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Cardiovascular risk and emotion regulation contribute to depression symptomatology in middle-aged and older autistic adults

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ABSTRACT

Background: Cardiovascular risk factors (CVRF) and executive function difficulties increase during later-life and are associated with depression symptoms among non-autistic older people. These associations, however, have not yet been explored among middle-aged and older autistic people.
Methods: Using data collected via Simons Foundation Powering Autism Research (SPARK), Research Match, we examined the frequency of CVRF, and associations between CVRF, executive function and depression symptoms in 387 middle-aged and older autistic people (aged 40–83 years).
Results: Autistic adults reported high rates of CVRF (two, 28.9%; three or more, 23.2%). Rates of high cholesterol and obesity were greater among middle-aged and older autistic adults compared to the general population. CVRF, age, and emotion regulation (but not inhibitory control), were significantly associated with depression symptoms in middle-aged and older autistic adults.
Conclusions: CVRF occur at high rates in middle-aged and older autistic adults, and it is important that healthcare providers monitor risk factors in order to implement preventative strategies. CVRF are associated with depressive symptoms among middle-aged and older autistic adults, but may not be as important as difficulties with emotion regulation.

1. Introduction

Many health problems become more common as people age into midlife and old age. Cardiovascular risk factors (CVRF) may be particularly important as they are associated with an elevated risk of stroke, vascular dementia and depression (Alexopoulos et al., 1997; Mahmood et al., 2014; Roman, Erkinjuntti et al., 2002). Cardiovascular health problems in mid-life are thought to be an

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important etiological factor for the development of depression in later life, forming the basis of the vascular depression hypothesis (Alexopoulos, 2019). CVRF include hypertension, obesity, hyperglycaemia often associated with diabetes, and hyperlipidaemia often characterised by high cholesterol and triglycerides. CVRF often co-occur, and combinations of these CVRF have been described as a metabolic syndrome (Reaven, 1993). Few studies have explored overall physical health and cardiovascular issues among autistic adults. Those that have suggest that many health conditions including CVRF occur at higher rates among autistic people compared to the general population. In studies utilising US Medicaid, Medicare, or electronic health record data, autistic people had higher rates of CVRF and cardiovascular disease (Bishop-Fitzpatrick et al., 2018, aged 4–89; Bishop-Fitzpatrick & Rubenstein, 2019, aged 40–88; Croen et al., 2015, Mean age = 29; Hand et al., 2020, age 65 years and older). As observed in the general population, rates of CVRF were increasingly common with older age, but rates of CVRF were significantly higher among autistic compared to non-autistic people across adulthood (Bishop-Fitzpatrick et al., 2018; Croen et al., 2015; Hand et al., 2020). In a study of autistic Medicaid beneficiaries aged over 40 years old, 46.2% of autistic adults had claims for CVRF and 49% had claims for cardiovascular disease (Bishop-Fitzpatrick & Rubenstein, 2019), with a similar pattern observed among autistic Medicare beneficiaries aged 65 and older (Hand et al., 2020). Given the cascade of difficulties associated with CVRF, it is important to understand more about the impact of CVRF on autistic people particularly in later life.

In the general population, presence of CVRF in middle-age has been associated with risk of cognitive difficulties and poor quality of life in older age (Daviglus et al., 2003; Olaya et al., 2019). CVRF may be particularly impactful in later life when they are associated with increased risk of stroke, but also with an increased risk of executive function difficulties and mood disorders (Alexopoulos et al., 1997; Dunbar et al., 2008; Mahmood et al., 2014). Across adulthood, presence or accumulation of multiple CVRF is associated with depression symptoms and development of depression in later life (Charlton et al., 2014; Dunbar et al., 2008; Foley et al., 2010; Kinder et al., 2004; Moulton et al., 2015). Even a small number of CVRF can have a significant negative impact on mood, and a higher number of CVRF is associated with higher self-rated depression scores (Lamar et al., 2015). CVRF are also associated with poorer executive function (more so than with other cognitive domains) among both middle-aged and older people (Leritz et al., 2011; Nishtala et al., 2014). Strong bi-directional associations exist between depression and executive function, with depression being both an outcome of poor executive function, and a risk for executive function difficulties (Bhalla & Butters, 2011). Simultaneity of depression, executive function difficulties, and slow walking speed is associated with the presence of CVRF among older people (Hajjar et al., 2009). In spite of the increased prevalence of CVRF and cardiovascular disease in autistic adults, studies have not yet examined the vascular depression hypothesis among middle-aged and older autistic people. If the association between CVRF and depression is similar among autistic compared to non-autistic people, then autistic adults may be at elevated risk of vascular depression due to existing high rates of CVRF relative to the general population.

Various mechanisms have been suggested to explain the associations between CVRF and depression. CVRF are hypothesised to reduce cortical blood flow, leading to white matter damage and disruption of fronto-subcortical pathways that support emotional regulation (Manning & Steffens, 2018). Although disruption of emotional regulation pathways are hypothesised to be a mechanism underlying vascular depression in middle-aged and older adults (see Alexopoulos, 2019 for details), studies rarely examine the self-regulation of emotion during this developmental window (Smoski et al., 2014). However, there is substantial literature exploring links between emotion regulation and depression among young adults (Joormann & Stanton, 2016). Of note, autistic people may demonstrate increased difficulties with the cognitive aspects of emotion regulation (Conner et al., 2021; Mazefsky et al., 2013); therefore exploring this association in later-life may be important. Alternatively, it has been suggested that both CVRF and depression may cause inflammation and disruption to the hypothalamus–pituitary–adrenal axis due to stress (Marazziti et al., 2014). While these mechanisms suggest that CVRF are causally linked to depression, evidence suggests that history of depression may be a risk factor for later cardiovascular health problems (Kinder et al., 2004; Marazziti et al., 2014). Apathy and disrupted eating habits associated with depression have been shown to increase likelihood of developing CVRF (Marazziti et al., 2014). Some studies suggest that dyslipidaemia (which may include high cholesterol) and obesity in particular may predict future development of depression (Akbaraly et al., 2009; Almeida et al., 2009). Whether this relates to purely cardiovascular risk or is impacted by psychosocial factors, including those associated with weight-stigma (i.e., sizeism) is not clear (Pausé et al., 2021). Overall there is strong evidence of a significant association between CVRF and depression, both across adulthood and particularly in later life in the general population (Marazziti et al., 2014; Repousi et al., 2018) yet this relationship has not been examined among autistic adults.

Autistic adults experience high rates of depression (Hand et al., 2020; Happe et al., 2016). A study of middle-aged and older (age range 40–88 years) Medicaid beneficiaries reported claims for depression treatment for nearly one-third of autistic people (28%) (Bishop-Fitzpatrick & Rubenstein, 2019). Similar rates of treatment for depression (35.9%) were observed among autistic Medicare beneficiaries aged over 65 years old (Hand et al., 2020), and in adults (18–74 years, Mean age = 30) receiving a first autism diagnosis (35%; Happe et al., 2016). High lifetime rates of depression among autistic people may be a risk factor for recurrent depression in later-life (Heun & Hein, 2005). Among both autistic and non-autistic people, depression and other mental health conditions have a significant impact on well-being and everyday functioning (Conry et al., 2011; Mason et al., 2018). Although a small number of studies have indicated that rates of CVRF and depression are high among autistic adults, no studies have yet examined associations between physical health and mental health difficulties in autistic people. Understanding whether CVRF are associated with depression for middle aged and older autistic people and how risk of late-life depression can be mitigated will be important to inform treatment and prevention activities for older autistic people.

Executive function difficulties, for example in inhibitory control and task switching, are also common among autistic adults (Johnston et al., 2019; Wallace et al., 2016), and this includes the cognitive aspects of emotional regulation (Conner et al., 2021; Mazefsky et al., 2013). Difficulties in emotional regulation are associated with higher rates of depressive symptoms in both autistic and non-autistic people (Joormann & Stanton, 2016; Morie et al., 2019). Young autistic adults report lower levels of executive function

ability (i.e. inhibitory control, planning, working memory, etc.) compared to a matched comparison group, with some (but not all) aspects of poorer executive function being associated with lower quality of life (Dijkhuis et al., 2017). Executive function difficulties may be particularly important for depression, as they are common in older depressed people and residual executive dysfunction often may remain even after depression symptoms reduce (Alexopoulos et al., 2005; Barch et al., 2012). Executive difficulties in middle-age and later-life are associated with CVRF, and interactions between executive function, depression and CVRF are likely to be important for outcomes such as risk of dementia (Bhalla & Butters, 2011; Charlton et al., 2006).

Emerging evidence suggests that CVRF, depression and executive function difficulties are common across the adult lifespan for autistic people. Whether CVRF and executive function can, in part, explain the high prevalence of depression among autistic people has not yet been assessed. Lifelong heightened presence of CVRF among autistic people may mean that autistic older adults are at increased risk for vascular depression and associated executive function difficulties in later life. The purpose of this study is to examine the associations between CVRF, executive function and depressive symptoms in a middle-aged and older autistic population. We hypothesise that middle-aged and older autistic adults will report high rates of CVRF, and that CVRF and executive function difficulties in the domains of inhibitory control and emotional regulation will be associated with depressive symptoms.

2. Methods

2.1. Participants

Autistic adults were recruited online via Simons Foundation Powering Autism Research (SPARK; Feliciano et al., 2018) Research Match. Participants were recruited to a larger online study examining adult development/ageing and were compensated $25 for their time. All 387 autistic participants were 40–83 years of age with 42 participants aged 65–74 and four aged over 75 years old. Characteristics of the sample are reported in Table 1. Autistic adults were mostly female (N = 224; 57.9%) and white (N = 321; 82.9%) and were, on average, 52.05 (SD=9.22) years old at the time that data were collected. The study was approved by the local institutional review board and followed procedures in accordance with the Declaration of Helsinki. All participants provided informed consent.

All individuals were "independent" autistic adults, as designated by SPARK. These individuals can consent for themselves and thus are unlikely to have a co-occurring intellectual disability. None of the participants in the current study reported intellectual disability as a prior medical diagnosis on a detailed health history questionnaire. In order to be included in the SPARK registry, participants had received a prior autism spectrum diagnosis by medical/clinical professionals. Moreover, a recent study validated these diagnoses within a portion of the overall participant registry. Based on review of electronic health records ~99% of these autism spectrum

Table 1
Demographic data (mean, standard deviation, range or count) for whole sample, and by number of CVRF.

	Whole Sample N = 387	No CVRF N = 81	1 CVRF N = 104	2 CVRF N = 112	3 CVRF N = 64	4 CVRF N = 26
Age	52.05 (9.22)	48.89 (7.61)	51.62 (8.89)	53.52 (9.61)	52.96 (9.37)	55.13 (10.73)
	40–83	40–73	40–74	40–83	40–75	42–78
Sex assigned at birth (m,f)[a]	163,224	28,53 (35%,	38,66 (37%,	52,60 (46%,	33,31 (52%,	12,14 (46%,
	(42%, 58%)	65%)	63%)	54%)	48%)	54%)
Race, count	321	71	80	94	48	23
White,	11	2	3	2	4	0
African-American,	7	0	3	4	3	0
Asian,	5	1	1	2	1	0
Native American/Alaska	38	7	13	9	6	3
Native,	4	0	4	1	5	0
Multiracial,						
Other						
Ethnicity, count	26	4	6	7	6	3
Latinx,	356	75	97	104	58	22
Not Latinx,	5	2	1	1	0	1
Unknown						
Percentage of CVRF endorsement	42.4%	0%	26.9%	45.5%	92.9%	100%
Obesity	46.5%	0%	20.2%	65.2%	93.8%	100%
Hypertension	57.6%	0%	51%	79.5%	85.9%	100%
High Cholesterol	14.7%	0%	1.9%	9.8%	28.1%	100%
Diabetes						
Autistic Traits (AQ-28) score	86.50 (10.62)	86.64 (11.31)	87.34 (9.37)	85.93 (10.74)	86.02 (11.78)	86.42 (10.17)
	55–110	67–110	55–105	65–110	55–109	65–108
Depression (PHQ-9) score	10.19 (7.22)	9.13 (7.07)	9.73 (7.03)	10.20 (7.20)	11.46 (7.18)	12.13 (8.32)
	0–27	0–25	0–27	0–26	0–27	0–26
Inhibitory Control (BDEFS) score	39.73 (10.82)	40.44 (12.05)	38.81 (10.92)	38.97 (10.22)	40.86 (10.09)	41.58 (10.82)
	19–75	22–75	19–73	21–68	23–63	24–68
Emotional Regulation (BDEFS)	30.84 (9.64)	32.60 (9.00)	29.99 (9.72)	30.68 (9.45)	29.92 (10.17)	31.73 (10.58)
score	13–52	15–52	13–52	13–52	13–51	14–52

[a] n = 387; BDEFS = Barkley Deficits in Executive Functioning Scale

diagnoses were confirmed (Fombonne et al., 2022). To further validate the autism spectrum diagnoses, participants were asked to complete the 28-item self-report Autism Spectrum Quotient-28 (AQ-28; Hoekstra et al., 2011). Nearly all participants completed the AQ-28 (386 of 387), and 97.7% of these participants reported scores > 65 (indicating a positive screen for ASD).

Data used in this study is held by SPARK and qualified researchers can apply to access SPARK data through Simons Foundation Autism Research Initiative (SFARI) Base (https://base.sfari.org/).

3. Measures

3.1. Demographic Information

Participants provided detailed demographic information including age, race, ethnicity, and sex assigned at birth.

CVRF. CVRF were rated as present or absent based on self-reported history of hypertension, high cholesterol, and diabetes (either type 1 or type 2). Participants reported their height and weight, and Body Mass Index (BMI) was calculated using CDC age- and sex-based norms to identify presence of co-occurring obesity (BMI≥30). Rates of CVRF are reported in Table 1. Total number of CVRF endorsed was calculated based on having hypertension, high cholesterol, diabetes and obesity (range 0–4).

3.2. Executive Function

Executive function in the domains of Inhibitory Control (Self-Restraint sub-scale) and Emotional Regulation (Self-Regulation of Emotion sub-scale) were measured using the self-report Barkley Deficits in Executive Functioning Scale (Barkley, 2011). These scales were selected to explore executive control (inhibition), which is often associated with late-life depression, and the cognitive aspects of emotional regulation implicated in depression across the lifespan. Inhibitory Control is measured on 19 items, such as "I make decisions impulsively"; and Emotional Regulation is measured on 13 items, such as "I remain emotional or upset longer than others". Responses are on a 4-point Likert scale from 1 ("Never or rarely") to 4 ("Very often"). Thus, the range of scores for Inhibitory Control is 19–76, and for Emotional Regulation is 13–52. The Barkley Deficits in Executive Functioning Scale has good internal consistency (Cronbach's alphas=0.91–0.95), interobserver agreement (r = 0.66–0.79), and test-retest reliability (between r = 0.62 and r = 0.84) across the scales (Barkley & Murphy, 2011; Barkley, 2014).

3.3. Depression

Self-reported depressive symptoms were assessed using the 9-item Patient Health Questionnaire (PHQ-9; Kroenke et al., 2001), which has been validated for use with autistic people (Arnold et al., 2020; Cassidy et al., 2018). Participants reported the presence/frequency of depressive symptomatology on a 4-point Likert scale ("Not at all," "Several days," "More than half the days," "Nearly every day"). Scores range from 0 to 27, with scores ≥ 10 indicating moderate or severe depression. Using a cut-off of ≥ 10 the PHQ-9 has been shown to have 88% sensitivity and specificity for major depressive disorder (Kroenke et al., 2001). On average, the middle-aged and older autistic adults in our sample had a depression score of 10.19 (SD=7.22), which is above the clinical cut-off for depression on the PHQ-9.

3.4. Statistical Analysis

Hypotheses were planned in advanced but were not pre-registered. Statistical analysis was performed using SPSS (version 27; IBM Corp, 2020). The frequency of CVRF among autistic older people was examined. Stepwise linear regressions were conducted to explore the extent to which CVRF and executive function uniquely (after accounting for covariates) contributed to the models explaining depressive symptoms among middle-aged and older autistic people. Hence the dependent variable was PHQ-9 scores. Independent variables in Model 1 were age, sex assigned at birth, and number of CVRF; with AQ-28 scores added in Model 2; and Inhibitory Control and Emotional Regulation scores added in Model 3. Associations (non-parametric correlations) between the independent variables were reported in order to allow examination of shared variance.

4. Results

The frequency and number of CVRF reported by autistic adults are presented in Table 1. High cholesterol was the most frequent CVRF, occurring in 57.6% of participants in the current study. Obesity (42.4%; note a further 32% meet criteria for overweight; thus 74.4% of autistic adults had BMI values consistent with either obesity or overweight) and hypertension (46.5%) were both common, although rates of diabetes were lower (14.7%). Three or more CVRF (hypertension, diabetes, high cholesterol, obesity) were present in 23.2% of participants.

4.1. Regression analysis

Stepwise regression models explored the variables that were associated with depressive symptoms. In Model 1, after accounting for demographic factors (age and sex assigned at birth), CVRF contributed a small but significant proportion of variance to the model ($\beta = 0.165$, $p = .001$; $F=7.58$. $p < .001$). In Model 2, autistic traits were added. The pattern of results remained the same, with demographic

factors, autistic traits and CVRF contributing to the variance in depressive symptoms. In Model 3, inhibitory control and emotion regulation were added. Emotion regulation contributed significantly to the model ($\beta = 0.496$, $p < .001$), as did CVRF ($\beta = 0.168$, $p < .001$) and age ($\beta = -0.185$, $p < .001$; Final model: $F=52.69$, $p < .001$). The beta weights for CVRF and age were at similar levels to the previous models. Model 3 explained substantially more variance than the previous models with the addition of emotional regulation. However inhibitory control, sex assigned at birth and autistic traits did not contribute significantly to the final model (see Table 2). In order to allow examination of possible shared variance, correlations between independent variables are presented in Table 3. The false discovery rate (FDR) multiple comparison correction procedure was applied and all correlations survived FDR corrections ($q<0.05$). Inhibitory control and emotional regulation were significantly correlated with one another. Age (negatively) and AQ scores (positively) correlated significantly with both inhibitory control and emotional regulation.

5. Discussion

In this paper we report the rates of CVRF in a relatively large sample of middle-aged and older autistic adults. High cholesterol, obesity and hypertension were common among these autistic adults, but diabetes was less common. In this sample 23.2% of the participants reported that they have three or more CVRF, which is a slightly lower proportion than diagnoses reported in similar aged non-autistic samples (Butnoriene et al., 2018, 34% with 3 + CVRF; Tournoy et al., 2010, 32% with 3 + CVRF). The frequency of hypertension (46.5%) and diabetes (14.7%) are similar to the US population rates (hypertension=49.6%, https://www.cdc.gov/nchs/fastats/hypertension.htm; diabetes=10.5%, https://www.cdc.gov/diabetes/data/statistics-report/index.html). Compared to a previous study of Medicaid claims data for similar aged non-intellectually disabled autistic people, the current sample rates of hypertension are higher (46.5% compared to 22%) but rates of diabetes are lower (14.7% compared to 23%; Bishop-Fitzpatrick & Rubenstein, 2019). The rates of high cholesterol (57.6%) in the current sample are much higher than rates in both the US population (11.5%; https://www.cdc.gov/nchs/fastats/cholesterol.htm) and Medicaid data for similar aged non-intellectually disabled autistic people (dyslipidemia 27%; Bishop-Fitzpatrick & Rubenstein, 2019). Rates of obesity are slightly higher (42.2%) in the current sample than in the US population (34.3%; https://www.cdc.gov/obesity/data/index.html), although frequency of being overweight is similar (SPARK sample=32%; US population=37.7%, https://www.cdc.gov/obesity/data/index.html). Disparate findings between our study and previous studies may reflect the limitations of self-report data in accurately capturing diagnoses, limitations of claims data in capturing chronic conditions, the large proportion of our sample that was assigned female at birth, barriers to healthcare access and engagement (and diagnoses that may result from interfacing with the healthcare system), and/or differences between autistic adults who are or are not Medicaid-eligible. It is also possible that self-reported CVRF are under-estimates, due to reduced access to and engagement with healthcare by autistic people. The results suggest that autistic adults without intellectual disabilities may be at particular risk of having or developing high cholesterol and/or obesity, which could be particularly important in ageing as these conditions increase risk for stroke and vascular dementia. Whether these risk factors are associated with lifestyle factors linked to being autistic (i.e. restricted eating; sensory sensitivities related to exercise) or to yet unknown genetic or biological mechanisms underlying heightened risk of CVRF in autistic people, cannot be resolved in the current study but this open question warrants further exploration. Future studies should investigate whether the pattern of increased risk for high cholesterol and obesity are also present among middle-aged and older autistic people with intellectual disabilities.

This study also explored whether the pattern of associations between CVRF, executive function and depressive symptoms observed in numerous studies in the general population (Alexopoulos et al., 1997; Mahmood et al., 2014) was also observed in a sample of middle-aged and older autistic adults. After accounting for age-effects, CVRF contributed significantly to the model explaining depressive symptoms. The pattern of results observed in this study are similar to those seen in non-autistic young adults (Kinder et al.,

Table 2
Results of stepwise regressions explaining variance in depression symptoms.

	Standardised Beta-weights	R^2 Change and F change at each step
Model 1		
Age	$\beta = -0.164$, $p = .001$	$R^2 = .022$; $F= 8.77$, $p = .003$
Number of CVRF	$\beta = 0.165$, $p = .001$	R^2 change= 0.023; $F= 9.33$, $p = .002$
Sex assigned at birth	$\beta = 0.104$, $p = .039$	R^2 change= 0.011; $F= 4.30$, $p = .039$
Model Summary	**R^2= .056; F= 7.58, p < .001**	
	All variables included in model	
Model 2		
AQ	$\beta = 0.160$, $p = .001$	R^2 change= 0.024; $F= 9.64$, $p = .002$
Age	$\beta = -0.164$, $p = .001$	R^2 change= 0.022; $F= 8.82$, $p = .003$
Number of CVRF	$\beta = 0.172$, $p = .001$	R^2 change= 0.025; $F= 10.39$, $p = .001$
Sex assigned at birth	$\beta = 0.112$, $p = .026$	R^2 change= 0.012; $F= 5.02$, $p = .026$
Model Summary	**R^2= .074; F= 8.71, p < .001**	
	All variables included in model	
Model 3		
Emotional Regulation	$\beta = 0.496$, $p < .001$	$R^2 = .242$; $F= 122.60$, $p < .001$
Age	$\beta = -0.185$, $p < .001$	R^2 change= 0.024; 12.30, $p = .001$
Number of CVRF	$\beta = 0.168$, $p < .001$	R^2 change= 0.027; $F= 14.64$, $p < .001$
Model Summary	**R^2= .293; F= 52.69, p < .001**	

Excluded variables: Sex assigned at birth, $\beta = 0.071$, $p = .105$; AQ scores, $\beta = 0.071$, $p = .104$; Inhibitory Control, $\beta = -0.002$, $p = .972$.

Table 3
Nonparametric correlations between variables.

	Age	Number of CVRF	AQ scores	Inhibitory Control
Number of CVRF	rho= 0.185			
AQ scores	rho= −0.001	rho= −0.042		
Inhibitory Control[a]	rho= −0.167 * ** ǂ	rho= 0.056	rho = 0.148 * * ǂ	
Emotional Regulation[a]	rho= −0.154 * * ǂ	rho= −0.053	rho = 0.203 * ** ǂ	rho = 0.669 * ** ǂ

[a] BDEFS (Barkley Deficits in Executive Functioning-Scale) total scores with test correction for age and sex used in the analysis; * ** ≤.001, * *≤ 0.01; ǂ indicates correlations that survive false discovery rate multiple comparison correction (q<0.05).

2004), people with late-life depression and euthymic older people (Charlton et al., 2014; Kinder et al., 2004; Mahmood et al., 2014); however, the strength of the association between CVRF and depression is much weaker in this sample of middle-aged and older autistic people. Although CVRF contributed to the final model (at a similar level in each model), the strongest association was between emotional regulation and depressive symptoms in Model 3 (see Table 2). This association is in keeping with results in young people from the general population with depression (Joormann & Stanton, 2016). However, few studies in middle-age and later life have examined the cognitive domain of self-regulation of emotion (most have focused on the age-related positivity effect - the finding that older people tend to be more attentive to positive compared to negative stimuli - using experimental methods, see Isaacowitz et al., 2018; Mather, 2012). While late-life depression is strongly associated with executive function difficulties, most studies have focused on aspects of executive function such as inhibitory control or working memory (Alexopoulos et al., 2005; Barch et al., 2012). These studies demonstrate poorer inhibitory control in depressed compared to non-depressed older people (Katz et al., 2010). In contrast, in the current study, inhibitory control did not contribute to the model explaining depressive symptoms. Results suggest that while CVRF may contribute to depressive symptoms in middle-aged and older autistic adults, they seem to explain a smaller proportion of the variance in depressive symptoms compared to findings in the general ageing population (Charlton et al., 2014; Lamar et al., 2015). For autistic people in middle- and old-age, previous episodes of depression, lifelong stressors and related inflammatory responses may be more important than CVRF for explaining depressive symptoms (Heun & Hein, 2005). Inhibitory control was not significantly associated with depressive symptoms, suggesting that emotional regulation is particularly important rather than global executive function per se. Overall these results suggest that for older autistic people the pattern of associations with depressive symptoms may differ to that seen in non-autistic older people.

The current study should be considered with certain limitations in mind. Although intellectual ability was not measured in this study, the cognitive demands of the survey and the participants' relatively high rates of postsecondary educational attainment suggest that participants have abilities within the average range or higher. Therefore, people included in this study do not reflect the experiences of all autistic adults (e.g., those with co-occurring intellectual disability). This study included a relatively high proportion (58%) of autistic adults assigned female at birth compared to US population-based expectations (e.g. Dietz et al., 2020). Although the inclusion of a large number of autistic adults assigned female at birth may not be comparable to most other studies of autism, it is a benefit to include this largely neglected and under-studied segment of the autism population. The determination of CVRF was based on self-report and rated as present or absent, which will be less accurate and include less variance than direct, interval-level measurement of CVRF. However, the advantage of this study is that it includes a prospectively ascertained community-based sample of middle-aged and older autistic people. The sample also includes a large number of autistic people from understudied groups including middle-aged and older autistic adults (Mason et al., 2022).

Further studies, particularly those employing longitudinal designs, are required to examine the impact of CVRF on psychosocial- and health-related outcomes for autistic older people and to further explore this and other factors important for late-life depression. In summary, CVRF are common among middle-aged and older autistic adults, consistent with rates observed in the general population. CVRF are modestly associated with presence of depressive symptoms among autistic people, although other factors such as emotional regulation may be more important for depressive symptoms in middle-age and later life.

Lay summary

Health problems that affect the heart and blood vessels are common in later life. Such heart-related health problems and the ability to regulate one's own emotions can influence depression symptoms. There is growing evidence that autistic people may be at risk for heart-related health problems. We do not know whether heart-related health problems and the ability to regulate one's emotions are linked to depression among middle-aged and older autistic people. We found high rates of heart-related health problems for middle-aged and older autistic people. Heart-related health problems are related to depression symptoms in autistic people to a medium degree in middle aged and older autistic people. The ability to regulate one's emotions is related to depression symptoms to a large degree in middle aged and older autistic people.

Declarations

Ethics

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

Helsinki.

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CRediT authorship contribution statement

Rebecca A. Charlton: Conceptualization, Methodology, Investigation, Formal analysis, Writing – original draft. **Goldie A. McQuaid:** Conceptualization, Methodology, Investigation, Data curation, Writing – review & editing. **Lauren Bishop:** Conceptualization, Writing – review & editing. **Gregory L. Wallace:** Conceptualization, Methodology, Investigation, Resources, Supervision, Data curation, Writing – review & editing.

Declaration of Conflicts of Interest

The authors have no conflicts of interest to declare.

Data Availability

The authors do not have permission to share data.

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Contribution Statement

The study was conceived and designed by Rebecca Charlton and Gregory Wallace. Material preparation and data collection were performed by Gregory Wallace and Goldie McQuaid. Data analysis was performed by Rebecca Charlton and Gregory Wallace. The first draft of the manuscript was written by Rebecca Charlton and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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