Depressive symptoms are not associated with clinically important levels of digital home blood pressure in the electronic Framingham Heart Study

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BACKGROUND Depressive symptoms are common and share many biopsychosocial mechanisms with hypertension. Association studies between depressive symptoms and blood pressure (BP) have been inconsistent. Home BP monitoring may provide insight.

OBJECTIVE To investigate the association between depressive symptoms and digital home BP.

METHODS Electronic Framingham Heart Study (eFHS) participants were invited to obtain a smartphone app and digital BP cuff at research exam 3 (2016–2019). Participants with ≥3 weeks of home BP measurements within 1 year were included. Depressive symptoms were measured using the Center for Epidemiological Studies Depression Scale (CES-D). Multivariable linear mixed models were used to test the associations of continuous CES-D score and dichotomous depressive symptoms (CES-D ≥16) (independent) with home BP (dependent), adjusting for age, sex, cohort, number of weeks since baseline, lifestyle factors, diabetes, and cardiovascular disease.

RESULTS Among 883 participants (mean age 54 years, 59% women, 91% White), the median CES-D score was 4. Depressive symptom prevalence was 7.6%. Mean systolic and diastolic BP at exam 3 were 119 and 76 mm Hg; hypertension prevalence was 48%. A 1 SD higher CES-D score was associated with 0.9 (95% CI: 0.18–1.56, $P = .01$) and 0.6 (95% CI: 0.06–1.07, $P = .03$) mm Hg higher home systolic BP and diastolic BP, respectively. Dichotomous depressive symptoms were not significantly associated with home BP ($P > .2$).

CONCLUSION Depressive symptoms were not associated with clinically substantive levels of home BP. The association between depression and cardiovascular disease risk factors warrants more data, which may be supported by mobile health measures.

KEYWORDS Mobile health; Blood pressure; Depression; Mental health; Home blood pressure monitoring

(Cardiovascular Digital Health Journal 2024;5:50–58)

Introduction

The estimated prevalence of depressive symptoms in US adults is 8.5% and tripled during the COVID-19 pandemic.[1] Depressive symptoms, including subthreshold levels for depression, are known to be associated with incident cardiovascular disease (CVD) and mortality.[2–4] Biopsychosocial mechanisms have been proposed to explain the association between depressive symptoms and CVD, including numerous biologic processes that underlie hypertension.[4] Depression has been implicated as a risk factor for hypertension. However, many studies have investigated the association between depressive symptoms and blood pressure (BP), with inconsistent results.

Large cross-sectional studies have reported a negative association between depression or depressive symptoms and BP,[5,6] as well as no association.[7] Large prospective studies have observed an association between greater depressive symptoms and higher average systolic and diastolic BP in older adults[8,9] and incident hypertension in adults.[10–13] A meta-analysis reported a 42% increased risk of hypertension in people with depression with a mean follow-up period of a decade.[14] In contrast, 2 large prospective studies combining symptoms of depression and anxiety found lower systolic BP (SBP) over the longer term, 2–3 decades later.[15,16]

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2666-6936/

https://doi.org/10.1016/j.cvdhj.2024.01.001

How depressive symptoms relate to BP warrants further investigation.

Mobile health devices promise more precise tracking of data and more patient-centered care and can facilitate home BP monitoring (HBPM). HBPM has some advantages compared to office-based measurements, including enabling the diagnosis of white-coat and masked hypertension,[17] being more reproducible,[18] and better predicting CVD morbidity and mortality.[19] HBPM can also support the management of hypertension over a lifecourse, as risk varies with age.[20] Presently, association studies between depressive symptoms and home BP have been limited to populations with hypertension[21,22] and 2 general population samples of Japanese adults, with incongruent results.[23,24] None seem to have used home BP readings collected for longer than 4 weeks. Thus, we aimed to investigate the association between depressive symptoms and home BP measured for up to 1 year in a large, community-based cohort, the electronic Framingham Heart Study (eFHS).

Methods

Study sample

The Framingham Heart Study (FHS) is a multigenerational cohort study that was initiated to investigate risk factors for CVD. The FHS recruited the FHS Third Generation Cohort (n = 4095), multiracial and multiethnic Omni Group 2 Cohort (n = 410), and New Offspring Spouse Cohort (n = 103) from 2002 to 2005. These participants underwent in-person research examinations every 6–8 years.[25] At research exam 3 (2016–2019, n = 3521), English-speaking participants who owned a smartphone were invited to enroll in the eFHS (n = 2151). If the invited participants owned an iPhone with iOS version 9 or later, they were offered a wireless Nokia Withings BP cuff for HBPM (n = 1167). Participants were excluded if they did not transmit a minimum of 3 weeks of BP measurements (n = 282) or if they had problematic data owing to device malfunction (n = 2), leaving a study sample of 883 participants (Figure 1). Most eFHS participants were assisted with app registration and new device pairing at the research center. In addition, each participant was provided a written protocol and was able to enroll remotely if they preferred. All participants provided written informed consent. The FHS and the eFHS were approved by the Institutional Review Board at Boston University Medical Center.

Depressive symptoms and antidepressant medication use

Trained technicians administered the Center for Epidemiological Studies Depression Scale (CES-D) at research exam 3. The CES-D is a widely used, validated self-report tool for measuring depressive symptomology in the general population.[25,26] It consists of 20 questions about symptoms and feelings, such as reduced appetite and loneliness. The answers to each question were scored from 0 to 3 based on their frequency during the past week. For 16 of the questions a higher score indicates a higher frequency of depressive symptoms. For the remaining 4 questions, a higher score indicates a lower frequency of depressive symptoms. We reversed the scores of the 4 questions and summed up the individual question scores to construct the CES-D score. Total CES-D scores range from 0 to 60. A total CES-D score of 16 or higher indicates the presence of depressive symptoms, as this cut-off has been shown to have acceptable specificity and sensitivity for clinical depression.[27] Participants self-reported all medications used at the time of each exam, and most used a medication bag provided to bring prescription bottles to the exam for verification. Antidepressant medications were recorded, and we identified antidepressant medications such as sertraline, fluoxetine, and citalopram. We included antidepressant use at exam 3 in one of the definitions of depressive symptoms in the statistical analysis, because antidepressant medication use may influence BP.[28,29]

Mobile home BP

Participants who opted to receive a wireless BP cuff were asked to download the Nokia Withings Health Mate app, enable data sharing, and measure home BP once a week, ideally on the same day of the week and time of day. Participants were instructed to sit in a comfortable position and rest quietly with feet flat on the ground for 5 minutes with left elbow and wrist supported and palm up before taking a measurement. All BP recordings were time stamped and transmitted to the eFHS. We included participants in our analysis if they returned at least 3 weeks of home BP measurements. A minimum of 3 home BP measurements has been shown to provide a reliable estimate of home BP[30,31] and aligns with current American Heart Association recommendations.[32] Previous work from our group also demonstrated similar results using 3 BP measurements compared with a threshold of 9 BP measurements.[33] The primary home BP outcomes were defined as repeated home SBP and repeated home diastolic BP (DBP), while the secondary outcome was the prevalence of home hypertension. Home hypertension was defined as home SBP $\geq$130 mm Hg, home DBP $\geq$80 mm Hg, and/or use of antihypertensive medication, which was self-reported at research exam 3.

Covariates

Demographic variables were measured at exam 3. Body mass index was calculated as weight in kilograms divided by the square of the measured height in meters. A questionnaire was used to obtain the following information: education (categorized as less than high school, high school or some college, and bachelor's degree or higher); physical activity (measured with the Physical Activity Index, a composite score of hours spent per activity level with weights of 1, 1.1, 1.5, 2.4, and 5 assigned to sleep, sedentary, slight, moderate, and heavy, respectively)[34]; smoking status (categorized as current smoker vs nonsmoking); alcohol intake (defined as average drinks per week); and use of

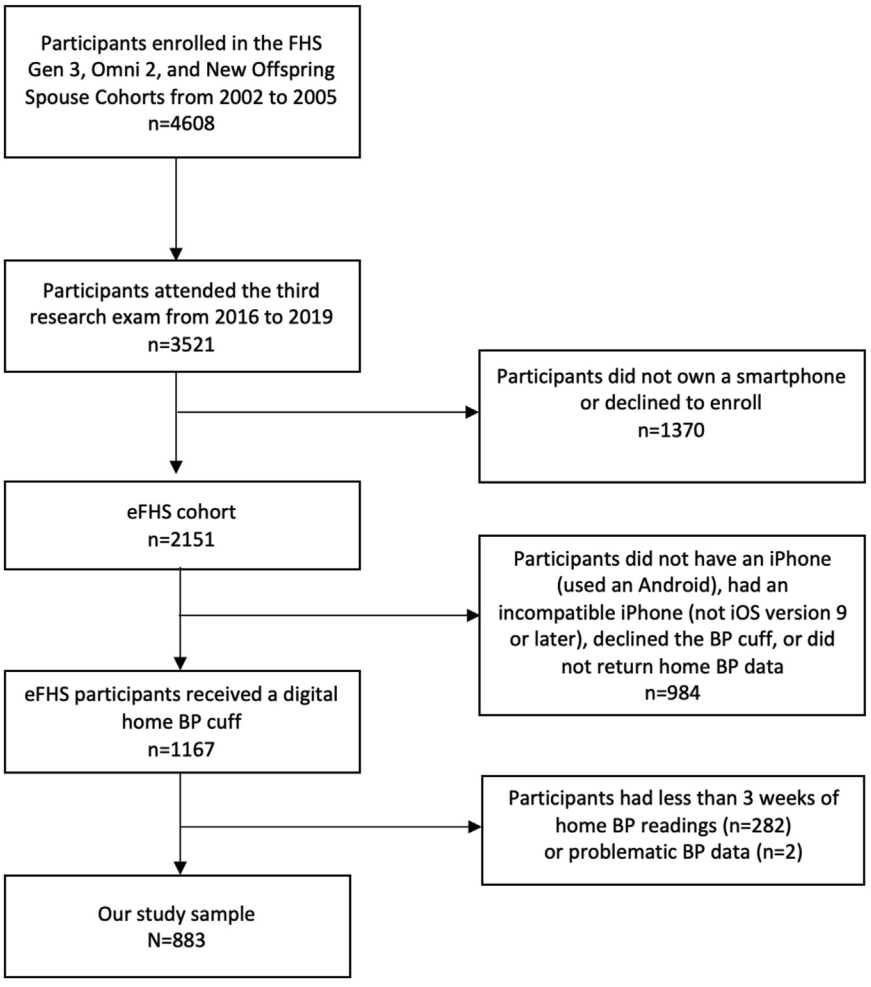

Figure 1 Flowchart of study sample inclusion. BP = blood pressure; eFHS = electronic Framingham Heart Study; FHS = Framingham Heart Study.

antihypertensive medication (coded as yes/no). The antihypertensive medications taken by the participants included, but were not limited to, angiotensin-converting enzyme inhibitors (eg, lisinopril), calcium channel blockers (eg, amlodipine), beta blockers (eg, metoprolol), and diuretics (eg, hydrochlorothiazide). Prevalent CVD was defined as heart failure, coronary heart disease (myocardial infarction, angina), stroke, or intermittent claudication adjudicated by a committee of investigators using all available evidence, including hospital records and written standardized criteria. Diabetes was defined as prior diagnosis, use of diabetes medications, HbA1C $\geq$6.5%, fasting blood glucose $\geq$126 mg/dL, or random plasma glucose $\geq$200 mg/dL and coded as yes/no.

Statistical analysis

Baseline characteristics were defined as mean (SD) or median (25th percentile, 75th percentile) if they were continuous variables and as counts (%) if they were categorical variables. BP variability between the groups with and without depressive symptoms was qualitatively assessed with crude data by plotting home SBP and DBP over the 52 weeks from time of enrollment. Linear mixed-effects models were conducted to test the effect of continuous and dichotomous depressive symptoms on repeated home SBP and home DBP and were adjusted for relevant covariates mentioned in the previous section (primary models). We also adjusted for the number of weeks of home BP measurements since the initial BP return. Continuous depressive symptoms were defined as continuous CES-D per 1 SD, and dichotomous depressive symptoms were defined as dichotomous CES-D $\geq$16 with or without antidepressant use in the primary models. Additionally, we checked for effect modification by sex on these associations by introducing multiplicative interaction terms (ie, CES-D $\times$ sex and dichotomous depressive symptoms $\times$ sex), then we performed sex-stratified analyses for all the associations in the primary models. In our secondary analyses, generalized linear mixed-effects models with logit link were used to evaluate the associations of continuous and dichotomous depressive symptoms with home hypertension. The secondary models were adjusted for the same covariates as in the primary models, except for antihypertensive medication.

Table 1 Characteristics of the study sample

Variable	eFHS participants with ≥3 weeks of digital home BP measurements (N = 883)
Age (years), mean ± SD	54 ± 9
Sex, female, n (%)	518 (58.7%)
Multiethnic Omni 2 cohort, n (%)	75 (8.5%)
Education, bachelor's degree or higher	605 (68.5%)
Systolic BP at exam 3 (mm Hg), mean ± SD	119 ± 14
Diastolic BP at exam 3 (mm Hg), mean ± SD	76 ± 8
Depressive symptom measures	
CES-D score, median (25th, 75th percentile)	4 (1, 7)
CES-D ≥16, n (%)	67 (7.6%)
Antidepressant use, n (%)	148 (16.8%)
Covariates	
Body mass index (kg/m^2), median (25th, 75th percentile)	27.2 (24.3, 30.4)
Physical Activity Index score, median (25th, 75th percentile)	32.6 (30.1, 35.6)
Current smoking, n (%)	34 (3.97)
Alcohol consumption (average drinks per week), mean ± SD	5.2 ± 6.2
Diabetes,[†] n (%)	49 (5.5%)
Hypertension,[‡] n (%)	420 (47.6%)
Cardiovascular disease,[§] n (%)	33 (3.7%)
Antihypertensive use, n (%)	197 (22.3%)
Home digital BP	
Number of weeks of HBPM, median (25th, 75th percentile)	23 (10, 47)
Digital home systolic BP (mm Hg), repeated (SD)	123 (16)
Digital home diastolic BP (mm Hg), repeated (SD)	76 (10)

Values are shown as n (%), mean ± SD, or median (25th, 75th percentile).

BP = blood pressure; CES-D = Center for Epidemiological Studies Depression Scale; eFHS = electronic Framingham Heart Study; HBPM = home blood pressure monitoring.

[†]Prior diagnosis, use of diabetes medications, HbA1C ≥6.5%, fasting blood glucose ≥126 mg/dL, or random plasma glucose ≥200 mg/dL.

[‡]BP ≥130/80 mm Hg and/or taking antihypertensive medication at exam 3.

[§]Prevalent heart failure, myocardial infarction, angina, stroke, and/or intermittent claudication.

All statistical analyses were conducted using R version 4.0. We used 2-tailed $P < .05$ for significance.

Results

Among the 883 participants (mean [SD] age 54 [9] years; 58.7% women; 8.5% non-White) in our study sample, the median CES-D score was 4 (25th percentile 1, 75th percentile 7), 7.6% had depressive symptoms (ie, CES-D score ≥16), 16.8% reported taking antidepressant medication, and nearly half had hypertension at exam 3 (Table 1). The eFHS participants were younger (53 years vs 57 years), were more likely to be female (56.2% vs 50.1%), and had fewer depressive symptoms (8.1% vs 12.8%) compared to FHS participants at research exam 3 who did not enroll in eFHS (Supplemental Appendix 1).

In an unadjusted descriptive analysis for visual inspection, the home SBP and DBP of participants with CES-D ≥16 vs participants with CES-D <16 were plotted across each week in Figure 2 and by CES-D and antidepressant use status in Figure 3. The dropout rates of participants returning digital BP in the 2 groups across time were comparable. The group with CES-D ≥16 had greater average SBP and DBP in the second half of the follow-up period and greater variability in SBP and DBP, compared to the group with CES-D <16 (Figure 2). Note that there was a large difference in sample sizes between the 2 groups (67 in the group with CES-D ≥16 vs 816 in the group with CES-D <16 in week 1). Including antidepressant use in the group with CES-D ≥16 almost tripled the sample size compared to CES-D ≥16 without antidepressant use. The group with CES-D ≥16 or antidepressant use exhibited similar average SBP (75.1 mm Hg vs 75.7 mm Hg) and DBP (122.7 mm Hg vs 123 mm Hg) compared to the other group over time, with the observed variability appearing to be greater (Figure 3). However, it is important to note that a substantial difference in sample sizes (186 in the group with CES-D ≥16 or antidepressant use vs 697 in the group with CES-D <16 and no antidepressant use in week 1) still existed between these 2 groups.

Continuous depressive symptoms had a small positive association with home BP, where a 1 SD higher CES-D score corresponded with 0.87 mm Hg ($P = .01$) and 0.56 mm Hg ($P = .03$) higher home SBP and DBP, respectively, in the multivariable adjusted model (Table 2). Dichotomous depressive symptoms (CES-D ≥16) was not significantly associated with home SBP or DBP ($P > .2$) whether or not antidepressant use was included in the definition. Effect modification by sex was not observed in all primary models mentioned above ($P > .05$). Despite the lack of evidence for effect modification, we noted that 1 SD increments in CES-D were associated with 1.12 mm Hg ($P = .01$) higher SBP in

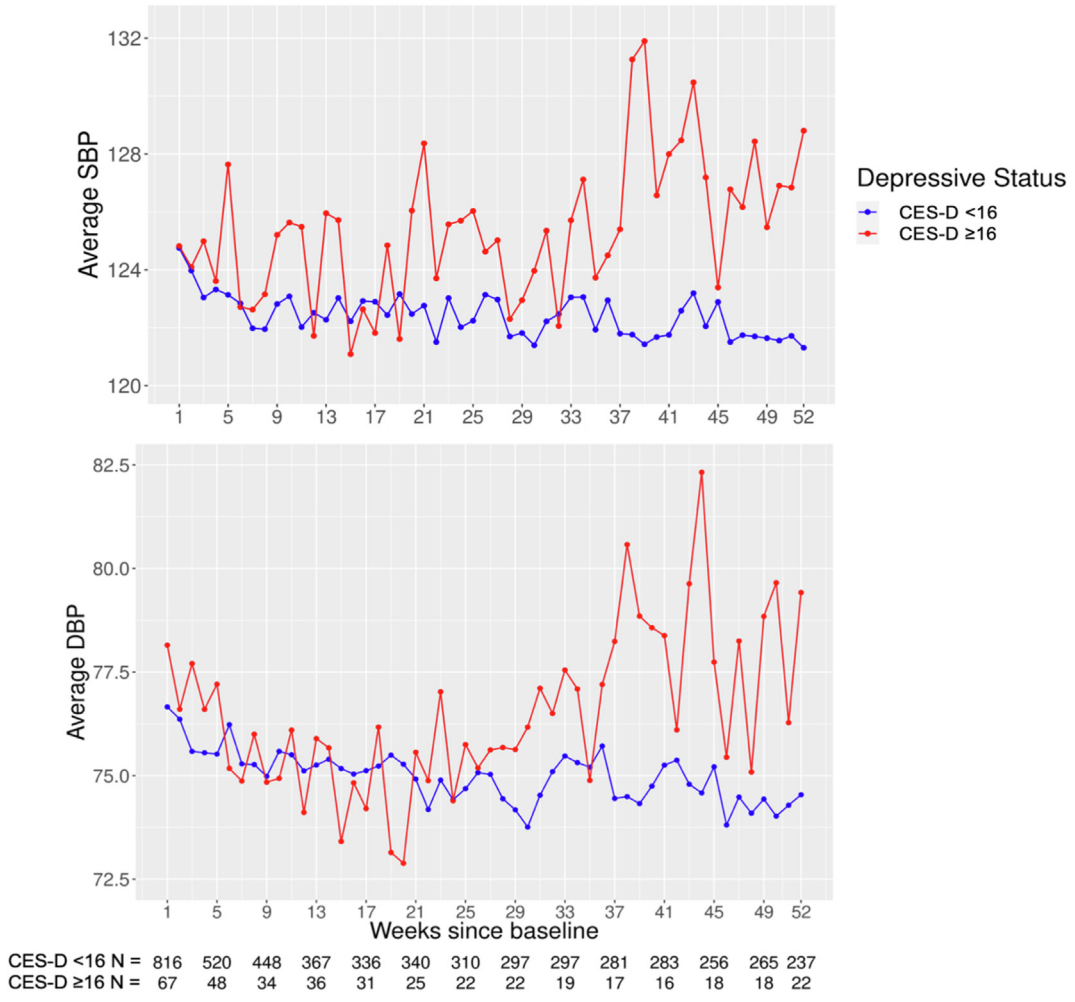

Figure 2 Average home systolic blood pressure (SBP; top panel) and diastolic blood pressure (DBP; bottom panel) each week across 1-year follow-up in participants with Center for Epidemiological Studies Depression Scale score (CES-D) ≥16 vs CES-D <16.

women, while no significant association was observed in men ($P = .7$) (Supplemental Appendix 2). In addition, continuous and dichotomous depressive symptoms were not significantly associated with the prevalence of home hypertension (OR = 1.16, 95% CI: 0.89–1.51 for 1 SD increase in CES-D scores, $P = .26$; OR = 1.77, 95% CI: 0.72–4.36 for participants with CES-D ≥16, $P = .22$; OR = 1.2, 95% CI: 0.66–2.18 for participants with CES-D ≥16 or antidepressant use, $P = .55$).

Discussion

In the present study we examined the association of depressive symptoms with digital home BP measured weekly for up to 1 year in middle-aged and older community-dwelling adults. In our study sample, we detected greater BP variability in the participants with depressive symptoms or antidepressant use compared to those without depressive symptoms and antidepressant use through a descriptive unadjusted analysis. We observed a small positive, but clinically insubstantial, association between continuous CES-D score and digital home BP. We did not observe an association between dichotomous depressive symptoms and digital home BP even in models that included antidepressant use in the depressive symptoms group. In our secondary analysis, we failed to observe any associations between the prevalence of home hypertension and both continuous and dichotomous depressive symptoms. Our study examined home BP measurements taken over a longer time period than other reports[23,24] but did not identify clinically meaningful associations with depressive symptoms. Our sample sizes for some of our association analyses were modest and may have contributed to ability to identify associations.

In contrast to our findings, other large cross-sectional studies have reported a negative association between depressive symptoms and BP in French, Dutch, and Chinese cohorts.[5,6,35] These prior studies used different measures for depressive symptoms, including self-reported history of a major depressive episode or treatment for depression, the major depressive episode module of the Mini International Neuropsychiatric Interview,[5] the Composite International Diagnostic Interview,[6] and the 9-item Personal Health Questionnaire,[35] and they evaluated BP with 2 or 3 in-office

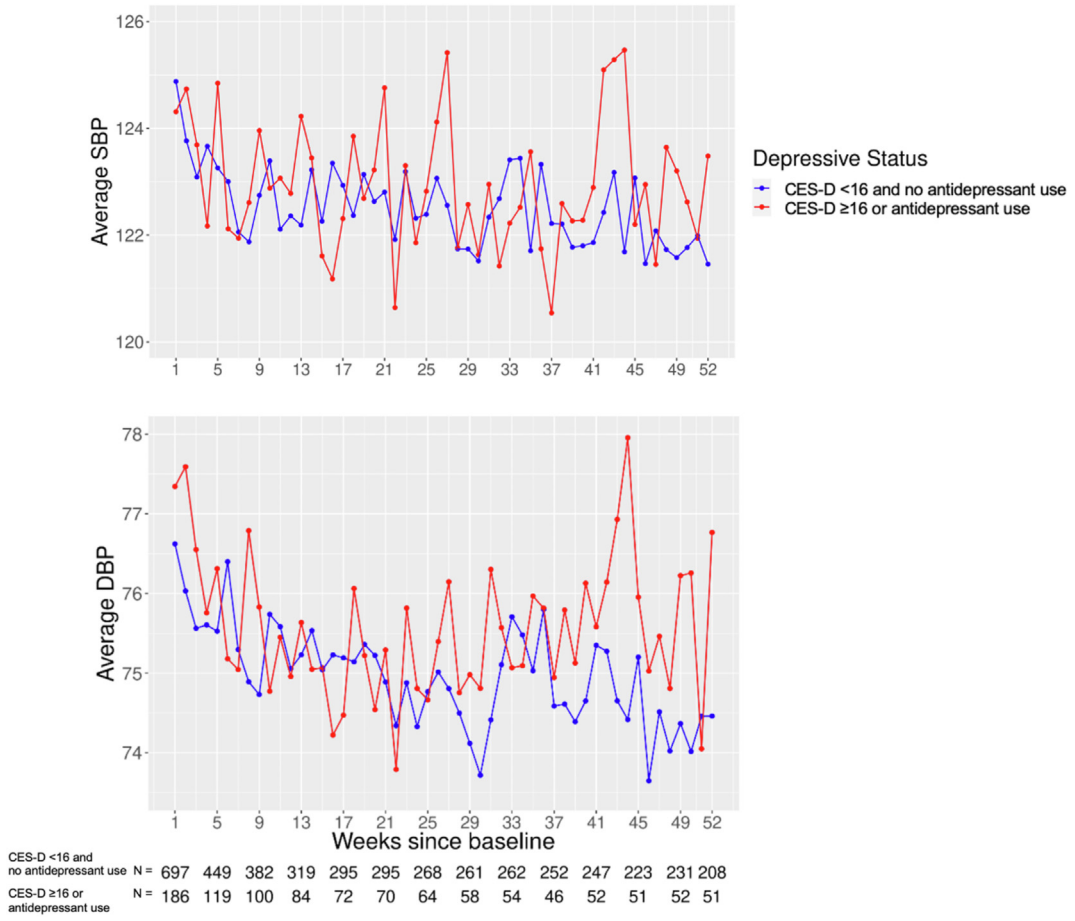

Figure 3 Average home systolic blood pressure (SBP; top panel) and diastolic blood pressure (DBP; bottom panel) each week across 1-year follow-up in participants with Center for Epidemiological Studies Depression Scale score (CES-D) ≥16 or antidepressant use vs CES-D <16 and no antidepressant use.

measurements at the time of interview. Our results may have differed owing to our utilization of the CES-D, home BP vs office BP, and a longer duration of BP measurements.

Another factor to consider when evaluating the association between depressive symptoms and BP is the age and sex distribution of the sample. A prospective study from the Baltimore Longitudinal Study of Aging spanning 29 years found CES-D to be positively associated with BP in older adults (≥ median 58.8 years) and younger women, and negatively associated with SBP in younger men.[8] An important difference is that our study was cross-sectional, but our sample did have a high proportion of female subjects and a narrow age distribution of middle-aged participants.

Population-based studies investigating depressive symptoms and home BP are sparse and used the Geriatric Depression Scale (GDS-15) to quantify depressive symptoms. One study found home SBP to negatively associate with depressive symptoms (GDS >11) in older Japanese adults aged >70 years,[23] while the other study found mild depressive symptoms (GDS 1–15) were positively associated with 7-day home SBP in Japanese adults aged 32–79 years (mean 60 years).[24] Our study used the CES-D to measure depressive symptoms, but we similarly found a positive association

Table 2 Association between depressive symptoms and mobile home blood pressure

	SBP			DBP		
Home BP	β	95% CI	*P* value	β	95% CI	*P* value
CES-D, 1 SD	0.87	(0.18, 1.56)	.014	0.56	(0.06, 1.07)	.030
CES-D ≥16	1.23	(-1.17, 3.62)	.314	1.10	(-0.66, 2.85)	.220
CES-D ≥16 or taking antidepressants	0.90	(-0.68, 2.48)	.264	0.67	(-0.49, 1.83)	.261

Adjusted for age, sex, multiethnic Omni 2 cohort, education, body mass index, physical activity, smoking, alcohol intake, history of diabetes or cardiovascular disease, use of antihypertensive medication, and the number of weeks of home BP measurements. The sample size was 883 in total: n = 67 with CES-D ≥16; n = 186 with CES-D ≥16 or taking antidepressants (1 SD CES-D = 6.8 units/points).

BP = blood pressure; CES-D = Center for Epidemiological Studies Depression Scale; DBP = diastolic blood pressure; SBP = systolic blood pressure.

between continuous depressive symptoms and home BP, while finding no association between dichotomous depressive symptoms and home BP, in middle-aged participants. Longitudinal studies may help us better understand the association between depressive symptoms and increased risk of hypertension[14] and CVD.

Our study observed that participants with depressive symptoms had greater average SBP and DBP only in the second half of the follow-up compared to the participants without depressive symptoms in a descriptive unadjusted analysis. The differences in the average BP between the first half and second half of the study follow-up may be attributed to the following 2 reasons. First, during follow-up, we observed a substantial sample size reduction in both groups, with the number of participants decreasing from 816 to 237 for those without depressive symptoms and from 67 to 22 for those with depressive symptoms. This reduction may be partly attributed to informative dropout, where participants withdrew from the study owing to their BP levels. Notably, individuals with normal BP levels might have considered home BP monitoring unnecessary and consequently stopped measuring and transmitting weekly home BP readings (dropped out). On the contrary, individuals with elevated BP levels may have been more inclined to monitor their health, leading to their prolonged participation in the study. The impact of informative dropout was more pronounced in the depressive symptom group owing to its smaller sample size, resulting in a higher average BP level in this group compared to the group without depressive symptoms. Second, participants with depressive symptoms at the beginning of our study may have experienced increased levels of chronic stress over time, potentially leading to elevated BP levels during follow-up. Besides, participants with depressive symptoms may have experienced an increase in unhealthy behaviors or a decrease in physical activity over time, which can contribute to higher BP.

Negative psychological factors have been associated with BP through both health behaviors and shared underlying biological mechanisms.[4] For example, depressive symptoms are associated with lower levels of physical activity,[36,37] and higher physical activity levels are associated with lower home BP.[33] Other health behaviors affected by depression include weight gain, alcohol intake, smoking, and medication nonadherence.[38–40] Genetic predisposition[41] and biological processes likely simultaneously play a role in both depression and BP, including dysregulation of the autonomic nervous system with higher catecholamine levels in response to stress,[42,43] increased inflammation,[44] and hyperactivation of the hypothalamic-pituitary-adrenal axis with higher awakening cortisol levels.[45] One recent study performed a systematic review of the association between mental illness and BP variability.[46] The study showed that previous studies using short-term and ultrashort-term BP variability found mental illness such as depression has dysregulated autonomic function. This dysregulation was evident through increased BP variability among young and middle-aged participants. However, the association was not clear for long-term BP variability. Our own study contributes to this understanding by highlighting that depressive symptoms may play a role in the deterioration of autonomic function, as reflected in mid- to long-term BP variability over a 1-year follow-up period. Finally, people with depression use healthcare services more often than other insured Americans and may have a greater opportunity for diagnosis of hypertension.[47,48] Increased interaction with the healthcare system could also explain why depression as a comorbidity is associated with BP control.[49] Hence efforts to improve psychological health and improve associated health behaviors may lead to lower BP.[4]

The 2017 Hypertension Clinical Practice Guidelines focus on self-monitoring with emphasis on out-of-office BP measurement.[50] As a convenient measure of out-of-office BP, HBPM has become important not only for the diagnosis of hypertension but also for stratifying risk and improving BP reduction and control.[20,51] A survey of a nationally representative sample of US adults aged 50–80 years revealed that among those with hypertension or a BP-related health condition, more than half owned and used a BP monitor.[52] The only factors associated with regular monitoring were BP monitor ownership, clinician recommendations to measure home BP, and excellent or good self-rated mental health.[52] Higher depressive symptoms have been associated with lower engagement with digital device use.[53,54] Targeted interventional strategies to support digital device use may result in improvement in regular and longer-term self-home BP management in this group. Interventions could also address disparities in age, educational attainment, and household income, which are known to be associated with lower wearable device use. Promisingly, the vast majority of all users were willing to share their health data with clinicians.[55] Smartphones and digital devices can provide real-world measures of depression and BP, improve patient engagement and empowerment, and aid in the diagnosis and treatment of these 2 chronic conditions.

Strengths of this study are its sample size for home BP data and the embedded aspect of eFHS, in which participants are well characterized, allowing for adjustment of many confounders. There are several limitations to the study that merit comment. First, the study design does not permit inferences about causality or directionality. Depressive symptoms were captured at 1 point in time. The eFHS study sample is primarily White, well educated, and healthier than all exam attenders, limiting generalizability to more diverse samples. Importantly eFHS participants who returned sufficient BP measurements for analysis had lower levels of depressive symptoms than FHS participants who did not enroll in eFHS (Supplemental Appendix 1), so we may be underestimating the association of depressive symptoms. Depressive symptoms were measured by CES-D score, which is not the gold standard for diagnosing depression but has been validated for use in population studies.[26,27] We cannot account for other possible confounders, including adherence to medications and diet.

Conclusion

In our community-based sample of middle-aged adults, CES-D score was observed to have a small positive association with digital home BP measured for up to 1 year, but the magnitude of the associations was clinically unsubstantial. Extending evaluation of mental health indicators and home BP to multiple assessments over time may provide important insights into the relationships between depressive symptoms and BP. Mobile health technologies, including digital home BP and digital assessments of mental health, can be leveraged to empower people to engage with self-management of these health conditions in their home environments to improve cardiovascular and overall health.

Funding Sources

This project was supported by Boston University School of Medicine's Medical Student Summer Research Program; the National Heart, Lung, and Blood Institute of the National Institutes of Health (NIH) under Award Numbers T35HL139444 and R01HL141434; and the FHS contract 75N92019D00031.

Disclosures

DDM has received research support from Apple Inc, Bristol-Myers Squibb, Boehringer-Ingelheim, Pfizer, Flexcon, Samsung, Philips Healthcare, and Biotronik, and has received consultancy fees from Heart Rhythm Society, Bristol-Myers Squibb, Pfizer, Flexcon, Boston Biomedical Associates, and Rose Consulting. Dr McManus also declares financial support for serving on the Steering Committee for the GUARD-AF study (NCT04126486) and Advisory Committee for the Fitbit Heart Study (NCT04176926). All other authors have no conflicts to disclose.

Authorship

All authors attest they meet the current ICMJE criteria for authorship.

Patient Consent

All patients provided written informed consent.

Ethics Statement

The authors designed the study and gathered and analyzed the data according to the Helsinki Declaration guidelines on human research. The FHS and the eFHS were approved by the Institutional Review Board at Boston University Medical Center.

Disclaimer

Given his role as Editor-in-Chief, David McManus had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to David Duncker, MD, FESC, FEHRA.

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.cvdhj.2024.01.001.

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