RESEARCH ARTICLE

Cardiovascular disease risk factors in autistic adults: The impact of sleep quality and antipsychotic medication use

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Abstract

Approximately 40% of American adults are affected by cardiovascular disease (CVD) risk factors (e.g., high blood pressure, high cholesterol, diabetes, and overweight or obesity), and risk among autistic adults may be even higher. Mechanisms underlying the high prevalence of CVD risk factors in autistic people may include known correlates of CVD risk factors in other groups, including high levels of perceived stress, poor sleep quality, and antipsychotic medication use. A sample of 545 autistic adults without intellectual disability aged 18+ were recruited through the Simons Foundation Powering Autism Research, Research Match. Multiple linear regression models examined the association between key independent variables (self-reported perceived stress, sleep quality, and antipsychotic medication use) and CVD risk factors, controlling for demographic variables (age, sex assigned at birth, race, low-income status, autistic traits). Overall, 73.2% of autistic adults in our sample had an overweight/obesity classification, 45.3% had high cholesterol, 39.4% had high blood pressure, and 10.3% had diabetes. Older age, male sex assigned at birth, and poorer sleep quality were associated with a higher number of CVD risk factors. Using antipsychotic medications was associated with an increased likelihood of having diabetes. Poorer sleep quality was associated with an increased likelihood of having an overweight/obesity classification. Self-reported CVD risk factors are highly prevalent among autistic adults. Both improving sleep quality and closely monitoring CVD risk factors among autistic adults who use antipsychotic medications have the potential to reduce risk for CVD.

Lay Summary

This study found that about 75% of autistic adults had at least one risk factor for heart disease and that being older, being male, and sleeping badly were related to how many heart disease risk factors autistic adults had. It also found that autistic adults who used antipsychotic medications were more likely to have diabetes and that autistic adults who sleep badly are more likely to have overweight or obesity status.

KEYWORDS

antipsychotic medications, cardiovascular disease, health, sex differences, sleep quality

INTRODUCTION

Cardiovascular disease (CVD) is the leading preventable cause of morbidity and mortality in the Unites States

(Benjamin et al., 2017) and globally (Kaptoge et al., 2019; Roth et al., 2018), and we have reason to believe that autistic people are disproportionately affected and at risk (Bishop-Fitzpatrick, Movaghar,

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et al., 2018; Croen et al., 2015; Hirvikoski et al., 2016; Mandell, 2018). The annual direct and indirect cost of CVD in the United States is \$316.1 billion, and it accounts for a greater proportion of total health expenditures than any other category of diagnoses (Benjamin et al., 2017). Combined, CVD and its risk factors (e.g., high blood pressure, high cholesterol, diabetes, and overweight or obesity) affect approximately 41.5% of Americans (Benjamin et al., 2017), and CVD is responsible for nearly 18 million annual deaths worldwide (Roth et al., 2018).

Multiple groups have identified high prevalence of CVD and its risk factors in several population-based and convenience samples of autistic people (Bishop-Fitzpatrick, Movaghar, et al., 2018; Croen et al., 2015; Hirvikoski et al., 2016). For instance, Croen et al. (2015) found that 37% of primarily young autistic adults, compared to 23% of primarily young non-autistic adults have CVD. Bishop-Fitzpatrick and colleagues (2018) also found high prevalence of CVD in a primarily middle aged and older adult sample: both valvular disease (27% compared to 16%) and congestive heart failure (37% compared to 26%) were elevated in autistic people compared to non-autistic people. In a national sample of Medicare beneficiaries aged 65+, Hand et al. (2020) found elevated prevalence of heart disease (54% compared to 37%) and cerebrovascular disease (12% compared to 8%) in autistic older adults compared to nonautistic older adults. In a study by Bishop-Fitzpatrick and Rubenstein (2019), prevalence of CVD (49.0%) and its risk factors (46.2%) were elevated among middle aged and older autistic Medicaid beneficiaries. These figures from previous research described above, all of which are derived from representative claims datasets of autistic adults in the United States, suggest that the prevalence of CVD is elevated in autistic people. These findings are echoed by recent work that assesses the prevalence of self-reported non-communicable physical health conditions (including CVD) among a convenience sample of autistic adults who reside primarily United Kingdom and finds increased risk for CVD in autistic adults, although percentages were not reported (Weir et al., 2021, 2022). Indeed, CVD is highly prevalent and accounts for the largest attributable fraction of deaths in autistic people (Hirvikoski et al., 2016; Mandell, 2018).

Although a growing body of research suggests that CVD and its primary risk factors are elevated in autistic people, limited research has focused specifically on potential mechanisms underlying this high prevalence of CVD or its risk factors among autistic people. A mechanistic understanding of the high prevalence of associated conditions like CVD in autistic people is necessary to develop primary and secondary prevention strategies that have the potential to extend life expectancy and improve quality of life (Rubenstein & Bishop-Fitzpatrick, 2019). In the general population, social, psychosocial, and lifestyle

determinants of health impact risk for CVD by increasing risk for primary CVD risk factors, including high blood pressure, high cholesterol, diabetes, and overweight or obesity (Dimsdale, 2008; Giurgescu et al., 2019; Mozaffarian et al., 2008; Richardson et al., 2012). Modifying social, psychosocial, and lifestyle factors that are associated with increased prevalence of primary CVD risk factors may be most important for primary prevention (Mozaffarian et al., 2008), and it is imperative to understand how autistic people are affected by both primary and secondary risk factors.

Research in non-autistic adults suggests that both poorer sleep quality and higher levels of perceived stress are associated with increased CVD risk factors, and both are elevated in autistic relative to non-autistic adults. A recent meta-analysis that reviewed data from 23 studies that included 118,696 adults in the general population found that high levels of perceived stress increased risk of incident coronary heart disease by 27% (Richardson et al., 2012). Autistic adults experience higher levels of perceived stress than non-autistic adults (Bishop-Fitzpa-2017; Bishop-Fitzpatrick, DaWalt, et al., Mazefsky, et al., 2018a; Hirvikoski & Blomgvist, 2015), which may increase risk for CVD in autistic people (Rubenstein & Bishop-Fitzpatrick, 2019). A 2011 metaanalysis that reviewed data from 15 studies that included 474,684 adults from the general population found that both short and long sleep duration—both markers of poor sleep quality—increased risk for coronary heart disease mortality by 48% and 38%, respectively (Cappuccio et al., 2011). A growing body of evidence suggests that sleep quality is poorer in autistic adults compared to nonautistic adults (Baker & Richdale, 2015; Hohn et al., 2019; Jovevska et al., 2020; McLean et al., 2021).

Like autistic people, people with serious mental illness-including schizophrenia, schizoaffective disorders, and mood disorders with psychotic features—are also at risk of early mortality and have heightened prevalence of CVD and its risk factors (Walker et al., 2015). Although the mechanisms underlying this high prevalence of CVD and its risk factors in people with serious mental illness are multifactorial, one factor that increases risk of CVD and its risk factors for this population is antipsychotic medication use. A body of research suggests that antipsychotic medications may, both directly and indirectly, increase risk for developing CVD risk factors (Kahl et al., 2018; Kovacs & Arora, 2008; Mwebe & Roberts, 2019; Walker et al., 2015). Second-generation antipsychotics, specifically, have the potential to increase the risk of developing CVD risk factors such as overweight and obesity, high cholesterol, diabetes, and metasyndrome (American Diabetes Association, American Psychiatric Association, American Association Clinical Endocrinologists, & Obesity. Saari, 2004). Antipsychotics are often used to treat irritability and emotion dysregulation in autistic people. The median international prevalence of antipsychotic drug

use in autistic adults among studies included in a recent systematic review with predominantly adult samples is high (42.8% with a range from 28.7% to 55.6%; Jobski et al., 2017) and accordingly, we have reason to believe that autistic adults may experience the downstream cardiovascular effects of these elevated levels of antipsychotic medication use.

Our goal was to fill these gaps in the literature by investigating the prevalence of self-reported CVD risk factors and testing the association between known predictors of CVD risk factors in the general population and in people with serious mental illness in autistic adults. Specifically, we aimed to: (1) describe self-reported CVD risk factors in a sample of autistic adults without intellectual disability; and (2) test the associations between CVD risk factors and antipsychotic medication use, sleep quality, and perceived stress. We hypothesized that autistic adults would have a high prevalence of CVD risk factors and that antipsychotic medication use, poor sleep quality, and high perceived stress would be associated with elevated CVD risk factors in autistic adults.

METHODS

Data and sample

We recruited participants aged 18+ through the Simons Foundation Powering Autism Research (SPARK; (Feliciano et al., 2018)) Research Match service, and we compensated participants \$25 for completing a series of questionnaires. Data for this study came from a broader study of adult development, and participants were recruited to the broader adult development study, not a study focused specifically on CVD risk factors. The study was approved by The George Washington University institutional review board, and all participants provided informed consent. A more in-depth description of the broader SPARK study can be found in Feliciano et al. (2018).

For this study, we included only data from the 545 autistic adults with complete data on medication use, out of a total possible sample of 899. We chose to use listwise deletion instead of multiple imputation because of the likely inaccuracy of imputed medication use data and the likelihood that medication use data are not missing at random. The autistic adults in our sample were mostly assigned female sex at birth (N = 350; 64.2%) and white (N = 437; 80.2%), and they ranged in age from 18 to 77 years (Mean = 41.0 years, SD = 13.45). Participants were geographically representative: based on U.S. Census Bureau designations, 31.6% (N = 172) were from the South, 26.5% (N = 145) were from the West, 23.9% (N = 130) were from the Midwest, and 16.0% (N = 87)were from the Northeast. A minority of participants (N = 11) did not provide geographic information. The geographic distribution of participants in our study

mirrors the distribution of the US population (U.S. Census Bureau, 2021).

All autistic adults in our sample were legally able to provide informed consent (did not have a legal guardian), and no autistic adults in our sample reported a cooccurring intellectual disability on their health history questionnaire. Like all participants in the SPARK registry, participants in this study self-disclosed a professional autism spectrum disorder diagnosis, which is highly likely given that SPARK partners with specialty autism clinics throughout the United States for recruitment (Feliciano et al., 2018). A recent study provides added validity for this supposition—98.8% of participants in a large subsample of SPARK participants had a confirmed ASD diagnosis as ascertained via electronic medical records (Fombonne et al., 2022). Finally, and consistent with participants' self-disclosed autism diagnoses, more than 95% of autistic adults included in our sample scored above the screening cutoff (>65) for autism spectrum disorder on the Autism Spectrum Quotient (AQ)-28 (Fombonne et al., 2022; Hoekstra et al., 2011).

Measures

Demographic information

We collected self-reported demographic data on age, race, income, sex assigned at birth, and autistic traits as measured using the AQ-28 (Hoekstra et al., 2011). For analyses, we dichotomized sex (male or female), race (white or non-white), and income (low-income versus not, as defined by household income less than \$20,000 per year; approximately 150% of the U.S. federal poverty guideline for a single adult). Race, sex, and income were included in analyses due to the body of literature that suggests that women, people from minoritized racial groups (in the United States, people who are not white), and people who are low-income have a higher prevalence of CVD risk factors (Clark et al., 2009; McWilliams et al., 2009; Mosca et al., 2011; O'Neil et al., 2018; Thomas et al., 2005).

Cardiovascular disease risk factors

Participants self-reported the presence or absence of a history of hypertension, high cholesterol, and diabetes. We assessed the presence or absence of overweight and obesity by calculating body mass index (BMI) based on self-reported height and weight, with overweight or obesity indicated as scores greater than or equal to 25 using the age- and sex-based norms developed by the Centers for Disease Control and Prevention for adults younger than age 65. For autistic adults who were 65 years or older, overweight was indicated by a score greater than or equal to 31 given BMI guidelines for older adults;

there is no obesity category for older adults (Winter et al., 2014). For the purpose of analyses, we collapsed "overweight" and "obesity" into a single category because there is no "obesity" category for older adults. We computed a summary score of CVD risk factors that ranged from 0 to 4, with a score of 0 indicating the presence of no CVD risk factors and a score of 4 indicating the presence of hypertension, high cholesterol, diabetes, and obesity/overweight.

Antipsychotic medication use

We asked participants to report any medications that they were taking at the time of data collection in a free text field. If participants typed into the free text field that they were taking too many medications to list or they typed that they preferred not to say which medications they were taking, we listed their current medications as unknown and excluded them from the sample used for this analysis. We then broadly classified medications using MedlinePlus. Because of the known association between antipsychotic medications and some cardiovascular disease risk factors, we created a "antipsychotic medication use" variable coded as yes (2) or no (1) for typical (e.g., haloperidol and loxapine) or atypical (e.g., clozapine and risperidone) antipsychotics.

Perceived stress

We measured self-reported perceived stress using the Perceived Stress Scale (Cohen et al., 1983), a 10-item scale rated on a 5-point Likert scale where higher scores indicate greater perceived stress. Questions that assess perceived stress include: "In the last month, how often have you been upset because of something that happened unexpectedly?"; "In the last month, how often have you felt nervous and 'stressed'?"; "In the last month, how often have you found that you could not cope with all the things that you had to do?"; and "In the last month, how often have you been angered because of things that were outside of your control?", among others. Cronbach's alpha reliability ranges from 0.78 to 0.91 in numerous national surveys in non-autistic people (Cohen & Janicki-Deverts, 2012; Cohen & Williamson, 1988), and research has found strong reliability in both autistic adults without intellectual disability ($\alpha = 0.87$; Bishop-Fitzpatrick, Mazefsky, et al., 2018) and autistic adults with and without intellectual disability ($\alpha = 0.76$; Hong et al., 2016). In the current study, the internal consistency of the PSS is strong ($\alpha = 0.89$; McQuaid et al., 2022).

Sleep quality

We measured self-reported sleep quality using the Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989)

which provides indices across seven domains. For this study, we used the global sleep quality domain. Questions included in this domain are: "When have you usually gone to bed?"; "How long has it taken you to fall asleep at night?"; "During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?"; and "During the past month, how much of a problem has it been for you to keep up enthusiasm to get things done?". The PSQI has strong internal consistency ($\alpha = 0.83$) in non-autistic adults (Buysse et al., 1989), and adequate internal consistency (both $\alpha = 0.68$) in two recent samples of autistic without intellectual disability adults (Baker Richdale, 2015; McLean et al., 2021). In the current study, the internal consistency of the PSQI is strong ($\alpha = 0.74$).

Analyses

We first conducted preliminary analyses to ensure that parametric tests were appropriate. Next, we summarized prevalence of CVD risk factors using descriptive statistics. We tested differences in CVD risk factors based on sex assigned at birth using chi-square tests. We then used multiple linear regression to examine the associations between our key independent variables (perceived stress, global sleep quality, and antipsychotic medication use) and number of CVD risk factors, controlling for demographic variables (age, sex assigned at birth, race, lowincome status, autistic traits). We chose to use multiple linear regression rather than ordinal logistic regression because our CVD risk factors variable violates the assumption of proportional odds because CVD risk factors are sometimes cumulative (e.g., metabolic syndrome), and individuals therefore do not have the same odds of having one CVD risk factor compared to four CVD risk factors. We generated standardized regression coefficients (b) as an effect size metric to assess the strength of these associations (Nieminen et al., 2013). Finally, a series of four exploratory logistic regression models tested associations between key independent variables included in Model 1 and individual CVD risk factors (hypertension, high blood pressure, diabetes, and overweight or obesity), controlling for the same demographic characteristics used in Model 1.

RESULTS

Descriptive findings and differences based on sex assigned at birth

Overall, 73.2% (N = 399) of autistic adults in our sample had co-occurring overweight or obesity status (BMI \ge 25), while 45.3% (N = 247) had high cholesterol, 39.4% (N = 215) had high blood pressure, and 10.3% (N = 56) had diabetes. The average BMI in our sample was 31.70

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TABLE 1 Demographic characteristics

	Overall ($N=5$	45)	Autistic men (A	V = 195)	Autistic women		
Continuous variables	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	<i>p</i> -value
Age	41.02 (13.45)	18.50-77.33	42.28 (14.62)	18.50-73.25	40.31 (12.73)	19.08-77.33	0.101
Perceived stress	23.31 (7.22)	0.00-40.00	21.83 (7.38)	0-40	24.14 (7.00)	2-40	< 0.001
Global sleep quality	9.78 (4.44)	21.00-9.78	8.67 (4.39)	1–19	10.41 (4.36)	1-21	< 0.001
Autism Quotient-28	85.77 (10.98)	54.0-110.00	84.58 (11.17)	54–110	86.44 (10.83)	54-110	0.058
BMI	31.09 (8.66)	15.03-70.41	30.00 (7.23)	15.03-54.24	31.70 (9.32)	15.62-70.41	0.028
Number of CV risk factors	1.68 (1.05)	0.00-4.00	1.84 (1.09)	0-4	1.59 (1.02)	0–4	0.008
Categorical variables	N	%	N	%	N	%	<i>p</i> -value
Male	195	35.80	_	_	_	_	_
White	437	80.20	161	82.56	276	78.86	0.298
Low income	179	32.80	55	28.21	124	35.43	0.085
BMI category							0.002
Underweight	16	2.90	5	2.56 ^a	11	3.14 ^a	
Normal weight	130	23.90	44	22.56 ^a	86	24.57 ^a	
Overweight	156	28.60	75	38.46 ^a	81	23.14 ^a	
Obesity	243	44.60	71	36.41 ^a	172	49.14 ^a	
Overweight or obesity	399	73.20	146	74.85	253	72.29	0.513
Hypertension	215	39.40	98	50.26	117	33.42	< 0.001
Hyperlipidemia	247	45.30	94	48.21	153	43.71	0.313
Diabetes	56	10.30	21	10.77	35	10.00	0.777
Uses antipsychotic medications	82	15.00	21	10.77	61	17.43	0.037

Abbreviations: BMI, body mass index; N, number; SD, standard deviation.

(SD = 9.32) for autistic women and 30.00 (SD = 7.23)for autistic men, although autistic men and autistic women did not differ significantly on BMI. Within the overweight or obesity category, 44.6% (N = 243) had a BMI score consistent with obesity status while 28.6% (N = 156) had a BMI consistent with overweight status. Only 2.9% (N = 16) of participants in our sample had a BMI consistent with underweight status. In terms of number of cardiovascular risk factors, only about one eighth of autistic adults (12.7%; N = 69) had no CVD risk factors, while 33.4% (N = 182) of autistic adults had one CVD risk factor, 31.4% (N = 171) had two CVD risk factors, 18.2% (N = 99) had three CVD risk factors, and 4.4% (N = 24) had all four CVD risk factors. Autistic men were more likely than autistic women to have high blood pressure ($\chi^2 = 15.17$, p < 0.001), but autistic men and women had similar rates of high cholesterol, diabetes, and overweight or obesity, even though autistic men had a higher average number of CVD risk factors than autistic women (t = -2.65, p = 0.004) and autistic women had BMI scores that were higher, on average, compared to autistic men (t = 2.209, p = 0.014).

A minority of autistic adults in our sample (15.00%; N = 82) reported taking one or more antipsychotic medications. Autistic women (17.4%; N = 61) were significantly more likely than autistic men (10.8%; N = 21) to report antipsychotic medication use ($\chi^2 = 3.35$,

p=0.037). Autistic women had significantly higher levels of perceived stress (M=24.14, SD = 7.00) compared to autistic men (M=21.83, SD = 7.38; t=3.62, p<0.001), and autistic women also had significantly poorer sleep quality (M=10.41, SD = 4.36) compared to autistic men (M=8.67, SD = 4.39; t=4.46, p<0.001). Both autistic men and autistic women experience high levels of perceived stress and poor sleep quality based on standardized norms in the general population for the PSS (Cohen & Janicki-Deverts, 2012) and PSQI (Buysse et al., 1989), respectively. Of note, 86.5% (N=475) of autistic adults in our sample exceeded a cutoff score of 5 on the PSQI, which is indicative of possible sleep disorders (Buysse et al., 1989). Descriptive findings are detailed in Table 1.

Prediction of number of CVD risk factors

Results of our multiple linear regression analysis (Table 2) revealed a significant, positive association between sleep quality and number of CVD risk factors, $\beta = 0.123$, p = 0.011, $\text{sr}^2 = 0.011$, when controlling for age, sex, race, low-income status, autistic traits, perceived stress, and antipsychotic medication use, such that better sleep quality (indicated by a lower score on the PSQI) was associated with fewer CVD risk factors. Older age

^aDoes not add up to 100% due to rounding error.

TABLE 2 Multiple linear regression predicting number of cardiovascular disease risk factors

	β	SE	t
Age	0.286	0.003	6.906***
Male	0.123	0.091	2.957**
White	0.045	0.108	1.100
Low Income	0.043	0.094	1.018
Autism Quotient-28	0.063	0.004	1.450
Anti-Psychotic Use	0.049	0.121	1.178
Perceived Stress	-0.047	0.007	-0.968
Sleep Quality	0.123	0.011	2.599**

^{*}p < 0.05.

was associated with a greater number of CVD risk factors, $\beta = 0.286$, p < 0.001, $sr^2 = 0.078$, when controlling for sex, race, low-income status, autistic traits, perceived stress, sleep quality, and antipsychotic medication use. There was a negative association between sex assigned at birth and CVD risk factors, $\beta = 0.123$, p = 0.003, $sr^2 = 0.014$, such that women had fewer CVD risk factors than men, when controlling for age, race, low-income status, autistic traits, perceived stress, sleep quality, and antipsychotic medication use. Race, low-income status, autistic traits, perceived stress, and antipsychotic medication use were not significantly associated with number of CVD risk factors.

Predicting individual CVD risk factors

Diabetes

Results of our exploratory logistic regression models (Table 3) indicate that autistic adults who took antipsychotic medications had a 106.5% increased likelihood of having diabetes, B = 0.73, $\chi^2(1) = 4.14$, p = 0.04, exp(B) = 2.065. The likelihood of having diabetes was increased by 3.6% for each additional year of age, B = 0.04, $\chi^2(1) = 10.33$, p > 0.001, exp(B) = 1.036. Participants who were classified as having a low income had an 88.9% increased likelihood of having diabetes compared to participants who were not classified as having a low income, B = 0.64, $\chi^2(1) = 4.39$, p = 0.04, exp(B) = 1.889. Race, sex, autistic traits, perceived stress, and sleep quality were not significantly associated with diabetes.

High cholesterol

The likelihood of having high cholesterol was increased by 6.7% for each additional year of age, B = 0.07, $\chi^2(1) = 68.53$, p > 0.001, $\exp(B) = 1.067$. Sex, race, low-

income status, autistic traits, antipsychotic use, sleep quality, and perceived stress were not associated with the likelihood of high cholesterol.

High blood pressure

The likelihood of having high blood pressure was increased by 2.8% for each additional year of age, $B=0.03, \chi^2(1)=15.33, p>0.001, \exp(B)=1.028.$ Autistic men were 119.5% more likely than autistic women to have high blood pressure, $B=0.79, \chi^2(1)=16.19, p<0.001, \exp(B)=2.195.$ Finally, a one-unit increase in autism symptomatology was associated with a 2.2% increase in the likelihood of having high blood pressure, $B=0.02, \chi^2(1)=5.87, p=0.02, \exp(B)=1.022.$ Race, low-income status, perceived stress, sleep quality, and antipsychotic use were not associated with the likelihood of having high blood pressure.

Overweight or obesity

Each additional unit of poorer sleep quality was associated with a 6.5% increase in the likelihood that an autistic adult's BMI was in the range of overweight or obesity, B = 0.06, $\chi^2(1) = 5.82$, p = 0.02, $\exp(B) = 1.065$. Age, sex, race, low-income status, autistic traits, perceived stress, and antipsychotic use were not significantly associated with overweight or obesity.

DISCUSSION

In this study we aimed to describe and identify correlates of CVD risk factors in a large sample of autistic adults. Our analyses demonstrated that CVD risk factors were highly prevalent in autistic adults; 476 of the 545 autistic adults had one or more CVD risk factors, with overweight or obesity being the most common CVD risk factor among our sample of autistic adults aged 18-77. Older age, male sex assigned at birth, and poorer sleep quality were associated with a higher number of CVD risk factors. Using antipsychotic medications was associated with an increased likelihood of having diabetes, but not other CVD risk factors. Poorer sleep quality was associated with an increased likelihood of having a BMI that was in the overweight or obesity range. Our hypothesis that higher levels of perceived stress were associated with a greater number of CVD risk factors was not supported.

Self-reported CVD risk factor prevalence

Our study identified high prevalence of self-reported CVD risk factors in autistic adults. In non-autistic adults,

^{**}p < 0.01.

^{***}p < 0.001.

TABLE 3 Exploratory binary logistic regression predicting individual cardiovascular disease risk factors

	Diabetes N = 56			$\frac{\text{High cholesterol}}{N = 247}$			$\frac{\text{High blood pressure}}{N = 215}$			Overweight or obesity $N = 399$		
	В	SE	O.R.	В	SE	O.R.	В	SE	O.R.	В	SE	O.R.
Age	0.35	0.011	1.036***	0.065	0.008	1.067***	0.027	0.007	1.028***	-0.006	0.007	0.994
Male	0.241	0.310	1.272	0.121	0.202	1.128	0.786	0.195	2.195***	0.229	0.211	1.257
White	0.222	0.350	1.248	0.341	0.237	1.407	0.227	0.230	1.254	-0.149	0.243	0.862
Low income	0.636	0.304	1.889*	0.108	0.209	1.114	0.039	0.202	1.039	0.010	0.215	1.020
Autism quotient	0.001	0.014	1.001	0.009	0.009	1.009	0.022	0.009	1.022*	-0.004	0.010	0.996
Anti-psychotic use	0.725	0.356	2.065*	0.245	0.265	1.277	-0.093	0.265	0.911	-0.013	0.016	1.188
Perceived stress	-0.004	0.24	-0.996	-0.020	0.016	0.981	-0.001	0.015	0.999	-0.013	0.016	0.987
Sleep quality	0.062	0.039	1.064	0.022	0.025	1.022	0.035	0.024	1.035	0.063	0.026	1.065*

Note: Number (N) indicates the number of participants who reported having the relevant cardiovascular disease risk factor. †p < 0.1, *p < 0.05, **p < 0.01, ***p < 0.001.

a study using population-level data found that 46.5% have one or more CVD risk factor (Fryar et al., 2012). We found that 87.3% of autistic adults in our sample selfreported a diagnosis of at least one CVD risk factor including diabetes, high cholesterol, high blood pressure, and overweight or obesity—while 4.4% of autistic adults in our sample reported all four. Within our sample, 73.2% had BMI scores in a range associated with overweight or obesity, 45.3% had high cholesterol, 39.4% had high blood pressure, and 10.3% had diabetes. The rate of any CVD risk factor in the current study is notably higher than previously reported figures among autistic people using claims data. Bishop-Fitzpatrick and Rubenstein (2019) found that 46.2% of autistic adults had Medicaid claims for at least one CVD risk factor and Croen et al. (2015) found in their sample of autistic adults that 33.9% had obesity, 22.8% had dyslipidemia, 25.6% had hypertension, and 7.6% had diabetes.

There are several potential reasons why we identified a higher prevalence of CVD risk factors in our survey sample compared to population-level samples. Although administrative data are generally considered the gold standard for identifying CVD and its risk factors (Psaty et al., 2016), self-reported CVD risk factors data generally agree with administrative data at >80% in large, population-level studies in the general population (Muhajarine et al., 1997; Newell et al., 1999; Robinson et al., 1997; Tisnado et al., 2006; Yasaitis et al., 2015). However, the agreement between self-reported health data and electronic health record (EHR) or claims data has not been specifically tested in autistic adults. It is possible that system- or provider-level factors such as diagnostic overshadowing or lack of provider knowledge about autism that drive disparities in receipt of highquality healthcare among autistic adults (Nicolaidis et al., 2015) are associated with underdiagnosis of CVD risk factors in autistic adults or underreporting of diagnosed CVD risk factors in the EHRs or insurance claims of autistic adults. Neurodiversity-related discrimination may lead providers to not test autistic adults for comorbidities because of perceptions about the difficulty of diagnostic procedures (e.g., blood draws needed to test for diabetes and dyslipidemia) and/or to treat autistic adults' autism diagnosis rather than the health conditions that they present with (Bishop-Fitzpatrick & Kind, 2017; Bishop-Fitzpatrick, Movaghar, et al., 2018; Nicolaidis et al., 2015). The lack of training for healthcare professionals focused on how to treat and interact with autistic adults may contribute to underdiagnosis of co-occurring conditions (Nicolaidis et al., 2015). Finally, participants in our survey sample may have been motivated to participate in a study about adult development and aging because they are experiencing aging-related health changes such as CVD.

It is likely that the true prevalence of CVD risk factors lies in between estimates of prevalence reported in this study and others, although the concordance between claims and self-reports for CVD and its risk factors in the general population is relatively high (Tisnado et al., 2006). Taken together, data from this study and previous studies suggest that CVD risk factors are highly prevalent in autistic adults, pointing towards the need to increase the level of focus in autism research on CVD disparities in autistic people, as well as to increase awareness among general practitioners to screen for CVD in autistic people, particularly as they age.

The association between sleep quality and CVD risk factors

We found that poorer sleep quality was associated with both a higher total number of CVD risk factors as well as an increased likelihood of having a BMI in the range of overweight or obesity. The link between sleep quality and CVD risk factors is well-established: reduced sleep quality has been linked in meta-analytic studies with increased risk for both metabolic syndrome and coronary heart disease (Cappuccio et al., 2011; Lian et al., 2019), and our study suggests that this association also exists

among autistic adults. Notably, the odds ratios identified in our study were within the range identified by a recent meta-analysis of predominantly general population adults (Lian et al., 2019), suggesting that the magnitude of association between sleep quality and cardiovascular disease risk factors is similar. This is concerning because autistic adults, overall, report very poor sleep quality (Baker & Richdale, 2015; McLean et al., 2021), and we could expect that a larger proportion of autistic adults compared to adults in the general population will develop CVD risk factors if the correlational link between poor sleep quality and increased risk of CVD risk factors identified by this study is causal.

The association between antipsychotic medication use and CVD risk factors

Among our sample of autistic adults, we found that using antipsychotic medications was associated with having diabetes but was not associated with either number of CVD risk factors or with overweight and obesity, high cholesterol, or high blood pressure. Although our subsample of 82 autistic adults who used antipsychotic medications represented only 15.0% of our sample and we may have thus been underpowered to detect associations, this study provides preliminary evidence that suggests that antipsychotic medication use is associated with an increased likelihood of diabetes among autistic adults. Future research that leverages larger samples of autistic adults who use antipsychotic medications will help us to determine whether antipsychotic use is associated with increased risk for overweight and obesity or high blood pressure as in adults with serious mental illness who use medications (American antipsychotic Diabetes Association et al., 2004; Kahl et al., 2018; Kovacs & Arora, 2008; Mwebe & Roberts, 2019; Saari, 2004; Walker et al., 2015).

The association between perceived stress and CVD risk factors

Counter to our hypotheses, perceived stress was not associated with the presence of self-reported CVD risk factors. It is possible that the link between perceived stress and CVD identified within the general population (Richardson et al., 2012) simply does not exist among autistic adults. The fact that autistic adults have, overall, very high levels of perceived stress (Bishop-Fitzpatrick, Mazefsky, et al., 2018; Bishop-Fitzpatrick, Minshew, 2017b; Mazefsky, & Eack, Hirvikoski Blomqvist, 2015) may have attenuated the association between high levels of perceived stress and the presence of CVD risk factors. It is also possible that the relatively high correlation between perceived stress and sleep quality (r = 0.49), which is not over the r > 0.70 cutoff for

multicollinearity and thus does not violate regression assumptions, indicates that poorer sleep quality results from high levels of perceived stress, thus representing a causal pathway that could be tested in future longitudinal work.

Limitations

Our findings should be interpreted within the context of several limitations. First, our sample is a convenience sample that included a greater proportion of women than men. This documented sex ratio is reflective of other online studies of autistic adults (Rubenstein & Furnier, 2021). Furthermore, the sample did not include any autistic adults with co-occurring intellectual disability; therefore, it is not representative of the full population of autistic adults. Participants were not recruited to this study for the purpose of studying CVD risk factors in autistic adults (rather, adult development more broadly). Thus, our findings are not representative of the full population of autistic adults. However, this study does include a large proportion of participants who represent understudied groups within the autistic community, specifically women and middle aged and older adults. Second, our primary outcome variables (CVD risk factors) were selfreported and not confirmed by a medical professional. This may have led to error in terms of either over- or particularly under-reporting of CVD risk factors. Third, other variables that may be relevant to CVD risk factor development or CVD itself such as smoking, alcohol consumption, physical activity, and diet were unmeasured. The diagnosed prevalence of CVD or metabolic syndrome was also unmeasured in our sample. Although this study provides preliminary data that can inform future research on CVD in autistic adults, future research should specifically study the emergence of CVD to fully understand mechanisms underlying CVD emergence. Fourth, although our hypotheses framed perceived stress, sleep quality, and antipsychotic medication use as predictors of CVD risk factors, this study's design precluded a test of causal mechanisms underlying CVD risk factors in autistic adults given that data were cross-sectional. Future studies that investigate mechanisms underlying CVD in autistic adults should use longitudinal methods and include clinical diagnosis and/or confirmation of CVD and its risk factors. These future studies should also investigate historical antipsychotic use, dosage, and duration of antipsychotic use in order to disentangle mechanisms driving the link between antipsychotic use and CVD risk factors in autistic adults.

CONCLUSIONS

This study found that self-reported CVD risk factors are highly prevalent among autistic adults. It also found that

poorer sleep quality was associated with an increased number of CVD risk factors and with an increased likelihood of overweight/obesity, while using antipsychotic medications was associated with an increased likelihood of diabetes. Findings are highly suggestive that CVD risk factors represent a major risk factor for premature mortality among autistic adults and deserve increased attention in both clinical work and research (Mandell, 2018). Importantly, sleep quality and antipsychotic medication use are both mutable factors that can be altered with targeted intervention. Improving sleep quality and carefully monitoring CVD risk factors among autistic adults who take antipsychotic medications both have the potential to improve the quality of autistic adults' health and lives.

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DATA AVAILABILITY STATEMENT

Research data are not shared.

ETHICS STATEMENT

The study was approved by the local institutional review board and followed procedures in accordance with the Declaration of Helsinki.

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