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Network analysis of adverse childhood experiences and cardiovascular diseases

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ABSTRACT

Significance: The findings to date indicate that adverse childhood experiences (ACEs) increase the risk of cardiovascular disease (CVD) in later life. We demonstrate how network analysis, a statistical method that estimates complex patterns of associations between variables, can be used to model ACEs and CVD. The main goal is to explore the differential impacts of ACE components on CVD outcomes, conditioned on other ACEs and important covariates using network analysis. We also sought to determine which ACEs are most synergistically correlated and subsequently cluster together to affect CVD risk.

Methods: Our analysis was based on cross-sectional data from the 2020 Behavioral Risk Factor Surveillance System, which included 31,242 adults aged 55 or older (54.6% women, 79.8% whites, mean age of 68.7 ± 7.85 years). CVD outcomes included angina/coronary heart disease (CHD) and stroke prevalence. Mixed graphical models were estimated using the R-package *mgm,* including all variables simultaneously to elucidate their one-to-one inter-relationships. Next, we conducted Walktrap cluster detection on the estimated networks using the R-package *igraph.* All analyses were stratified by gender to examine group differences.

Results: In the network for men, the variable "household incarceration" was most strongly associated with stroke. For women, the strongest connection was between "physical abuse" and stroke, followed by "sexual abuse" and angina/CHD. For men, angina/CHD and stroke were clustered with several CVD risk factors, including depressive disorder, diabetes, obesity, physical activity, and smoking, and further clustered with components of household dysfunction (household substance abuse, household incarceration, and parental separation/divorce). No clusters emerged for women.

Conclusions: Specific ACEs associated with CVDs across gender may be focal points for targeted interventions. Additionally, findings from the clustering method (especially for men) may provide researchers with valuable information on potential mechanisms linking ACEs with cardiovascular health, in which household dysfunction plays a critical role.

1. Introduction

Adverse childhood experiences (ACEs) are among the most intensive stressors to negatively impact later-life health and well-being (Centers for Disease Control and Prevention, 2022). ACEs include emotional, physical, and sexual forms of abuse, as well as household dysfunction factors, such as parental substance abuse, mental illness, and violence. Studies have found that higher exposure to ACEs is associated with an increased risk of adopting risk-taking behaviors and having health issues, disabilities, or premature death (Hughes et al., 2017).

The study by Felitti et al. (1998) was the first to propose that ACEs lead to the development of chronic conditions in late adulthood, including cardiovascular diseases (CVDs). Since then, other studies have replicated this finding. One systematic review with meta-analysis showed that cumulative ACEs increased the risk of myocardial infarction in adulthood after controlling for CVDs and psychosocial factors (Jacquet-Smailovic et al., 2021). In a meta-analysis by Hughes et al. (2017), individuals with four or more ACEs had higher risks of developing CVD when compared to individuals with no ACEs. One meta-analysis of 23 studies reported that a reduction of approximately

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20.0% of CVD cases would occur if ACEs were to end in North America (Bellis et al., 2019).

To date, commonly applied statistical approaches examining the effects of ACEs on CVD are often referred to as a "cumulative approach," where individual experiences are added to generate an unweighted, composite ACE score (i.e., an index of cumulative risk). Although informative, the cumulative approach implicitly assumes that all ACEs are equally influential and interchangeable in their impact. Accordingly, which type of ACEs have the most impact is unclear. To account for such methodological challenges, some researchers favored a "selective approach," studying only one or two ACEs, or a specific category of adversity (e.g., household dysfunction) and exploring the impacts on CVD (Dong et al., 2004; Scott et al., 2011). However, this approach could miss the apparent effects of co-occurring adverse experiences. When co-occurrence is not considered, researchers might be biased towards the implicit assumption that the effect of one type of ACE will not vary in relation to the presence of other ACEs. Recent studies of mental disorders adopted a "dimensional approach," such as latent class analysis or factor analysis to account for ACEs (Brodbeck et al., 2018; Westermair et al., 2018). However, this approach cannot fully capture the complex nature of ACEs either. In latent variable models, unobserved latent variables account for the correlations between ACEs, referring to discrete latent (in latent class analysis) or continuous latent variables (in factor analysis). After imposing a latent variable, no direct effects between ACEs are assumed to remain (de Vries et al., 2022).

Network analysis explores complex patterns of relationships between variables (i.e., between variables when conditioned on all other network variables; Borsboom & Cramer, 2013). Specifically, it uses a graphical statistical technique enabling easy observation of the distance and strength of correlations between variables, making it superior to traditional analytics (Borsboom & Cramer, 2013). In the study context, network analysis could clarify the direct (and indirect) associations between ACEs (given its capability to model conditional associations between ACEs) or between ACEs and CVD outcomes in a single mathematical model. It has been previously used to identify pathways between different types of ACEs and personality dimensions (Schouw et al., 2020), clusters of psychotic symptoms (Isvoranu et al., 2016), and mental disorders (Breuer et al., 2020) in adulthood. However, no studies have assessed the interactions of different types of ACEs and CVDs integratively in later life through network analysis. We hope to address that here.

Herein, we also argue that considering the role of gender on ACE's impact on CVD is critical. Although gender-related differences in this field have been under-examined (Basu et al., 2017), the general trend from earlier studies suggests that women are more vulnerable to the detrimental effects of ACEs on CVD outcomes compared with men, and stronger associations between ACE and CVD were generally found in women (Batten et al., 2004; Hosang et al., 2013; Korkeila et al., 2010) and were stronger for early-onset CVD (Soares et al., 2020). Yet, conclusions from these previous studies are based on composite ACE scores, and this type of cumulative approach is particularly problematic given that gender differences exist in the types of ACEs that individuals experience (Jones et al., 2022). Although some research has evaluated the effects of different ACE dimensions or categories on CVD outcomes, respectively, for men and women (Fuller-Thomson et al., 2012; Goodwin & Stein, 2004; Hosang et al., 2013; Soares et al., 2020), these studies adopted a selective approach, which again, does not account for the effects of co-occurring adverse experiences. Using network analysis to gain insights into which specific adversities are associated with others, and conjunctively with CVD outcomes of interest within one network by gender may produce more comprehensive conclusions regarding the gender discrepancy.

1.1. Study aims

In summary, this study investigates the relationships between ACEs and CVDs through network analysis. The main focus is to explore the differential impacts of ACE components on CVD outcomes in later life, conditioned on other ACEs and important covariates **(Aim 1)**. In addition, because ACEs are complex and individual ACEs dynamically co-occur, integrated analyses should be favored over one-to-one associations. Thus, the study further explores which ACEs are most synergistically related and subsequently appear to cluster together to affect CVD risk **(Aim 2)**. Given the prior evidence on gender differences in CVD outcomes, analyses were stratified by gender.

In the current study, the age of individuals was restricted to 55 years or older as the "young-old" (first developmental epoch in later life) begins at age 55, consistent with the age cut in the literature (Jeuring et al., 2019; Klokgieters et al., 2019; Suanet et al., 2009). This cut-off age has also been utilized in life-span research to examine the roles of adversity and trauma in populations' later health (Yang & Hedeker, 2020), including cardiovascular conditions (Jacquet-Smailovic et al., 2021). Furthermore, one study demonstrated that age screening using a cut-off of 55 years can detect 86.0% of all first CVD events arising in the population, which makes this cut-off a meaningful value for the current study's participants (Wald et al., 2011).

2. Methods

2.1. Study design and sample population

The current study follows a cross-sectional design using data from the 2020 Behavioral Risk Factor Surveillance System (BRFSS) sponsored by the Centers for Disease Control and Prevention. The BRFSS is a nationwide, state-based, annual telephone survey targeting a sample of non-institutionalized adults (aged 18 years or older) within the fifty United States (U.S.), the District of Columbia, and U.S. territories. The sample was selected via random-digit-dialing methods. A state agency reached potential participants at their home telephone numbers, and only one person per household was interviewed. The survey mainly collects information on health-related risk behaviors, chronic health conditions, and preventive health practices. Full descriptions of these methods are available at www.cdc.gov/brfss.

A total of 217,920 adults ages 55 and older were interviewed during the 2020 BRFSS. Those who had not replied to the ACE module or CVD outcome questions were excluded ($n = 152{,}004$). In addition, only those who identified themselves as cisgender were selected (answered "no" to the question: Do you consider yourself to be transgender?) ($n = 37{,}110$) as evidence, including systematic reviews and a meta-analysis, suggests that the influence and outcome of ACEs in transgender people or those with non-conforming gender identities are different (Friedman et al., 2011; Rothman et al., 2011; Wilsnack et al., 2012). Finally, entries with missing values within variables of interest (i.e., covariates) ($n = 5{,}868$) were excluded (listwise deletion) from the data set since network analysis cannot handle missing values and these entries were completely random (p-value = .533; Little et al., 2022). The aforementioned processes produced a final sample size of 31,242 individuals (54.6% women, 79.8% whites, mean age of 68.7 ± 7.85 years).

The BFRSS data are weighted to reflect the participant's probability of selection as well as the age-, gender-, and race-specific population of the state. However, in the present study, weights could not be assigned to the data during statistical testing as the appropriate role of survey weights in network analysis methodology is not yet known.

2.2. Measurements

2.2.1. Cardiovascular disease (CVD) outcomes

The following self-reported CVD outcomes were assessed for this study: angina/coronary heart disease (CHD) and stroke. Individuals were asked if they had ever been diagnosed with these conditions by a healthcare professional. Those who responded positively to the question were identified as having that condition.

2.2.2. Adverse childhood experiences (ACEs)

The BRFSS ACE module includes eleven questions that examine eight categories of adverse experiences during their childhood (prior to 18 years of age): household mental illness (one item; "living with depressed or mentally ill"), household substance abuse (two items; "living with problem drinker or alcoholic" and "living with medications/drugs abuser"), household incarceration (one item; "living with anyone who served time in prison"), parental separation/divorce (one item), witnessing household violence (one item; "parents punch or beat each other"), physical abuse (one item; "parents beat or physically hurt you"), emotional abuse (one item; "parents beat or physically hurt you"), and sexual abuse (three items; "adult touch you sexually", "adult try to make you touch them sexually", and "adult force you to have sex"). The response options for the first five items are coded as "yes" or "no" based upon whether the individual reported experiencing the adverse events for that ACE in any capacity, while the response options for the rest are coded for the frequency of experience as "never," once," and "more than once."

2.2.3. CVD risk factors (covariates)

Using the previous review by Jacquet-Smailovic et al. (2021), covariates were selected to include variables that mediate mechanisms between ACEs and CVD outcomes. These are depressive disorder (yes/no), diabetes (yes/no), obesity (yes/no), physical activity (yes/no), heavy alcohol consumption (yes/no), and smoking status (current smoker, every day; current smoker, some days; former smoker; or never smoked). More details on how the response options for each covariate were coded can be found in the Supplemental Table S1.

2.3. Statistical analysis

All analyses were conducted separately by gender with the statistical programming language R and its available packages. R codebase is shared in Supplemental Table S2. Descriptive analyses were initially performed to examine baseline characteristics. For Aim 1, a mixed graphical model implemented in the R-package *mgm* (Haslbeck & Waldorp, 2020) estimated the network structure including all variables (i.e., eleven items of ACEs, covariates, and CVD outcomes). For Aim 2, a Walktrap cluster detection algorithm implemented in the R-package *igraph* was utilized for network clustering.

2.3.1. Network estimation (Aim 1)

The *mgm* method calculates associations between mixed variables (i.e., categorical, count, or continuous variables) that can be illustrated in undirected graphical models, where variables of interest are represented as "nodes" and conditional (partial) correlations between nodes are represented as "edges" within the network. Since ACEs are often binary, the Ising model (Finnemann et al., 2021) is often the most appropriate. However, mixed graphical models are suitable for our data because the frequency of ACEs is defined using a three-level response scale.

A statistical penalty, namely the least absolute shrinkage and selection operator (LASSO; Tibshirani, 1996), was applied to the model estimation to limit false positive findings. This is done by shrinking spurious or non-significant edges to zero, thus removing them from the network. The shrinkage was performed using an Extended Bayesian Information Criterion (EBIC; Foygel & Drton, 2010). Following the recommendation (Epskamp & Fried, 2018), the EBIC tuning hyperparameter γ was set to 0.25 for a more conservative network estimation. The k parameter was set to 2 to indicate pairwise associations. In addition, node predictability was estimated to quantify the proportion of node variance that is explained by all other nodes in the model using *predict()* function in *mgm*. Here we specified the proportion of correct classification (or accuracy, "CC") for categorical variables. Estimates are provided on a scale of 0 to 1, in which 1 reflects full predictability.

The network models were visualized using the Fruchterman–Reingold algorithm ("spring" layout in the R-package *qgraph*) (Epskamp et al., 2012). In this layout, highly correlated nodes are placed closer together, such that strongly correlated nodes are located near the center of the network and weakly correlated nodes are pushed to the periphery. Grey edges represent pairwise interactions wherein no sign is specified (i.e., interactions including categorical variables). Thicker (thinner) lines indicate strong (weak) correlations. Predictability was depicted as the filled portions of the circle around the nodes.

Lastly, the *resample*() function in *mgm* was used to conduct a bootstrap analysis of network edge stability. We applied 100 bootstrapped samples. The *plotRes*() function in *mgm* was used to plot the resulting sampling distribution of all edges and the proportion of estimates whose absolute values were larger than zero. For instance, stability of 90.0% indicates that the edge was found to be larger than zero in 90 of 100 bootstrap runs.

2.3.2. Network clusters (Aim 2)

For Aim 2, the Walktrap algorithm was employed to test whether the certain nodes cohere (i.e., cluster) as subnetworks in the model. The Walktrap algorithm uses the random walk principle: random walks throughout the network tend to detect subnetworks (areas of the network with high edge density, often referred to "communities") as there are only few links that lead outside a given community (Pons & Latapy, 2005). The modularity ratio was used to evaluate the communities' goodness-of-fit by comparing the density of edges within a community to the density of edges outside a community. Modularity ratio ranges from 0 to 1, with higher values signifying a higher number of within-community edges than what's expected at random and indicating a strong community structure. Conventionally, modularity values between 0.3 and 0.7 indicate the presence of sub-clusters in the network (Newman & Girvan, 2004). The Walktrap algorithm is one of the most reliable methods of community detection. Simulations demonstrated that the Walktrap algorithm, when used with the LASSO model, generated more accurate and less biased findings than other community detection methods (Christensen et al., 2020).

3. Results

Table 1 presents the background characteristics of the participants by gender. The mean ages of the men and women in this study were 68.1 years (standard deviation [SD] = 7.75) and 69.1 years (SD = 7.90), respectively. Table 2 summarizes the predictability for CVD outcomes, CVD-ACEs edge weights, and stability of nonzero edges for men and women each.

In the network for men (Fig. 1), when controlling for interrelatedness, the largest edge weight between the constructs of ACEs and the CVD outcomes was between "household incarceration" and stroke (edge weight = 0.158). Stability analyses indicated robust associations between this node (nonzero in 86.0% of bootstrapped analyses). In addition, "physical abuse" had some correlation with angina/CHD (edge weight = 0.016) and stroke (edge weight = 0.046). The "physical abuse"–angina/CHD edge and "physical abuse"–stroke edge were nonzero in 57.0% and 48.0% of the bootstrap analyses, respectively. The angina/CHD predictability was 87.2%, as indicated by the black pie chart around the node. The stroke predictability was 93.5%. Further, ACEs also displayed interesting relationships with the covariates (i.e., CVD risk factors). For example, "household incarceration" exhibited an association with smoking status (edge weight = 0.265, nonzero in 100.0% of bootstraps). "Household substance abuse (living with medications/drugs abuser)" was correlated with heavy alcohol consumption (edge weight = 0.174, nonzero in 94.0% of bootstraps) and smoking status (edge weight = 0.149, nonzero in 98.0% of bootstraps), and "household mental illness" was correlated with depressive disorders (edge weight = 0.565, nonzero in 100.0% of bootstraps). Moreover, strong edges were found between the nodes for "emotional abuse" and depressive disorder (edge weight = 0.188, nonzero in 100.0% of bootstraps), "sexual abuse (ever touch you sexually)" and depressive disorder (edge weight =

Table 1
Gender differences in general characteristics.

Variables	Gender, *n* (%)	
	Men (*n* = 14,193)	Women (*n* = 17,049)
Angina/coronary heart disease		
yes	1,678 (11.8%)	1,082 (6.3%)
No	12,515 (88.2%)	15,967 (93.7%)
Stroke		
yes	850 (6.0%)	925 (5.4%)
no	13,343 (94.0%)	16,124 (94.6%)
Household mental illness		
yes	1,125 (7.9%)	2,114 (12.4%)
no	13,068 (92.1%)	14,935 (87.6%)
Household substance abuse 1 (living with problem drinker or alcoholic)		
yes	2,497 (17.6%)	3,447 (20.2%)
no	11,696 (82.4%)	13,602 (79.8%)
Household substance abuse 2 (living with medications/drugs abuser)		
yes	768 (5.4%)	805 (4.7%)
no	13,425 (94.6%)	16,244 (95.3%)
Household incarceration		
yes	476 (3.4%)	513 (3.0%)
no	13,717 (96.6%)	16,536 (97.0%)
Parental separation/divorce		
yes	2,232 (15.7%)	2,833 (16.6%)
no	11,961 (84.3%)	14,216 (83.4%)
Witnessing household violence		
never	12,509 (88.1%)	14,914 (87.5%)
once	505 (3.6%)	548 (3.2%)
more than once	1,179 (8.3%)	1,587 (9.3%)
Physical abuse		
never	10,864 (76.5%)	13,830 (81.1%)
once	893 (6.3%)	991 (5.8%)
more than once	2,436 (17.2%)	2,228 (13.1%)
Emotional abuse		
never	10,382 (73.1%)	12,677 (74.4%)
once	696 (4.9%)	825 (4.8%)
more than once	3,115 (21.9%)	3,547 (20.8%)
Sexual abuse 1(ever touch you sexually)		
never	13,461 (94.8%)	14,860 (87.2%)
once	351 (2.5%)	866 (5.1%)
more than once	381 (2.7%)	1323 (7.8%)
Sexual abuse 2 (try to make you touch sexually)		
never	13,620 (96.0%)	15,695 (92.1%)
once	286 (2.0%)	555 (3.3%)
more than once	287 (2.0%)	799 (4.7%)
Sexual abuse 3 (force you to have sex)		
never	13,932 (98.2%)	16,275 (95.5%)
once	93 (0.7%)	246 (1.4%)
more than once	168 (2.0%)	528 (3.1%)
Depressive disorder		
yes	1,653 (11.6%)	3,411 (20.0%)
no	12,540 (88.4%)	13,638 (80.0%)
Diabetes		
yes	3,026 (21.3%)	3,020 (17.7%)
no	11,167 (78.7%)	14,029 (82.3%)
Obesity		
yes	4,658 (32.8%)	5,207 (30.5%)
no	9,535 (67.2%)	11,842 (69.5%)
Physical activity		
yes	10,916 (76.9%)	12,340 (72.4%)
no	3,277 (23.1%)	4,709 (27.6%)
Heavy alcohol consumption		
yes	808 (5.7%)	856 (5.0%)
no	13,385 (94.3%)	16,193 (95.0%)
Smoking status		
current smoker, everyday	1,165 (8.2%)	1,224 (7.2%)
current smoker, some days	360 (2.5%)	438 (2.6%)
former smoker	5,329 (37.5%)	4,720 (27.7%)
never smoked	7,339 (51.7%)	10,667 (62.6 %)

Table 2
CVD predictability and CVD-ACEs edge weights/stability considering all the variables used in the network model.

	Men (*n* = 14,193)		Women (*n* = 17,049)	
Overall angina/CHD predictability	0.872		0.930	
Overall stroke predictability	0.935		0.941	
	CVD-ACEs edge weights (stability)			
	Angina/ CHD	Stroke	Angina/ CHD	Stroke
Household mental illness	X	X	X	X
Household substance abuse 1 (living with problem drinker or alcoholic)	X	X	0.032 (67.0%)	0.039 (62.0%)
Household substance abuse 2 (living with medications/ drugs abuser)	X	X	X	X
Household incarceration	X	0.158 (86.0%)	X	X
Parental separation/divorce	X	X	X	X
Witnessing household violence	X	X	0.028 (78.0%)	X
Physical abuse	0.016 (57.0%)	0.046 (48.0%)	0.024 (55.0%)	0.056 (71.0%)
Emotional abuse	X	X	X	X
Sexual abuse 1(ever touch you sexually)	X	X	X	X
Sexual abuse 2 (try to make you touch sexually)	X	X	X	X
Sexual abuse 3 (force you to have sex)	X	X	0.053 (83.0%)	0.025 (45.0%)

Note. X = no edge between CVD and ACEs, % of 100 bootstraps for which the edge weight was non-zero in parentheses
ACE = adverse childhood experiences; CHD = coronary heart disease; CVD = cardiovascular disease

0.152, nonzero in 100.0% of bootstraps), and "sexual abuse (force you to have sex)" and depressive disorder (edge weight = 0.133, nonzero in 91.0% of bootstraps).

In the network for women (Fig. 2), the strongest edge weight

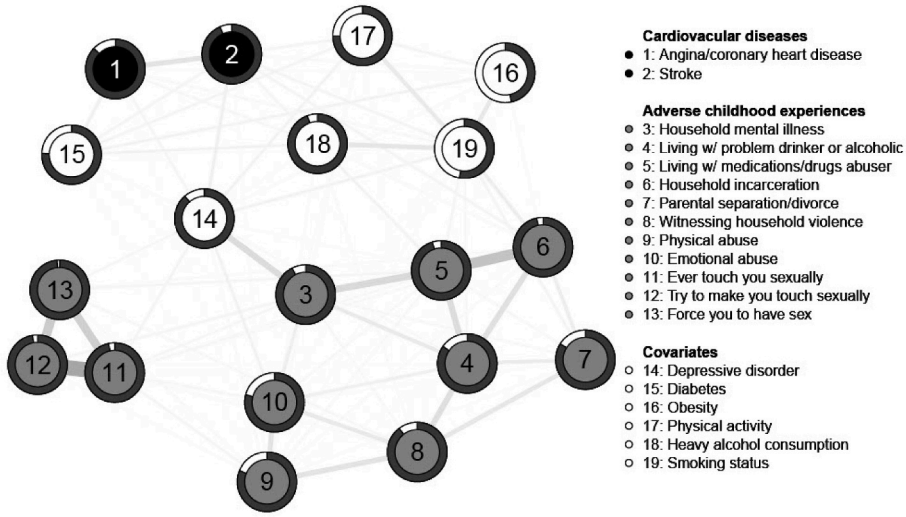

Fig. 1. Mixed graphical model network for men (n = 14,193).
Note. Grey edges represent pairwise interactions wherein no sign is defined (i.e., interactions including categorical variables). The thickness of an edge reflects the strength of the association.

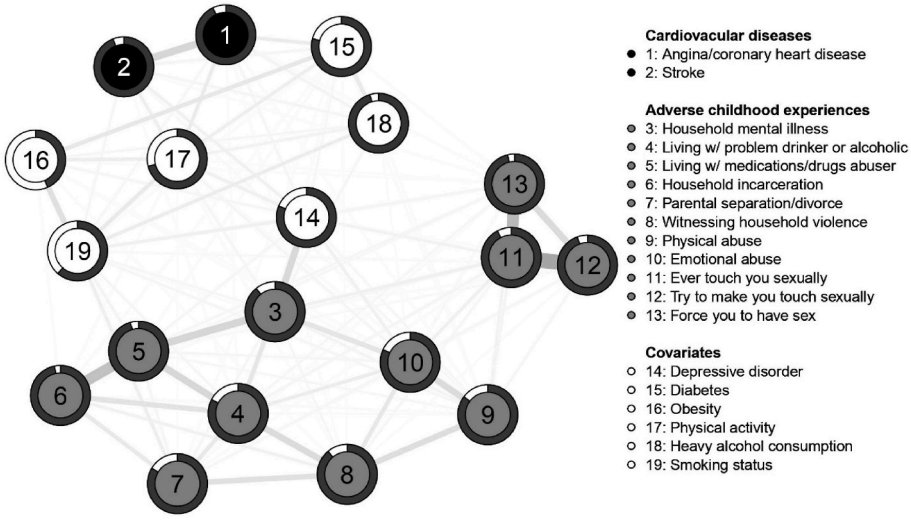

Fig. 2. Mixed graphical model network for women (n = 17,049).
Note. Grey edges represent pairwise interactions wherein no sign is defined (i.e., interactions including categorical variables). The thickness of an edge reflects the strength of the association.

between ACEs and the CVD outcome was between "physical abuse" and stroke (edge weight = 0.056, nonzero in 71.0% of bootstraps), followed by the edge between "sexual abuse (force you to have sex)" and angina/CHD (edge weight = 0.053, nonzero in 83.0% of bootstraps). Of interest, edges were found between "witnessing household violence" and angina/CHD and "sexual abuse (force you to have sex" and stroke, which were not observed in the network for men, although the edge weight was somewhat weak (edge weight = 0.028, nonzero in 78.0% of bootstraps; 0.025, nonzero in 45.0% of bootstraps). In addition, "household substance abuse (living with problem drinker or alcoholic)" was proximal to angina/CHD (edge weight = 0.032) and stroke (edge weight = 0.039), with smaller edge weights and stability (nonzero in 67.0% and 62.0% of bootstraps, respectively). Similar to men, "physical abuse" also demonstrated relatively weak associations with angina/CHD (edge weight = 0.024, nonzero in 55.0% of bootstraps). The angina/CHD and stroke predictability values were 93.0% and 94.1%, respectively. Further, strong edges were found between the nodes for "household mental illness" and depressive disorder (edge weight = 0.547, nonzero in 100.0% of bootstraps), "household substance abuse (living with medications/drugs abuser)" and smoking status (edge weight = 0.136, nonzero in 100.0% of bootstraps), "parental separation/divorce" and smoking status (edge weight = 0.202, nonzero in 100.0% of bootstraps), and "emotional abuse" and depressive disorder (edge weight = 0.176, nonzero in 100.0% of bootstraps). Both "sexual abuse (ever touch you sexually)" and "sexual abuse (force you to have sex)" were associated with depressive disorder (edge weight = 0.164, nonzero in 100.0% of bootstraps; edge weight = 0.128, nonzero in 100.0% of bootstraps).

Fig. 3 illustrates the clusters in the estimated networks. The number of connections was greater between variables and CVD outcomes in men (modularity value = 0.30). The clusters and their respective nodes are illustrated in different colors. Two clusters of strongly associated nodes were identified in the network for men. In particular, angina/CHD and stroke were located in the blue cluster with several CVD risk factors, including depressive disorder, diabetes, obesity, physical activity, smoking, and certain constructs of ACEs (i.e., "household substance abuse [living with problem drinker or alcoholic])", "household

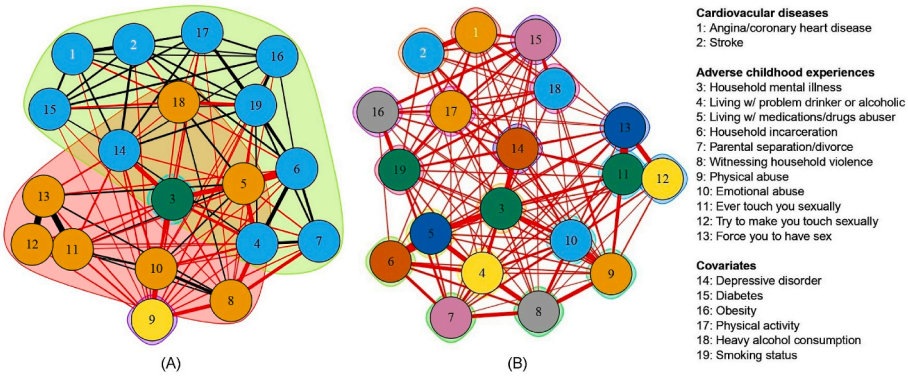

Fig. 3. Network clusters for men (A) and women (B).

incarceration", and "parental separation/divorce"). Other constructs of ACEs, including three items of sexual abuse, "household substance abuse (living with medications/drugs abuser)", "witness to household violence", and "emotional abuse", co-occurred as expected and were located in orange clusters with heavy alcohol consumption. As depicted in Fig. 3, no clusters were detected for women.

4. Discussion

The current study contributes to the burgeoning body of literature on ACEs and CVD outcomes by offering nuanced insights on the role of specific types of ACEs towards angina/CHD and stroke while considering the complex patterns of correlations among other variables. We also explored the clustering patterns of ACEs and how they were linked to CVD outcomes in a national representative sample, which has provided empirical evidence on potential mechanisms underlying these associations. The findings of this study can further inform the development of gender-specific interventions to reduce rates of CVD.

Our study findings have highlighted the distinct role of household incarceration, among other ACEs, in influencing stroke among men. This is consistent with the seminal work on ACEs demonstrating that the incarceration of a household member critically damages individual's long-term health (Felitti et al., 1998) and other evidence based on BRFSS data from previous years where the associations between ACEs and stroke are observed (Campbell et al., 2016; Gilbert et al., 2015). However, prior work on ACEs and stroke tend to either conceptualize the influence of each type of ACEs on stroke as independent (Campbell et al., 2016) or use a composite score for ACEs assuming the equal importance of each type of ACEs in its relationship to stroke (Gilbert et al., 2015), creating missed opportunities to locate the specific type of ACEs most salient to stroke after accounting for their complex relationships. Household incarceration has a profound impact on health beyond childhood. Children exposed to parental incarceration are seldom recognized as a distinct population with unique needs within the protection systems and there is no government agency responsible for their well-being (Williams et al., 2012). Existing services, not surprisingly, are patchy and rarely tailored to their needs (Beresford et al., 2020). Additionally, individuals exposed to household incarceration tended to stay silent about their experiences, which provides another possible explanation of why they are more likely to experience health challenges than others (Jones et al., 2013). Future services should move beyond an individual-focused approach and attend to the needs of the family influenced by incarceration, especially children, to effectively reduce a major risk factor for stroke in later life.

For men in our study, individuals exposed to household incarceration also tend to have experienced other two types of household dysfunction (i.e., household substance abuse and parental separation/divorce), further encountered multiple chronic conditions and risk behaviors (i.e., depressive disorder, diabetes, obesity, physical activity, and smoking) and CVD outcomes. This sheds light on the potential mechanisms underlying the link between ACEs and CVD outcomes. Aligned with previous evidence, household incarceration seems to play a central role in an individual's exposure to ACEs in our study. Children of incarcerated parents are challenged with nearly five times of other types of ACEs when compared with their counterparts without exposure to incarcerated parents (Turney, 2018). Our finding supports earlier evidence on possible mechanisms where early adversities can interfere with normal psychosocial development and increase the likelihood of various mental, behavioral, and physical health problems, leading to higher CVD risks. (Maguire et al., 2015; Naughton et al., 2013). Furthermore, our study presents complex interrelationships contributing to the susceptibility to CVD, which challenges the common assumptions in previous studies where the focus is usually a single mechanism versus interactions across different mechanisms. Interesting to note here is the role of smoking. Both household incarceration and household substance abuse are associated with smoking behaviors in our study. This might suggest smoking as a salient mechanism underlying the ACEs–CVD link where men use smoking to cope with adversity and stress and are vulnerable to CVD risk as indicated by the long-established link between smoking and CVD (Ockene & Miller, 1997).

Among all types of ACEs, our findings emphasize the crucial role of childhood physical and sexual abuse in later life CVD risks among women even after accounting for all other interrelationships in the network. Basu et al. (2017) found a stable connection between childhood maltreatment and elevated CVD risks including stroke and CHD in their review of 40 studies and called for future studies to examine such relationships by gender. As a response to their call, our study further articulates the gender differences in the well-established connections between childhood physical and sexual abuse and CVD where such relationships are only observed among women in our study. No clustering of ACEs, CVD risk factors, and CVD outcomes were observed for women in our study despite women exposed to childhood sexual abuse tend to develop depressive disorders in our study. This might be due to the chronic nature of depressive disorders measured in our study, which cannot reflect or capture the depressed mood and stress that usually serve as the acute triggers of major cardiac events as indicated in a meta-analysis (Steptoe & Kivimäki, 2013).

Our study has revealed important gender differences in both the link between ACEs and CVD and its potential mechanisms, which is well-aligned with established literature on differences across epidemiology, interventions/treatments, and outcomes by gender (The EUGenMed et al., 2016). Specifically, physical and sexual abuse emerge as salient components of ACEs to develop CVD for women compared to men though there were no huge differences in prevalence in physical and sexual abuse exposure across genders in our study. This is also consistent with prior evidence where stronger associations between childhood maltreatment and CVD were found among women (Soares et al., 2020) and suggests the interactions of gender and ACEs from early life in

shaping CVD disparities across genders. Gendered coping mechanisms of adversity were also overserved. In contrast with men who use alcohol and smoking as a way of coping with adversity and stress in our study, women exposed to childhood sexual abuse tend to develop depressive disorders in our study. This further supports the needs to assess the gender-specific mechanisms besides shared mechanisms in future intervention efforts to address modifiable risk factors for CVD.

In the present study, edge weights were fairly small across the constructs of ACEs and CVD outcomes within the network. This finding may reflect the true strength of associations, given that numerous factors determine cardiovascular health. However, several points should be considered regarding the findings. First, we performed the model selection using the EBIC, leading to a conservative network that could miss significant associations (Epskamp et al., 2018). Although this permits a good recovery of the overall network structure, it might exclude adversities that rarely occur or have a weak connection with other adversities (de Vries et al., 2022). Future research can perform a simulation to obtain more insight into these issues and examine how well simulated network structures can be retrieved with different model selection techniques. Second, this study may not have included certain edges due to missing data. Third, some associations could have changed in magnitude after controlling for the number of covariates.

4.1. Limitations

This study has several broad limitations. First, the cross-sectional design makes it challenging to infer the directionality of the associations between variables. It is possible that the investigated associations, for instance, between CVD risk factors and CVD outcomes, are in fact bidirectional; with individuals possibly altering their health behaviors upon diagnosis with CVD. Thus, results should be interpreted with caution. Still, ACE measures relative to current health outcomes provide some temporality, as CVD risk factors or CVD at an average age of 68.7 years is generally unlikely to be associated with whether participants had experienced ACEs or whether participants accurately reported experiencing ACEs. Second, the CVD diagnosis data is self-reported without validation using actual clinical records, potentially resulting in an under- or overestimate of true prevalence. Indeed, research argues that discrepancies between self-reported and objective data exist for CVD conditions in the general population (Muggah et al., 2013; Woodfield & Sudlow, 2015), and which method is most accurate to examine presence of CVD is inconclusive (Fortin et al., 2017). Yet, BFRSS has been reported to produce similar prevalence estimates for most health indicators and chronic diseases with other national surveys relying on self-reporting (Li et al., 2012; Pierannunzi et al., 2013), which provides some confidence in validity and reliability of BRFSS measures. Third, other critical covariates for ACEs and CVD outcomes were not considered, given the unavailability of such variables in the BRFSS dataset. For instance, ACEs must be evaluated within the comprehensive scope of the social determinants of health (Havranek et al., 2015; Suglia et al., 2020). Adults who have experienced ACEs tend to live in challenged neighborhoods exposed to poor food security or higher levels of air pollution, and interactions between these factors further influence the risk of CVD and the risk factors, including diabetes and obesity (Chilton et al., 2015; Daniels et al., 2011; Hazlehurst et al., 2018).

We additionally acknowledge the methodological limitations of ACE measurement used in the current study. First, the score used in the BRFSS ACE module weights all ACE categories equally (e.g., using options of either “yes/no” or “never/once/more than once”), neglecting interindividual differences in manifestations (Anda et al., 2020). Recently, most attention has focused on the importance of assessing the severity, timing, and chronicity of each experience (Lacey & Minnis, 2020; Portwood et al., 2021), all of which should be further explored in future studies. For example, with more validated ACE measures, more granular information on the frequency and severity of ACEs can be leveraged in mixed graphical models (e.g., including count/continuous variables to present frequency/severity). Incorporating the timing of ACEs requires models that permit the inclusion of repeated measurements of ACE occurrence (e.g., cross-lagged prospective network analysis; Epskamp, 2020). Second, ACEs were assessed retrospectively, making the results prone to recall bias. Currently, no consensus has been reached on the validity of adult retrospective reports of ACEs. One comprehensive review concluded that retrospective recall is sufficiently valid since bias is not significant enough to invalidate retrospective studies of major adversities (Hardt & Rutter, 2004). Contrastingly, some argue that it is not reliable to assume that the health correlates of retrospective ACE reports are equivalent to the long-term consequences of adversity assessed during childhood, or that the risk mechanisms through which health problems surface in the two groups identified by retrospective or prospective measures are equivalent (Danese, 2020). One meta-analysis concluded that these two forms of ACE measures had a low agreement, and further reported that the agreement was higher in studies that used interviews instead of questionnaires or in studies with small sample sizes (Baldwin et al., 2019). Reuben et al. (2016) also argued that, relative to prospective measures, retrospective ACE measures underestimated the influence of ACEs on ‘objective’ adult outcomes and overestimated the influence of ACEs on ‘subjective’ adult outcomes. Thus, one should recognize these critical measurement differences and carefully interpret the current study’s findings.

4.2. Strengths and implications

Despite these limitations, this study has strengths and important implications. Foremost, we considered a wide range of ACEs and CVD outcomes on the symptom level, considering their high interrelatedness via network analysis, and produced a differentiated picture compared to other studies.

Based on the findings, pondering the potential advantages of contemplating the role of ACEs in CVD and identifying strategies to negate these effects is crucial. For instance, ACE is an underrecognized and insufficiently discussed topic in routine cardiovascular encounters (Godoy et al., 2021). As such, screening for ACE exposure can promote awareness that these practices are relevant for patient care. In this regard, trauma-informed care (TIC) can serve as an important framework for guiding health care for CVD patients with a history of ACEs (Su et al., 2015). TIC entails engaging individuals with a history of trauma, recognizing its presence and role in their lives (Raja et al., 2015). Su et al. (2015) argues that designing clinical trials to evaluate the effectiveness of integrated TIC on cardiovascular health is worthwhile due to the remaining lack of evidence. In addition to implementing TIC, following the American Heart Association’s strategic impact 2020 goals and beyond, early intervention and increased exposure of children to stable, safe, and nurturing environments are also emphasized to prevent the long-lasting consequences of ACEs.

There are important considerations and recommendations for future ACE research utilizing network analysis. First, no consensus exists on what constitutes ACEs, and there is substantial heterogeneity in how researchers operationalize ACEs (Lacey & Minnis, 2020). As edges between nodes are strongly dependent upon the variables entered into the network model, the findings might vary among studies (e.g., different ACE measures), hampering comparisons. Thus, future replication studies may consider employing conceptually similar ACEs. Second, we stratified the analysis solely by gender as an initial effort to advance this critical yet unexplored field of study. Gender was of particular interest to us as the integration of the gender dimension in ACE-CVD research is an important understudied area that requires timely evaluation (Basu et al., 2017), and the impact of gender as a social determinant of health is likely to represent a composite of the effects of social roles, socioeconomic status, poverty, and interpersonal relationships (Phillips, 2005), all which render gender a priority factor to be addressed in ACE studies. Nevertheless, we emphasize that this is an exploratory, preliminary investigation, and future studies should examine how network

structures can be constructed according to diverse identities such as class or race (or intersection of these), which this study did not fully analyze. Third, it is worth mentioning that, although we only focused on cisgender (with rationale) in this study, we fully acknowledge the need for future studies to extend to gender minorities, a group which has not yet received attention in ACE-CVD research. Unfortunately, BRFSS was comprised predominantly of cisgender people with approximately 0.42% transgender people in the entire collected data and network analysis was unsuitable with such a small data size. Although there are no "rules of thumb" for sample size requirements for network analysis, with a small-to-moderate sample (and possibly a low absolute number of childhood adversity cases, reducing the statistical power), it is typically challenging to obtain precise estimates regarding edges between nodes. Fourth, ACE is the product of various protective factors, including socioeconomic resources, resilience, and genetics, that can manage the impact of ACEs on an individual (Traub & Boynton-Jarrett, 2017). Researchers can include these factors in a moderated network model (Haslbeck, 2022) to assess whether such factors moderate the relationships between individual ACEs, or between ACEs and CVD outcomes. For instance, an important next question after this study is: Are conditional associations between ACEs and CVD moderated by social support? This query could elucidate mechanisms that may buffer the deleterious effects of childhood adversity.

5. Conclusion

Network analysis provides a valuable guide for examining multiple relationships between ACEs and CVD outcomes in later life. The ACEs with connections to CVD in the present study are potential gender-specific intervention targets to decrease the burden of future CVD. Nevertheless, we reemphasize that this is an exploratory, preliminary investigation, and readers must view these findings as emerging from an extensive national survey analysis with a diverse participant group. The quality of research can be improved with further prospective analyses, more validated measures of ACEs, direct clinical assessments of CVD events, and a detailed subgroup analysis. Researchers may use a more sophisticated statistical approach to network analysis to incorporate important covariates or moderators unaccounted for in this study to address various research questions in this field. Future studies evaluating the effectiveness of trauma-informed intervention in reducing the influence of ACEs on CVD risk could also be beneficial.

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Data statement

The data are publicly available for download on the BRFSS website (www.cdc.gov/brfss).

Ethical considerations

BRFSS is a publicly available deidentified dataset. A secondary analysis of publicly available data does not require Institutional Review Board approval according to the corresponding author's institution.

Author contributions

Chiyoung Lee: Conceptualization; Data curation; Methodology; Formal analysis; Writing - original draft. Jiepin Cao: Writing - original draft; Writing - review & editing, Data curation. Meghan Eagen-Torkko: Conceptualization; Supervision; Writing - review & editing. Selina A. Mohammed: Conceptualization; Supervision; Writing - review & editing.

Declaration of competing interest

None.

Data availability

The data are publicly available for download on the BRFSS website (www.cdc.gov/brfss).

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ssmph.2023.101358.

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