Cardiometabolic conditions in people with autism spectrum disorder: a nationwide prospective cohort study from the Netherlands

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Abstract

Little is known about the association between autism spectrum disorder (ASD) and cardiometabolic conditions across the lifespan. We conducted the largest cohort study, using Dutch register data of 8,690,286 individuals aged 12–65 years. These individuals were followed up from January 1, 2014 to their first incidence of cardiometabolic conditions, emigration, death, or December 31, 2020. Cox proportional-hazards models indicated ASD was associated with higher risks of cardiometabolic conditions (hazard ratio (HR): 1.20, 95% confidence interval (CI): 1.18–1.23, specifically hypertension (HR: 1.16; CI: 1.14–1.19), dyslipidemia (HR: 1.17; CI: 1.12–1.23), diabetes (HR: 1.22; CI: 1.14–1.30), stroke (HR: 1.23; CI: 1.14–1.34), and heart failure (HR: 1.28; CI: 1.07–1.53). Sex-stratified findings were similar. Associations were observed in adolescent, young (18–30 years), and middle-aged (31–40 years), but not older individuals, indicating earlier onset in autistic compared to non-autistic individuals. Our results underscore the need of monitoring and treatment of cardiometabolic conditions among individuals with ASD.

Main

Autism spectrum disorder (ASD) is a lifelong neurodevelopmental condition that typically manifests during early childhood [1]. ASD often co-exists with various psychiatric and somatic conditions [2-4]. Cardiometabolic conditions such as hypertension and diabetes have recently been reported as important comorbidities of ASD, which can worsen disparities in quality of life and life expectancy [5]. However, research focusing on the comorbidity of ASD and cardiometabolic conditions is limited.

The association between ASD and cardiometabolic conditions across the lifespan remains largely unknown. A recent meta-analysis revealed an association between ASD and diabetes, dyslipidemia, and heart disease [5]. However, most existing studies, including this meta-analysis, rely on cross-sectional data from children and young adults, with small sample sizes [5-11]. Given that the risk of cardiometabolic conditions generally increases with age [12], it is important to broaden existing evidence by investigating prospective associations across the lifespan, extending beyond children and young adults to older age groups. Furthermore, ASD and metabolic syndrome are more prevalent in males than females [13-15]. However, it remains unclear whether the associations in males differ from females.

Another notable limitation in most existing research is the absence of adjustment for potential confounders [5], such as socioeconomic status (SES) and psychiatric conditions that co-occur with ASD, which may alter the interpretation of observed associations. SES is associated with both ASD [16] and cardiometabolic conditions [17]. Additionally, ASD is highly comorbid with other psychiatric conditions, which on their own may increase the risk of cardiometabolic conditions [3,18,19]. For example, previous research has shown that the risk of somatic conditions varies with comorbid intellectual disabilities in young autistic individuals [3]. Similarly, another study revealed that attention-deficit/hyperactivity disorder (ADHD) is associated with a broad range of cardiovascular diseases [19] and it is well known that ASD and

ADHD often co-occur [20,21]. However, there is a notable lack of understanding of how SES and comorbid psychiatric conditions may be relevant to the association between ASD and cardiometabolic conditions.

Objectives

This study aimed to investigate the prospective association between ASD and cardiometabolic conditions across the lifespan. Using medical claims data from the Dutch nationwide population register, we examined associations with various cardiometabolic conditions, including hypertension, diabetes, dyslipidemia, stroke, angina pectoris, myocardial infarction, and heart failure. We analyzed the associations stratified by sex and age. Furthermore, we investigated whether and to what extent any observed associations were altered after adjusting for SES and comorbid psychiatric conditions.

Results

Cohort description

As shown in Table 1, the study cohort contained 8,690,286 individuals born between 1949 and 2002 with a mean age of 36.11 (standard deviation (SD): 15.01) years at baseline 2014. Among these, 111,795 (1.29%) were diagnosed with ASD, of whom 82,434 (73.74%) were male. The average age at baseline in the ASD group was 24.58 (SD: 12.42) years, while it was 36.26 (SD: 14.98) years in the non-ASD group. Comorbid psychiatric conditions diagnosed before baseline (between 2011 and 2014) were present in 45,285 individuals (40.51%) in the ASD group and in 500,248 individuals (5.83%) in the non-ASD group. Table 1 also presents the incidence and age at new onset of each outcome during the follow-up period.

Table 1. Characteristics of the study population

Characteristic	Total N=8,690,286	Non-ASD n=8,578,491	ASD n=111,795
Sex (male), n (%)	4,511,656 (51.92)	4,429,222 (51.63)	82,434 (73.74)
Birth year, n (%)			
[2002,1997]	1,168,587 (13.45)	1,124,945 (13.11)	43,642 (39.04)
(1997,1984]	2,351,148 (27.05)	2,311,309 (26.94)	39,839 (35.64)
(1984,1974]	1,553,801 (17.88)	1,541,797 (17.97)	12,004 (10.74)
(1974,1964]	1,786,116 (20.55)	1,775,948 (20.70)	10,168 (9.10)
(1964,1949]	1,830,634 (21.07)	1,824,492 (21.27)	6,142 (5.49)
Age in 2014 (years), mean (SD)	36.11 (15.01)	36.26 (14.98)	24.58 (12.42)
Socioeconomic classification in 2014, n (%)			
Employee	6,644,163 (79.32)	6,567,269 (79.45)	76,894 (69.14)
Benefit recipient	966,315 (11.54)	940,426 (11.38)	25,889 (23.28)
Pension recipient	247,099 (2.95)	244,517 (2.96)	2,582 (2.32)
Student	64,438 (0.77)	63,437 (0.77)	1,001 (0.90)
No income	454,757 (5.43)	449,915 (5.44)	4,842 (4.35)
Gross income (yearly, euros) in 2014, mean (SD)	43,825.47 (44,768.64)	43,884.94 (44,772.93)	39,407.31 (44,225.84)
Prevalence of psychiatric conditions during 2011-2014, n (%)			
Any psychiatric comorbidity	545,533 (6.28)	500,248 (5.83)	45,285 (40.51)
Depressive disorders	190,415 (2.19)	179,768 (2.10)	10,647 (9.52)
Anxiety disorders	163,983 (1.89)	154,407 (1.80)	9,576 (8.57)
Personality disorders	144,115 (1.66)	136,224 (1.59)	7,891 (7.06)
ADHD	135,551 (1.56)	114,423 (1.33)	21,128 (18.90)

Characteristic	Total N=8,690,286	Non-ASD n=8,578,491	ASD n=111,795
Substance use disorders	74,155 (0.85)	69,816 (0.81)	4,339 (3.88)
Schizophrenia	36,379 (0.42)	33,462 (0.39)	2,917 (2.61)
Bipolar disorders	22,931 (0.26)	21,746 (0.25)	1,185 (1.06)
Eating disorders	19,817 (0.23)	18,690 (0.22)	1,127 (1.01)
Intellectual disability	15,661 (0.18)	10,913 (0.13)	4,748 (4.25)
Incidence of cardiometabolic conditions during 2014-2020[a], n (%)			
Any cardiometabolic condition	1,113,030 (12.81)	1,101,573 (12.84)	11,457 (10.25)
Diabetes	136,178 (1.57)	134,925 (1.57)	1,253 (1.12)
Hypertension	858,477 (9.88)	849,347 (9.90)	9,130 (8.17)
Dyslipidemia	354,405 (4.08)	352,235 (4.11)	2,170 (1.94)
Stroke	96,225 (1.11)	95,498 (1.11)	727 (0.65)
Angina pectoris	65,756 (0.76)	65,430 (0.76)	326 (0.29)
Myocardial infarction	42,329 (0.49)	42,119 (0.49)	210 (0.19)
Heart failure	21,279 (0.24)	21,125 (0.25)	154 (0.14)
Age at new onset of cardiometabolic conditions during 2014-2020, (years) median (IQR)			
Any cardiometabolic condition	51 (38, 59)	51 (38, 59)	29 (20, 47)
Diabetes	48 (35, 57)	48 (35, 57)	35 (25, 49)
Hypertension	51 (37, 59)	51 (37, 59)	26 (20, 45)
Dyslipidemia	57 (50, 62)	57 (50, 62)	49 (40, 57)
Stroke	55 (47, 62)	55 (47, 62)	44 (25, 54)
Angina pectoris	57 (51, 63)	57 (51, 63)	53 (46, 60)
Myocardial infarction	57 (50, 62)	57 (50, 62)	53 (47, 60)
Heart failure	58 (50, 64)	58 (50, 64)	49 (31, 58)

Abbreviations: SD, standard deviation; IQR, interquartile range; ASD, autism spectrum disorder; ADHD, attention-deficit/hyperactivity disorder.

[a] This sample did not include individuals who had a history of diagnosis or medication dispensation for cardiometabolic conditions (ATC codes: C, A10A, and A10B) before baseline (2014).

Main results

Overall, there was a lower cumulative incidence of cardiometabolic conditions in individuals with ASD than in those without ASD at the end of the follow-up period (10.3% vs. 13.2%) due to the average younger age of people with ASD. Among the different age groups (12-17, 18-30, 31-40, and 41-50 years), individuals with ASD had a higher cumulative incidence of cardiometabolic conditions than those without ASD (eTable 1 and eFigure 1).

As shown in Figure 1, adjusted for birth year and sex, individuals with ASD had an increased risk of having any cardiometabolic condition (hazard ratio (HR): 1.20, 95% confidence interval (CI): 1.18-1.23) compared with non-ASD group (Model 1). Specifically, associations were observed for hypertension, dyslipidemia, diabetes, stroke, and heart failure (Model 1). After adjusting for SES, the association was slightly reduced (HR: 1.11, 95% CI: 1.09-1.13) but remained statistically significant (Model 2). Subsequent inclusion of each psychiatric comorbidity further reduced the associations without eliminating statistical significance (Models 3_a-3_i, eTable 2).

To further illustrate the influence of comorbid psychiatric conditions, the HRs of individuals with both ASD and psychiatric comorbidities were compared to those without ASD. After adjusting for covariates (Table 2, Model 2), we found that individuals with ASD and comorbid psychiatric disorders, except intellectual disability, had a greater risk of developing cardiometabolic conditions than those without ASD. The highest increased risk was observed in individuals with ASD and eating disorders (HR: 2.03, 95% CI: 1.77-2.33) (Table 2, Model 2).

Table 2. Hazard ratios (HR) with 95% confidence intervals (CI) of developing any cardiometabolic condition in people with ASD and psychiatric comorbidities, compared with those without ASD

Predictors[a]	Model 1		Model 2	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value
ASD and depressive disorders	1.55 (1.48-1.63)	<.001	1.39 (1.32-1.46)	<.001
ASD and anxiety disorders	1.76 (1.67-1.86)	<.001	1.57 (1.49-1.66)	<.001
ASD and personality disorders	1.53 (1.45-1.61)	<.001	1.32 (1.25-1.39)	<.001
ASD and ADHD	1.27 (1.21-1.33)	<.001	1.17 (1.12-1.23)	<.001
ASD and substance use disorders	1.65 (1.53-1.79)	<.001	1.39 (1.29-1.50)	<.001
ASD and schizophrenia	1.52 (1.38-1.67)	<.001	1.23 (1.12-1.35)	<.001
ASD and bipolar disorders	1.81 (1.58-2.07)	<.001	1.58 (1.38-1.81)	<.001
ASD and eating disorders	2.24 (1.96-2.57)	<.001	2.03 (1.77-2.33)	<.001
ASD and intellectual disability	1.19 (1.09-1.31)	<.001	1.04 (0.94-1.14)	0.441

Abbreviations: HR, hazard ratio; CI, confidence interval; ASD, autism spectrum disorder; ADHD, attention-deficit/hyperactivity disorder.

Model 1 was adjusted for birth year and sex.

Model 2 was further adjusted for socioeconomic classification and income.

[a] Individuals were classified as “non-ASD” (as the reference group), “ASD without a specific comorbid psychiatric condition” (e.g., ASD without ADHD), or “ASD with the specific comorbid psychiatric condition” (e.g., ASD co-occurring with ADHD) in each model. The HRs of “ASD without a specific comorbid psychiatric condition” (not in the table) were slightly lower than those with ASD and the specific comorbid psychiatric condition, except for intellectual disability, ranging between 1.23 to 1.28 in Model 1 and 1.14 to 1.19 in Model 2.

Subgroup analyses

When stratified by age subgroups, a significant HR identified for any cardiometabolic condition in the main analysis was observed in the age groups 12-17, 18-30, and 31-40 years (Figure 2), but not in older individuals. This decreasing trend in the associations across young and older individuals is indicative of an earlier onset of these cardiometabolic conditions in individuals with ASD (Figure 2 and eFigure 2). When stratified by sex, associations were observed in both males and females (Figure 2 and eFigure 3).

Sensitivity analyses

The results from the sensitivity analyses using ASD as a time-independent predictor were comparable to the main results (eTable 3).

Discussion

To our knowledge, this is the largest nationwide cohort study to examine the prospective associations between ASD and cardiometabolic conditions across the lifespan. Among over 8 million Dutch residents, we found that individuals with ASD were at an increased risk of developing cardiometabolic conditions such as hypertension, dyslipidemia, diabetes, stroke, and heart failure. However, no significant association was observed of ASD with angina pectoris or myocardial infarction. Our findings further showed that the estimates for men and women were similar, indicating that the presence of ASD does not alter the potential sex differences in the presence of cardiometabolic conditions in the general population. Associations were particularly prominent in the younger age groups, indicating an earlier age at onset of cardiometabolic conditions in ASD. Finally, the presence of co-occurring psychiatric conditions typically added to the strength of associations.

Our results showed robust associations between ASD and hypertension, dyslipidemia, and diabetes. These associations support findings from a few published studies that predominantly used a cross-sectional design and small sample sizes [6-11,22], including a recent meta-analysis suggesting associations of ASD with diabetes and dyslipidemia [5]. This meta-analysis also found an association between ASD and hypertension but only in children. Our study extends previous findings by confirming the association between ASD and hypertension in adolescents and young adults. Additionally, the associations persisted regardless of SES and psychiatric conditions, which has rarely been explored. Moreover, for the first time, we have identified an elevated risk of stroke (in adolescents and young adults) and heart failure (in young adults) in autistic people. However, these findings need to be interpreted with caution given limited number of cases in the ASD group (for stroke: n=107 in adolescents and n=153 in young adults; heart failure: n=32 in young adults).

An important finding of our study was that individuals with ASD have an earlier onset of cardiometabolic conditions. To illustrate, following the exclusion of all people who had developed a cardiometabolic condition before baseline, we found an average age of newly diagnosed hypertension of 26 years in autistic individuals compared to 51 years in non-autistic individuals. A similar pattern was also observed of other cardiometabolic conditions (Table 1). Additionally, associations between ASD and cardiometabolic conditions were observed in adolescents, young, and middle-aged adults but not in older individuals (41-65 years). Notably, these age-stratified findings warrant consideration of the changes in the recognition of ASD over time. Historically, the recognition of ASD has been notably low, but this has been significantly increased in recent times owing to improved clinician training and heightened public awareness. This history of recognition has likely led to under- or misdiagnosis of ASD in current older generations and a potential overdiagnosis in the current younger generation [23]. Our data likely reflect both trends: although the overall prevalence of 1.3% in our sample aligns with the 1-2% reported in the literature [24,25], we estimated a prevalence of 3.7% among adolescents, whereas

individuals aged 41-65 years exhibited a notably lower prevalence of 0.5%. Thus, the younger groups likely contain individuals with milder forms of ASD, whereas older groups probably consist of individuals with more severe forms of ASD, often with comorbid intellectual disabilities [26,27]. The misclassifications would underestimate the associations between ASD and cardiometabolic conditions in both younger (non-autistic individuals who have a lower risk of cardiometabolic conditions were misclassified as ASD, therefore attenuating the risk in the ASD group) and older individuals (autistic individuals who have a higher risk of cardiometabolic conditions were misclassified as non-ASD, therefore enhancing the risk in the non-ASD group). Given that fewer individuals with ASD were identified in older groups, this may partially explain the absence of an association.

The absence of differences between autistic and non-autistic individuals in older age groups may also reflect the premature mortality of autistic individuals, as shown by both our study and previous research [28,29]. In a nationwide study in Sweden, the estimated average age of death in the autistic population was 54 years, compared to 70 years in non-autistic controls from the general population [28]. Our study also indicated a higher cumulative risk of mortality in individuals with ASD than in those without ASD across all age subgroups (eTable 1 and eFigure 1). This finding suggests that the associations may be attenuated in older age groups due to survival bias. This can also partially explain the absence of an association with angina pectoris or myocardial infarction, which are more severe forms of cardiovascular conditions with a later onset than hypertension, diabetes, and dyslipidemia.

A final interesting finding in our study is that eating disorders showed the highest increased risk (HR: 2.03) among the nine comorbid psychiatric conditions that we studied. Autistic people are at a higher risk of developing eating disorders, such as binge eating and selective eating (e.g., high-calorie foods), which may be attributed to difficulties in emotional regulation and rigid thinking [30-32]. Therefore, comorbid eating disorders in individuals with ASD may increase the risk of developing obesity, insulin resistance, and dyslipidemia, thereby raising the risk of cardiometabolic conditions [31,32] in line with our current findings.

Limitations

Some limitations of this study need to be noted. First, the DBC system only includes diagnoses from specialists rather than general practitioners, potentially leading to under-classification of cardiometabolic conditions, especially milder forms. In addition, since data on the diagnoses of cardiometabolic conditions were accessible from 2013 and our study began in 2014, there was a relatively short wash-out period (one year) to exclude individuals with pre-existing cardiometabolic conditions, leading to a potential under-classification. Nevertheless, we mitigated these limitations by integrating data on medication dispensation (from 2006 to 2020) in addition to diagnoses to determine the occurrence of cardiometabolic conditions. Second, due to the historical under- or misdiagnosis of ASD in older generations and a potential over-diagnosis in younger generations, the associations between ASD and cardiometabolic conditions may be underestimated. Third, the causality was not

examined. For example, this could be addressed through a Mendelian Randomization study [33], but it requires data from well-powered genome-wide association studies (GWAS), which are currently unavailable for ASD. Further research is needed to gain a mechanistic understanding of this association.

Conclusions

Individuals with ASD, particularly adolescents and young adults, are at an elevated risk of developing cardiometabolic conditions, including hypertension, dyslipidemia, diabetes, stroke, and heart failure. These findings highlight the importance of monitoring and treating cardiometabolic conditions in people with ASD. Additional research is required to investigate the mechanisms underlying this association.

Methods

Data Sources

Nationwide register-based data were derived from Statistics Netherlands (Centraal Bureau voor de Statistiek, CBS) [34]. We used data on birth date, sex, SES (including socioeconomic classification and personal income), emigration status, and date of death. Additionally, we used medical claims data, including information on diagnoses from the specialist medical care and medication dispensation register, as part of the Dutch Diagnosis Treatment Combination (DBC) system [35]. Specifically, somatic conditions were coded using specific DBC diagnosis codes assigned by specialists; DBC-based psychiatric conditions were coded according to the Diagnostic and Statistical Manual of Mental Diseases, 4th edition (DSM-IV). The medications were coded using the Anatomical Therapeutic Chemical Classification System (ATC). In the Netherlands, all residents must purchase statutory healthcare insurance, and the majority of both outpatient and inpatient care for adults is covered by medical claims data [36]. This also applies to non-adults, particularly for somatic conditions. However, since 2015, diagnoses of psychiatric conditions for non-adults are no longer included in the CBS database. Medication dispensation includes all medications prescribed in primary and specialist care. We used the medical claims data across the following available years (eFigure 4): for somatic conditions, from 2013 to 2020; for psychiatric conditions, from 2011 to 2020 for adults and from 2011 to 2014 for non-adults; and for medication dispensation, from 2006 to 2020. The starting years were the earliest years in which data became accessible.

Study Population and Study Design

As shown in Figure 3, the study population included all individuals born in the Netherlands between 1949 and 2002. We excluded individuals who (1) had a record of diagnosis or medication dispensation of cardiometabolic conditions (ATC codes: C, A10A and A10B) before January 1, 2014 and (2) died or had the first record of emigration before January 1, 2014, yielding a total of 8,690,286 individuals in our study sample.

These individuals were followed up from January 1, 2014, to their first incidence of any cardiometabolic condition (including hypertension, diabetes, dyslipidemia, stroke, angina pectoris, myocardial infarction, and heart failure), emigration, death, or the end of follow-up on December 31, 2020, whichever occurred first (Figure 3).

ASD was determined as a single broad category using the DSM-IV criteria, which includes autistic disorder, Rett's disorder, childhood disintegrative disorder, Asperger syndrome, and pervasive developmental disorders-not otherwise specified [37]. This ascertainment was conducted between 2011 and 2020 for adults, and between 2011 and 2014 for non-adults.

Incident cardiometabolic events were defined as the first occurrence of cardiometabolic conditions between 2014 and 2020. To identify the occurrence of stroke, angina pectoris, myocardial infarction, and heart failure, we used the first diagnostic record (DBC diagnosis codes). For hypertension, diabetes, and dyslipidemia, in addition to the diagnosis, we used the first record of medication dispensation between 2014 and 2020 (ATC codes for hypertension: C02, C03, C07, C08, and C09; diabetes: A10A and A10B; dyslipidemia: C10) [38].

Covariates

In the subsequent models, we adjusted for the following potential confounders: sex, birth year, and SES (socioeconomic classification and personal income). Furthermore, we studied the potential influence of comorbid psychiatric conditions, including depressive disorders, anxiety disorders, personality disorders, ADHD, substance use disorders, schizophrenia, bipolar disorders, eating disorders, and intellectual disabilities. The SES data were obtained from the CBS, considering the main source of income. We classified the registered socioeconomic categories into five groups: 1) employees; 2) benefit recipients (recipients of unemployment, sickness, invalidity, or social benefit); 3) pension recipients; 4) students; and 5) individuals without income. Personal income includes employee wage, income from self-employment, benefits, and pensions. Parents’ SES and income were used for people below 25 years of age. Comorbid psychiatric conditions were ascertained before baseline (2011-2014).

Statistical analysis

Descriptive analyses

Age at baseline was described by mean and standard deviation (SD), given the normal distribution; age at cardiometabolic condition diagnosis was described by median and interquartile range (IQR), given the non-normal distribution. All other variables were categorical and were described as frequencies and percentages.

Main analyses

First, overall, sex-, and baseline age-specific cumulative incidences of any cardiometabolic condition were estimated by the subdistribution function accounting for competing risk of death using the "cmprsk" package in R [39,40]. This analysis describes the cumulative risk of developing cardiometabolic conditions during the study period. Second, the association between ASD and cardiometabolic conditions was estimated by hazard ratios (HRs) and 95% confidence intervals (CIs) using Cox proportional-hazards models, with attained age within 2014-2020 as the underlying time variable. In the main analyses, ASD was modelled as a time-varying dichotomous predictor to prevent potential immortal time bias [41]. That is, individuals were given an additional "immortal time" before receiving an ASD diagnosis. Throughout this timeframe, they were exempt from death or development of cardiometabolic conditions by design. To address this, individuals diagnosed with ASD before baseline were categorized as "exposed", while those who received a diagnosis during follow-up were initially considered "unexposed" until their diagnosis and were subsequently included in the "exposed" group from their diagnosis onwards.

We aimed to study "any cardiometabolic condition" as the primary outcome and analyzed each cardiometabolic condition separately. Three models were fitted, in which we increasingly adjusted for covariates. Model 1 was adjusted for birth year and sex, and Model 2 was additionally adjusted for SES and income. Stratified subgroup analyses were additionally conducted to investigate whether the findings differed based on sex and age (12-17, 18-30, 31-40, 41-50, 51-65 years at baseline).

Models 3_a-3_i were built on Model 2 and additionally accounted for the presence of comorbid psychiatric conditions before the baseline (ascertained between 2011 and 2014). Each model explored whether the association between ASD and cardiometabolic conditions were altered in the presence of a specific comorbid psychiatric condition.

Finally, models 1 and 2 were rerun to quantify the influence of having both ASD and comorbid psychiatric conditions. Individuals were classified as "non-ASD" (as the reference group), "ASD without a specific psychiatric comorbidity" (e.g., ASD without ADHD), or "ASD with the specific psychiatric comorbidity" (e.g., ASD co-occurring with ADHD). These analyses showed the strength of associations when both ASD and a comorbid psychiatric condition were present. All statistical tests were two-sided.

Sensitivity analyses

In the sensitivity analysis, ASD was modelled as a time-independent predictor. Specifically, individuals were categorized into the "exposed" group if they had been diagnosed with ASD between 2011 and 2020. While not considering potential immortal time bias, this sensitivity analysis was performed assuming, in line with the common definition, that ASD is a lifelong disorder with an onset in early childhood.

Declarations

Inclusion and ethics statement

This study was conducted through a collaborative effort involving researchers from the Netherlands, China, and Sweden. All contributors have been listed as coauthors in acknowledgment to their work. This publication has considered the Global Code of Conduct. The results are based on calculations by the authors using non-public microdata made available by the Statistics Netherlands (CBS). No informed consent is required for register-based studies using anonymized data.

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Council. The funder of the study had no role in the study design, data collection, data analysis, data interpretation, or manuscript writing.

Author Contributions

Yiran Li had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Yiran Li, Tian Xie, Lin Li, Harold Snieder, Catharina A. Hartman

Acquisition, analysis, or interpretation of data: Yiran Li, Tian Xie, Catharina A. Hartman

Drafting of the manuscript: Yiran Li

Critical review of the manuscript for important intellectual content: All authors.

Statistical analysis: Yiran Li

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Competing interests

The authors declare no competing interests.

Data availability

Under certain conditions, these microdata are accessible for statistical and scientific research. For further information: microdata@cbs.nl.

Code availability

Code for the main analysis is publicly available at https://github.com/yiranli-hi/ASD_cardiometabolic/tree/main

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Figures

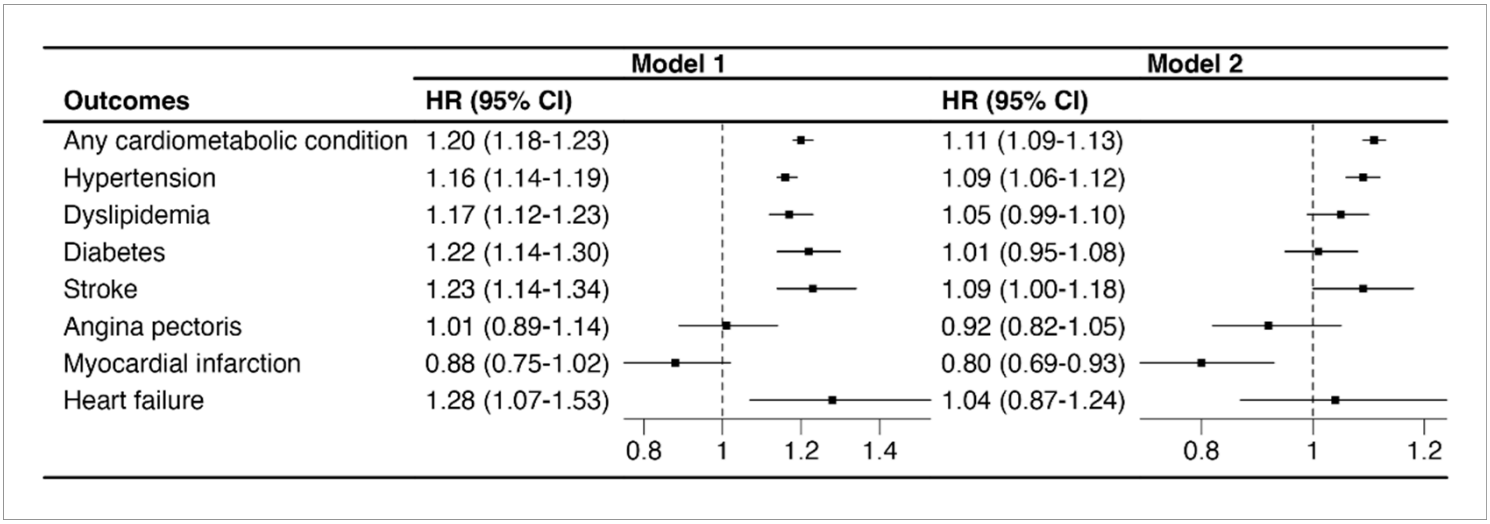

Figure 1

Hazard ratios (HR) with 95% confidence intervals (CI) of developing cardiometabolic conditions among individuals with ASD, compared with those without ASD

Abbreviations: HR, hazard ratio; CI, confidence interval; ASD, autism spectrum disorder.

Model 1 was adjusted for birth year and sex.

Model 2 was further adjusted for socioeconomic classification and income.

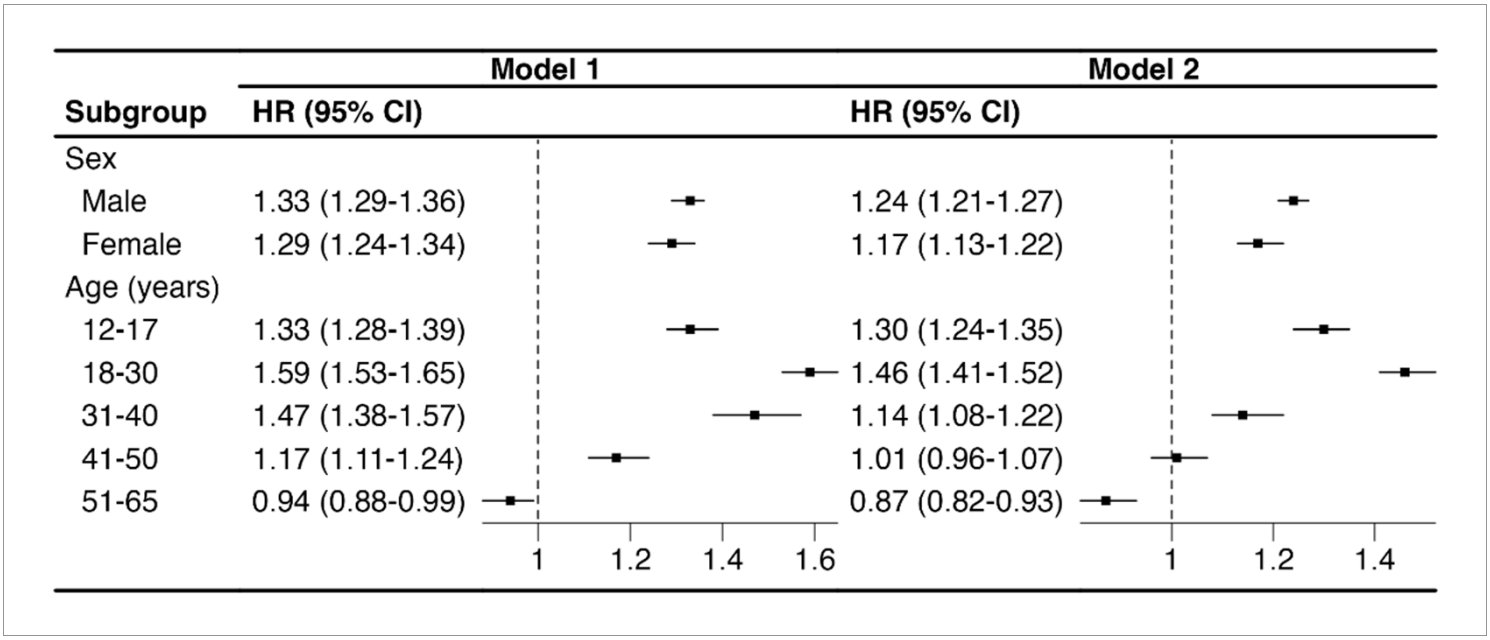

Figure 2

Sex- and baseline age-specific hazard ratio (HR) with 95% confidence interval (CI) of developing any cardiovascular condition among individuals with ASD, compared with those without ASD

Abbreviations: HR, hazard ratio; CI, confidence interval; ASD, autism spectrum disorder.

Model 1 was adjusted for birth year and sex.

Model 2 was further adjusted for socioeconomic classification and income.

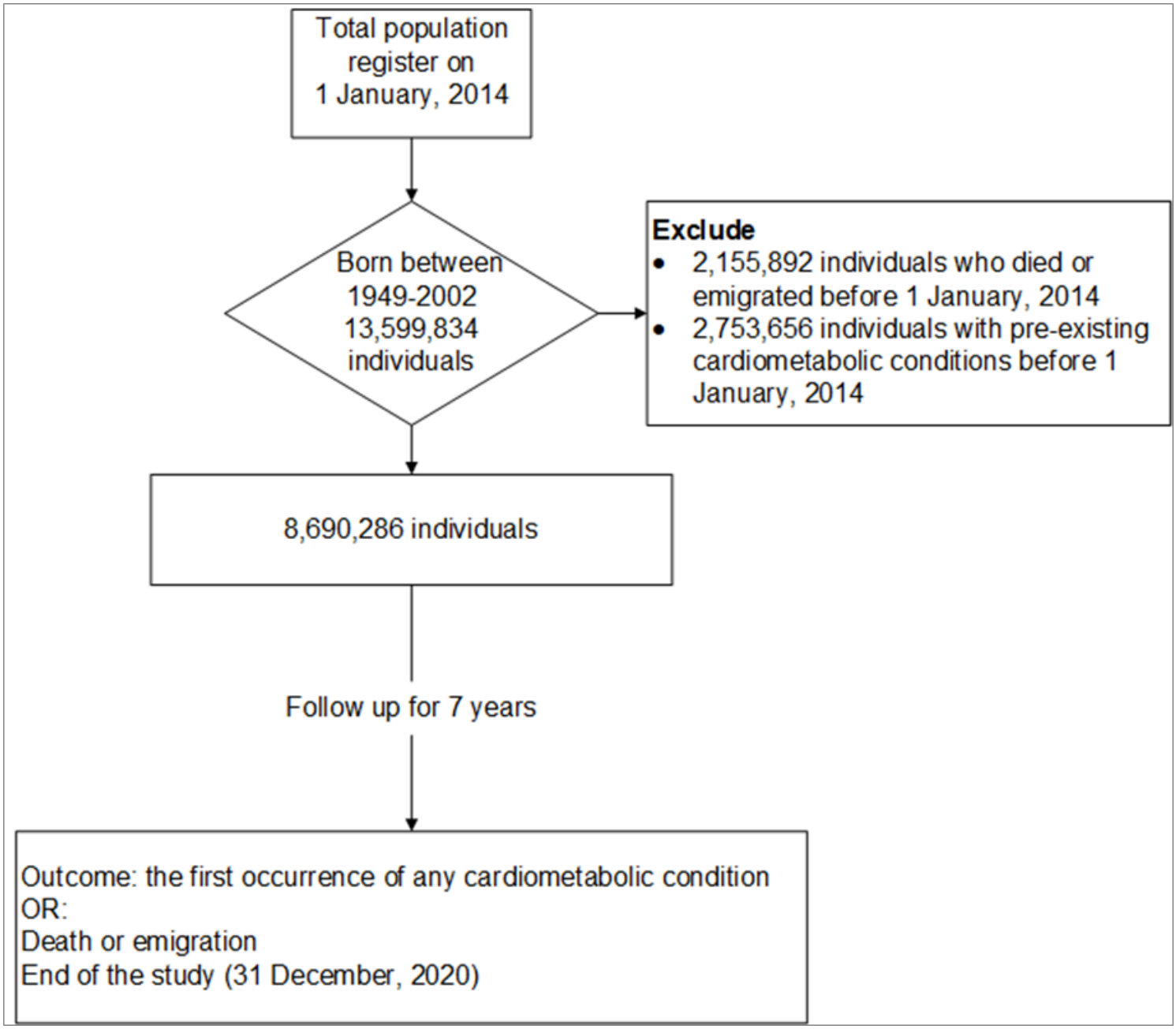

Figure 3

Flowchart of sample inclusion and exclusion

Abbreviations: ASD, autism spectrum disorder

Supplementary Files

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- SupplementMaterials.docx