% CI: 1.1, 2.1 vs. $PR_{\text{fully adjusted for women}}$: 1.0, 95% CI: 0.7, 1.5).

Antidepressant use at wave 4 (without concurrent high depressive symptoms) was associated with an increase in diastolic, but not systolic blood pressure, in fully adjusted models (Table 5). In fully adjusted models, antidepressant use (without concurrent high depressive

symptoms) was associated with an average increase in DBP of 1.6 mmHg (95% CI: 0.46, 2.7). Further, differences by sex were observed ($B_{\text{fully adjusted DBP for Men}}$: 3.0, 95% CI: 1.1, 5.0; $B_{\text{fully adjusted DBP for Women}}$: 0.76, 95% CI: −0.59, 2.1) (data not shown in table). Non-SSRI antidepressant use (without concurrent high depressive symptoms) was associated with an increase in DBP in fully adjusted models (B: 2.9, 95% CI: 1.0, 4.7) and no differences by sex were observed.

We conducted several sensitivity analyses including: 1) analyses using categorization of high depressive symptoms as a nine-item CES-D score of 10 or higher, 2) a complete case analysis of 10,536 participants, and 3) inclusion of wave 3 hypertensive participants. Findings were robust across all analyses. Longitudinal and cross-sectional models of high depressive symptoms, antidepressant medication use, and hypertension are provided in eTables 2–4.

DISCUSSION

In a nationally representative sample of US adolescents who transitioned to young adults, we note both cross-sectional and longitudinal relations between use of antidepressants and hypertension in young adulthood, but no relation between depressive symptoms and hypertension in young adulthood. An association between SSRIs and non-SSRIs and hypertension was observed, with a stronger association observed for non-SSRI medications.

Some studies have noted a prospective association between major depressive disorder diagnosis and hypertension.[4,9] However, in our sample of young adults, results from the most distal exposure (wave 1) to the most proximal exposure (wave 4), as well as prolonged exposure to depressive symtoms (chronic symptoms), are consistent with studies that suggest no association between depressive symptoms and hypertension. Instead, our findings suggest an association between antidepressant use and hypertension. Strongest associations are noted in cross-sectional analyses, which we interpret as the most proximal exposure to medication use in relation to hypertension, although the temporal relationship between exposure and outcome cannot be confirmed. An association between antidepressant use and hypertension could be due to a number of factors. Antidepressant use may indicate major depressive disorder, and the disorder, rather than just depressive symptoms, may increase risk of hypertension. Those with active, diagnosed major depressive disorder may adopt a more sedentary lifestyle and/or change eating habits leading to weight gain. However, the noted associations between antidepressant use and hypertension in our study remained even after accounting for physical activity, alcohol consumption, and dietary behaviors.

Alternatively, medication side effects could be responsible for the rise in blood pressure. In our study, we observe a relation between SSRI and non-SSRI antidepressants use and hypertension. Our findings are consistent with non-SSRI medication trials in children, adolescents, and adults that demonstrated mild increases in blood pressure, potentially clinically significant high blood pressure, or increased risk for hypertension for participants taking TCAs and some SNRIs.[14,17,19,41,42] Because of small sample size, we could not further examine subtype differences in the non-SSRI antidepressant use category.

In contrast, our results which note those participants on SSRIs were more likely to be hypertensive differ from findings of trials of sertraline (one kind of SSRI),[15,18,41] which note no association between sertraline and increased blood pressure and/or hypertension. Differences between these trials and the current study in participants' age and health status, as well as sample size and study design, may contribute to differences in findings. Our study consisted of a large sample of young adults (n = 11,183), who ranged in age from 24 to 32 years and were not included or excluded based on any prior health condition with the exception of current pregnancy (exclusion criteria). Glassman and colleagues[18] limited their study to adults with a recent history of acute myocardial infarction or angina and Brent and colleages[41] limited their sample to adolescents who had previously been taking SSRI medications. All three trials[15,18,41] had sample sizes considerably smaller than the present study. More broadly, many SSRI and non-SSRI antidepressants studies limit their samples to children and adolescents under 18 years of age[15,17,18,41,42] or include a sample of adults whose mean age is 50 or 60 years.[18,19] The young adults of our sample (ages 18–32) represents a group of participants that is included in adult studies, but often in small numbers such that findings from adult studies may not speak to their specific risk. Finally, our study is not a clinical trial and while we adjust for potential confounders, we recognize that this is an observational study and subject to other sources of unmeasured confounding that may link antidepressant use with hypertension.

There are a number of limitations worth mentioning. First, there are participants who were lost during follow-up; however, we used multiple imputation to address missing data, as well as longitudinal sampling weights, which adjust the sample to be representative of sample characteristics at baseline. Second, to approximate incident hypertension assessment, we excluded participants who self-reported high blood pressure, hypertension or anti-hypertensive medication use at wave 3. This exclusion may contribute to an underestimation of the depression and wave 4 hypertension relation, but in sensitivity analyses not reported in this manuscript, we included these participants and did not observe an association between depressive symptoms at any wave and hypertension at wave 4. Third, our assessment of blood pressure was conducted at only one point in time (wave 4) and we have no objective measure of blood pressure in adolescence (wave 1) or at wave 3; multiple, objective assessments of blood pressure at all time points would provide a more reliable measure of hypertension in this sample. Fourth, as noted in prior studies, the prevalence of hypertension in this national sample of young adults is higher than in other nationally representative samples.[43,44] If the prevalence of hypertension is associated with inaccurate measurement then this would have likely biased our results towards the null. We rely on an abridged version of the CES-D to assess depressive symptoms and not a diagnostic measure of depression. The CES-D is a widely used measure with well documented reliability and validity[28,45–47] and the abridged version has been used in studies using Add Health data with good reliability.[29–31] Given our use of a screening and not a diagnostic measure of depression, we cannot discern whether the noted association with antidepressants is due to a diagnosis of depression, where more frequently medication would be prescribed, or is a result of the medication itself. Future work that makes further distinctions between high depressive symtoms and diagnosed depression, separate from medication use, would be important in studies of depression and hypertension.

Finally, although antidepressant use in wave 4 was assessed through review of actual dispensed medication, we rely on self-reported use of medication for 'depression or stress' at wave 3. Evidence suggests that self-reported medication history is a valid measure of medication use,[35,48] but the wording of the question does not allow us to ascertain the specificity of the medication used and, as such, there may be some misclassification of medications for stress that may not be antidepressants. If these medications have a different effect on blood pressure than antidepressants, this may lead to a washing out of observed effects.

In this nationally representative sample of young adults, we noted no association between depressive symptoms and hypertension, but rather an association between antidepressant use and increased prevalence of hypertension even after accounting for depressive symptomatology and behavioral factors. Although antidepressant use might indicate clinical diagnosis of depression, which was not assessed in this study, future studies should examine the incidence of hypertension among those using antidepressant medications, as well as differences in incidence between those with diagnosed depression who are using and not using antidepressants. We suggest that additional research with young adult populations be conducted because there is an underrepresentation of young adults in this literature and some evidence of mixed findings in the literature regarding antidepressant use and cardiovascular outcomes more generally.[49] Future research on this topic should continue to examine sex differences and timing of exposure (e.g., adolescence vs. young adulthood) in the relationship between depression, antidepressant use, blood pressure, and hypertension.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Sources of funding: This work was supported by grants from the National Institute of General Medical Sciences (R25-GM062454); the National Institutes of Health (R01-DK102932); the National Institute on Alcohol Abuse and Alcoholism (K01AA021511); and the National Heart, Lung and Blood Institute (HL125761).

References

1. Nwankwo T, Yoon SS, Burt V, Gu Q. Hypertension among adults in the United States: National Health and Nutrition Examination Survey, 2011–2012. NCHS data brief. 2013; (133):1–8.
2. Kishi S, Teixido-Tura G, Ning H, Venkatesh BA, Wu C, Almeida A, Choi E-Y, Gjesdal O, Jacobs DR, Schreiner PJ. Cumulative blood pressure in early adulthood and cardiac dysfunction in middle age: the CARDIA Study. Journal of the American College of Cardiology. 2015; 65(25):2679–2687. [PubMed: 26112189]
3. Allen NB, Siddique J, Wilkins JT, Shay C, Lewis CE, Goff DC, Jacobs DR, Liu K, Lloyd-Jones D. Blood pressure trajectories in early adulthood and subclinical atherosclerosis in middle age. Jama. 2014; 311(5):490–497. [PubMed: 24496536]
4. Licht CM, De Geus EJ, Seldenrijk A, Van Hout HP, Zitman FG, Van Dyck R, Penninx BW. Depression is associated with decreased blood pressure, but antidepressant use increases the risk for hypertension. Hypertension. 2009; 53(4):631–638. [PubMed: 19237679]
5. Shinn EH, Poston WSC, Kimball KT, Jeor STS, Foreyt JP. Blood pressure and symptoms of depression and anxiety: a prospective study. American Journal of Hypertension. 2001; 14(7):660–664. [PubMed: 11482304]

6. Hildrum B, Mykletun A, Holmen J, Dahl AA. Effect of anxiety and depression on blood pressure: 11-year longitudinal population study. The British Journal of Psychiatry. 2008; 193(2):108–113. [PubMed: 18669991]
7. Goldstein BI, Fagiolini A, Houck P, Kupfer DJ. Cardiovascular disease and hypertension among adults with bipolar I disorder in the United States. Bipolar disorders. 2009; 11(6):657–662. [PubMed: 19689508]
8. Rutledge T, Hogan BE. A quantitative review of prospective evidence linking psychological factors with hypertension development. Psychosomatic Medicine. 2002; 64(5):758–766. [PubMed: 12271106]
9. Stein DJ, Aguilar-Gaxiola S, Alonso J, Bruffaerts R, De Jonge P, Liu Z, Caldas-de-Almeida JM, O'Neill S, Viana MC, Al-Hamzawi AO. Associations between mental disorders and subsequent onset of hypertension. General hospital psychiatry. 2014; 36(2):142–149. [PubMed: 24342112]
10. Meng L, Chen D, Yang Y, Zheng Y, Hui R. Depression increases the risk of hypertension incidence: a meta-analysis of prospective cohort studies. Journal of hypertension. 2012; 30(5): 842–851. [PubMed: 22343537]
11. Davidson K, Jonas BS, Dixon KE, Markovitz JH. Do depression symptoms predict early hypertension incidence in young adults in the CARDIA study? Archives of internal medicine. 2000; 160(10):1495–1500. [PubMed: 10826464]
12. Yan LL, Liu K, Matthews KA, Daviglus ML, Ferguson TF, Kiefe CI. Psychosocial factors and risk of hypertension: the Coronary Artery Risk Development in Young Adults (CARDIA) study. Jama. 2003; 290(16):2138–2148. [PubMed: 14570949]
13. Biffi A, Scotti L, Corrao G. Use of antidepressants and the risk of cardiovascular and cerebrovascular disease: a meta-analysis of observational studies. European Journal of Clinical Pharmacology. 2017:1–11.
14. Thase ME. Effects of venlafaxine on blood pressure: a meta-analysis of original data from 3744 depressed patients. The Journal of clinical psychiatry. 1998; 59(10):502–508. [PubMed: 9818630]
15. Wilens TE, Biederman J, March JS, Wolkow R, Fine CS, Millstein RB, Faraone SV, Geller D, Spencer TJ. Absence of cardiovascular adverse effects of sertraline in children and adolescents. Journal of the American Academy of Child & Adolescent Psychiatry. 1999; 38(5):573–577. [PubMed: 10230189]
16. Goldstein BI, Carnethon MR, Matthews KA, McIntyre RS, Miller GE, Raghuveer G, Stoney CM, Wasiak H, McCrindle BW. Major Depressive Disorder and Bipolar Disorder Predispose Youth to Accelerated Atherosclerosis and Early Cardiovascular Disease A Scientific Statement From the American Heart Association. Circulation. 2015; 132(10):965–986. [PubMed: 26260736]
17. Otasowie J, Castells X, Ehimare UP, Smith CH. Tricyclic antidepressants for attention deficit hyperactivity disorder (ADHD) in children and adolescents. The Cochrane Library. 2014
18. Glassman AH, O'connor CM, Califf RM, Swedberg K, Schwartz P, Bigger JT Jr, Krishnan KRR, van Zyl LT, Swenson JR, Finkel MS. Sertraline treatment of major depression in patients with acute MI or unstable angina. Jama. 2002; 288(6):701–709. [PubMed: 12169073]
19. Delaney JA, Oddson BE, Kramer H, Shea S, Psaty BM, McClelland RL. Baseline depressive symptoms are not associated with clinically important levels of incident hypertension during two years of follow-up. Hypertension. 2010; 55(2):408–414. [PubMed: 20065156]
20. Shah AJ, Ghasemzadeh N, Zaragoza-Macias E, Patel R, Eapen DJ, Neeland IJ, Pimple PM, Zafari AM, Quyyumi AA, Vaccarino V. Sex and age differences in the association of depression with obstructive coronary artery disease and adverse cardiovascular events. Journal of the American Heart Association. 2014; 3(3):e000741. [PubMed: 24943475]
21. Rhee SJ, Kim EY, Kim SH, Lee HJ, Kim B, Ha K, Yoon DH, Ahn YM. Subjective depressive symptoms and metabolic syndrome among the general population. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2014; 54:223–230. [PubMed: 24975752]
22. Harris, KMH., Carolyn, T., Whitsel, Eric, Hussey, Jon, Tabor, Joyce, Entzel, Pamela, Udry, J Richard. [Accessed November 30, 2016] The national longitudinal study of adolescent health: Study design. http://www.cpc.unc.edu/projects/addhealth/design
23. Harris, KM. The Add Health STudy: Design and Accomplishments. Chapel Hill, NC: Carolina Population Center, University of North Carolina at Chapel Hill; 2013.

24. Allison, PD. Quantitative Applications in the Social Sciences. Thousand Oaks, CA: Sage publications Ltd; 2002. Missing data.
25. Moons KG, Donders RA, Stijnen T, Harrell FE. Using the outcome for imputation of missing predictor values was preferred. Journal of clinical epidemiology. 2006; 59(10):1092–1101. [PubMed: 16980150]
26. Sterne JA, White IR, Carlin JB, Spratt M, Royston P, Kenward MG, Wood AM, Carpenter JR. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. Bmj. 2009; 338:b2393. [PubMed: 19564179]
27. Sullivan TR, Salter AB, Ryan P, Lee KJ. Bias and precision of the "multiple imputation, then deletion" method for dealing with missing outcome data. American journal of epidemiology. 2015; 182(6):528–534. [PubMed: 26337075]
28. Radloff L. The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. Applied Psychological Measurement. 1977; 1(3):385–401.
29. Fish JN, Pasley K. Sexual (minority) trajectories, mental health, and alcohol use: A longitudinal study of youth as they transition to adulthood. Journal of youth and adolescence. 2015; 44(8): 1508–1527. [PubMed: 25956289]
30. McPhie ML, Rawana JS. The effect of physical activity on depression in adolescence and emerging adulthood: A growth-curve analysis. Journal of adolescence. 2015; 40:83–92. [PubMed: 25721258]
31. Schuler MS, Vasilenko SA, Lanza ST. Age-varying associations between substance use behaviors and depressive symptoms during adolescence and young adulthood. Drug and alcohol dependence. 2015; 157:75–82. [PubMed: 26483358]
32. Keyes KM, Cheslack-Postava K, Westhoff C, Heim CM, Haloossim M, Walsh K, Koenen K. Association of hormonal contraceptive use with reduced levels of depressive symptoms: a national study of sexually active women in the United States. American journal of epidemiology. 2013; 178(9):1378–1388. [PubMed: 24043440]
33. Cook EC, Pflieger JC, Connell AM, Connell CM. Do specific transitional patterns of antisocial behavior during adolescence increase risk for problems in young adulthood? Journal of abnormal child psychology. 2015; 43(1):95–106. [PubMed: 24893667]
34. Tabor, JW., Eric, A. Add Health Wave IV Documentation: Prescription Medication Use. Chapel Hill, NC: Carolina Population Center, University of North Carolina at Chapel Hill; 2010.
35. Kwon A, Bungay KM, Pei Y, Rogers WH, Wilson IB, Zhou Q, Adler DA. Antidepressant use: concordance between self-report and claims records. Medical care. 2003; 41(3):368–374. [PubMed: 12618640]
36. Entzel, P., Whitsel, EA., Richardson, A., Tabor, J., Hallquist, S., Hussey, J., Halpern, CT., Mullan Harris, K. Add Health wave IV documentation: Cardiovascular and anthropometric measures. Chapel Hill, NC: Carolina Population Center, University of North Carolina At Chapel Hill; 2009.
37. Law M, Wald N, Morris J, Jordan R. Value of low dose combination treatment with blood pressure lowering drugs: analysis of 354 randomised trials. Bmj. 2003; 326(7404):1427. [PubMed: 12829555]
38. Clark CJ, Everson-Rose SA, Alonso A, Spencer RA, Brady SS, Resnick MD, Borowsky IW, Connett JE, Krueger RF, Suglia SF. Effect of partner violence in adolescence and young adulthood on blood pressure and incident hypertension. PloS one. 2014; 9(3):e92204. [PubMed: 24658452]
39. Rothman, KJ., Greenland, S., Lash, TL. Modern epidemiology. Lippincott Williams & Wilkins; 2008.
40. Chen, PC., Kim. Guidelines for Analyzing Add Health Data. Chapel Hill, NC: Carolina Population Center, University of North Carolina at Chapel Hill; 2014.
41. Brent D, Emslie G, Clarke G, Wagner KD, Asarnow JR, Keller M, Vitiello B, Ritz L, Iyengar S, Abebe K. Switching to another SSRI or to venlafaxine with or without cognitive behavioral therapy for adolescents with SSRI-resistant depression: the TORDIA randomized controlled trial. Jama. 2008; 299(8):901–913. [PubMed: 18314433]
42. Prakash A, Lobo E, Kratochvil CJ, Tamura RN, Pangallo BA, Bullok KE, Quinlan T, Emslie GJ, March JS. An open-label safety and pharmacokinetics study of duloxetine in pediatric patients

with major depression. Journal of child and adolescent psychopharmacology. 2012; 22(1):48–55. [PubMed: 22251023]

43. Nguyen QC, Tabor JW, Entzel PP, Lau Y, Suchindran C, Hussey JM, Halpern CT, Harris KM, Whitsel EA. Discordance in national estimates of hypertension among young adults. Epidemiology. 2011; 22(4):532–41. [PubMed: 21610501]
44. Chyu L, McDade TW, Adam EK. Measured blood pressure and hypertension among young adults: a comparison between two nationally representative samples. Biodemography and social biology. 2011; 57(2):184–99. [PubMed: 22329087]
45. Andresen EM, Malmgren JA, Carter WB, Patrick DL. Screening for depression in well older adults: evaluation of a short form of the CES-D (Center for Epidemiologic Studies Depression Scale). American Journal of Preventive Medicine. 1994; 10(2):77–84. [PubMed: 8037935]
46. Boey KW. Cross-validation of a short form of the CES-D in Chinese elderly. International Journal of Geriatric Psychiatry. 1999; 14(8):608–17. [PubMed: 10489651]
47. Bradley KL, Bagnell AL, Brannen CL. Factorial validity of the Center for Epidemiological Studies Depression 10 in adolescents. Issues in Mental Health Nursing. 2010; 31(6):408–12. [PubMed: 20450343]
48. Mojtabai R, Olfson M. National trends in long-term use of antidepressant medications: results from the US National Health and Nutrition Examination Survey. The Journal of clinical psychiatry. 2013; 75(2):169–177.
49. Penninx BW. Depression and cardiovascular disease: Epidemiological evidence on their linking mechanisms. Neuroscience & Biobehavioral Reviews. 2017; 74:277–286. [PubMed: 27461915]

Table 1

Participants Characteristics by Hypertension Status in Young Adulthood, Add Health Study (N = 11,183), United States, 1994–2009

Characteristics[a]	n	Weighted %
Race		
White	6028	66
Black	2328	16
Hispanic	1746	12
Asian	773	4
Other	308	3
Completed education		
Less than High School	794	8
High School	2146	21
Some College	4467	39
College	3772	32
Male	5307	53
Depression and antidepressant use at wave 3, age 22		
High depressive symptoms only[b]	830	7
Antidepressant use only	393	4
High depressive symptoms and antidepressant use	125	1
Depression and antidepressant use at wave 4, age 29		
High depressive symptoms only[b]	943	9
Antidepressant use only	545	5
High depressive symptoms and antidepressant use	185	2
Hypertension at wave 4[c]	2105	20
Anti-hypertensive use at wave 4	266	3
Smoking status		
Current Smoker[d]	2326	24
Former Smoker	2431	23
Frequent sugar sweetened beverage consumption[e]	7281	67
Frequent fast food consumption[f]	1700	15
Frequent alcohol consumption[g]	1231	12
Physically inactive[h]	5200	46

Abbreviations: BMI, Body mass index; SE, standard error; SBP, systolic blood pressure; DBP, diastolic blood pressure.

[a] Non-imputed values are reported for the sample

[b] High depressive symptoms defined as a CES-D score of 11 or higher

[c] Hypertension defined as SBP greater than or equal to 140mmHg or DBP greater than or equal to 90mmHG or anti-hypertensive medication use

[d] Current smoker defined as smoking 1 cigarette per day for the past 30 days

[e] Frequent sugar sweetened beverage consumption defined as 7 or more times in the past week

[f] Frequent fast food defined as eating at a fast food establishment 7 or more days in the past week

[g] Frequent alcohol consumption defined as drinking at least 3–5 days per week over the past 12 months

[h] Physically inactive defined as engaged in physical activity fewer than 5 days in the past week

Table 2

Depressive Symptoms and Hypertension in Young Adulthood Among Add Health Participants (N = 11,183), United States, 1994–2008

	Model A[a]				Model B[b]			
	RR	**95% CI**	**PR**	**95% CI**	**RR**	**95% CI**	**PR**	**95% CI**
High depressive symptoms, age 16	0.99	0.85, 1.2			0.96	0.83, 1.1		
High depressive symptoms, age 22	0.98	0.81, 1.2			0.95	0.79, 1.2		
High depressive symptoms, age 29	1.0	0.85, 1.2			1.0	0.86, 1.2		
Chronic high depressive symptoms								
None			1.0	Referent			1.0	Referent
1 time point			1.0	0.89, 1.2			1.0	0.89, 1.2
2 time points			1.0	0.78, 1.3			1.0	0.77, 1.3
3 time points			0.88	0.53, 1.4			0.80	0.49, 1.3

Abbreviations: CI, confidence interval; PR, prevalence ratio; RR, relative risk.

[a] adjusted for age, education, race and sex

[b] additionally adjusted for body mass index, smoking status, alcohol consumption, fast food consumption, sugary sweetened beverage consumption, and physical activity

Table 3

Antidepressant Use and Hypertension in Young Adulthood Among Add Health Participants (N = 11,183), United States, 1994–2008

	Model A[a]				Model B[b]			
	RR	**95% CI**	**PR**	**95% CI**	**RR**	**95% CI**	**PR**	**95% CI**
Antidepressant use, age 22	1.2	0.96, 1.5			1.2	0.97, 1.5		
Antidepressant use, age 29			1.4	1.2, 1.7[c]			1.3	1.1, 1.6[c]
Antidepressant use by type, age 29								
None			1.0	Referent			1.0	Referent
SSRI			1.3	1.1, 1.6[c]			1.2	1.0, 1.5[c]
Non-SSRI			1.6	1.3, 2.1			1.5	1.2, 2.0

Abbreviations: CI, confidence interval; PR, prevalence ratio; RR, relative risk.

[a] adjusted for age, education, race and sex

[b] additionally adjusted for body mass index, smoking status, alcohol consumption, fast food consumption, sugary sweetened beverage consumption, and physical activity

[c] interaction with sex observed

Table 4

Depressive Symptoms, Antidepressant Use and Hypertension, Longitudinal (Wave 3) and Cross-sectional (Wave 4) Associations (N = 11,183), United States, 1994–2008

	Model A[a]				Model B[b]			
	RR	**95% CI**	**PR**	**95% CI**	**RR**	**95% CI**	**PR**	**95% CI**
Wave 3, age 22								
Low depressive symptoms and no antidepressants	1.0	Referent			1.0	Referent		
High depressive symptoms and antidepressants	1.2	0.75, 1.8			1.1	0.70, 1.7		
High depressive symptoms only	0.96	0.78, 1.2			0.94	0.77, 1.2		
Antidepressants only	1.2	0.94, 1.5			1.2	0.96, 1.6		
Wave 4, age 29								
Low depressive symptoms and no antidepressants			1.0	Referent			1.0	Referent
High depressive symptoms and antidepressants			1.3	0.93, 1.8			1.2	0.84, 1.7
High depressive symptoms only			0.98	0.81, 1.2			1.0	0.84, 1.2
Antidepressants only			1.4	1.2, 1.7[c]			1.4	1.2, 1.7[c]
Wave 4, age 29								
Low depressive symptoms and no antidepressants			1.0	Referent			1.0	Referent
High depressive symptoms and SSRI use			1.3	0.84, 2.0			1.1	0.73, 1.8
High depressive symptoms and non-SSRI use			1.4	0.78, 2.4			1.3	0.75, 2.2
High depressive symptoms only			0.98	0.82, 1.2			1.0	0.84, 1.2
SSRI use only			1.3	1.0, 1.7[c]			1.3	1.0, 1.6[c]
Non-SSRI use only			1.7	1.3, 2.2			1.6	1.2, 2.1

Abbreviation: CI, confidence interval; PR, prevalence ratio; RR, relative risk; SSRI, selective serotonin reuptake inhibitors.

[a] adjusted for age, education, race and sex

[b] additionally adjusted for body mass index, smoking status, alcohol consumption, fast food consumption, sugary sweetened beverage consumption, and physical activity

[c] interaction with sex observed

Table 5

Depressive Symptoms, Antidepressant Use and Systolic and Diastolic Blood Pressure, Longitudinal (Wave 3) and Cross-sectional (Wave 4) Associations (N = 11,183), United States, 1994–2008

	Model A[b]		Model B[c]	
	B	95% CI	B	95% CI
Systolic blood pressure[a]				
Wave 3, age 22				
Low depressive symptoms and no antidepressants	0.0	Referent	0.0	Referent
Depressive symptoms and antidepressants	0.14	−3.0, 3.2	−0.60	−3.3, 2.2
Depressive symptoms only	0.01	−1.3, 1.3	−0.40	−1.6, 0.82
Antidepressants only	0.31	−1.3, 2.0	0.39	−1.2, 2.0
Wave 4, age 29				
Low depressive symptoms and no antidepressants	0.0	Referent	0.0	Referent
Depressive symptoms and antidepressants	−0.73	−2.8, 1.4	−1.9	−4.0, 0.15
Depressive symptoms only	−0.58	−1.8, 0.67	−0.34	−1.5, 0.80
Antidepressants only	1.7	0.15, 3.3	1.3	−0.11, 2.8
Wave 4, age 29				
Low depressive symptoms and no antidepressants	0.0	Referent	0.0	Referent
Depressive symptoms and SSRI use	−0.04	−2.5, 2.4	−1.6	−4.3, 1.0
Depressive symptoms and non-SSRI use	−2.0	−5.7, 1.8	−2.5	−5.8, 0.83
Depressive symptoms only	−0.58	−1.8, 0.67	−0.34	−1.5, 0.80
SSRI use only	1.5	−0.42, 3.5	1.2	−0.51, 2.9
Non-SSRI use only	2.2	−0.50, 4.9	1.6	−0.91, 4.1
Diastolic blood pressure[a]				
Wave 3, age 22				
Low depressive symptoms and no antidepressants	0.0	Referent	0.0	Referent
Depressive symptoms and antidepressants	−0.26	−2.4, 1.9	−0.75	−2.7, 1.2
Depressive symptoms only	−0.23	−0.76, 1.2	−0.06	−1.0, 0.92
Antidepressants only	0.47	−0.88, 1.8	0.44	−0.90, 1.8
Wave 4, age 29				
Low depressive symptoms and no antidepressants	0.0	Referent	0.0	Referent
Depressive symptoms and antidepressants	0.17	−1.0, 2.4	−0.11	−1.9, 1.7
Depressive symptoms only	−0.33	−1.3, 0.60	−0.26	−1.1, 0.60
Antidepressants only	1.9	0.68, 3.1[d]	1.6	0.46, 2.7[d]
Wave 4, age 29				
Low depressive symptoms and no antidepressants	0.0	Referent	0.0	Referent
Depressive symptoms and SSRI use	0.33	−1.8, 2.4	−0.71	−3.0, 1.6[d]
Depressive symptoms and non-SSRI use	1.4	−1.3, 4.2	0.96	−1.6, 3.6
Depressive symptoms only	−0.33	−1.3, 0.60	−0.26	−1.1, 0.60
SSRI use only	1.2	−0.30, 2.6[d]	0.95	−0.42, 2.3[d]
Non-SSRI use only	3.3	1.3, 5.2	2.9	1.0, 4.7

Abbreviations: CI, confidence interval; SSRI, selective serotonin reuptake inhibitors.

[a] Blood pressure corrected if participants were taking anti-hypertensive medications (+9 mmHg for systolic blood pressure, +6 mmHg for diastolic blood pressure)

[b] adjusted for age, education, race and sex

[c] adjusted for age, education, race, sex, BMI, smoking status, alcohol consumption, fast food consumption, sugary sweetened beverage consumption, and physical activity

[d] interaction with sex observed