Effect Heterogeneity of Loneliness and Social Support on Incident Hypertension in Older, Normotensive Populations

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Although social isolation is known to impact those with cardiovascular disease, its relationship with incident hypertension is unclear. In this retrospective cohort study, we used data from the *All of Us* research program. Participants were enrolled between May 2017-April 2023, aged 50+ years, and had at least 60-days of EHR data pre-index date. We identified incident hypertension during follow-up. Those classified as hypertensive at or prior to the index date were excluded. We defined low social support and loneliness as binary variables. Using causal forests, we estimated treatment effects as unweighted and overlap-weighted risk differences (RD). A total of 24,720 participants with a median follow-up of 2.6 years were included. While loneliness and social support were not significantly associated with incident hypertension in the overall population, causal forests revealed meaningful effect heterogeneity, with socially isolated male (RD: 0.038, 95% CI 0.002 to 0.075; overlap-weighted RD: 0.027, 95% CI -0.005 to 0.059) and Gay or Lesbian participants (RD: 0.108, 95% CI 0.011 to 0.205; overlap-weighted RD: 0.11, 95% CI 0.008 to 0.211) experiencing a significantly elevated risk. This illustrates how machine learning, when embedded within epidemiologic frameworks, can detect subgroup vulnerability that other approaches may obscure, enabling targeting of limited resources.

Key words: Heterogenous Treatment Effects, Social Support, Machine Learning (ML), Hypertension, Loneliness.

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Introduction

Hypertension is highly prevalent, affecting nearly 50% of the US adult population[1,2]. It is also a powerful risk factor for cardiovascular disease (CVD), a leading cause of morbidity and mortality[2]. Consequently, modifiable risk factors for incident hypertension should be identified to inform public health interventions[2,3].

Although lifestyle factors have long been a focus of cardiovascular health efforts, social isolation has recently gained greater attention, especially among older adults[3-5]. Lack of social support, defined as limited or no availability of emotional, practical, or tangible assistance from others, is a well-established risk factor for adverse outcomes in older populations and in populations with existing CVD[4-6]. However, its relationship with incident hypertension is unclear. Additionally, the evidence for loneliness–a state of discomfort due to the perception that one is alone–in primary and secondary prevention of CVD and its risk factors is mixed[4,5]. Nevertheless, numerous biological pathways are purported to link social support and loneliness with cardiovascular health, including activation of the hypothalamic–pituitary–adrenocortical axis and the sympathetic nervous system, as well as increased oxidative stress and inflammation[4,7-9].

Populations at greater risk for social isolation include older individuals, immigrants, and Lesbian Gay Bisexual Transgender Queer Asexual populations, while evidence of inequities by race and ethnicity is mixed[4,10]. Given that disparities in hypertension burden are well-documented in these populations, studies should explore whether social isolation accounts for part of this increased risk[11-13].

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In this retrospective cohort study, we applied causal forests, a novel machine learning approach designed to estimate heterogeneous treatment effects in observational data, to determine whether social support and loneliness are associated with an increased risk of incident hypertension in a large, diverse population of normotensive older US adults. Given inequities in hypertension across various subpopulations, we explored effect heterogeneity by socio-demographic subpopulations.

Methods

Data Source and Population

This study examines data from the *All of Us* research program, which consists of linked survey and electronic health record (EHR) data from participants across the US normalized to the Observational Medical Outcomes Partnership (OMOP) common data model[14,15]. *All of Us* collects detailed clinical, lifestyle, and social determinants data, permitting exploration of overall population effects and by numerous socio-demographics not often captured in clinical studies[14]. Recruitment for *All of Us* is ongoing; however, participants considered for our study were enrolled between May 31, 2017- April 1, 2023. This study was approved by the Northeastern University Institutional Review Board (IRB #23-5-21). The data underlying this article were provided by the National Institutes of Health by permission. Data can be accessed by requesting permission at https://allofus.nih.gov/[14].

We defined the index date as the date each participant took The Basics survey, as completion of this survey was required for participation in *All of Us*. We included all participants aged 50 years or older with at least 60-days of EHR data pre-index date. We only required that a participant

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have started the four study questionnaires used for the analysis (The Basics, Lifestyle, Personal/Family Health History, and Social Factors of Health; note that the latter 3 are available after completion of The Basics survey). We excluded participants with the study outcome at or prior to the index date. Beginning at the index date, we followed participants longitudinally for incident hypertension.

Covariables and Outcome

Based on a literature review, we created a directed acyclic graph (DAG) to elucidate the causal structure of our study question and identify covariables to include in the models (**Figure 1**). In this DAG, edges from the 'Subpopulations' node, indicating membership in socio-demographic subgroups, represents increased risk caused by social stress and marginalization[16]. We defined EHR-based variables using validated phenotypes and derived social and behavioral measures from validated survey instruments[17-27]. To enhance replicability and reliability, we used standardized concepts in the OMOP CDM whenever possible[15,28]. All covariables and exposures were defined at or before the index date.

See **Table S1** and **Table S2** for definitions of study covariables, exposures, and outcome. Covariables include age (years), body mass index (BMI, kg/m^2), race (Asian alone, Black alone, Hispanic alone, Middle Eastern/ North African [MENA] alone, multi-race, other race alone [includes other race, American Indian/ Alaska Native alone, Native Hawaiian/ Pacific Islander alone], or White alone), sex at birth (female, male), US born (binary), sexual orientation (asexual, bisexual, gay/ lesbian, not sure, queer/ other, straight), family history of atherosclerotic CVD (binary), family history of cardiometabolic risk factors (binary), current smoking (binary),

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current use of nicotine products (binary), current alcohol misuse (binary), education (never to eleven years, twelve years or General Educational Development [GED], college one to three years, college graduate, advanced degree), income per year in US dollars (less than 10k, 10k to <25k, 25k to <35k, 35k to <50k, 50k to <75k, 75k to <100k, 100k to <150k, 150k to <200k, 200k or more), insurance (dual eligible, government, Medicaid, Medicare, private, other, uninsured), and current unipolar depression (binary). Given that diabetes and hypercholesteremia were bias-inducing colliders in our DAG, we did not control for these covariables in our analysis.

The exposure variables social support and loneliness were collected using the Medical Outcomes Study (MOS) Social Support Survey and revised UCLA Loneliness 8 item Scale, respectively (see **Table S1** for survey questions)[17,18]. These variables were scored based on the guidelines of their respective questionnaires[18,29]. The MOS Social Support Survey, coded as an average of the 8 questions, ranges from 1-5, with a higher score indicating greater social support. The UCLA Loneliness scale, coded as the sum of all questions, ranges from 0-24, with a higher score indicating greater loneliness. We converted continuous scores to binary by categorizing those at or above the 90th percentile of loneliness as exposed and unexposed otherwise, and those at or below the 10th percentile of social support as exposed and unexposed otherwise.

We defined the study outcome of hypertension using two pathways in the EHR data: (1) The presence of two or more systolic or diastolic blood pressures>=140/90 mm Hg within the same year and not on the same day; or (2) the presence of one or more International Classification of Diseases 10th Revision Clinical Modification hypertension codes and a prescription for an

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antihypertensive medication within a year of the code (**Table S2**). This hypertension algorithm has been extensively validated in EHR data[23,24]. Additionally, use of blood pressures to detect hypertension cases is essential, as hypertension is frequently undiagnosed and is not adequately captured solely using prescriptions and diagnosis codes[24,30].

Statistical Analysis

We first assessed missingness across study variables. Then, assuming a missing at random (MAR) mechanism, we adjusted for missing data using stabilized inverse probability (IP) weights[31]. To generate the weights, we fit two generalized linear models (GLM): an intercept-only model for the numerator and, for the denominator, a covariable-adjusted model restricted to variables with < 1.5% missingness (10 of 18 variables; see **Table S3**). We assessed model assumptions and reviewed weight distributions to identify extreme weights. We then generated weights proportional to the IP of having complete data which were used in the subsequent analyses[31].

We then performed omnibus tests to determine the presence of effect heterogeneity using two complementary approaches developed by Yadlowsky, Athey, and Wager based on generalized random forests (GRFs) and implemented in the grf package in R: rank-weighted average treatment effects (RATE) and average treatment effects (ATE)[32-36]. Compared to traditional non-parametric approaches, GRFs used in both approaches offer improved performance in high-dimensional settings and enhanced power to detect effect heterogeneity[33]. Further, in contrast to ATE, RATE enables exploration of effect heterogeneity without relying on prespecified subgroups[36].

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Both the RATE and ATE approaches have the same initial steps. First, two nuisance functions are estimated: (i) Outcome regressions marginalized over exposure (hypertension given loneliness or low social support) and (ii) Exposure propensities (probability of being lonely or having low social support). Given the high degree of correlation between social support and loneliness (Pearson correlation = -0.60) and convergence issues noted in the GLMs when modeling them jointly, we ran separate models for each exposure. Although GRFs typically employ regression trees with missingness incorporated as attributes (MIA), we instead used GLMs weighted by the IP of having complete data for nuisance estimation. This decision reflected the presence of missing exposure data, as MIA is not validated when the dependent variable itself is missing, as is the case when generating exposure propensities for loneliness and social support in our study[37,38].

In the second step, the two approaches diverge. In the ATE approach, the entire dataset and estimated nuisance functions are passed to a GRF called a causal forest. Causal forests extend the classification and regression tree (CART) approach to focus explicitly on heterogeneity in treatment effects under the assumption of unconfoundedness[33,34]. By aggregating many trees, causal forests generate stable estimates of individual treatment effects[34]. We then performed an omnibus test using the differential forest prediction coefficient, a significant p-value of which indicates effect heterogeneity is present[35].

In the RATE approach, the dataset and nuisance functions are divided into equally sized training and test datasets[35,36]. The training data is then passed to two causal forests: one that serves as a

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CATE estimator and a second that serves as a RATE estimator. The held-out data is then passed to the trained CATE estimator to generate treatment effects. Finally, the RATE estimator and the treatment effects are used to generate a doubly robust RATE estimate, calculated as the weighted sum of the area under the targeting operator characteristic (AUTOC) curve[35,36]. A 95% CI of the AUTOC that does not overlap with zero indicates that effect heterogeneity is present[35].

For both approaches, we grew 2500 trees with 10 sub-trees to generate estimates and standard errors. We tuned forest hyperparameters, including minimum node size, sample fractions, total number of variables considered for each split, honesty parameters, alpha, and imbalance penalties, using cross-validation and out-of-bag (OOB) errors[32,35]. Covariables included in each model are provided in **Table S3**. We reviewed GLM diagnostics to ensure model assumptions were met. We also reviewed the distribution of the exposure propensity scores for sufficient overlap to evaluate positivity violations.

Finally, as an exploratory analysis, we generated the ATE and conditional average treatment effects (CATEs) in pre-specified subpopulations as risk differences (RD). After following the ATE approach outlined above, the individual treatment effect estimates generated by the causal forest were combined via a doubly robust augmented inverse probability weighting (AIPW) estimator to obtain population-level ATEs and subgroup-specific CATEs. We reported both unweighted and overlap weighted RDs. Overlap weighting estimates is recommended when exposure propensities are close to 0 or 1[39].

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Given the exploratory nature of our study, we took numerous measures to control the type 1 error rate. First, we prespecified four subpopulations for subgroup analysis: race, sex at birth, US birth status, and sexual orientation, yielding 16 possible subpopulations. To ensure stability of estimates for binary outcomes, we further restricted analyses to subgroups with at least 200 incident hypertension events during follow up[40]. This resulted in 10 eligible subpopulations for CATE estimation.

We determined statistical significance based on 95% confidence intervals. For descriptive measures, we reported means, standard deviations (SD), counts, and percentages. All analyses were performed in R version 4.4.0.

Sensitivity Analysis

We conducted three sensitivity analyses. First, to assess whether differing lengths of observation among participants impacted our findings, we restricted the follow up period to 6 months. Second, given that the study surveys can be completed at different times, we evaluated our assumption that loneliness and social support are not time varying by restricting our population to participants who completed the loneliness and social support measures within 6 months of the index date. Third, given that dichotomization of exposures in our main analysis limits interpretation to those in the extreme of these measures, we treated social support and loneliness as continuous exposures and generated RDs as average partial effects (APE) and conditional average partial effects (CAPE). To simplify comparison between the two exposures, we reversed the social support scale (a greater score indicates less social support) and standardized both variables. We then followed the same approach as the ATE analysis, except we generated the

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exposure propensities using generalized propensity scores (GPS)[41]. In this approach, we fit an ordinary least squares model regressing continuous loneliness and social support on the baseline covariables, using the resulting coefficients and residual variance to generate a GPS density distribution. We then extracted each participant's GPS from this distribution based on their observed value of exposure[41].

Results

Study Population and Missing Data

Of 304,754 participants aged 50 years or older consenting to join the *All of Us* Research Program within the study period, a total of 43,182 participants were eligible for the study. Of these participants, 24,720 had complete data across all study variables (see **Figure S1** for a flow diagram). However, the fraction of missing information by variable was low (**Table S4**). BMI had the most missingness, with 11.1% (n=4,805) of participants having missing data. Participants with any missing data were similar to those with complete data, with the largest absolute differences observed on private insurance (34.7% and 45.1%, respectively) and white race alone (78.6% and 83.2%, respectively). The missingness GLM indicated no violations of model assumptions, and we noted no extreme weights. The maximum and minimum stabilized IP weights were 2.28 and 0.74, respectively.

Table 1 summarizes study population characteristics overall and by levels of perceived social support and loneliness. In the overall study population, the most common educational attainment levels were advanced degree (38.9%, n=9,605) and college graduate (29.7%, n=7,349). The most common annual incomes were $100-150,000 per year (20.2%, n=5,004) and $50-75,000 per year

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(15.5%, n=3,827). By race, 1.8% (n=436) were Asian alone, 5.6% (n=1,377) were Black alone, 4.3% (n=1,052) Hispanic alone, 0.3% (n=83) were MENA alone, 3.9% (n=968) were multiple races, 1.0% (n=241) were other race alone, and 83.2% (n=20,563) were white alone. A total of 65.1% (n=16,081) of the population was female. Although straight was the most common sexual orientation (93.5%, n=23,109), 4.0% (n=982) identified as Gay or Lesbian and 1.9% (n=471) identified as bisexual.

The average age and BMI were 63.9 years (SD=8.4) and 28.2 kg/m² (SD=6.4), respectively. The majority of participants reported a family history of ASCVD or cardiometabolic risk factors. A total of 6.7% (n=1,644) had current unipolar depression. Although the percent of those with alcohol misuse was high (36.4%, n=9,004), similar findings were reported in another study using the study questionnaire[42]. A total of 5.3% (n=1,315) and 4.3% (n=1,059) reported smoking or nicotine use, respectively.

The 90th percentile of loneliness was 14, and the 10th percentile of social support was 2.38. A total of 9.7% (n=2,410) and 10.6% (n=2,637) of participants reported low social support or loneliness, respectively. Compared to those not lonely or with normal/high social support, these participants tended to have a higher BMI, lower levels of income and education, higher rates of unipolar depression, were more often current smokers, and had lower rates of alcohol misuse. During a mean and median of 2.8 and 2.6 years of follow up, respectively, the study outcome occurred in 25.7% (n=6,348) of participants.

Omnibus Tests, ATE, and CATE

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The GLMs used to generate outcome and exposure probabilities showed no violations of model assumptions. Estimated exposure propensities for both loneliness and social support demonstrated good overlap between exposed and unexposed, with no evidence of positivity violations. After tuning, the final hyperparameters of both GRFs were 50% sample fraction, 27 variables considered at each split, honesty fraction=50%, alpha=0.05, imbalance penalty=0, and minimum node size of 5.

For loneliness, both omnibus tests indicated that effect heterogeneity was not present (differential forest prediction coefficient -0.42, p-value<0.90; AUTOC -0.02, 95% CI -0.04 to 0.004). The ATEs and CATEs also agreed with this (**Table 2**): loneliness was not significantly associated with incident hypertension (RD: -0.004, 95% CI -0.02 to 0.016; overlap weighted RD: -0.002, 95% CI –0.02 to 0.016) and we did not detect any statistically significant RD CATEs by subpopulation.

However, for social support, the differential forest prediction coefficient indicated effect heterogeneity was present (0.56, p-value<0.02) while the RATE did not (AUTOC 0.01, 95% CI -0.01 to 0.04). It should be noted that non-significant AUTOC may indicate that the algorithm was unable to predict heterogeneity effectively, rather than it being absent. Although social support was not statistically significantly associated with incident hypertension in the overall population (RD: 0.004, 95% CI -0.016 to 0.025; weighted RD: -0.0005, 95% CI -0.019 to 0.018), we did detect effect heterogeneity in subpopulations (**Table 2)**. Participants identifying as Gay or Lesbian with low social support had a statistically significant increased risk of hypertension compared to Gay or Lesbian participants with high social support (RD: 0.108, 95% CI 0.011 to

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0.205; overlap weighted RD: 0.11, 95% CI 0.008 to 0.211). Further, male participants with low social support also exhibited an elevated risk of incident hypertension compared to males with high social support (RD: 0.038, 95% CI 0.002 to 0.075), although this finding was limited to the non-overlap weighted analysis.

Sensitivity Analysis Results

Our sensitivity analyses limiting follow-up to the first 6 months and restricting to individuals who completed the loneliness and social support questionnaires within 6 months of the index date agreed with our primary findings (**Table S5** and **Table S6**, respectively). This includes non-significant RDs in the overall population and Gay or Lesbian and male participants with low social support exhibiting elevated risk of incident hypertension, although these did not reach statistical significance. The third sensitivity analysis treating loneliness and social support as continuous exposures also agreed with the main findings, with no marginal effects but statistically significant elevated risk of incident hypertension in male and Gay or Lesbian participants (**Table S7**).

Discussion

After controlling for numerous lifestyle, socioeconomic, and clinical factors, we found that loneliness and low social support were not associated with a statistically significant increased risk of incident hypertension in a diverse, normotensive older population. However, variability in effect size was notable and associations were statistically significant in some subpopulations. Our findings contribute novel information on the impact of loneliness and social support on the risk of hypertension in older adults.

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The National Academies of Sciences, Engineering, and Medicine consensus study on social isolation in older adults summarized the numerous impacts of social isolation, including on cardiometabolic risk factors and CVD[4]. Following the report, a statement from the American Heart Association summarized the numerous adverse impacts of social isolation on cardiovascular and brain health[5]. However, the statement also reported that consistency in evidence varies, as social isolation is well-established to be an important risk factor in those with existing CVD yet plays an unclear role in first-time cardiovascular events[5]. Consistent with this, the literature on the impact of social isolation on blood pressure in normotensive populations is mixed. A meta-analysis of the association between ambulatory blood pressure and social support in mostly healthy populations did not support an association[43]. A systematic review of cross-sectional studies assessing the association between social support and nocturnal blood pressure dipping in healthy participants suggested a relationship but noted that more research is needed due to heterogeneity in findings[43,44].

These mixed findings may be driven in part by individual variation in psychological responses to social isolation. Emotional coping and regulation are suggested to be important determinants of blood pressure regulation[45,46]. A study of normotensive young adults found that differing emotional regulation strategies influenced blood pressure variability, an important predictor of cardiovascular outcomes[47-49]. Another study using fMRI brain imaging found that blood pressure varied with emotion-related brain activity[50]. In this vein, a large, prospective study of the U.K. Biobank found that although loneliness was predictive of incident hypertension, a subsequent Mendelian Randomization analysis did not support a causal relationship[51]. This led the authors to

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posit that loneliness itself is not a causal driver but rather is a surrogate variable[51]. Taken together, the effects of loneness and social support on cardiovascular outcomes may be moderated by an individual's psychological response. That said, given that indicators of emotional regulation are not available in *All of Us*, we are unable to explore this. Future studies should disentangle whether emotional regulation and psychological processes moderate the relationship between social isolation and cardiovascular outcomes.

However, the purported role of emotional regulation should be interpreted in the context of broader social forces when considering the elevated risk observed in select socio-demographic populations in our study. We found Gay or Lesbian participants and participants of male sex experienced a significant increase in the risk of incident hypertension associated with low social support, despite there being no apparent marginal effects. The relationship between sex, isolation, and adverse outcomes is highly complex, driven by cultural and structural forces[52]. Hegemonic masculinity, defined as the normative or idealized way of being a man, is theorized to be detrimental to men's emotional and physical health[53,54]. Additionally, because of longstanding bias, stigma, and discrimination, Gay or Lesbian populations may experience greater impacts when socially isolated, as strong social networks are important to mental and physical well-being of these communities[55-57]. However, given the exploratory and observational nature of our study, these findings should be interpreted cautiously.

Complicating the relationship between social isolation and hypertension is that the effect size may be small. Indeed, a meta-analysis and systematic review of social support and blood pressure reported small effects sizes with continuous blood pressure[43,44]. Consistent with this, a

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cross-sectional study of the association between loneliness and hypertension reported an OR of 1.31 (95% CI 1.04-1.66)[58]. A longitudinal study of high baseline social support and incident hypertension reported an incident rate ratio of 0.64 (95% CI 0.41-0.97), while a longitudinal study of loneliness found a 1.40 OR (95% CI 1.09-1.79) of incident hypertension[59,60]. A key methodological strength of our study is the application of causal forests, a powerful machine learning approach tailored to estimate heterogeneous treatment effects in observational data[33,34]. Unlike conventional regression models, causal forests are designed to detect subgroup-specific variation in effects while maintaining valid inference[33]. Thus, our study's estimation of effect heterogeneity supports interventions in subpopulations that experience clinically meaningful risks associated with social isolation.

Limitations

Our study has limitations. Measures of loneliness and social support vary by study[43,44,51,58-61]. Although we used psychometrically robust measures of these concepts, use of differing measures of loneliness and social support may increase variability of effect estimates[17,18]. Because study surveys are only collected at baseline, we could not explore time-varying effects of social support and loneliness or mediation by health behaviors. Further, as participants complete study surveys at their own pace, this requires the assumption that loneliness and social support do not change over time. While we rigorously accounted for missing data, IP weighting is inefficient and may have limited our ability to detect statistically significant effects. Even though the *All of Us* Research Program endeavors to enroll diverse populations often underrepresented in clinical trials, our findings may have limited external validity. Further, the loss of participants due to missing data, albeit adjusted for through IP weighting, may nevertheless result in residual

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selection bias. Although the exploratory nature of effect heterogeneity could inflate the type 1 error rate, we reduced this risk by limiting the number of subpopulations included in the analysis.

Finally, it is unclear whether health behaviors are mediators or confounders in the relationship between social isolation and adverse health outcomes[4,5]. We treated smoking, nicotine use, and alcohol misuse as confounders; thus, our estimates quantify the direct effect of low social support and loneliness on risk of incident hypertension. However, the relationship between these behaviors and social isolation is likely bidirectional[4,5]. If these health behaviors are indeed mediators between social isolation and incident hypertension, the total effect of social isolation may be larger. Studies using time-varying methods should determine the sequence of these variables and conduct effect decompositions to inform public health program design[4,5].

Conclusion

In our study of older adults, we found that loneliness and low social support were not statistically significantly associated with an increased risk of incident hypertension. However, we detected significant effect heterogeneity among male and Gay or Lesbian participants. Future research should explore the role of emotional responses to social isolation and elucidate the sequence of health behaviors and social isolation to better prioritize limited public health resources.

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Disclosure Statement

There was no funding for this study. The authors have no conflicts of interest to declare.

Data Availability Statement

The data underlying this article were provided by the National Institutes of Health by permission.

Data can be accessed by requesting permission at https://allofus.nih.gov/.

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Table 1. Socio-Demographic Characteristics of Normotensive, Older Adults Overall and Stratified by Loneliness and Social Support, May 2017-April 2023.

		Social Support		Loneliness	
Variable	Total Population (n=24,720)	High (Unexposed) (n=22,310)	Low (Exposed) (n=2,410)	Not Lonely (Unexposed) (n=22,083)	Lonely (Exposed) (n=2,637)
Age (Years)	63.9 (8.4)	63.9 (8.3)	63.7 (8.5)	64.2 (8.4)	61.8 (8.1)
BMI (kg/m²)	28.2 (6.4)	28.0 (6.3)	29.2 (7.0)	28.0 (6.2)	29.7 (7.8)
Education					
Never to 11 Years	346 (1.4%)	295 (1.3%)	51 (2.1%)	289 (1.3%)	57 (2.2%)
12 Years or GED	1859 (7.5%)	1617 (7.2%)	242 (10.0%)	1566 (7.1%)	293 (11.1%)
College 1- 3 Years	5561 (22.5%)	4827 (21.6%)	734 (30.5%)	4772 (21.6%)	789 (29.9%)
College Graduate	7349 (29.7%)	6677 (29.9%)	672 (27.9%)	6630 (30.0%)	719 (27.3%)
Advanced Degree	9605 (38.9%)	8894 (39.9%)	711 (29.5%)	8826 (40.0%)	779 (29.5%)
Alcohol Misuse	9004 (36.4%)	8317 (37.3%)	687 (28.5%)	8261 (37.4%)	743 (28.2%)
Family History					
ASCVD	16517 (66.8%)	15059 (67.5%)	1458 (60.5%)	14778 (66.9%)	1739 (65.9%)
CM Risk Factors	17616 (71.3%)	16013 (71.8%)	1603 (66.5%)	15730 (71.2%)	1886 (71.5%)
Hypertension	6348 (25.7%)	5616 (25.2%)	732 (30.4%)	5546 (25.1%)	802 (30.4%)
Non-USA Born	2101 (8.5%)	1819 (8.2%)	282 (11.7%)	1881 (8.5%)	220 (8.3%)
Income (Per Year)					
< 10k	826 (3.3%)	611 (2.7%)	215 (8.9%)	600 (2.7%)	226 (8.6%)
10k to < 25k	1797 (7.3%)	1381 (6.2%)	416 (17.3%)	1339 (6.1%)	458 (17.4%)
25k to <35k	1365 (5.5%)	1128 (5.1%)	237 (9.8%)	1108 (5.0%)	257 (9.7%)
35k to <50k	2090 (8.5%)	1794 (8.0%)	296 (12.3%)	1774 (8.0%)	316 (12.0%)
50k to <75k	3827 (15.5%)	3434 (15.4%)	393 (16.3%)	3392 (15.4%)	435 (16.5%)
75k to <100k	3615 (14.6%)	3340 (15.0%)	275 (11.4%)	3341 (15.1%)	274 (10.4%)
100k to < 150k	5004 (20.2%)	4688 (21.0%)	316 (13.1%)	4650 (21.1%)	354 (13.4%)
150k to <200k	2520 (10.2%)	2414 (10.8%)	106 (4.4%)	2379 (10.8%)	141 (5.3%)
200k or More	3676 (14.9%)	3520 (15.8%)	156 (6.5%)	3500 (15.8%)	176 (6.7%)
Health Insurance					
Dual	573 (2.3%)	420 (1.9%)	153 (6.3%)	378 (1.7%)	195 (7.4%)
Other Government	445 (1.8%)	398 (1.8%)	47 (2.0%)	379 (1.7%)	66 (2.5%)
Medicaid	1330 (5.4%)	1048 (4.7%)	282 (11.7%)	988 (4.5%)	342 (13.0%)
Medicare	10395 (42.1%)	9391 (42.1%)	1004 (41.7%)	9497 (43.0%)	898 (34.1%)
Other	450 (1.8%)	392 (1.8%)	58 (2.4%)	397 (1.8%)	53 (2.0%)
Private	11139 (45.1%)	10341 (46.4%)	798 (33.1%)	10130 (45.9%)	1009 (38.3%)
Uninsured	388 (1.6%)	320 (1.4%)	68 (2.8%)	314 (1.4%)	74 (2.8%)
Depression	1644 (6.7%)	1426 (6.4%)	218 (9.0%)	1317 (6.0%)	327 (12.4%)
Nicotine Use	1059 (4.3%)	910 (4.1%)	149 (6.2%)	878 (4.0%)	181 (6.9%)
Race					
Asian Alone	436 (1.8%)	381 (1.7%)	55 (2.3%)	397 (1.8%)	39 (1.5%)
Black Alone	1377 (5.6%)	1162 (5.2%)	215 (8.9%)	1171 (5.3%)	206 (7.8%)
Hispanic Alone	1052 (4.3%)	902 (4.0%)	150 (6.2%)	959 (4.3%)	93 (3.5%)
MENA Alone	83 (0.3%)	-	> 20	-	> 20
Multiple Races	968 (3.9%)	837 (3.8%)	131 (5.4%)	817 (3.7%)	151 (5.7%)
Other Race	241 (1.0%)	209 (0.9%)	32 (1.3%)	203 (0.9%)	38 (1.4%)

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White Alone	20563 (83.2%)	18747 (84.0%)	1816 (75.4%)	18465 (83.6%)	2098 (79.6%)
Female Sex	16081 (65.1%)	14611 (65.5%)	1470 (61.0%)	14337 (64.9%)	1744 (66.1%)
Sexual Orientation					
Asexual	24 (0.1%)	-	> 20	-	> 20
Bisexual	471 (1.9%)	412 (1.8%)	59 (2.4%)	375 (1.7%)	96 (3.6%)
Gay or Lesbian	982 (4.0%)	868 (3.9%)	114 (4.7%)	818 (3.7%)	164 (6.2%)
Not Sure	83 (0.3%)	-	> 20	-	> 20
Queer or Other	51 (0.2%)	-	> 20	-	> 20
Straight	23109 (93.5%)	20898 (93.7%)	2211 (91.7%)	20764 (94.0%)	2345 (88.9%)
Smoker	1315 (5.3%)	1070 (4.8%)	245 (10.2%)	1065 (4.8%)	250 (9.5%)

Abbreviations: ASCVD indicates atherosclerotic cardiovascular disease; CM indicates cardiometabolic; GED indicates general educational development; MENA indicates Middle Eastern or North African.

[a] A cell containing "> 20" indicates a suppressed cell due to *All of Us* privacy requirements.

[b] A cell containing "-" indicates complimentary suppression to prohibit back-calculation of the suppressed value.

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Table 2. Average Treatment Effects and Conditional Average Treatment Effects of Social Support and Loneliness on Risk of Incident Hypertension Among Normotensive, Older Adults, May 2017-April 2023.

	Loneliness		Social Support	
Population	RD (95% CI)	Overlap-Weighted RD (95% CI)	RD (95% CI)	Overlap-Weighted RD (95% CI)
Overall	-0.004 (-0.025, 0.016)	-0.002 (-0.02, 0.016)	0.004 (-0.016, 0.025)	0 (-0.019, 0.018)
Non-USA Born	-0.039 (-0.11, 0.03)	-0.019 (-0.077, 0.039)	0.013 (-0.048, 0.075)	0.001 (-0.053, 0.056)
Race				
Black, NH	0.031 (-0.055, 0.119)	0.01 (-0.056, 0.076)	0.056 (-0.033,0.145)	0.011 (-0.054, 0.077)
Hispanic	-0.031 (-0.14, 0.076)	0.008 (-0.089, 0.105)	0 (-0.088, 0.087)	-0.012 (-0.089, 0.065)
Multiple Races, NH	-0.006 (-0.093, 0.081)	0.025 (-0.055, 0.105)	0.034 (-0.054, 0.123)	0.016 (-0.07, 0.103)
White, NH	-0.006 (-0.029, 0.017)	-0.008 (-0.028, 0.012)	0 (-0.022, 0.023)	-0.002 (-0.024, 0.019)
Sexual Orientation				
Bisexual	0.053 (-0.073, 0.18)	0.055 (-0.046, 0.158)	-0.09 (-0.208, 0.027)	-0.027 (-0.155, 0.099)
Gay or Lesbian	0.068 (-0.014, 0.15)	0.078 (-0.006, 0.163)	0.108 [a] (0.011, 0.205)	0.11 [a] (0.008, 0.211)
Straight	-0.007 (-0.029, 0.014)	-0.007 (-0.027, 0.011)	0.003 (-0.018, 0.024)	-0.003 (-0.023, 0.016)
Sex at Birth				
Male	-0.021 (-0.059, 0.015)	-0.004 (-0.036, 0.028)	0.038 [a] (0.002, 0.075)	0.027 (-0.005, 0.059)
Female	0.004 (-0.02, 0.03)	-0.001 (-0.023, 0.021)	-0.014 (-0.039, 0.011)	-0.017 (-0.041, 0.006)

Abbreviations: NH indicates non-Hispanic; RD indicates risk difference.

[a] Superscript "a" indicates a statistically significant result.

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Figure Titles and Legends

Figure 1. Study Directed Acyclic Graph.

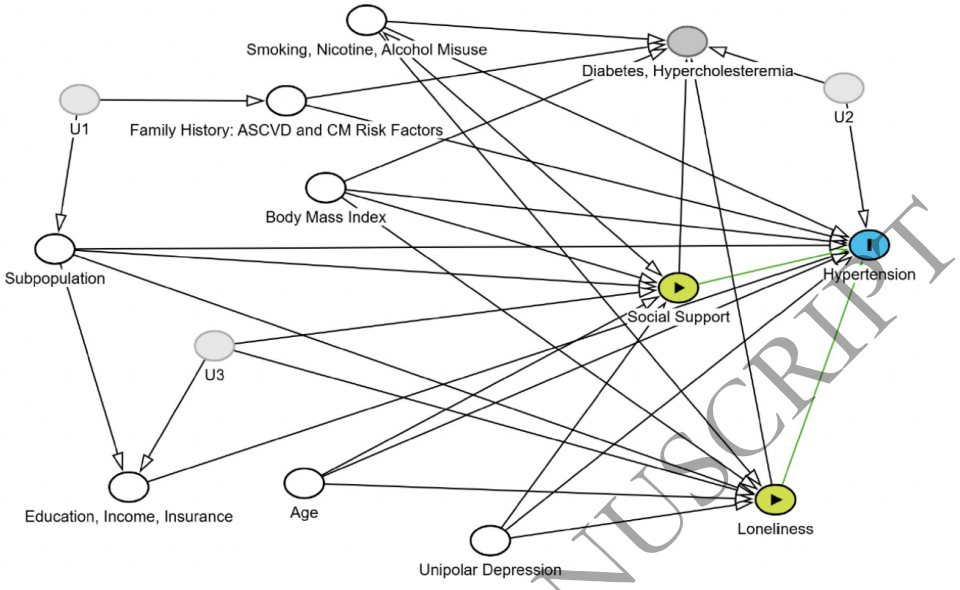
Abbreviations: ASCVD = Atherosclerotic cardiovascular disease; CM = cardiometabolic; U1,

U2, U3 = unmeasured variable.

Alt Text: A directed acyclic graph depicting the causal relationships between the study exposures loneliness and social support and the study outcome hypertension.

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