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Neighbourhood disadvantage and behavioural problems during childhood and the risk of cardiovascular disease risk factors and events from a prospective cohort

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ABSTRACT

Both low socioeconomic status (SES) and behavioural problems in childhood are associated with cardiovascular disease (CVD) in adulthood, but their combined effects on CVD are unknown. Study objectives were to investigate the effect of neighbourhood level SES and behavioural problems during childhood on the development of CVD risk factors and events during adulthood. Participants were from a longitudinal cohort (n = 3792, baseline: 6–13 years of age) of Montreal children, followed from 1976 to 2010. SES was a composite measure of neighbourhood income, employment, education, and single-parent households separately assessed from census micro data sets in 1976, 2001, and 2006. Behavioural problems were assessed based on sex-specific peer assessments. CVD events were from medical records. Sex-stratified multivariable Cox regression models adjusted for age, frequency of medical visits, and parental history of CVD. Males from disadvantaged neighbourhoods during childhood were 2.06 (95% CI: 1.09–3.90, $p = 0.03$) and 2.51 (95% CI: 1.49–4.22, $p = 0.0005$) times more likely to develop a CVD risk factor or an event, respectively, than males not from disadvantaged neighbourhoods. Aggressive males were also 50% more likely to develop a CVD risk factor or event. Females from disadvantaged neighbourhoods during childhood were 1.85 (95% CI: 1.33–2.59, $p = 0.0003$) times more likely to develop a CVD risk factor. Future studies should aim to disentangle the interpersonal from the socioeconomic effects on CVD incidence.

1. Background

The association between low socioeconomic status (SES) and health is well documented (Kaplan, 2006; Kaplan and Keil, 1993; Havranek et al., 2015; Hanson and Chen, 2007). The risk starts early: children from low-income households have worse health outcomes on a number of key indicators, including obesity and cardiovascular disease (Gupta et al., 2007). Indeed, these children are considered high-risk for not only chronic physical health conditions, but also mental health issues (Costello et al., 2001) and internalizing and externalizing behavioural problems (such as aggression and withdrawal) (Costello et al., 2001; Costello et al., 2003), which have been associated with an increased risk of future cardiovascular disease (Caspi et al., 2006; Chida and Steptoe, 2009; Valtorta et al., 2016). In adulthood, these behavioural problems manifest as psychopathology, substance use, crime, and poorer social functioning, all of which are associated with lower academic and occupational achievement and ongoing health problems (Reef et al., 2011; Vaillancourt et al., 2013).

As these behavioural problems have been shown to be stable over time (Rubin et al., 2009), youth from low SES environments already exhibiting aggression or withdrawal during childhood may be particularly vulnerable to future cardiovascular disease (CVD) risk. However, the combined effects of behavioural problems and low SES on future CVD are poorly understood.

As CVD is the leading cause of death (Minino et al., 2011), improving our understanding of the longitudinal association between SES

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and childhood behavioural problems on future CVD is a critical public health objective. Through the use of a large, prospective cohort with nearly 30 years of follow-up, this study aimed to examine the effect of low SES and behavioural problems during childhood on the risk of developing CVD. As internalizing and externalizing behavioural problems in childhood are associated with SES (Reef et al., 2011; Vaillancourt et al., 2013) as well as long-term health risk (Puder and Munsch, 2010; Suglia et al., 2013), the effect of low SES on future health was assessed separately, as well as in combination with behavioural problems.

2. Methods

2.1. Data source

Participants were from the Concordia Longitudinal Research Project (Concordia Project). The Concordia Project is an ongoing, prospective cohort study initiated in 1976 to identify predictors of developmental problems and psychopathology from a targeted sample of high-risk youth. This targeted sample was selected to demonstrate the consequences of early-life SES inequalities and internalizing/externalizing behavioural problems on future health and development. The study was conducted in collaboration with the French-language public school board and with the permission and support of school directors, teachers, teachers' unions and parents' committees. Study procedures have been previously published and are briefly described here (Schwartzman et al., 1985; Serbin et al., 1998).

French-speaking children of European descent attending 22 public schools serving inner-city neighbourhoods of Montreal in Grade 1, 4, or 7 (ages 6–7, 9–10, or 12–13, respectively) were invited to participate. Over 95% of the children in these classes participated in the study (n = 4109). Data collection measures included baseline measurements and provincially-available data such as medical records, and neighbourhood characteristics, described in further detail.

2.2. Measures

Access and permission to the provincial-level data were provided by the Commission d'Accès à l'Information du Québec for the medical services data, the Canadian Census Micro Data Set for neighbourhood SES, and la Régie de l'assurance-automobile du Québec to confirm the current address of participants throughout the study. Although data collection procedures also included questionnaires collected several times throughout the study duration, many of these measurements could not be integrated with the subsequent data extractions of provincial-level data. This was due to the de-nominalization of provincial data in order to maintain participant confidentiality. Thus, this study exclusively focuses on data available for all participants such as questionnaires completed by the parents at baseline and provincially available data such as medical records and census data.

2.2.1. Low SES

SES was measured with 1976, 2001, and 2006 Canadian Census Micro Data Sets, representing childhood (1976) and adulthood neighbourhood SES (2001 and 2006) (Martin-Storey et al., 2013). The SES measure was comprised of four neighbourhood characteristics based on the participant's forward sortation area (first three digits of their home or school postal code): (1) percentage of families with an annual household income < $10,000 per year (1976) or < $20,000 per year (2001, 2006), (2) percentage of unemployed adults, (3) percentage of single-parent households, and (4) percentage of households with less than a high-school diploma. Forward sortation areas define a subset of stable and well-defined geographic regions and have been previously used in the literature to assess neighbourhood walkability scores and neighbourhood fast-food availability in Canada (Hajna et al., 2015; Hollands et al., 2014). The details of this measure are further outlined separately for childhood and adulthood neighbourhood SES.

2.2.1.1. SES during childhood. To ease interpretations for SES during childhood, these variables were dichotomized to reflect whether the neighbourhood was worse off than the rest of Quebec (e.g., the prevalence of single-parent households for that neighbourhood was higher than the Quebec-wide prevalence of 17%). These proportions were based on the published estimates for 1976. Due to the initial recruitment efforts to target at-risk youth, the population at baseline was homogeneous in SES. Thus, only a single binary variable (such as whether the child lived in a neighbourhood that was disproportionately poor compared to the rest of Québec) was necessary as > 90% were also living in neighbourhoods that were disproportionately high on other neighbourhood disadvantage measures.

2.2.1.2. SES during adulthood. In contrast, due to neighbourhood disadvantage changes over time and upward social mobility, neighbourhood disadvantage in 2001 and 2006 was more heterogeneous. Nevertheless, the four neighbourhood characteristics loaded highly on a single factor in Mplus software, suggesting that they all still represented a latent variable for neighbourhood disadvantage (Martin-Storey et al., 2013). Thus, adulthood neighbourhood disadvantage was a composite score of the four neighbourhood SES characteristics (proportion of (1) low income, (2) unemployed adults, (3) low education, and (4) single-parent households), where higher scores indicated greater neighbourhood disadvantage. Current neighbourhood disadvantage was the most recent neighbourhood measure prior to the CVD risk or CVD event, as described in future sections.

2.2.2. Social behaviours

Using peer-nomination according to the Pupil Evaluation Inventory (PEI), each child's social behaviours reflecting aggression, withdrawal, and likeability (Pekarik et al., 1976) was assessed, which has been shown to have good test-retest reliability (> 0.75) and internal consistency (Cronbach's α > 0.80) (Johnston et al., 1988; Martin-Storey et al., 2013). These scores accounted for the normative values based on sex, age and classroom and enabled the classification of children into standardized high-aggression, withdrawal, or likeability (≥ 95th percentile).

2.2.3. CVD

All medical services for permanent residents of Québec are covered by the Régie de l'Assurance-Maladie du Québec. These medical services include any and all contact with the Québec health care system including emergency care visits, specialist visits, and routine inpatient and outpatient care. For this study, all medical service codes were assessed and codes pertaining to a cardiovascular disease event (such as angina, cardiac arrest, myocardial infarctions, among others) were considered for inclusion.

2.2.4. CVD risk

In recognition of the likelihood that many participants may not be advanced in age enough for the development of CVD events, a secondary outcome was to assess for the incidence of CVD *risk factors* (essential and secondary hypertension, type II diabetes, hypercholesterolermia, hyperlipidemia, and obesity).

2.2.5. Covariates

Other covariates in the model included demographic and health characteristics such as sex, age, the average number of medical visits in a year, and whether there was a parental history of CVD or CVD risk based on a medical diagnosis between the years of 1981–2006. A small number of mothers and fathers did not have any provincial medical records (n = 122) due to moving out of province or death. Parental history of CVD was conservatively noted as absent for these

Table 1
Descriptive statistics of the study population, Concordia Longitudinal Research Project, Montreal, 1976–2006.

Characteristic	Males (n = 1911) n (%)[a]	Females (n = 1909) n (%)[a]	*p*
Childhood			
Age in years, mean (SD) (range: 5–15)	9.60 (2.64)	9.43 (2.60)	0.04
High prop. low income neighborhood[b]	1775 (93)	1755 (92%)	0.27
High aggression (≥ 95th percentile)	351 (18)	334 (17)	0.48
High withdrawal (≥ 95th percentile)	305 (16)	320 (17)	0.50
High likeability (≥ 95th percentile)	338 (18)	345 (18)	0.76
Adulthood			
High prop. low income[c]	556 (29)	532 (28)	0.40
High prop. education < 9th grade[c]	1407 (74)	1436 (75)	0.26
High prop. single-parent households[c]	1317 (69)	1188 (62)	< 0.0001
High prop. unemployment[c]	749 (39)	698 (36)	0.09
Neighbourhood SES factor score	0.04 (1.0)	− 0.04 (1.0)	0.007
Medical record data			
Number of visits per year, mean (SD)	4.09 (3.61)	6.99 (4.17)	< 0.0001
Follow-up in years, mean (SD) (range: 0.05–26)	20.71 (5.51)	21.32 (5.61)	0.001
Developed cardiovascular disease	237 (12)	245 (13)	0.69
Angina	45 (2)	27 (1)	
Arrhythmia or cardiac arrest	72 (4)	98 (5)	
Ischemia or myocardial infarction	43 (2)	26 (1)	
Pulmonary	12 (0.2)	18 (0.1)	
Other	65 (3)	76 (4)	
Developed cardiovascular disease risk factor	405 (21)	662 (35)	< 0.0001
Diabetes	45 (2)	94 (5)	
Hypercholesterolemia or hyperlipidemia	22 (1)	20 (1)	
Hypertension	192 (10)	132 (7)	
Obesity	146 (8)	416 (22)	

[a] n (%) unless otherwise indicated.
[b] High proportion in baseline defined as proportions greater than the Quebec average of 8% low income (annual household income < $10,000/year).
[c] High proportion in adulthood defined as proportions greater than the Quebec average of 8% of low income between 1976 and 2001 (annual household income < $10,000/year), and 20% between 2001 and 2006 (annual household income < $20,000/year), education < 9th grade of 17% (1976–2001) or 14% (2001–2006), single-parent households of 17% (1976–2006), and unemployment of 8% (1976–2001) and 7% (2001–2006).

participants, but a sensitivity analysis which excluded these participants did not affect our results. Due to obesity being a mediator for CVD events, weight status was not adjusted in analyses as adjustment may result in biased associations (Chiolero et al., 2012). Although neighbourhood disadvantage in adulthood was weakly correlated with household income in 2001 ($r < 0.25$), the independent effect of neighbourhood disadvantage on CVD risk and events after controlling for individual-level household income could not be assessed as household income was only available in a small subset of the sample (n = 387).

2.3. Statistical analysis

All analyses were conducted with SAS 9.4. Descriptive statistics between men and women during childhood and adulthood were tested with *t*-tests and chi-square. Due to evidence of an interaction between sex and CVD, all results were then stratified by sex. Descriptive statistics between SES and social behaviours were tested with correlations. To allow this descriptive analysis to detect differences between specific features of SES (proportion of: low income, unemployed adults, low education, and single-parent households in the neighbourhood), the factor scores were used in this unadjusted comparison. In contrast, in the multivariable analyses, SES was dichotomized as previously described to ease interpretation. Nevertheless, a sensitivity analysis utilizing SES as binary to test for an association with social behaviours in unadjusted *t*-tests did not affect conclusions.

For the multivariable results, in order to incorporate subject-level variation in follow-up time and the prospective nature of this study, a Cox regression model with sandwich estimators was used. As the analytic considerations and statistical methodology were the same for both objectives, the process will only be described for CVD. Due to an inherent bias in subjects with multiple diagnoses of CVD, only the first diagnosis was used.

Thus for each participant, study follow-up time was calculated as the time to either the first CVD diagnosis (event), or the end of the study follow-up (censored). Using this same methodology, the medical visit rates were calculated. As the incidence of CVD risk factors precede subclinical and clinical outcomes (O'Donnell and Elosua, 2008), < 20% of those with a first risk factor outcome were among those who also later experienced a first CVD event. Thus by focusing on the incidence of CVD risk factors, and the incidence of CVD events, we minimized the overlap between our two outcomes. The assumptions of Cox regression models were tested. The proportional hazards assumption was violated for several continuous variables (age of the participant, number of medical service visits in the past year). To correct this violation, these variables were dichotomized based on survival curves indicating the approximate point in time at which the change in the hazards occurred (when the participant was age 40 or older and when the participant had at least 12 medical visits per year, respectively) and modeled alongside their interaction with time.

Two multivariable Cox regressions were assessed. Model 1 tested the association between SES during childhood and incidence of CVD after controlling for age, clinic visit rate, and whether there was a parental history of CVD. Model 2 additionally adjusted for social behaviours during childhood (aggression, withdrawal and likeability levels). Due to evidence of an interaction between aggression and withdrawal, results were further stratified by withdrawal scores (≥ 95th percentile, Model 3a and Model 3b, respectively) where aggression percentiles (≥ 95th percentile) were then assessed separately based on these withdrawal score dichotomizations. Maintaining these standardized scores as continuous did not affect results.

Sensitivity analyses re-tested all the above models after additionally adjusting for current (adulthood) neighbourhood disadvantage. This measure also failed to meet the proportional hazards assumption. As SES was among the main variables of interest, to maintain interpretability of the parameter estimate in the model, SES was modeled as time-varying where the most recent census value that occurred prior to the event or censoring was used. This analytic decision also ensured

temporality in the estimates as current SES always occurred prior to the event or censoring. The implications of utilizing this measure for current neighbourhood disadvantage are described in the discussion section.

3. Results

Of the original cohort (n = 4109), participants who moved out of the province and had no provincial medical records (n = 205), were diagnosed with CVD at the start of follow-up (n = 7), or were missing any of the covariates or main predictor of interest (n = 77) were excluded, resulting in a final analytic sample of 3820 participants (92% of the original sample).

The incidence of CVD and CVD risk factors was 13% and 28%, respectively (Table 1). Several age differences in childhood social behaviours were noted: the youngest males and youngest females (< 8 years of age at study entry) were significantly more likely to be more withdrawn and aggressive than their older counterparts (males: 55% vs 45%, $p < 0.0001$; females: 59% vs 40%, $p < 0.0001$, respectively, data not shown). Due to the initial recruitment objectives of targeting a sample of disadvantaged youth, 92% of the sample was living in disproportionately low-income households in childhood.

3.1. Development of CVD

After adjusting for covariates, males with disproportionately disadvantaged neighbourhoods in childhood (Model 1) had shorter survival times to developing CVD (Hazards Ratio [HR]: 1.68, 95% Confidence Intervals [CI]: 0.98–2.90, $p = 0.06$; Table 2; Fig. 1) than males from neighbourhoods which were not disproportionately disadvantaged. The association between neighbourhood disadvantage in childhood and a first CVD event differed based on the child's withdrawal and aggressive levels. For males who displayed average or low withdrawal levels during childhood (Model 3a), living in disproportionately disadvantaged neighbourhoods in childhood was associated with two times the risk of developing CVD (HR: 2.06, CI: 1.09–3.90, $p = 0.03$). Among these males with average or low withdrawal levels, additionally exhibiting high aggression levels were associated with 1.5 times the risk of developing CVD (HR: 1.51, CI: 1.08–2.11, $p = 0.01$). However, among males who displayed high levels of withdrawal during childhood, neither neighbourhood disadvantage during childhood nor aggression levels were associated with the risk of CVD events.

Among the females, living in disadvantaged neighbourhoods during their childhoods was not associated with the likelihood of developing CVD (Model 1). In contrast to the males, no associations between childhood neighbourhood disadvantage or aggression scores were noted among females with average or low withdrawal levels (Model 3a). In addition, among females with high withdrawal levels (Model 3b), high aggression levels were associated with a *decreased* risk of developing CVD, However, further investigation of the study sample revealed an interaction between aggression and age such that the most aggressive girls were also the youngest (< 8 years of age at baseline). Thus after incorporating the interaction between age and aggression into the model, aggression levels were no longer protective against CVD events (Table 4).

3.2. Development of CVD risk factors

The Cox regression models consistently indicated that males and females with childhoods in disproportionally disadvantaged neighbourhoods were significantly more likely to develop a CVD risk factor (Table 3) than males and females from neighbourhoods which were not disproportionately disadvantaged (Model 1 (males): HR: 2.40, CI: 1.49–3.85, $p = 0.0003$, (females): HR: 1.77, CI: 1.31–2.39, $p = 0.0002$, respectively).

Among the males and females with average or low withdrawal levels during childhood, also being from disproportionately disadvantaged neighbourhoods during childhood were (Model 3a (males): HR: 2.51, CI: 1.49–4.22, $p = 0.0005$ and (females): HR: 1.85, CI: 1.33–2.59, $p = 0.0003$) more likely to have a CVD risk factor than males and females from neighbourhoods that were not disproportionately disadvantaged, respectively. For males and females who were highly withdrawn, childhood and adulthood neighbourhood disadvantage was not associated with CVD risk factors. That is, for highly withdrawn children the advantage of being from a relatively more advantaged neighbourhood was not found.

Similar to the CVD results, the effect of aggression on CVD risk factors in the females was masked by an interaction between age and aggression among the highly withdrawn females. For instance, compared to aggressive girls who are older than 8 years of age at baseline, aggressive girls who are 8 years and younger at baseline are twice as likely to experience a CVD risk factor (HR: 2.12, $p < 0.0001$).

Table 2
Multivariable Cox regression model testing for the risk of developing cardiovascular disease based on childhood and adulthood neighbourhood disadvantage and childhood social behaviours, Concordia Longitudinal Research Project, Montreal, 1976–2006.

	Model 1[a]		Model 2[b]		Model 3a: average or low withdrawal[c]		Model 3b: high withdrawal[d]	
	OR	*p*	OR	*p*	OR	*p*	OR	*p*
Males								
Neighbourhood disadvantage[e]	1.68 (0.98–2.90)	0.06	1.71 (0.99–2.94)	0.05	2.06 (1.09–3.90)	0.03	0.77 (0.27–2.22)	0.63
High aggression					1.51 (1.08–2.11)	0.01	0.54 (0.23–1.25	0.54
High withdrawal								
High likeability					0.98 (0.68–1.42)	0.93	0.98 (0.40–2.41)	0.98
Aggression × withdrawal				0.03				
Females								
Neighbourhood disadvantage[e]	1.51 (0.94–2.41)	0.09	1.51 (0.94–2.41)	0.09	1.49 (0.89–2.49)	0.13	1.56 (0.48–5.11)	0.46
High aggression					0.94 (0.62–1.41)	0.75	0.30 (0.13–0.68)	0.004
High withdrawal								
High likeability					1.07(0.75–1.52)	0.70	0.54 (0.17–1.76)	0.30
Aggression × withdrawal				0.02				

[a] In addition to variables shown here, adjusted for age, number of visits, parental history of cardiovascular disease; n = 1911 (males) and 1909 (females).
[b] Adjusted for all the same covariates as Model 1 with the addition of aggression, withdrawal, likeability, and the interaction between aggression and withdrawal; n = 1911 (males) and 1909 (females).
[c] Assessed only in those with low withdrawal (< 95th percentile), n = 1606 (males) and n = 1589 (females).
[d] Assessed only in those with high withdrawal (≥ 95th percentile), n = 305 (males) and n = 320 (females).
[e] Incorporated neighbourhood prevalence of low income, education < 9th grade, single-parent households and unemployment in 1976.

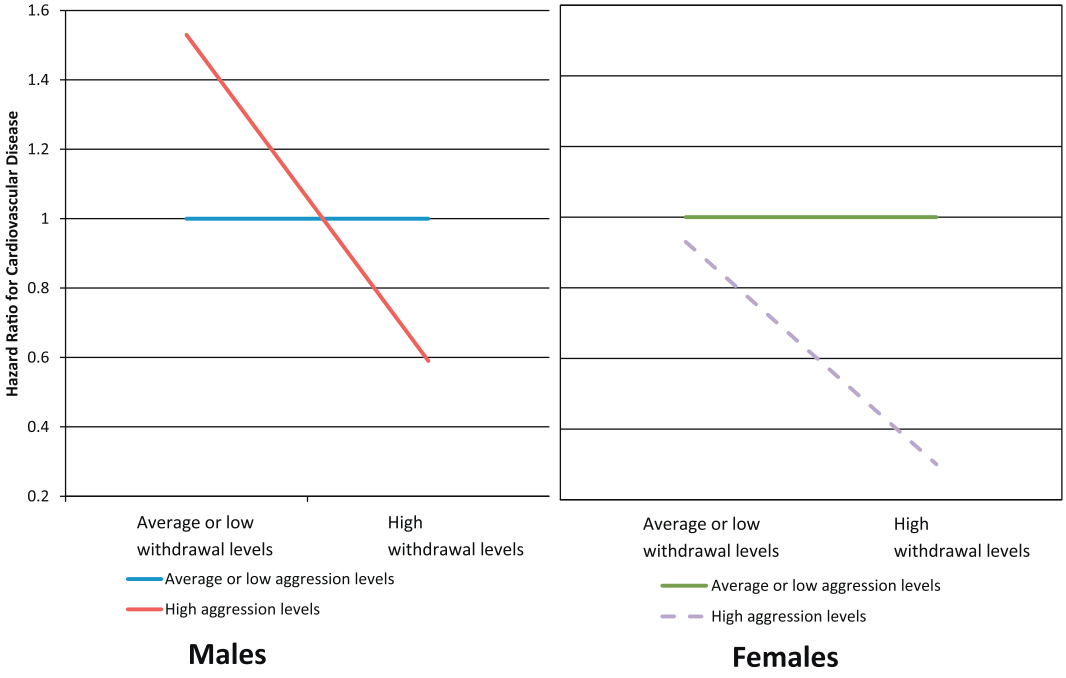

Fig. 1. Sex-stratified hazard ratios of developing cardiovascular disease based on aggression and withdrawal levels in childhood from multivariable Cox regression model, Concordia Longitudinal Research Project, Montreal, 1976–2006.
Caption: Adjusted for age, number of visits, parental history of cardiovascular disease; n = 1911 (males) and 1909 (females).

Table 3
Multivariable Cox regression model testing for the likelihood of developing cardiovascular disease risk factors based on childhood and adulthood neighbourhood disadvantage and childhood social behaviours, Concordia Longitudinal Research Project, Montreal, 1976–2006.

	Model 1[a]		Model 2[b]		Model 3a: average or low withdrawal[c]		Model 3b: high withdrawal[d]	
	OR	*p*	OR	*p*	OR	*p*	OR	*p*
Males								
Neighbourhood disadvantage[e]	2.40 (1.49–3.85)	0.0003	2.44 (1.52–3.92)	0.0002	2.51 (1.49–4.22)	0.0005	2.03 (0.63–6.47)	0.23
High aggression					1.45 (1.12–1.87)	0.004	0.66 (0.36–1.23)	0.20
High withdrawal								
High likeability					0.81 (0.60–1.09)	0.16	1.07 (0.58–1.98)	0.82
Aggression × withdrawal				0.03				
Females								
Neighbourhood disadvantage[e]	1.77 (1.31–2.39)	0.0002	1.79 (1.32–2.41)	0.0002	1.85 (1.33–2.59)	0.0003	0.94 (0.47–1.90)	0.86
High aggression					1.08 (0.85–1.37)	0.51	0.70 (0.43–1.13)	0.14
High withdrawal								
High likeability					0.90 (0.72–1.12)	0.34	0.93 (0.52–1.67)	0.82
Aggression × withdrawal				0.0002				

[a] In addition to variables shown here, adjusted for age, number of visits, parental history of cardiovascular disease risk factors; n = 1895 (males) and 1897 (females).
[b] Adjusted for all the same covariates as Model 1 with the addition of aggression, withdrawal, likeability, and the interaction between aggression and withdrawal; n = 1892 (males) and 1885 (females).
[c] Assessed only in those with average to low withdrawal (< 95th percentile), n = 1591 (males) and n = 1572 (females).
[d] Assessed only in those with high withdrawal (≥ 95th percentile), n = 301 (males) and n = 313 (females).
[e] Incorporated neighbourhood prevalence of low income, education < 9th grade, single-parent households and unemployment in 1976.

3.3. Sensitivity analysis

Based on forward sortation areas, nearly two-thirds of the sample experienced some degree of upward social mobility during adulthood. Indeed neighbourhood disadvantage factor scores during childhood (1976) and current neighbourhood disadvantage in adulthood had a weak correlation of 0.32 ($p < 0.0001$, data not shown). As forward sortation areas may be too imprecise as a proxy for current neighbourhood disadvantage, this additional adjustment was tested in sensitivity analyses only, and not in our primary result. There were no associations between neighbourhood disadvantage during childhood with social behaviours in either men or women (all $p > 0.05$), but childhood social behaviours were weakly correlated ($r < 0.10$, $p < 0.01$) with neighbourhood disadvantage during adulthood. However, additionally adjusting for current neighbourhood disadvantage did not impact the results in any of our multivariable Cox regression models (data not shown).

4. Discussion

In this large, prospective cohort of adults, results indicated that the high-risk youth living in disadvantaged neighbourhoods during childhood were at an increased risk of developing CVD or CVD risk. The results from the present study are consistent with the neighbourhood disadvantage CVD incidence and mortality literature (Foraker et al., 2011; Pedigo et al., 2011; Wen and Christakis, 2005). However, a number of important sex differences were detected. Females in this study from disproportionately disadvantaged neighbourhoods during

Table 4
Multivariable Cox regression model testing for the likelihood of developing cardiovascular disease events or risk factors based on childhood neighbourhood disadvantage among the highly withdrawn females, Concordia Longitudinal Research Project, Montreal, 1976–2006.

	CVD events[a,b]		CVD risk[a,c]	
	OR (CI)	*p*	OR (CI)	*p*
Neighbourhood disadvantage[d]	1.17 (0.35–3.91)	0.79	1.10 (0.55–2.20)	0.79
High aggression	0.47 (0.18–1.26)	0.13	0.29 (0.10–0.46)	< 0.0001
High likeability	0.81 (0.24–2.75)	0.74	0.92 (0.51–1.67)	0.79
Young age (< 8 years) at baseline	0.40 (0.07–2.17)	0.29	0.26 (0.11–0.61)	0.002
Young age at baseline × aggression	0.47 (0.07–2.98)	0.43	5.50 (2.02–15.01)	0.001

[a] In addition to variables shown here, adjusted for age, number of visits, parental history of cardiovascular disease risk factors or events.
[b] Assessed only in those with high withdrawal (≥ 95th percentile), n = 320.
[c] Assessed only in those with high withdrawal (≥ 95th percentile), n = 313.
[d] Incorporated neighbourhood prevalence of low income, education < 9th grade, single-parent households and unemployment in 1976.

childhood were significantly more likely to develop CVD *risk factors*, but not CVD *events*. As the onset of CVD occurs later in women in comparison to men (Adams et al., 2009; Dragano et al., 2007), it is possible that only CVD risk factors, and not events, are detectable among women in their early 30s. Whether these associations continue to persist into late-adulthood should be further assessed.

In addition, high aggression levels during childhood were an independent predictor for CVD risk and events, but only consistently among men. In contrast, high aggression levels during childhood were only an independent predictor for CVD risk among the highly withdrawn females. Results suggest that while childhood neighbourhood disadvantage has residual effects regardless of sex, aggression plays an independent role primarily among men. Indeed, the results among the men are consistent with previous studies linking hostility with CVD morbidity and mortality (Mwendwa et al., 2013; Reijneveld, 1998). A number of possible biologic mechanisms have been proposed, including inflammation and poor autonomic or neuroendocrine regulation (Boisclair Demarble et al., 2014; Möller-Leimkühler 2007; Suls 2013).

However, the biologic plausibility for how the combination of these social behaviours would result in a protective effect among women is unclear. In particular, as high aggression and high withdrawal are both highly correlated with social isolation (Rozanski et al., 1999) (another independent risk factor for CVD), these results in the women is counterintuitive. Nevertheless, several methodological differences may account for these findings. The high aggression and high withdrawal females and males were significantly younger than the less aggressive and less withdrawn peers. Thus the protective effect among high aggression and high withdrawal females may be an artifact of age; indeed, the effect disappears after accounting for initial age into the cohort. In addition, as these are same-sex comparative measures, high aggression and high withdrawal in females is not conceptually the same social behaviours in males. In previous studies with this cohort, women with high aggression and high withdrawal were more likely to experience interpersonal and internalizing problems such as substance abuse, teen pregnancies, and dropping out of school in early adulthood (Serbin et al., 1998). It is possible that these women continued to experience interpersonal problems that ultimately affected their healthcare needs beyond the time frame of the present study.

In addition, the underlying pathways through which SES and behavioural problems increase CVD risk in tandem is unknown. One theory posits that persons living in low SES environments are not only more frequently exposed to stressors, but also have an increased sensitivity to these stressors due to limited resources and reserves to develop appropriate responses (be it emotional capacities, social support, etc.) (Matthews and Gallo, 2011). Additional research measuring the biologic and psychological responses to stressors in these populations is needed.

Although SES is most commonly examined on the micro-level (individual's income, education, or occupation), it is increasingly being investigated on the neighbourhood and macro-levels (Wen and Christakis, 2005). Indeed, low neighbourhood SES is associated with increased overall mortality (Bosma et al., 2001; Marinacci et al., 2004; Martikainen et al., 2003; Osler and Prescott, 2003; Sloggett and Joshi, 1994) and CVD incidence and mortality rates (Borrell et al., 2004; Diez et al., 2004; Dragano et al., 2007; Engström et al., 2000; Macintyre et al., 2001). However, in this particular study, neighbourhood disadvantage was defined with forward sortation areas. Although these are stable units of measurement and have been previously used in the literature to assess walkability and fast-food density in the neighbourhood (Hajna et al., 2015; Hollands et al., 2014), forward sortation areas as a measure of neighbourhood SES is likely imprecise. Due to the targeted sampling approach at study inclusion in 1976, forward sortation areas were homogeneous and thus consistent with the initial study objectives of recruiting high-risk, low SES children and indicative of minimal measurement error. However, the measurement error from the use of forward sortation areas during adulthood is less clear. Sensitivity analyses were conducted with the additional adjustment for current neighbourhood disadvantage and did not differ from our main results.

With the exception of a small sub-sample with individual-level household income data in 2001 (n = 387), we were unable to connect neighbourhood- and provincial-level information with the individual SES characteristics of the study sample in adulthood. Nevertheless, although household income and neighbourhood disadvantage were weakly correlated (r < 0.25), as these data were only available in a small subset of the data, whether study results truly reflect neighbourhood disadvantage, or is an artifact of individual SES that is highly correlated with neighbourhood SES cannot be entirely ruled out.

While the use of standardized scores for aggression and withdrawal enables us to classify the sample into groups which utilize meaningful sex-specific comparative values, it diminishes our ability to compare and interpret the scores between males and females. Due to the original cohort study objective of targeting children from disadvantaged neighbourhoods, the cohort is not a representative sample and results may not be generalizable. However, the data are of an economically disadvantaged sample of children, and may thus best reflect the true population of interest. Lastly, when censoring rates are high, hazard ratios are reportedly underestimated (Persson and Khamis, n.d.). Yet study findings were largely consistent for both CVD events and risk factors and were significant, further highlighting the early detrimental effect of neighbourhood disadvantage on cardiovascular health.

Several strengths in this study's methodology increase our confidence in the results. In this large, longitudinal cohort study, loss to follow-up was minimal, resulting in a study population that encapsulates the risk from neighbourhood disadvantage during childhood even after three decades of follow-up. Importantly, due to the prospective nature of this cohort and the use of survival analysis, we were able to determine *incident* cases, which is less prone to recall bias than *prevalent* cases. Relatedly, recall bias and measurement error was minimized through the use of medical records and census data. Lastly, due to the use of a targeted sample of high-risk youth, results strongly highlight the risks of early-life SES inequalities on future health. Indeed, the incidence of CVD was 13%, which is significantly higher than the 1–3% of the general Canadian population of this same age demographic (Public Health Agency of Canada, 2009). Each one of these study strengths addresses an important limitation of the existing literature in methodology or analysis, further highlighting this study's unique contribution to the existing literature.

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elevate a child's risk for CVD. However, as this study is among the first to investigate these associations in a prospective cohort study with objective measures of neighbourhood disadvantage and CVD incidence, further study with larger samples, longer follow-up, and more precise measurements of neighbourhood disadvantage is warranted in order to further illuminate how the natural history of CVD is affected by neighbourhood disadvantage. In particular, disentangling the interpersonal from the socioeconomic effects separately for females and males in order to improve our understanding of their underlying mechanisms on CVD incidence should be the focus of future studies.

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Conflict of interest

The authors have no conflicts of interest to disclose.

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