Social support and C-reactive protein in a Québec population cohort of children and adolescents

Eloïse J. Fairbank1*, Jennifer J. McGrath1*, Mélanie Henderson2,3,4‡, Jennifer O'Loughlin4‡, Gilles Paradis5‡

1 Department of Psychology, Concordia University, Montréal, Québec, Canada, 2 Department of Pediatrics, Université de Montréal, Montréal, Québec, Canada, 3 Centre de Recherche CHU Sainte-Justine, Montréal, Québec, Canada, 4 School of Public Health, Department of Social and Preventive Medicine, Université de Montréal, Montréal, Québec, Canada, 5 Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montréal, Québec, Canada

* These authors contributed equally to this work.
‡ MH, JO and GP also contributed equally to this work.
* jennifer.mcgrath@concordia.ca

Abstract

Objective

Robust evidence exists for the health-enhancing benefits of social support in adults. Inflammatory processes are thought to be an important mechanism linking social support and health risk. Less is known about the relation between social support and chronic inflammation during childhood and adolescence, or when the association emerges during the lifespan.

Method

Data from the population-representative 1999 Quebec Child and Adolescent Health and Social (QCAHS) survey were analyzed. Youth aged 9, 13, and 16 years (N = 3613) and their parents answered questions about social support. A subsample (n = 2186) completed a fasting blood draw that was assayed for C-reactive protein (CRP).

Findings

Higher social support was significantly associated with lower hs-CRP log, after controlling for age, sex, body mass index (BMI Z-score), medication use, puberty, ethnoracial status (French-Canadian), smoking, household income, and parental education (F = 25.88, p < .001, Total $R^2_{adj} = 10.2\%$). The association was largely similar for boys and girls, and strengthened with age.

Conclusion

Greater social support was linked to lower chronic low-grade inflammation in a large sample of children and adolescents. Effect sizes were small and consistent with prior findings in the adult literature. Importantly, these findings provide evidence that the relation between social
Introduction

Chronic inflammation is a key contributor to the pathophysiology of multiple health outcomes [1]. Chronic low-grade inflammation is characterized by increased levels of cytokines that are the long-term response to threats overtime (e.g., stressor exposure, injury), and result in elevated susceptibility to disease [2]. Proinflammatory cytokines include interleukin (IL)-1, IL-6, C-reactive protein (CRP), and tumor necrosis factor-alpha (TNF-alpha) [2]. CRP is an acute phase reactant secreted in response to both acute and chronic inflammation. Although CRP initially works to restore the body after infection or injury, high circulating levels of CRP have been linked to adverse health outcomes [3]. In fact, higher levels of proinflammatory circulating markers have been associated with osteoporosis, certain cancers, cardiovascular disorders, type 2 diabetes, rheumatoid arthritis, Alzheimer’s disease, frailty and disability, and increased risk of all-cause of mortality [4, 5].

Social support is conceptualized as the perception that “one is valued, cared for, and loved by others in a social network” [6]. Social support encompasses numerous experiences within one’s network, both negative and positive [7], and has important links to health outcomes [8–14]. In adults, social support is often parsed into types: structural support is characterized by one’s integration within their network; functional support is characterized by the kind of support (e.g., emotional), and can be further distinguished as perceived or received support [15]. In children, however, social support is traditionally parsed by the source or the particular people within the child’s social network: parents, teachers, peers, siblings, others (e.g., relatives, neighbors, coaches). Studies in the child and adolescent literature predominantly present findings based on only one source (e.g., parents, peers) [16]. While children’s positive and negative social relationships are commonly measured using this singular source approach, this introduces an important construct gap in the field because focusing narrowly on a single source (e.g., parents) fails to capture having anyone within one’s social network who can contribute to feeling valued and supported. Interestingly, within the adult literature, studies using a broader conceptualization of social support (e.g., aggregated measures across sources and types of support) observed stronger associations with health [9, 10]. Ultimately, the perceived cumulative support across one’s entire social network provides a comprehensive representation of social support.

Social support, health, and inflammation

Social support is a robust predictor of health and well-being [8–14]. Indeed, social support has been found to be protective against cardiovascular disease, cancer, infectious disease, depression, and early mortality [14]. A seminal meta-analysis of over 300,000 adults indicated stronger social support was linked to 50% greater odds of survival, regardless of age, sex, initial health status, cause of death, or length of follow-up period [9]. In a study of over 100 countries, the association between social support and self-reported health was consistent across the socioeconomic gradient and geographic locations [10]. Inflammation, specifically proinflammatory cytokines (IL-6, CRP), has been found to be an important mechanism linking social support and health risk [17].
Social support is linked to inflammation through complex bidirectional processes. Two theories posit neurophysiological and behavioural pathways to explain these associations between social support and inflammation. The social signal transduction theory suggests that a lack of social support and/or interpersonal stress activate brain regions associated with cytokine release, which become repeatedly sensitized over time [18]. The sickness behavior theory postulates that sickness and resulting chronic cytokine exposure lead to altered social support (e.g., withdrawal, energy conservation, anxiety, hypervigilance) [19]. In other words, being sick may change how one interacts with others; they may reach out for support or isolate and stay home. Various studies also have considered plausible pathways that mediate the relation between social support and inflammatory processes, such as neurological, behavioural, psychological, and physiological mechanisms [20–23]. For example, animal models establish credibility of physiological causality linking social support and inflammation (e.g., unstable social environment and higher CRP in rabbits) [24]. Further, findings of an association between adverse social experiences and inflammation during adolescence provides preliminary evidence that cumulative exposure to strained or limited social support over the lifetime may not be necessary [25, 26]. The underlying pathophysiological mechanisms remain unclear and necessitate comprehensive approaches to disentangle the complex relations (and plausibly bi-directional relations) among social support, immune functioning, and inflammation.

**Social support and inflammation: Adulthood**

Among adults, evidence consistently links social support to lower levels of chronic low-grade inflammation. Insufficient social support during adulthood (i.e., social isolation) increases inflammatory responses while suppressing antiviral immunity, whereas positive social support (i.e., integration) decreases inflammation and strengthens antiviral responses [27]. For example, a population-based study in the United States found that higher levels of social support and lower levels of social conflict within one’s social network predicted lower levels of inflammatory markers throughout adulthood [25]. In a recent meta-analysis of 47 studies, social support was significantly related to lower levels of inflammatory markers ($r = -.073$) [17]. Specifically, social support (e.g., family, caregiver, friends, neighbours, supervisors/co-workers) was negatively associated with inflammatory markers (i.e., CRP) in clinical and non-clinical samples. Given the robust association of higher social support and lower inflammation in adults (albeit of a small magnitude), it is important to examine if and when this association emerges during childhood and adolescence [28].

**Social support and inflammation: Childhood and adolescence**

Compared to adulthood, less is known about the relation between social support and chronic inflammation during childhood and adolescence. Mounting evidence suggests that the association between social support and inflammation begins early in the lifespan [29–32]. Social support during childhood and adolescence (e.g., greater parent support, warmer family climate, lower interpersonal stress) has been linked to CRP [33–37], IL-4 [38], IL-6 production [39], and the inflammatory response [40]. For example, greater parental support is associated with lower levels of IL-4 [38], and has been found to moderate the association between CRP with depressive symptoms [33] and sympathetic activity [34] in adolescents. Warmer family climate (i.e., more emotional support, less conflict, less harsh) predicted IL-6 production trajectories over 18 months; and, having a less harsh family climate was a buffer when experiencing a major life event, leading to lower IL-6 production [39]. Curiously, although school environment (e.g., teachers, school connectedness) has been related to positive mental health...
outcomes and reduced health risk behaviours [41, 42], no studies to date have explored its relation to chronic inflammation. Strained social relationships, conversely related to emotional social support and warmth, have also been examined. For example, adolescents who reported more interpersonal stress across sources (i.e., peers, family, school) had higher levels of CRP ($\beta = .28$) [37]. Poor parental monitoring (e.g., lack of time or interest in teen’s activity) and negative parental behaviours (e.g., conflictual aggression) have been associated with higher CRP during adolescence [35, 36]. Additionally, fewer warm, supportive peer relationships predicted greater pro- and anti-inflammatory responses in adolescent girls six months later [40]. Less supportive home and neighborhood environments have also been associated with higher levels of CRP in children and adolescents [43, 44]. Together, these studies evidence modest associations between social support and inflammatory markers and suggest that this relation emerges early during development; however, the majority of studies were conducted with adolescents and largely focused on a singular source of social support.

**Rationale and objectives**

The importance of understanding the pathophysiology of inflammation from a young age is timely and has lasting implications for overall health. Childhood and adolescence are important periods for developing interpersonal skills and lifestyle behaviors. Inadequate social support during childhood (e.g., social isolation) is linked to higher levels of inflammation in adulthood nearly 40 years later [29–32]. Current findings suggest the association between greater social support and lower chronic inflammation, or alternatively more strained relationships and higher chronic inflammation, may emerge during adolescence. However, most studies conducted to date have been conducted in small samples (e.g., $N < 200$) and almost exclusively use narrow social support measures based on certain sources (e.g., parents, peers). Further, to the best of our knowledge, no studies have considered sex differences. Therefore, before we can advance our understanding of the pathophysiological mechanisms underlying the association between social support and inflammation, it is necessary to first establish whether the association exists at different ages across childhood and adolescence using large, population cohorts.

The aim of the present analysis was to test the association between social support and chronic low-grade inflammation (CRP) in a population-based sample of children and adolescents. To address the existing gaps within this literature, the specific objectives were to i) replicate previous findings among adults and adolescents that observed greater overall social support was associated with lower CRP; ii) extend previous work by examining the association during childhood; and, iii) examine this association within a large population sample. As a secondary aim, potential sex- and age-based differences were explored to test whether the relation was similar in boys and girls, and across 9-, 13-, and 16-year-olds.

**Methods**

**Population dataset**

The Quebec Child and Adolescent Health and Social Survey (QCAHS) was a multi-stage sample survey of Quebec youth aged 9 years ($n = 1267$), 13 years ($n = 1186$), and 16 years ($n = 1160$; Total $N = 3613$) that was population-representative at the time of sampling (1999). Complete survey design and methodology are reported elsewhere [45, 46]. The original QCAHS survey was approved by the Ethics Review Board of Direction Santé Québec, Institut de la Statistique du Québec, and CHU Sainte-Justine; secondary dataset use was approved by Concordia University’s Ethics Committee (UH2006-068).
Protocol
Research teams completed standardized assessments during morning sessions at schools of blood pressure, anthropometrics (height, weight, waist circumference), and >10 hr fasting blood draw. Parents and youth completed questionnaires of items previously validated and adapted from other Quebec or Canada population-based surveys (e.g., Canadian National Longitudinal Study of Children and Youth; Québec Enquête Sociale et de Santé). Questionnaires were administered in the language of instruction at the child’s school (e.g., French or English) [46].

Measures

**C-reactive protein (CRP).** Blood was obtained by venipuncture by a pediatric nurse and high-sensitivity C-reactive protein (CRP) concentrations were assessed with the IMMAGE® immunochemistry system (Beckman Coulter), with a lower detection limit of 0.20 mg/L per assay [47]. Assay values below the lower detection limit were imputed using multiple imputation, which is deemed preferable to assigning a static value of 0.20 mg/L [48]. CRP concentrations were log⁶-transformed to adjust for non-normality and positive skew [49]. Over half of the sample agreed to have blood drawn (N = 2475; age 9, 62%, n = 783; age 13, 69%, n = 818; age 16, 75%, n = 874). The present analyses include youth who completed the blood draw, consented to C-Reactive Protein assays, had sufficient plasma volumes, and had no chronic health condition known to affect CRP (e.g., diabetes, cystic fibrosis, inflammatory bowel disease; N = 2232; age 9, n = 710; age 13, n = 715; age 16, n = 807). CRP concentrations are remarkably stable over time with no seasonal variations and only occasional spikes due to acute infections; the consistency of measures repeated years apart is comparable to cholesterol (i.e., r = 0.50) [50, 51]. Previous QCAHS analyses examined non-response and/or selection bias; there were no statistically significant differences for blood draw completion for sex, pubertal status, smoking, weight status, parental smoking, parent education, household income, or school setting (rural or urban) [46]. Language spoken at home (age 9 only; 67% francophone, 53% anglophone) and physical activity levels (age 16 only; 72% active, 81% least active) were significantly different between those who did and did not complete the blood draw [46]. To address possible bias within the CRP subsample used in the present analyses, sample demographics were compared to the entire QCAHS sample. Effect sizes were estimated for continuous and categorical variables (Cohen’s d and φ Phi coefficient).

**Social support.** Youth and parents answered items about social support. QCAHS questionnaires included social support items drawn from surveys previously used in Quebec population surveys (e.g., Styles de vie des jeunes du secondaire en Outaouais study [52]; Ado, Familles et Milieu de vie study [53]) and some items adapted from the Social Support Rating Scale [16]. A panel of independent raters (n = 3) reviewed child and parent questionnaires to identify potential items that captured social support broadly (e.g., confiding, perceived, emotional, warmth) with any source (e.g., parents, siblings, peers, teachers, neighbors, relatives, friends). Raters had excellent agreement (kappa (κ) = .983, p < .001): 38 items were identified for children (age 9); 44 items were identified for adolescents (ages 13, 16; same 38 items, plus 6 additional items not answered by children). Examples of items included “Do you think your [friend] would really listen to you and help you feel better if you really needed it?”, “Do your neighbors help each other”, and “Do some of your teachers listen to you when you need to talk about your problems”. Items were rated on Likert scales (e.g., Completely disagree to Completely agree, -2 to 2; Never to Very often, 0 to 3) and harmonized to yield consistent directions (i.e., higher score = more social support). A cumulative social support score was derived across
items; summed scores could range from -60 to 60. In the present sample, the social support score evidenced good internal consistency (Cronbach’s α = .817).

**Covariates.** Youth reported their age and sex (response options only included boy or girl; insufficient information to discern biological sex assigned at birth versus identified gender. Sex is the assumed construct measured, consistent with prior QCAHS publications). Age was verified using Quebec Ministry of Education records, which were based on birth certificate information. Height and weight were recorded based on standardized protocols (see [46]). Body Mass Index (BMI) was calculated [weight (kg)/height²(m)] and converted into age- and sex-specific Z-scores based on the Centers for Disease Control and Prevention (CDC) standardized curves [54]. Pubertal status was defined as adrenarche stage (i.e., body hair, pubic, under-arm). Smoking status was defined as smoking a cigarette ever (age 9) or over past 30 days (age 13 and 16; 1994 Canadian Youth Smoking Survey [55]. Medication use was operationally defined as use of any over-the-counter medications or prescription drugs for possible infection or inflammation in the prior 2 weeks (e.g., antibiotics, pain/fever, cold/allergies, respiratory problems, pump/inhaler) [47]. Socioeconomic status (SES) was defined as parental education (no formal schooling to university) and total household income (1998, before taxes and deductions; <$10K to ≥$80K CAN) based on parent report. Ethnoracial background was defined by categorizing children as French-Canadian (i.e., parents born in Quebec or Canada, and French language spoken at home) or not. This variable has been used in prior QCAHS publications as a proxy for ethnoracial status (e.g., ethnicity, race), which was unavailable.

**Data integrity and missingness.** Assumptions of linearity, normality, and residuals (independent, normality with mean of zero, homogeneity) were verified [49]. Univariate outliers were retained when clinically plausible (e.g., BMI-Z score). Sensitivity analyses were conducted with and without CRP values exceeding 10 mg/L (n = 45), which is the designated clinical threshold suggesting active infection. Data were missing completely at random (MCAR χ² = 17.830, df = 18, p = .467; 12.2% total missingness). Multiple imputation with fully conditional specification (iterative Markov Chain Monte Carlo, MCMC) was used to impute 25 datasets that were inspected for multivariate outliers (n = 4). Sensitivity analyses were also conducted using imputed and non-imputed datasets. Results were largely identical; therefore, only imputed results are presented for parsimony. Analyses were performed using SPSS version 27.

**Hypothesis testing.** Linear regression using the General Linear Model (GLM) was used to test the hypothesized relation that greater social support would be associated with lower CRP. GLM is deemed preferential to TOBIT models (e.g., censored regression) when combined with multiple imputation to address data missing below-detectable-limits (e.g., non-detects) [48]. Prediction models adjusted for covariates (age, sex, BMI Z-score, medication use, puberty, smoking status, French-Canadian status, household income, parental education). Models were also stratified by sex (boy, girl) and by age (9, 13, 16 years) for secondary analyses to explore results and inform the interpretation. Effect sizes were estimated for models and covariates (R² and η², eta-squared). Finally, sensitivity analyses were conducted to examine the effects of CRP values above the clinical threshold and imputed data.

**Results**

**Sample demographics**

The present analyses were based on the CRP subsample (n = 2186) who completed the blood draw and consented to CRP assaying, as described above. Demographic data are presented in Table 1. This subsample included a similar percentage of boys and girls (48.5%, 51.5%, respectively), who were of normal weight status (BMI-Z avg = .203), predominantly non-smoking (80.8%), and lived in households with an average income of $48.25K CAN and with a parent
who completed a university degree or higher (70.3%; ≥16 yrs schooling). Youth had low hs-CRP levels (0.831 mg/L); girls had higher levels of hs-CRP than boys ($t = 3.713, p < .001; Cohen’s $d = 0.159$). Compared to the entire QCAHS sample, the CRP subsample was ~3 months older ($t = 3.173, p = .002; Cohen’s $d = 0.086$) and had slightly more advanced pubertal

| Table 1. Sample demographics. | QCAHS ($N = 3613$) | Present Analysis ($n = 2186$) | QCAHS vs. CRP |
|-----------------------------|-------------------|------------------|--------------|
|                             | Complete Sample   | Boys            | Girls        | CRP Subsample | Boys    | Girls   | Sex Comparison |
|                             | $M (SD)$          | $M (SD)$        | $M (SD)$     | $M (SD)$      | $M (SD)$| $M (SD)$|               |
| Age*                        | 12.49 (2.90)      | 12.45 (2.88)    | 12.53 (2.92) | 12.74 (2.91)  | 12.69   | 12.79   | $t = .829, \ p = .407, \ d = .028$ |
| BMI Z-Score*                | .192 (1.08)       | .233 (1.08)     | .154 (1.09)  | .203 (1.05)   | .217   | .189    | $t = .2.181, \ p = .029, \ d = .073$ |
| Pubertal stage*             | 2.57 (1.11)       | 2.46 (1.04)     | 2.67 (1.16)  | 2.65 (1.11)   | 2.48   | 2.76    | $t = .5.646, \ p < .001, \ d = .001$ |
| Income ($\text{K}$)*       | 48.29 (22.55)     | 48.33 (22.55)   | 48.25 (22.55)| 48.25 (22.59) | 48.53  | 47.98   | $t = .5.095, \ p < .001, \ d = .024$ |
| Education (years)*          | 14.13 (2.05)      | 14.13 (2.04)    | 14.13 (2.05) | 14.12 (2.04)  | 14.13  | 14.11   | $t = .2.30, \ p = .010, \ d = .004$ |
| CRP (mg/L)                  | 0.831 (1.38)      | .719 (1.26)     | 0.937 (1.47) | 1.06 (1.34)   | 1.03   | 1.00    | $t = .5.646, \ p < .001, \ d = .005$ |
| Social support              | 20.21 (10.28)     | 19.75 (10.05)   | 20.67 (10.48)| 20.23 (10.43) | 19.58  | 20.84   | $t = .5.646, \ p < .001, \ d = .005$ |
| Medication Use (yes)        | 1655 (45.80)      | 729 (41.0)      | 926 (50.5)   | 1046 (47.80)  | 457    | 589     | $\chi^2 = 18.856, \ p < .001, \ \phi = .093$ |
| French-Canadian (yes)       | 2892 (80.0)       | 1455 (81.80)    | 1437 (78.30) | 1746 (79.90)  | 882    | 864     | $\chi^2 = 13.605, \ p < .001, \ \phi = .079$ |
| Smoking (yes)               | 666 (18.40)       | 288 (16.2)      | 378 (20.6)   | 419 (19.2)    | 174    | 245     | $\chi^2 = 10.194, \ p < .001, \ \phi = .068$ |

Note.
*Test statistics (t-tests) calculated on all available data from QCAHS ($n<3613$).

https://doi.org/10.1371/journal.pone.0268210.001
development (0.08 adrenarche stage; t = 2.647, p = .008; Cohen’s d = 0.072); the observed effect sizes imply these differences were trivial. There were no differences for sex, BMI Z-score, current smoking status, medication use, household income, parental education, nor cumulative social support score.

Model testing

In the prediction model, known covariates (sex, age, BMI Z-score, pubertal status) were significantly associated with hs-CRP<sub>log</sub> (see Table 2). Additional covariates were retained in the prediction models for consistency with past QCAHS publications and because they have been previously linked to CRP in other youth samples (e.g., medication use, French-Canadian status, smoking status, household income, parental education) [56, 57]. A higher cumulative social support score was significantly associated with lower hs-CRP<sub>log</sub> after controlling for the aforementioned covariates. Social support accounted for 0.3% of the variance, yielding a small effect size, which is consistent with prior findings in the adult and adolescent literature. Overall, the prediction model accounted for 10.2% of the variance (see Table 2).

Secondary analyses stratified by sex and age yielded largely consistent associations (i.e., magnitude of effect). Analyses stratified by sex revealed that the findings were largely similar for boys and girls; however, these analyses failed to reach statistical significance (see Table 3). The slope and magnitude of the association between social support and hs-CRP<sub>log</sub> were comparable in boys and girls (Unstd. B = -.325, η² = .003; Unstd. B = -.304, η² = .003; respectively).

Analyses stratified by age revealed that the association between social support and hs-CRP<sub>log</sub> increased in magnitude across ages (see Table 4). While the beta coefficients for cumulative social support score in 13- and 16-year-olds were similar in magnitude to those of the non-stratified prediction model, they did not reach significance (η²<sub>p</sub> = .002 and .004, respectively). Specifically, beta coefficients increased in a gradient fashion with age (Unstd. B = .002, -.240, and -.367, respectively). Further, these similar effect sizes for social support were observed while controlling for other meaningful covariates, such as BMI Z-score. Finally, sensitivity analyses were conducted to examine the effects of including CRP values above the clinical threshold (>10) and using original (non-imputed) data; overall results were largely identical (not shown for parsimony).

Table 2. Prediction model.

| CRP Sample (N = 2186) | Unstd. B | Unstd. SE | t   | p  | η²<sub>p</sub> |
|-----------------------|----------|-----------|-----|----|--------------|
|                       | (F = 25.88, p < .001, Adjusted R² = .102) |       |     |    |              |
| Sex (ref: Boys)       | 0.138    | 0.032     | 4.345 | < .001 | .011 |
| Age                   | 0.047    | 0.010     | 4.547 | < .001 | .012 |
| BMI-Z Score           | 0.177    | 0.014     | 12.507 | < .001 | .076 |
| Medication Use (ref: No) | 0.059 | 0.031     | 1.878 | .061  | .002 |
| Pubertal status       | -0.070   | 0.027     | -2.578 | .010 | .004 |
| French-Canadian status (ref: No) | 0.028 | 0.041     | 0.670 | .503  | .000 |
| Smoking status (ref: No) | -0.044 | 0.043    | -1.006 | .315 | .001 |
| Household income      | 0.000    | 0.001     | -0.639 | .523 | .000 |
| Parental education    | -0.008   | 0.009     | -0.843 | .400 | .001 |
| Social support (cumulative score) | -0.311 | 0.150   | -2.078 | .038 | .003 |

https://doi.org/10.1371/journal.pone.0268210.t002
Discussion

This study aimed to test the relation between social support and low-grade chronic inflammation in a population-based sample of children and adolescents. As hypothesized, higher social support was significantly associated with lower CRP. The magnitude of the effect observed was comparable to previous research linking social support and inflammation in meta-analyses of the adult literature ($R^2 = .005$) [17] and emerging findings in the child and adolescent literature [33–40, 43, 44]. While small, these generally consistent effect sizes imply a robust association between social support and inflammation across the lifespan. The small magnitude is not unexpected given that inflammation is only one of many pathways linking social support to health; the complex nature of inflammatory processes and their unmeasured biological influences encumber the interpretation of the effects. Further, the construct of social support is not harmonized in the field: heterogeneous measurement of different sources and types of support hinders meaningful synthesis, and in turn, obscures interpretation of findings linking inflammation and social support. Given the similar strength of association between this study and those within adults, these findings are promising for the pediatric literature. Future research should explore the relation between social support and inflammation across sex and age.

Table 3. Prediction model by sex.

|                      | Boys                                  | Girls                                |
|----------------------|---------------------------------------|--------------------------------------|
|                      | Unstd. B | Unstd. SE | $t$   | $p$   | $\eta^2_p$ | Unstd. B | Unstd. SE | $t$   | $p$   | $\eta^2_p$ |
| Age                  | 0.034    | 0.013    | 2.498 | .013  | .007       | 0.060    | 0.014    | 4.127 | <.001 | .019       |
| BMI-Z Score          | 0.169    | 0.020    | 8.567 | .001  | .073       | 0.185    | 0.020    | 9.257 | <.001 | .079       |
| Medication Use       | 0.085    | 0.044    | 1.942 | .052  | .005       | 0.035    | 0.045    | 0.791 | .429  | .001       |
| Pubertal status      | -0.033   | 0.038    | -0.864 | .388  | .001       | -0.102   | 0.037    | -2.780 | .006  | .009       |
| French-Canadian status | 0.029  | 0.058    | 0.495 | .621  | .000       | 0.022    | 0.054    | 0.413 | .680  | .000       |
| Smoking status       | -0.098   | 0.064    | -1.526 | .128  | .003       | -0.006   | 0.057    | -0.113 | .910  | .000       |
| Household income     | -0.001   | 0.001    | -0.845 | .399  | .001       | 0.000    | 0.001    | -0.019 | .985  | .000       |
| Parental education   | 0.009    | 0.013    | 0.747 | .470  | .000       | -0.024   | 0.012    | -1.992 | .047  | .005       |
| Social support       | -0.325   | 0.221    | -1.472 | .142  | .003       | -0.304   | 0.207    | -1.466 | .143  | .003       |

Table 4. Prediction model by age.

|                      | 9-year-olds ($n = 696$) | 13-year-olds ($n = 704$) | 16-year-olds ($n = 786$) |
|----------------------|-------------------------|--------------------------|--------------------------|
|                      | Unstd. B | Unstd. SE | $t$   | $p$   | $\eta^2_p$ | Unstd. B | Unstd. SE | $t$   | $p$   | $\eta^2_p$ | Unstd. B | Unstd. SE | $t$   | $p$   | $\eta^2_p$ |
| Sex (ref: Boys)      | 0.162    | 0.052    | 3.090 | .002  | .016       | -0.043   | 0.059    | -0.727 | .468  | .002       | 0.231    | 0.053    | 4.315 | <.001 | .027       |
| BMI-Z Score          | 0.165    | 0.023    | 7.144 | <.001 | .080       | 0.219    | 0.025    | 8.818 | .000  | .118       | 0.156    | 0.026    | 5.886 | <.001 | .051       |
| Medication (ref: No) | 0.025    | 0.057    | 0.444 | .657  | .001       | 0.027    | 0.053    | 0.517 | .606  | .001       | 0.105    | 0.052    | 2.026 | .043  | .006       |
| Pubertal status      | -0.010   | 0.052    | -0.199 | .842  | .001       | -0.062   | 0.042    | -1.478 | .140  | .004       | -0.031   | 0.052    | -0.591 | .555  | .001       |
| French-Canadian status (ref: No) | -0.007 | 0.071    | -0.099 | .921  | .000       | -0.014   | 0.070    | -0.201 | .841  | .001       | 0.058    | 0.065    | 0.889 | .374  | .001       |
| Smoking status (ref: No) | -0.234 | 0.181    | -1.294 | .196  | .003       | -0.044   | 0.078    | -0.563 | .574  | .001       | -0.053   | 0.053    | -0.992 | .321  | .002       |
| Household income     | 0.000    | 0.001    | 0.138 | .890  | .000       | -0.002   | 0.001    | -1.498 | .135  | .004       | 0.000    | 0.001    | -0.055 | .956  | .000       |
| Parental education   | -0.010   | 0.015    | -0.668 | .505  | .001       | 0.000    | 0.015    | -0.033 | .974  | .000       | -0.014   | 0.015    | -0.948 | .344  | .002       |
| Social support (cumulative score) | 0.002 | 0.374    | 0.004 | .997  | .000       | -0.240   | 0.224    | -1.073 | .284  | .002       | -0.367   | 0.232    | -1.580 | .115  | .004       |

https://doi.org/10.1371/journal.pone.0268210.t003

https://doi.org/10.1371/journal.pone.0268210.t004
Among the emerging findings in children and adolescents, greater social support (feeling valued and cared for) has been previously linked to lower chronic inflammation. For example, higher parental support and positive behaviours have been related to lower CRP [33–36]. Inversely, negative aspects of social support (e.g., absence, poor quality, harsh climate) have been linked to higher chronic inflammation [37–40]. Results of the present study replicate these findings, and extend this work to a larger, population-representative sample across three age groups, and use a broader, more encompassing definition of social support. Conceptualizations of social support that include a wider network of home environment and neighborhood have shown that lower support (i.e., unsafe, fewer resources) are associated with higher levels of CRP in children and adolescents [43, 44]. Finally, prospective and retrospective evidence suggests the association between childhood social support and chronic inflammation tracks into adulthood [29–32]. The present findings indicate that the strength of the association emerges across age groups, with stronger associations observed among 13- and 16-year-olds. Altogether, findings suggest there is a social support gradient for inflammation across the life-span, beginning in early adolescence.

Questions remain about the pathways linking social support and chronic inflammation. Sex has been posited as a moderator within social isolation and social integration models (few studies have considered gender; see below) [58]. Social isolation is thought to have a threshold effect: insufficient social support increases health risk via negative psychological states, poor self-care, and risky health practices, leading to increased inflammation. Inversely, social integration is thought to have a graded relation: having greater social support (e.g., number of social roles) decreases health risk via more adaptive cognitions, better emotional state, and healthier behaviours [58], leading to lower inflammation. For example, in a systematic review of social support and cardiovascular health risk in adults, sex moderated the association between social support and health risk; men had graded effects (i.e., social integration) while women had both graded and threshold effects (i.e., social isolation) [58]. In the present analysis, a graded association between social support and chronic inflammation was observed similarly in boys and girls. For example, increasing perceptions of greater support from anyone in the social network (e.g., family, peers, teachers, school, neighbourhood) in both boys and girls were linked to decreasing levels of chronic inflammation. Further, the high majority of boys and girls reported high levels of social support and social integration; only 4% endorsed social isolation (i.e., social support cumulative score below zero). Sex is commonly included as a covariate in childhood studies testing the association between social support and chronic inflammation; while no studies-to-date present sex-stratified results, mean differences have been reported. Notably, in the stratified analyses of the present study, the magnitude of the association between social support and inflammation was similar to that of the overall non-stratified analyses, but was no longer significant due to likely power limitations. Similar to past findings, girls reported higher social support [59–61] and had higher CRP [62], compared to boys. Mean level differences observed between boys and girls may be attributable to biological (sex) and/or social (gender) differences. Biologically, males and females have differing levels of pubertal timing, hormone production, adiposity, and fat mass distribution, which alter the CRP trajectory [63–66]. Socially, there is evidence that feminine individuals both seek and perceive higher levels of social support from their networks than masculine individuals [67]; though, few studies have considered gendered effects in relation to inflammation and health. Future research should consider how sex/gender and related variables (pubertal status, same/different-sex relationships) contribute to bidirectional models linking social support and chronic inflammation.

CRP levels in the present study were comparable to those previously reported in the pediatric literature (most < 3mg/L) [68]. Values of CRP that were below the detectable limit were
imputed; this preferred approach to handle non-detects provides more accurate estimates and is deemed more robust against heteroscedasticity of errors [48]. CRP is low during adolescence and increases throughout adulthood [69]. The limited variability of CRP levels in this sample of youth (consistent with expected values), may have contributed to the null findings when stratified by age. In other words, when the CRP range is constrained, especially within 9-year-olds, there are power limitations to detect a significant association. Other inflammatory markers not assessed in this study (e.g., IL-4, IL-6, TNF-alpha) may be more prevalent at younger ages with lower fat mass and more sensitive to the developmental onset and progression of chronic inflammation. Furthermore, less invasive sampling methods (e.g., saliva) have been shown to have higher sensitivity to CRP and other inflammatory markers in adolescents [70]. Future research should assess additional early inflammatory markers and precursors as these may better reveal the emergence of the relation between social support and chronic inflammation early in the lifespan.

Covariates in this study included age, sex, BMI Z-score, medication use, puberty, ethnoracial status, smoking, household income, and parental education, all of which have been previously shown to be associated with inflammation. Unexpectedly, French-Canadian status, smoking status, household income and parental education were not associated with CRP in the present study. (Post-hoc exploratory analyses revealed the interactions of socioeconomic status with social support were also not significant.) The use of French-Canadian status as a proxy for race or ethnicity is a limitation of the dataset. It is plausible that other measures of ethnoracial status and/or culture may be related to social support and/or CRP. It is important for future research to examine the association between social support and chronic inflammation within a larger, cultural context. Additionally, prior researchers have also adjusted for physical activity, household smoking exposure, perceived and objective socioeconomic status, and stressor exposure (perceived or interpersonal) and their relation to CRP [71–73]. Future research should consider these covariates when testing the complex association between social support and inflammation and its myriad mediators and moderators. Higher order measurement of social support may help to delineate critical causal pathways and targetable predictors of chronic inflammation.

**Strengths, limitations, and future directions**

The richness and quality of the QCAHS dataset, despite noted limitations, was an important strength of this study. First, this multi-stage sample survey of Quebec youth was a large, population-representative study that included information about children and adolescents’ social support combined with CRP values. Most studies conducted to date have only included small samples of youth (N < 200) that pose generalizability limitations. Second, it is rare to have fasting blood draw data for such a large number of participants, especially in a pediatric sample. As described earlier, the present sample included those who consented to blood draw and CRP assays. Compared to the entire QCAHS sample, this CRP subsample was slightly older and more advanced adrenarche development (puberty). However, these differences are likely not meaningful, as the subsample was only 3 months older and 0.08 stages more advanced. Third, this dataset presented a unique opportunity to examine the cross-sectional relation between social support and chronic inflammation with generalizability to the larger population of children and adolescents in Quebec. It is recognized that cross-sectional data precludes the examination of causal inferences (e.g., mediation, direction of association). However, the sampling design included three distinct age groups (9-, 13-, 16-year-olds), which provides valuable information spanning childhood and adolescent development. We recognize that additional work needs to be done to evaluate whether processes may differ across the lifespan. Fourth, the
QCAHS was conducted in 1999, which could be deemed “old data”. While the data may no longer be population-representative (e.g., mean level of CRP may be higher given larger BMI trends over 2 decades), the association between social support and chronic inflammation would not necessarily be expected to change over time, which is the key focus of the present study. Ultimately, the QCAHS dataset provided an exceptional resource to examine the relation between social support and chronic inflammation in youth and to address important gaps in research within the extant literature.

The conceptualization and measurement of social support introduced strengths and weaknesses that merit consideration. The QCAHS survey was originally designed to examine social constructs and lifestyle behaviors linked to cardiovascular risk factors [46]. At the time of inception, the decision of which questionnaire items to include was guided by both the ability to make comparisons with other population-representative surveys at that time (e.g., Youth Smoking Survey [55]) and practical choices to minimize administration time, which is a common challenge for large epidemiological surveys. The secondary use of the QCAHS dataset precluded our ability to refine item wording or to use standardized measures of social support. We strived to optimize information available by creating a cumulative score for all items pertaining to social support. In fact, the aggregated score yielded remarkable psychometrics in the present study. Raters had excellent congruence in their selection of social support items, which included both source-specific and general questions about support in one’s social network. Further, the cumulative support score had good internal consistency. Nevertheless, the lack of a standardized measure of social support is a recognized limitation of the study. Most commonly used standardized social support measures for children and adolescents include the Student Social Support Scale (1999; 60 items) [74], the Child and Adolescent Social Support Survey (2002; 40 items) [75], the Social Support Scale for Children (2012; 24 items) [76], and the Social Support Questionnaire for Children (2016; 50 items) [77]. The majority of these scales have 40 to 60 items, require roughly 20 minutes for administration time, and therefore, few have been included in large population surveys (e.g, \( N > 1000 \)). Further, these measures use a source-centric approach and categorize social support from parents, teachers, peers, and other sources. Obviously, these standardized measures were not used as they were developed and validated after the implementation of the QCAHS survey in 1999.

Curiously, while a source-centric approach is dominant in the child and adolescent social support literature, more nuanced subconstructs are used within the adult literature. For example, in adults, social support is largely defined as the type of support one receives: structural or functional [15]. Structural characteristics include the size of one’s social network and/or the degree of social integration one experiences (i.e., number of support sources in one’s network). Functional characteristics include the support processes that these networks serve, which can be further divided into two functional processes: received and perceived support [15]. Received support (i.e., what support one “gets”) captures interactions that are experienced such as help or advice during a crisis. Perceived support (i.e., support one “perceives” as available) captures beliefs of support availability that one can acquire from their network if necessary. To date, while the conceptualization of social support during childhood and adolescence has not been defined from these perspectives, closer inspection of standardized questionnaire items reveals that the assessment of functional support is embedded within the language of the item wording (e.g., makes me feel better, helps me solve problems). It is not yet clear whether there is a ubiquitous conceptualization of social support, or its subconstructs, that is contiguous across the lifespan. Another conceptualization used in the literature applies a more encompassing, macro perspective of broader social support. In fact, in the seminal meta-analysis by Holt-Lunstad and colleagues [9], broader (multi-dimensional)
measures of social support yielded the strongest associations with longevity. Similarly, Kumar’s international study [10] demonstrated that a single question of broad social support (i.e., “If you were in trouble, do you have friends and relatives you can count on to help you whenever you need them, or not”) was significantly associated with self-reported health. A broader more encompassing conceptualization of social support, reflecting a possible higher order construct, may be more robustly associated with health than conceptual silos that parse social support narrowly by type or source. Nonetheless, parsing support by these narrow sub-constructs can be useful to uncover mechanistic processes as exposures and processes at every level of one’s social ecosystem, from macro to micro, interact to influence health. Importantly, multiple perspectives of the conceptualization of social support are complementary and advantageous for the field.

Over the past two decades, children’s relationship and social support processes have evolved parallel to advances in technology and social media. In 1999, at the time of the QCAHS study, most social media platforms did not exist. In 2017, 76% of adolescents report using social media and over 90% use social media to connect with friends every day (e.g., over 1h per day) [78, 79, as cited in 78]. Since the onset of the COVID-19 pandemic, social media use has been the predominant means by which people connect with others and experience social support given social distancing mandates [80]. Social media introduces challenges to the conceptualization and measurement of social support. Social media may simply present an alternative mode to connect with loved ones (i.e., modes include in-person, letters, phone, video, social media platforms). On the other hand, it may create new forms of social support not redundant with existing support. For example, connectedness with one’s social media network (e.g., receiving anonymous “likes” or tweets from strangers) provides unique opportunities for experiencing social support. It is plausible to consider that social media use and/or deriving social support from social media groups may differ across marginalized populations and ethnoracial groups. There are emerging findings that social media may create unique and important opportunities for individuals from minority groups to feel more connected to others [81, 82]. Altogether, the measurement of social support, selection of suitable standardized measures, broader social support conceptualizations, and modern advances of social media introduced methodological considerations within the current study.

There are key recommendations to advance work on social support and inflammation in youth and to elucidate these findings. This study should be replicated in large samples, including population-representative cohorts. As the present findings were cross-sectional, they precluded the examination of a bidirectional association between social support and inflammation, and no causality can be inferred; future prospective studies would provide valuable data to investigate the causal nature of the relation and information about the predictive utility of social support. Moving beyond associations, it is valuable to investigate mechanisms (e.g., IL-6 production, stress buffering) and moderators (e.g., sex, gender) of the association between social support and inflammation to better understand the pathophysiological process. The construct and measurement of social support should continue to be carefully considered in future research. There is some evidence that a broader, more encompassing conceptualization using higher order macro-level items may provide a complementary perspective to existing conceptualizations of social support that are source-centric or isolate subconstructs. The importance of using psychometrically-sound, empirically-validated measures of social support remains fundamental for either conceptualization approach. Relatedly, it will be imperative that the role of social media and online platforms be evaluated within social support conceptualizations in future work.
Conclusion
Social support predicts multiple health outcomes in adults, including those related to inflammation and immune functioning. There is less evidence for this relation in children and adolescents. In the present analyses, social support was associated with lower chronic inflammation across 9-, 13-, and 16-year olds. Remarkably, the magnitude of effect was similar to that previously observed among adults. The question remains how social support "gets under the skin" and leads to inflammation. Pathogenic mechanisms linking social support and CRP should be examined in future work. Pediatric studies offer a distinct advantage for investigating when and how chronic inflammation develops and its trajectory with social support across the lifespan. These findings contribute to the current state of knowledge about the relation between social support and inflammation and have implications for improving our understanding of the pathophysiology of systemic inflammation and susceptibility to disease.

Author Contributions
Conceptualization: Eloïse J. Fairbank, Jennifer J. McGrath, Jennifer O'Loughlin, Gilles Paradis.
Data curation: Jennifer J. McGrath.
Formal analysis: Eloïse J. Fairbank.
Funding acquisition: Eloïse J. Fairbank, Jennifer J. McGrath, Jennifer O'Loughlin, Gilles Paradis.
Investigation: Eloïse J. Fairbank, Jennifer J. McGrath, Jennifer O'Loughlin, Gilles Paradis.
Methodology: Jennifer J. McGrath, Jennifer O'Loughlin, Gilles Paradis.
Project administration: Jennifer O'Loughlin, Gilles Paradis.
Resources: Jennifer J. McGrath, Gilles Paradis.
Supervision: Jennifer J. McGrath.
Visualization: Eloïse J. Fairbank.
Writing – original draft: Eloïse J. Fairbank, Jennifer J. McGrath.
Writing – review & editing: Eloïse J. Fairbank, Jennifer J. McGrath, Mélanie Henderson, Jennifer O'Loughlin, Gilles Paradis.

References
1. Furman D, Campisi J, Verdin E, Carrera-Bastos P, Targ S, Franceschi C, et al. Chronic inflammation in the etiology of disease across the life span. Nat Med. 2019 Dec 5; 25(12):1822–32. https://doi.org/10.1038/s41591-019-0675-0 PMID: 31806905
2. Pahwa R, Goyal A, Bansal P, Jialal I. Chronic inflammation [Internet]. Treasure Island (FL): StatPearls Publishing [Updated 2020 Nov 20; cited 2021 June 1]. https://www.ncbi.nlm.nih.gov/books/NBK493173/
3. van Zanten JV. C-Reactive Protein (CRP). In: Gellman MD, Turner JR, editors. Encyclopedia of Behavioral Medicine. New York (NY): Springer; 2013.
4. Maggio M, Guralnik JM, Longo DL, Ferrucci L. Interleukin-6 in aging and chronic disease: a magnificent pathway. J Gerontol A Biol Sci Med Sci. 2006 Jun 1; 61(6):575–84. https://doi.org/10.1093/gerona/61.6.575 PMID: 16799139
5. Harris TB, Ferrucci L, Tracy RP, Corti MC, Wacholder S, Ettinger WH Jr, et al. Associations of elevated interleukin-6 and C-reactive protein levels with mortality in the elderly. Am J Med. 1999 May 1; 106(5):506–12. https://doi.org/10.1016/s0002-9343(99)00066-2 PMID: 10335721
6. Ruiz J, Prather CC, Kauffman EE. Social Support. In: Gellman MD & Turner JR, editors. Encyclopedia of Behavioral Medicine. New York (NY): Springer; 2013.

7. Rook KS. Investigating the positive and negative sides of personal relationships: through a glass darkly? In: Spitzberg BH, Cupach WR, editors. The dark side of close relationships. Mahwah, NJ: Lawrence Erlbaum; 1998. p. 369–93.

8. Cohen S. Social relationships and health. Am Psychol. 2004 Nov; 59(8):676–84. https://doi.org/10.1037/0003-066X.59.8.676 PMID: 15554821

9. Holt-Lunstad J, Smith TB, Layton JB. Social relationships and mortality risk: a meta-analytic review. PLoS Med. 2010; 7(7):e1000316. https://doi.org/10.1371/journal.pmed.1000316 PMID: 20668659

10. Kumar S, Calvo R, Avendano M, Sivaramakrishnan K, Berkman LF. Social support, volunteering and health around the world: Cross-national evidence from 139 countries. Soc Sci Med. 2012 Mar 1; 74(5):696–706. https://doi.org/10.1016/j.socscimed.2011.11.017 PMID: 22305947

11. Cacioppo JT, Cacioppo S. Social relationships and health: The toxic effects of perceived social isolation. Soc Personal Psychol Compass. 2014 Feb; 8(2):58–72. https://doi.org/10.1111/pspc.12087 PMID: 24839458

12. Umberson D, Karas Montez J. Social relationships and health: A flashpoint for health policy. J Health Soc Behav. 2010 Mar; 51(Supplement 1):SS4–66. https://doi.org/10.1177/0022146510383501 PMID: 20943583

13. Smith TB, Workman C, Andrews C, Barton B, Cook M, Layton R, et al. Effects of psychosocial support interventions on survival in inpatient and outpatient healthcare settings: A meta-analysis of 106 randomized controlled trials. PLoS Med. 2021 May 18; 18(5):e1003595. https://doi.org/10.1371/journal.pmed.1003595 PMID: 34003832

14. Uchino BN. Social support and health: a review of physiological processes potentially underlying links to disease outcomes. J Behav Med. 2006 Aug 1; 29(4):377–87. https://doi.org/10.1007/s10865-006-9056-5 PMID: 16758315

15. Lakey B, Cohen S. Social support theory and measurement. In: Cohen S, Underwood LG, Gottlieb BH, editors. Social support measurement and intervention: A guide for health and social scientists. Oxford University Press; 2000. p. 29–52. https://doi.org/10.1093/med.psych/9780195126709.003.0002

16. Cauce AM, Mason C, Gonzales N, Hiraga Y, Liu G. Social networks and social support in childhood and adolescence. Berlin, New York: de Gruyter; 2012. Chapter 6, Social support during adolescence: methodological and theoretical considerations; p. 89–108.

17. Uchino BN, Trettevik R, Kent de Grey RG, Cronan S, Hogan J, Baكوم BR. Social support, social integration, and inflammatory cytokines: A meta-analysis. Health Psychol. 2018; 37(5):462–71. https://doi.org/10.1037/hea0000594 PMID: 29565600

18. Slavich GM, Irwin MR. From stress to inflammation and major depressive disorder: a social signal transduction theory of depression. Psychol Bull. 2014 May; 140(3):774–815. https://doi.org/10.1037/a0035302 PMID: 24417575

19. Eisenberger NI, Moieni M, Inagaki TK, Muscatell KA, Irwin MR. In sickness and in health: the co-regulation of inflammation and social behavior. Neuropsychopharmacology. 2017 Jan; 42(1):242–53. https://doi.org/10.1038/npp.2016.141 PMID: 27480575

20. Hellermans KG, Benge LC, Olmstead MC. Adolescent enrichment partially reverses the social isolation syndrome. Developmental Brain Research. 2004 Jun 21; 150(2):103–15. https://doi.org/10.1016/j.devebrain.2004.03.003 PMID: 15158074

21. Karelina K, DeVries AC. Modeling social influences on human health. Psychosom Med. 2011 Jan; 73(1):67. https://doi.org/10.1097/PSY.0b013e3182002116 PMID: 21097660

22. Kiecolt-Glaser JK, Gouin JP, Hantsoo L. Close relationships, inflammation, and health. Neurosci Biobehav Rev. 2010 Sep 1; 35(1):33–8. https://doi.org/10.1016/j.neubiorev.2009.09.003 PMID: 19751761

23. Miller AH, Raison CL. The role of inflammation in depression: from evolutionary imperative to modern treatment target. Nat Rev Immunol. 2016 Jan; 16(1):22–34. https://doi.org/10.1038/nri.2015.5 PMID: 26711676

24. Nation DA, Gonzales JA, Mendez AJ, Zaia J, Szeto A, Brooks LG, et al. The effect of social environment on markers of vascular oxidative stress and inflammation in the Watanabe heritable hyperlipidemic rabbit. Psychosom Med. 2008 Apr 1; 70(3):269–75. https://doi.org/10.1097/PSY.0b013e3181646753 PMID: 18256340

25. Yang YC, Schorpp K, Harris KM. Social support, social strain and inflammation: Evidence from a national longitudinal study of US adults. Soc Sci Med. 2014 Apr 1; 107:124–35. https://doi.org/10.1016/j.socscimed.2014.02.013 PMID: 24607674
26. Fagunde CP, Bennett JM, Derry HM, Kiecort-Glas JK. Relationships and inflammation across the lifespan: Social developmental pathways to disease. Soc Personal Psychol Compass. 2011 Nov; 5(11):891–903. https://doi.org/10.1111/j.1751-9004.2011.00392.x PMID: 22125580

27. Leschak CJ, Eisenberger NI. Two distinct immune pathways linking social relationships with health: inflammatory and antiviral processes. Psychosom Med. 2019; 81(8):711–9. https://doi.org/10.1097/PSY.000000000000173 PMID: 31600173

28. Uchino BN. Understanding the links between social support and physical health: A life-span perspective with emphasis on the separability of perceived and received support. Perspect Psychol Sci. 2009 May; 4(3):236–55. https://doi.org/10.1111/j.1745-6924.2009.00122.x PMID: 26158961

29. Fagunde CP, Way B. Early-life stress and adult inflammation. Curr Dir Psychol Sci. 2014 Aug; 23(4):277–83.

30. Slopen N, Chen Y, Priest N, Albert MA, Williams DR. Emotional and instrumental support during childhood and biological dysregulation in midlife. Prev Med. 2016 Mar 1; 84:90–6. https://doi.org/10.1016/j.ypmed.2015.12.003 PMID: 26708307

31. Lacey RE, Kumari M, Bartley M. Social isolation in childhood and adult inflammation: Evidence from the National Child Development Study. Psychoneuroendocrinology. 2014 Dec 1; 50:85–94. https://doi.org/10.1016/j.psyneuen.2014.08.007 PMID: 26995316

32. Yang YC, Boen C, Gerken K, Li T, Schorpp K, Harris KM. Social relationships and physiological determinants of longevity across the human life span. Proc Natl Acad Sci U S A. 2016 Jan 19; 113(3):578–83. https://doi.org/10.1073/pnas.1511085112 PMID: 26729882

33. Guan SS, Bower JE, Almeida DM, Cole SW, Dahl RE, Irwin MR, et al. Parental support buffers the association of depressive symptoms with cortisol and C-reactive protein during adolescence. Brain Behav Immun. 2016 Oct 1; 57:134–43. https://doi.org/10.1016/j.bbi.2016.03.007 PMID: 26995316

34. Nelson BW, Byrne ML, Simmons JG, Whittle S, Schwartz OS, Reynolds EC, et al. Adolescent sympathetic activity and salivary C-reactive protein: The effects of parental behavior. Health Psychol. 2017 Oct; 36(10):955–65. https://doi.org/10.1037/he0000016 PMID: 28639820

35. Byrne ML, Badcock PB, Simmons JG, Whittle S, Pettitt A, Olsson CA, et al. Self-reported parenting style is associated with children’s inflammation and immune activation. J Fam Psychol. 2017 Apr; 31(3):374–80. https://doi.org/10.1037/fam0000254 PMID: 27819440

36. Byrne ML, Horne S, O’Brien-Simpson NM, Walsh KA, Reynolds EC, Schwartz OS, et al. Associations between observed parenting behavior and adolescent inflammation two and a half years later in a community sample. Health Psychol. 2017 Jul; 36(7):641–51. https://doi.org/10.1037/he0000502 PMID: 28530434

37. Fuligni AJ, Telzer EH, Bower J, Cole SW, Kiang L, Irwin MR. A preliminary study of daily interpersonal stress and C-reactive protein levels among adolescents from Latin American and European backgrounds. Psychosom Med. 2009 Apr; 71(3):329–33. https://doi.org/10.1097/PSY.0b013e3181921b1f PMID: 19196810

38. Chen E, Chim LS, Strunk RC, Miller GE. The role of the social environment in children and adolescents with asthma. Am J Respir Crit Care Med. 2007 Oct 1; 176(7):644–9. https://doi.org/10.1164/rccm.200610-1473OC PMID: 17556714

39. Miller GE, Rohleder N, Cole SW. Chronic interpersonal stress predicts activation of pro- and anti-inflammatory signaling pathways six months later. Psychosom Med. 2009 Jan; 71(1):57–62. https://doi.org/10.1097/PSY.0b013e318190d7de PMID: 19073750

40. Vaz S, Parsons R, Falkmer T, Passmore AE, Falkmer M. The impact of personal background and school contextual factors on academic competence and mental health functioning across the primary-secondary school transition. PloS One. 2014 Mar 7; 9(3):e89874. https://doi.org/10.1371/journal.pone.0089874 PMID: 24608366

41. McNeely C, Falcì C. School connectedness and the transition into and out of health-risk behavior among adolescents: A comparison of social belonging and teacher support. J Scho Health. 2004 Sep 1; 74(7):284–82.

42. Schmeer KK, Yoon AJ. Home sweet home? Home physical environment and inflammation in children. Soc Sci Res. 2016 Nov 1; 60:236–48. https://doi.org/10.1016/j.sssresearch.2016.04.001 PMID: 27712682

43. Broyles ST, Staiano AE, Drazba KT, Gupta AK, Sothern M, Katzmarzyk PT. Elevated C-reactive protein in children from risky neighborhoods: evidence for a stress pathway linking neighborhoods and inflammation in children. PloS One. 2012 Sep 25; 7(9):e45419. https://doi.org/10.1371/journal.pone.0045419 PMID: 23049799
45. Aubin J. Institut de la statistique du Québec. Enquête sociale et de santé auprès des enfants et des adolescents québécois 1999. Québec: Institut de la statistique du Québec; 2002. https://statistique.quebec.ca/en/fichier/enquete-sociale-et-de-sante-aupres-des-enfants-et-adolescents-quebecois-1999-rapport.pdf

46. Paradis G, Lambert M, O’Loughlin J, Lavallée C, Aubin J, Berthiaume P, et al. The Quebec Child and Adolescent Health and Social Survey: design and methods of a cardiovascular risk factor survey for youth. Can J Cardiol. 2003 Apr; 19(5):523–31. PMID: 12717488

47. Lambert M, Delvin EE, Paradis G, O’Loughlin J, Hanley JA, Levy E. C-reactive protein and features of the metabolic syndrome in a population-based sample of children and adolescents. Clin Chem. 2004 Oct 1; 50(10):1762–8. https://doi.org/10.1373/clinchem.2004.036418 PMID: 15308596

48. Uh HW, Hartgers FC, Yazdanbakhsh M, Houwing-Duistermaat JJ. Evaluation of regression methods when immunological measurements are constrained by detection limits. BMC immunology. 2008 Dec; 9(1):1–0. https://doi.org/10.1186/1471-2172-9-59 PMID: 18928527

49. Tabachnick BG, Fidell LS. Using multivariate statistics. Boston, MA: Pearson; 2019.

50. Pepys MB, Hirschfield GM. C-reactive protein: a critical update. J Clin Invest. 2003 Jun 15; 111(12):1805–12. https://doi.org/10.1172/JCI18921 PMID: 12813013

51. Markanday A. Acute phase reactants in infections: evidence-based review and a guide for clinicians. Open Forum Infect Dis. 2015 Sep 1; 2(3):ofv098. https://doi.org/10.1093/ofid/ofv098 PMID: 26258155

52. Deschesnes M, Demers S, Finès P. Styles de vie des jeunes du secondaire en Outaouais. Régie Régionale de la Santé et des Services Sociaux de l’Outaouais: Direction de la santé publique; 2003. http://www.santequebec.qc.ca/bibliothequetable/hyperion/2895770085.pdf

53. Cloutier RL, Champoux C, Jacques C. Enquête ados, familles et milieu de vie: la parole aux ados!. Québec: Université Laval; Centre de recherche sur les services communautaires; 1994. http://www.santequebec.qc.ca/Bibliothquevirtuelle/santecon/3556700000002326.pdf

54. Center for Disease Control (CDC). Defining childhood obesity [Internet]. 2019 Jul 3 [cited 2021 Jun 1]. https://www.cdc.gov/obesity/childhood/defining.html

55. Stephens T, Morin M. Youth Smoking Survey 1994: Technical report. Ottawa: Health Canada; 1996.

56. Dowd JB, Zajacova A, Aiello AE. Predictors of inflammation in US children aged 3–16 years. Am J Prev Med. 2010 Oct; 39(4):314–20. https://doi.org/10.1016/j.amepre.2010.05.014 PMID: 20837281

57. Le-Ha C, Beilin LJ, Burrows S, Oddy WH, Hands B, Mori TA. Gender and the active smoking and high-sensitivity C-reactive protein relation in late adolescence. J Lipid Res. 2014 Apr 1; 55(4):758–64. https://doi.org/10.1194/jlr.P045369 PMID: 24577623

58. Chin B, Cohen S. Review of the association between number of social roles and cardiovascular disease: Graded or threshold effect? Psychosom Med. 2020; 82(5):471–86. https://doi.org/10.1097/PSY.0000000000001039 PMID: 32515924

59. Dubow EF, Ullman DG. Assessing social support in elementary school children: The survey of children’s social support. J Clin Child Psychol. 1989; 18(1):52–64.

60. Colarossi LG. Adolescent gender differences in social support: Structure, function, and provider type. Soc Work Res. 2001 Dec 1; 25(4):233–41.

61. Furman AMW, Buhrmester D. Age and sex differences in perceptions of networks of personal relationships. Child Dev. 1992 Feb; 63(1):103–15. https://doi.org/10.1111/j.1467-8624.1992.tb03599.x PMID: 1551320

62. Mac Giollabhuí N, Alloy LB, Swistun D, Coe CL, Ellman LM, Moriarity DP, et al. Concurrent and longitudinal associations of sex and race with inflammatory biomarkers during adolescence. J Youth Adolesc. 2021; 50(4):711–23. https://doi.org/10.1007/s10964-020-01369-w PMID: 33449289

63. Konishi S, Parajuli RP, Takane E, Maharjan M, Tachibanaka K, Jiang H-W, et al. Significant sex differences in inflammation in adolescents: association with early-life factors, gender, and lifestyle. Am J Epidemiol. 2010; 171(1):72–82. https://doi.org/10.1093/aje/kwp320 PMID: 19917553

64. Bupp MR. Sex, the aging immune system, and chronic disease. Cell Immunol. 2015 Apr 1; 294(2):102–10. https://doi.org/10.1016/j.cellimm.2015.02.002 PMID: 25700766

65. Shanahan L, Copeland WE, Worthman CM, Erkanli A, Angold A, Costello EJ. Sex-differentiated changes in C-reactive protein from ages 9 to 21: The contributions of BMI and physical/sexual maturation. Psychoneuroendocrinology. 2013 Oct 1; 38(10):2209–17. https://doi.org/10.1016/j.psyneuen.2013.04.010 PMID: 23711900
67. Reevy GM, Maslach C. Use of social support: Gender and personality differences. Sex Roles. 2001 Apr; 44(7):437–59.

68. Rödöö P, Ridedfelt P, Aldrimer M, Niklasson F, Gustafsson J, Hellberg D. Population-based pediatric reference intervals for HbA1c, bilirubin, albumin, CRP, myoglobin and serum enzymes. Scand J Clin Lab Invest. 2013 Aug 1; 73(5):361–7. https://doi.org/10.3109/00365513.2013.783931 PMID: 23581477

69. Ferrucci L, Corsi A, Lauretani F, Bandinelli S, Bartali B, Taub DD, et al. The origins of age-related proinflammatory state. Blood. 2005 Mar 15; 105(6):2294–9. https://doi.org/10.1182/blood-2004-07-2599 PMID: 15572589

70. Byrne ML, O’Brien-Simpson NM, Walsh KA, Laughton K, Waloszek JM, et al. Acute phase protein and cytokine levels in serum and saliva: a comparison of detectable levels and correlations in a depressed and healthy adolescent sample. Brain Behav Immun. 2013 Nov 1; 34:164–75. https://doi.org/10.1016/j.bbi.2013.08.010 PMID: 23999491

71. Schmeer KK, Yoon A. Socioeconomic status inequalities in low-grade inflammation during childhood. Arch Dis Child. 2016 Nov 1; 101(11):1043–7. https://doi.org/10.1136/archdischild-2016-310837 PMID: 27371708

72. Freeman JA, Bauldry S, Volpe VV, Shanahan MJ, Shanahan L. Sex differences in associations between subjective social status and C-reactive protein in young adults. Psychosom Med. 2016 Jun; 78(5):542–51. https://doi.org/10.1097/PSY.0000000000000309 PMID: 26910797

73. Wilkinson JD, Lee DJ, Arheart KL. Secondhand smoke exposure and C-reactive protein levels in youth. Nicotine Tob Res. 2007; 9(2);305–7. https://doi.org/10.1080/14622200601078277 PMID: 17365732

74. Malecki CK, Elliott SN. Adolescents’ ratings of perceived social support and its importance: Validation of the Student Social Support Scale. Psychol Sch. 1999 Nov; 36(6):473–83.

75. Kerres Malecki C, Kilpatrick Demary M. Measuring perceived social support: Development of the child and adolescent social support scale (CASSS). Psychol Sch. 2002 Jan; 39(1):1–8.

76. Harter S. Social support scale for children: Manual and questionnaires. Denver, CO: University of Denver, 2012.

77. Gordon-Hollingsworth AT, Thompson JE, Geary MA, Schexnaildre MA, Lai BS, Kelley ML. Social support questionnaire for children: Development and initial validation. Meas Eval Couns Dev. 2016 Apr; 49(2):122–44.

78. Uhls YT, Ellison NB, Subrahmanyam K. Benefits and costs of social media in adolescence. Pediatrics. 2017 Nov 1; 140(Supplement 2):S67–70. https://doi.org/10.1542/peds.2016-1758E PMID: 29093035

79. Cole DA, Nick EA, Zalkowitz RL, Roeder KM, Spinelli T. Online social support for young people: does it recapitulate in-person social support; can it help?. Comput Human Behav. 2017 Mar 1; 68:456–64. https://doi.org/10.1016/j.chb.2016.11.058 PMID: 28993715

80. Wong A, Ho S, Olusanya O, Antonini MV, Lyness D. The use of social media and online communications in times of pandemic COVID-19. J Intensive Care Soc. 2021 Aug; 22(3):255–60. https://doi.org/10.1177/1751143720966280 PMID: 34422109

81. Selkie E, Adkins V, Masters E, Bajpai A, Shumer D. Transgender adolescents’ uses of social media for social support. J Adolesc Health. 2020 Mar 1; 66(3):275–80. https://doi.org/10.1016/j.jadohealth.2019.08.011 PMID: 31690534

82. Chen Y, Tian H, Chang J. Chinese first, woman second: Social media and the cultural identity of female immigrants. Asian J Women Stud. 2021 Jan 2; 27(1):22–45.