## Title

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# Childhood Socioeconomic Status, Telomere Length, and Susceptibility to Upper Respiratory Infection

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## Abstract

Low socioeconomic status (SES) during childhood and adolescence has been found to predict greater susceptibility to common cold viruses in adults. Here, we test whether low childhood SES is associated with shorter leukocyte telomere length in adulthood, and whether telomere length mediates the association between childhood SES and susceptibility to acute upper respiratory disease in adulthood.

At baseline, 196 healthy volunteers reported whether they currently owned their home and, for each year of their childhood, whether their parents owned the family home. Volunteers also had blood drawn for assessment of specific antibody to the challenge virus, and for $CD8^+CD28^-$ T-lymphocyte telomere length (in a subset, $n = 135$). They were subsequently quarantined in a hotel, exposed to a virus (rhinovirus [RV] 39) that causes a common cold and followed for infection and illness (clinical cold) over 5 post-exposure days.

Lower childhood SES as measured by fewer years of parental home ownership was associated with shorter adult $CD8^+CD28^-$ telomere length and with an increased probability of developing infection and clinical illness when exposed to a common cold virus in adulthood. These associations were independent of adult SES, age, sex, race, body mass, neuroticism, and childhood family characteristics. Associations with infections and colds were also independent of pre-challenge viral-specific antibody and season. Further analyses do not support mediating roles for smoking, alcohol consumption or physical activity but suggest that $CD8^+CD28^-$ cell telomere length may act as a partial mediator of the associations between childhood SES and infection and childhood SES and colds.



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Lower levels of socioeconomic status (SES) in childhood and adolescence, as measured by living conditions, family income, and parental education and employment, have repeatedly been found to be associated with poorer health and greater risk for premature mortality in adulthood (Aber et al., 1997; Cohen et al., 2010; Gissler et al., 1998; Nelson, 1992; Roberts and Power, 1996). Although this literature has primarily focused on mortality (Galobardes et al., 2004; Galobardes et al., 2008) and cardiovascular health (Pollitt et al., 2005), there has been increasing interest in the impact of low early childhood SES on adult immune competence and susceptibility to infectious diseases (Cohen et al., 2004; Miller et al., 2009; Ziol-Guest et al., 2012).

The aim of the present study is to investigate the possibility that low childhood SES contributes to shorter leukocyte telomere length that, in turn, increases susceptibility to virus infection. Shorter white blood cell telomere lengths have been suggested as markers of decreased immunocompetence (Effros and Pawelec, 1997; Effros, 2001). Consistent with this view, human adults with shorter peripheral blood mononuclear cell (PBMC) telomere lengths, especially in $CD8^+CD28^-$ T lymphocytes, have been found to be at greater risk for experimentally-induced upper respiratory infections (Cohen et al., 2013). $CD8^+$ T lymphocytes that have lost the capacity to express CD28, a costimulatory molecule important for antiviral function, exhibit an accelerated rate of telomere attrition (Schmid et al., 2002; Valenzuela & Effros, 2002). Shorter average telomere length in this cell population indicates a greater proportion of cells nearing replicative senescence and hence comparatively fewer effector cells available to respond to viral insult (Cohen et al., 2013).

Although childhood SES has not been directly associated with adult leukocyte telomere length, childhood exposures to stressful environments that are characteristic of the low childhood SES experience have been associated with shorter average PBMC telomere lengths measured decades later (e.g., Kiecolt-Glaser et al., 2011; Tyrka et al., 2010; reviewed by Price et al., 2013). Moreover, low childhood SES (parental education) has been related to shorter telomere length in children aged 7 to 13 years (Needham et al, 2012). That exposures during childhood may result in concurrent changes in telomere length that persist through adulthood is suggested by evidence that telomere length is quite stable over 10 or more years (Chen et al., 2011; Ehrlenbach et al., 2009) and is thought to operate as a stable marker of disease susceptibility over much of the life course (Cohen et al., 2012).

Home ownership is a comprehensive SES indicator, reflecting wealth, income and social status (Long and Caudill, 1992) and is thought to be a more sensitive measure of SES in women than husband's occupation or income (Pugh et al., 1991). Parental home ownership has been widely used as an indicator of childhood SES with ownership associated with less psychological and emotional distress (e.g., Boyle, 2002; Cairney, 2005), less of an inflammatory profile in asthmatics (Chen et al., 2006) and greater resistance to upper respiratory infection (Cohen et al, 2004). An advantage of home ownership as a retrospective marker of *childhood* SES is that people are confidently able to recall whether their parents owned the family home from fairly early childhood (Cohen et al., 2004). In this study, we operationalized childhood SES as the number of years during participants' childhoods (through age 18 years) that their parents owned the family home.

Here, we evaluate whether childhood SES, measured as years of parental home ownership, is associated with $CD8^+CD28^-$ T cell telomere length in young to mid-life adults. We further ask whether childhood SES predicts susceptibility to infection and upper respiratory illness as previously reported (Cohen et al., 2004) and whether these associations are wholly or partly mediated by $CD8^+CD28^-$ T cell telomere length. In all of these cases, we test whether the associations are independent of current (adult) SES and of other childhood

family characteristics such as parental divorce, number of children in the home, number of residence moves, and mother's age when the participant was born.

## Methods

### Participants

Participants were drawn from 212 healthy volunteers ages 18–55 from greater Pittsburgh, PA. Of these, the last 152 had blood drawn for assessment of telomere length. The participants were recruited by newspaper and posted advertisements, and each was paid $1,000. The study was conducted between 2007 and 2011 and was approved by the Institutional Review Boards of both Carnegie Mellon University and the University of Pittsburgh and all participants provided signed informed consent.

### Overview

Healthy adult participants answered questions about their childhood and current socioeconomic status, and had blood drawn for measurement of rhinovirus (RV) 39 antibody titer and $CD8^+CD28^-$ telomere length (subsample only). They were subsequently quarantined, administered nasal drops containing a rhinovirus that causes the common cold (RV39), and monitored in quarantine over 5 days for infection and objective signs of a cold.

### Procedures

Volunteers presenting for possible enrollment underwent medical screenings and were excluded if they were treated in the past year or hospitalized in the last five years for psychiatric illness; had a history of major nasal or otologic surgery, respiratory disorders, or cardiovascular disease; had abnormal urinalysis, complete blood count, or blood enzymes; were currently pregnant or lactating; tested seropositive for human immunodeficiency virus; or regularly taking medication other than birth control. Specific serum neutralizing antibody titer to RV39 was assessed at screening, and, in order to maximize the rate of infection, volunteers were also excluded if that titer was greater than 4. This assay was repeated on a blood sample taken 2–3 days before quarantine to be defined as the pre-viral challenge titer for use as a covariate. The last 152 participants also had their blood drawn during the pre-quarantine baseline interval between screening and viral challenge to be assayed for lymphocyte telomere length.

Qualifying volunteers were isolated in a local hotel for a 6-day period. During the first 24 hours of quarantine (before viral exposure), volunteers had a nasal examination and a nasal lavage, and baseline symptoms, nasal mucociliary clearance and nasal mucus production were assessed. Volunteers were dismissed from the study if they displayed signs or symptoms of a cold on that day, and data for any participant in whom a virus was isolated from the nasal lavage fluids collected on that day were excluded from all analyses. Then, participants were given nasal drops containing approximately 100 tissue culture infectious dose ($TCID_{50}$)/mL of RV39. The quarantine continued for five days. On each day, volunteers were assessed for nasal mucociliary clearance and nasal mucus production, and nasal lavage samples were collected for virus culture. Approximately 28 days after virus exposure, blood was collected for serological testing. Investigators were blinded to all predictor variables at all points of the trial. Telomere length was assayed after the trial was completed by technicians blinded to all other study data.

### Socioeconomic Status

**Childhood SES—**Data on parental home ownership were collected by self-report questionnaire during the baseline day in quarantine. For each year of their lives from age 1

through 18, participants were asked whether their parents owned their family home. Response alternatives included *yes*, *no*, and *I don't know*. Many ($n$ = 33) participants were unable to provide information on parental home ownership for the first 4 years of their childhoods. For this reason, our primary analyses in the parent study were limited to childhood SES based on data provided for ages 5–18. By assessing parental home ownership on a yearly basis, we were able to calculate the total number of years of home ownership from ages 1 through 18, as well as to assess exposure at specific ages.

**Current (adult) SES—**Current SES was assessed by self-report questionnaire during the baseline interval between screening and viral challenge. Participants were asked to report the highest level of educational attainment that they had completed. Nine response options were provided, ranging from didn't finish high school to doctoral degree. For analysis, education was coded into 3 indicator variables with bachelor's degree or higher as the referent category: high school or less; less than two years of college; 2 years of college + associate's degree. Participants also were asked whether they currently owned their own home (including paying a mortgage). Home ownership status was verified using the Allegheny County, Pennsylvania Department of Real Estate website for 154 participants whose addresses were listed in the county database with 100% concurrence.

## Control Variables

All control variables were collected during the 2-month period before viral challenge.

**Standard control variables—**These covariates were chosen based on *a priori* likelihood that they might be associated with both childhood SES and the outcome variable. Self-reported age, sex, and race (selected from white, black, Native American, Asian/Pacific Islander, Hispanic/Latino, or other, and coded as white and nonwhite because of small numbers reporting nonblack minority categories), body mass index (BMI; weight in kg/[height in m]$^2$) computed from measurements of participant's height and weight, and neuroticism (using a 10-item version of the emotional stability subscale from the International Personality Item Pool [IPIP] Big-Five Factor Markers [Goldberg et al., 2006]) were included in all analyses. Season of the year (winter, spring, summer) and pre-challenge neutralizing specific antibody titer as assessed from a blood sample collected 2–3 days before exposure to the virus were additional covariates in analyses predicting infection and disease.

**Controls for family characteristics—**The results from the earlier study on childhood SES and infection (Cohen et al., 2004) were potentially confounded by the possibility that family characteristics often related to SES accounted for the increased risk for infection with decreasing childhood SES. Here we queried participants on a number of these alternative explanations which we included as controls. These included: (1) whether the participant experienced parental marital dissolution prior to age 19 years; (2) the average number (per year from ages 5–18 years) of supervisory adults and (3) of other children in the home; (4) how often the participant moved residence between ages 6 and 18 (sum of responses to two 4-pt items inquiring about the time periods spanning ages 6 to 14 years and 15 to 18 years, respectively; 0 = *never*, 3 = *more than twice*); and (5) the age of the participant's mother when the participant was born. Because many participants could not recall the information required to calculate father's age when they were born, we were not able to include this variable.

## Telomere Length

Whole blood for telomere length assay was collected by standard venipuncture within an 8-week window before the day of viral-challenge. Lymphocyte subsets from each blood

sample were labeled with fluorochrome conjugated mouse antihuman monoclonal antibodies (BD Bioscience Pharmingen) in RosetteSep cocktails, isolated immediately using an automated immunomagnetic cell separator (RoboSep, StemCell Technologies), and then stored at −80°C. Because telomere length in the $CD8^+CD28^-$ population was the best predictor of both infection and colds in this sample (Cohen et al., 2013), analyses in this paper are limited to this cell population. We also assessed PBMC telomere length, the marker more commonly studied. However, the small number of participants with complete data required for the analyses reported here (N=120) provided insufficient power to test our hypotheses in this cell population.

Details on the measurement of telomere length in this sample have been published elsewhere (Cohen et al., 2013). In brief, DNA was extracted from $CD8^+CD28^-$ T cells and amplified using a real-time quantitative polymerase chain reaction assay (qRT-PCR) (7300 Fast Real Time PCR system, Applied Biosystems) as per a published protocol (O'Callaghan et al., 2008). Applied Biosystems SDS software was used to generate standard curves and to determine the dilution factors of standards corresponding to the telomere (T) and single-copy gene (S) amounts in each sample. From these data, a T:S ratio was computed, providing a relative index of average telomere length. Coefficients of variation were 12% and 13% for T and S, respectively.

## Infection, Signs of Illness, and Clinical Colds

**Infection—**Infection was defined as recovery of the challenge virus in nasal lavage samples on any of the five post-challenge days (cultured using standard procedures [Gwaltney et al., 1989]) or a four-fold rise or greater in virus-specific serum neutralizing antibody titer from pre-exposure to 28-days post-exposure (using microtiter neutralizing assay [Al Nakib and Tyrrell, 1988]).

**Signs of illness—**We used two objective markers of illness: mucus production (weight) and mucocilliary clearance function. Daily mucus production was assessed by collecting used tissues in sealed plastic bags on each day of quarantine (Doyle et al., 1988). The bags were weighed and the pre-use weight of the tissues and bags subtracted. Nasal mucociliary clearance function was assessed as the time required for a solution administered into the anterior nose to reach the nasopharnyx (Doyle et al., 1988).

Baseline-adjusted daily scores for each measure were calculated by subtracting the appropriate baseline score from each of the five post-exposure daily scores. Negative adjusted scores were re-assigned a value of 0. Total scores for mucus weight and nasal clearance were calculated by summing the respective adjusted daily scores over the five post-challenge days.

**Colds—**Volunteers were considered to have developed a clinical cold if they were both infected with the challenge virus and met the illness criterion. The criterion for signs of illness required a total adjusted mucus weight of at least 10 grams or a total adjusted nasal mucociliary clearance time of at least 35 minutes (Cohen et al., 1997).

## Health Behaviors

Health behaviors were assessed by self-report questionnaires administered during baseline. Participants were asked whether they currently smoke on a daily basis and, if so, how many cigarettes/cigars/bowls of tobacco they typically smoke per day; whether they consume alcohol at least once a week and, if so, the average number of drinks they usually have per day (1 drink = 1 glass of wine, 12 oz of beer, or 1 shot of hard liquor); and the number of days per week that they engage in regular physical activity long enough to work up a sweat.

For analysis, non-smokers, non-drinkers, and those who do not exercise were assigned a score of 0 for the relevant variable. For analysis, drinks per day was converted to drinks per week. Smoking and drinking rate variables were $\log_{10}$-transformed to reduce skew.

### Statistical Analysis

Complete childhood SES and control variable data were available for 196 participants. Lymphocyte telomere length was assessed in a substudy that included only the last 152 participants in the main study. $CD8^+CD28^-$ T cell telomere length data were available for 144 subjects (see Cohen et al., 2013), 135 of whom also had complete childhood SES data. Hence analyses addressing telomere length as either an outcome or mediator are based on these 135 participants. However, for analyses not including telomere length (evaluating the role of childhood SES in infection and colds), we present results for both the larger (N=196) and smaller (N=135) samples.

Multiple linear regressions were used to identify significant predictors of telomere length, a continuous outcome. There, we report the unstandardized regression coefficient (*B*), standard error (SE), beta (β), and *p*-value. Logistic regression was used to predict binary study outcomes, presence/absence of a cold or of infection. In these cases, we present the odds ratio (OR) and 95% confidence intervals (CI). Standard covariates described in the methods section (5 for models predicting telomere length and 7 for models predicting infection and illness) were included in all regression models. Other covariates were added to the model when addressing alternative explanations. To assess mediation, we added potential mediators to the model containing the standard controls and numbers of years of parental home ownership and assessed the extent to which the addition of the proposed mediator reduced the association between parent home ownership and infection and clinical illness.

## Results

Participant characteristics are presented in Table 1 for the 196 participants with complete data and for the subset of 135 (of the 196) enrolled in the telomere substudy. Focusing on the SES variables, more years of parental home ownership was associated with higher participant educational attainment ($F[3, 192] = 8.14$, $p < 0.001$), but not participant home ownership ($t[194] = 0.88$, $p = 0.38$). Specifically, post-hoc comparisons showed that participants with less than 2 years of college reported fewer years of parental home ownership relative to participants who attained at least a bachelor's degree ($p$s < 0.01).

### Childhood SES and Telomere Length

In a model that controlled for age, sex, race, BMI, and neuroticism, lower childhood SES as indicated by fewer years of parental home ownership was associated with shorter average $CD8^+CD28^-$ cell telomere length ($B$=0.05, SE=0.02, β=0.24, $p < 0.01$). This translates to a 5% decrease in telomere length for each decrease of 1 year in parental home ownership. These results are summarized by tertiles of years of parent home ownership in Figure 1. As indicated by the figure, adult average $CD8^+CD28^-$ telomere length was shorter among participants whose parents owned their home for 6 or fewer years when compared to both those whose parents owned their homes for 7 to 13 years ($p$ for contrast of tertiles = 0.03) and whose parents owned their homes throughout the participant's childhood and adolescence ($p$ for contrast = 0.01).

### Controls for adult SES and family characteristics

The association of parental home ownership with $CD8^+CD28^-$ telomere length was not affected by either the addition of control variables for adult SES ($B$=0.05, SE=0.02, β =

0.24, $p < 0.01$) or by those reflecting family characteristics ($B$=0.05, SE=0.02, β = 0.27, $p$ = 0.02).

### When does childhood SES matter most?

We were also interested in whether the association reported above based on the average of 14 years of childhood SES represents an equivalent strength of association between parental home ownership and $CD8^+CD28^-$ telomere length at different ages. Figure 2 presents the effect size for the association between parental home ownership at each 2-year age interval (each coded as 0, 1 or 2 years ownership) and $CD8^+CD28^-$ telomere length. As is apparent from the figure, the effect size (regression coefficient) is consistent across childhood and adolescence.

### Childhood SES Infection and Colds

For the main study (N=196), the risk of developing a cold after experimental virus exposure increased with decreasing years of parental home ownership (OR = 1.09, CI = 1.02–1.17), independent of age, sex, race, BMI, season, neuroticism, and pre-challenge viral specific Ab. Specifically, for each decrease of one year in parental home ownership, the participants' odds of developing a cold increased by approximately 9%. This is illustrated in Figure 3 with years of parental home ownership presented in tertiles. There, participants with parental home ownership during their childhood and adolescence of 6 or fewer years were at significantly greater risk of developing a cold when compared to those whose parents owned their homes for the entire 14 years (OR = 2.68, CI = 1.16–6.17) and at marginally greater risk than those whose parents owned their homes for 7 to 13 years (OR = 2.28, CI = 0.91–5.72). There was no difference when comparing those whose parents owned their homes 7–13 years versus 14 years.

**Control for adult SES and family characteristics—**Adding adult SES to the model predicting colds from the continuous parental home ownership variable did not change the level of association (OR = 1.10, CI = 1.02–1.17). In contrast, the addition of all family characteristics variables marginally reduced the association between childhood SES and colds (OR = 1.06, CI = 0.98–1.15). Further examination revealed that this reduction was entirely attributable to the number of times the participant moved during childhood, as the association of childhood SES with colds was unaffected when moving was excluded from the family characteristics analysis (OR = 1.09, CI = 1.02–1.18). Moving was correlated −0.53, $p < 0.001$ with years of home ownership.

**Increased infection or increased illness among the infected?—**Because our definition of clinical colds combines infection with signs of illness, the observed association between parental home ownership and adult susceptibility to clinical colds could have resulted from a decreased risk for infection and/or a decreased expression of illness among infected persons. We fit two regression models to address this issue. The first model predicted *infection* in the entire sample of 196. The second predicted *colds*, but was limited to the 146 participants who were infected, thus examining more specifically whether parental home ownership is associated with post-infection expression of signs of illness. Decreasing years of parental home ownership was similarly associated with *both* greater risk for infection (OR = 1.07, CI = 1.00–1.15) and greater risk for illness among infected participants (OR = 1.07, CI = 1.00–1.15).

**When does childhood SES matter most?—**As above in the telomere length analysis, we represented childhood SES at 2-year intervals (e.g., ages 5–6, age 7–8, etc.) and fit separate models with standard covariates testing the association of parental home ownership at each age with colds. As shown in Figure 4, the relationship between parental home

ownership and colds is fairly consistent over all ages from 5 to 18 years, with somewhat larger effects of home ownership during adolescence.

### Does Telomere Length Mediate the Association between Parental Home Ownership and Colds?

Because telomere length was assessed only in a subsample of participants ($n$ = 135), we first refit the regressions with all 7 standard controls and parental home ownership predicting infection and colds, respectively, with that smaller sample. Even with the substantially reduced sample size, parental home ownership remained associated with infection (OR = 1.10, CI = 1.00–1.20) and marginally associated with colds (OR=1.08, CI=0.98–1.19). To evaluate whether telomere length might mediate these associations we refit the models adding telomere length as a covariate. This procedure reduced the effect size by 27% ([$B$=0.091 without telomere length – $B$=0.066 with telomere length]/0.091) for predicting infection and by 22% ([$B$=0.074 without telomere length – $B$=0.058 with telomere length]/0.074) for predicting colds. These data are consistent with telomere length acting as a partial but limited mediator in the relationships between childhood SES and adult susceptibility to infection and illness.

### Do Health Behaviors Mediate the Association between Childhood SES and Colds?

Adding adult smoking, drinking and exercise rates to the model including the standard covariates did not at all reduce the association between childhood SES and colds (OR = 1.09, CI=1.01, 1.17). Hence these factors did not operate as mediators of the childhood SES association with colds.

## Discussion

### Childhood SES and Telomere Length

We found that fewer years of parental home ownership during the participant's childhood and adolescence was associated with shorter average $CD8^+CD28^-$ cell telomere length during adulthood. This association was driven primarily by the substantially shorter (over ½ a standard deviation) telomere length for the subgroup of participants that spent the fewest (0 to 6) years in parent-owned homes. This suggests that relatively extreme childhood SES conditions may be required to trigger telomere shortening. Analyses of exposures at different ages suggest that the association between childhood SES and shorter telomere length is not dependent on when during childhood and adolescence (from 5 to 18 years of age) the experience of having lower SES occurs.

We considered the possibility that those with low childhood SES are more likely to have low adult SES, and it is low adult SES exposure that is responsible for shorter telomere length. However, our analyses showed that the childhood SES association with telomere length is independent of adult SES. Consequently, it is likely that the association is attributable to effects on behavioral or biological trajectories begun during childhood (Cohen et al., 2010; Miller et al., 2009; Miller, Chen and Parker, 2011). For example, low childhood SES is associated with an array of known risks for shorter telomeres including experiences of childhood adversity and abuse (Kiecolt-Glaser et al., 2011; Tyrka et al., 2010; review by Price et al, 2013), cytomegalovirus infections (Dowd et al., 2009) and younger paternal age at conception (Unryn et al., 2005). Each of these correlates of low childhood SES constitutes a potential trajectory through which childhood SES could affect adult telomere length.

We also found that the association between childhood SES and telomere length occurs above and beyond potential effects of family characteristics (e.g., divorce, supervisory adults in the home, other children in the home, residential mobility) associated with childhood

SES. Excluding these alternatives suggests the potential importance of income, wealth and social status (as indicated by home ownership) as driving forces.

We focused on T cytolytic cells because they play an important role in fighting infection. Our particular interest in the $CD8^+CD28^-$ cell population reflects the fact that telomere shortening in this population indicates reduced numbers of effector cells available to respond to the virus. This interpretation is consistent with a published comparison from this same data set indicating that telomere length in this cell population predicted infection above and beyond telomere length in PBMC, $CD4^+$ and $CD8^+CD28^+$ cells (Cohen et al., 2013).

### Childhood SES Infection and Colds

We replicated earlier results from a different sample indicating that the continuous measure of the number of years during childhood that one's parents owned their own home was associated with colds (Cohen et al., 2004). Here we found that with each decrease of one year of home ownership there was a 9% increase in risk for developing a cold. The association was driven primarily by those in the group with the lowest levels of childhood SES being at the greatest risk. This association was independent of adult measures of SES, indicating that the effect is not attributable to lower SES children growing up to be lower SES adults, but rather to some host resistance-related trajectory set in childhood or adolescence. Also like the earlier study, the association held for both the risk of infection and the risk of expressing signs of illness during infection. These results suggest that childhood exposures typical of a low SES environment impact a broad range of immune system functions including fighting infection and regulating the local inflammatory response that contributes to the production of signs and symptoms of illness.

Controlling for other family characteristics had only a minimal influence on the size of the associations between childhood SES and infection and childhood SES and colds. Here we found that controls for parental separation or divorce at any time before participants reached 19 years of age, average number (per year) of supervisory adults in the home, and of children in the home, and mother's age did not affect the association. However, frequency of moving during childhood marginally reduced the association. This finding is difficult to interpret because owning one's own home and moving are intrinsically confounded variables: families who own their own homes are less likely to move because of the associated personal and financial commitments. This leaves some ambiguity as to whether it is the income, social status and wealth associated with home ownership or less residential mobility that accounts for the health benefits of home ownership. Interestingly, however, while parental home ownership was associated with telomere length, moving was not (data not reported).

Controlling for neuroticism, a personality factor that generally predicts biases in reporting evaluative data (Costa and McCrae, 1985), did not influence the associations reported here. Moreover, controlling for body mass eliminated the potential role of obesity in both telomere length (Buxton et al., 2011) and host resistance. It is also important to note that while home ownership may be an insensitive measure of income and wealth in places with highly inflated housing costs such as New York City or San Francisco, our participants were for the most part reared in the mid-Atlantic states, where home ownership is a more sensitive measure of economic circumstances.

An inconsistency between the results of this and our earlier study (Cohen et al., 2004) relates to the importance of exposure to low SES during the adolescent years. The earlier study clearly indicated that the effect sizes were greatest in early childhood and dropped as one got older, with no statistical significance at 15 years and older. Here, because of a combination of a smaller sample and the inability of some participants to confidently remember parental

home ownership prior to 5 years of age, we were not sufficiently powered to examine the early childhood effects. Moreover, unlike the earlier study, we found a strong association with colds for parental home ownership during adolescence. We have no explanation for this inconsistency. It is possible that the SES levels in this sample were more stable throughout childhood and adolescence (e.g., those who lived in parent-owned homes during their teens were also more likely to have lived in parent-owned homes during early childhood), or that the present sample is fundamentally different from the earlier sample in some other important way. These explanations are unlikely, nonetheless, because the two populations were demographically similar with no obvious differences. Overall, then, we must consider the possibility that SES in adolescence does play a significant role in predicting disease susceptibility.

### Does Telomere Length Mediate the Association between Parental Home Ownership and Colds?

Our analyses showed that childhood SES predicted $CD8^+CD28^-$ telomere length, and that adding telomere length to the models relating childhood SES to infection and colds, respectively, reduced both associations (although the reductions were small to moderate). These reductions in association are consistent with the argument that the reduced ability of $CD8^+$ cells to fight infection provides a partial explanation for why low childhood SES is associated with greater risk for infection and colds. However, it is also possible (but not directly testable in the present sample due to insufficient power) that telomere length also plays a role in the post-infection inflammatory response thought to be responsible for the expression of the signs of illness.

### Limitations

One limitation of this study was that parental home ownership was reported retrospectively. However, participants showed considerable confidence in the accuracy of their recall and we excluded the early years of life where they were less confident. Also, a substantial number of participants did not provide parental home ownership data relevant to early childhood (ages 1 through 4). Accordingly, we were not sufficiently powered to conduct a fair evaluation of the relative importance of parental SES during early childhood versus middle childhood and adolescence as it pertains to associations with telomere length and colds.

### Conclusions

In summary, we found that exposure to low SES during childhood and adolescence is associated with shorter $CD8^+CD28^-$ cell telomeres in adulthood. This association was independent of the standard control variables as well as a number of associated childhood family factors, and adult SES at the time of viral-challenge. We also replicated earlier work establishing an association between low SES during childhood and increased susceptibility to developing an infection and illness when exposed to a common cold virus. This association also held up to multiple control factors including adult SES. Unlike the previous study, here we found that the association was as strong for SES during adolescence as it was for SES during earlier childhood. Finally, our analyses were consistent with $CD8^+CD28^-$ cell telomere length playing a small to moderate role as a mediator of the associations of childhood SES and infection, and childhood SES and colds. These data strongly support the potential role of childhood environments in host resistance to infection and suggest the need for identifying what it is in the childhood SES experience that drives these effects. Moreover, while providing preliminary evidence for a mediating role of telomere length in linking childhood SES to infectious susceptibility it suggests the need to pursue the role of other pathways as well.

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## Research Highlight

Lower childhood SES is related to shorter CD8+CD28− telomere length and poorer resistance to the common cold, with telomere length partly mediating the SES-cold association.

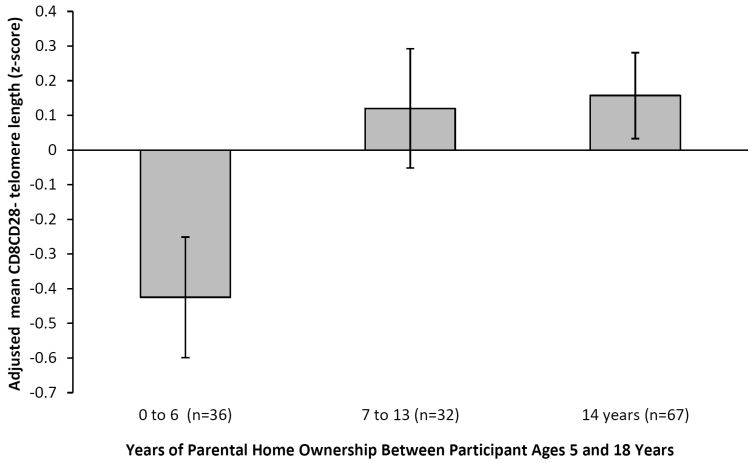


**Figure 1.**

Association of years of parental home ownership (from 5 through 18 years of age) and CD8+CD28− lymphocyte telomere length assessed during adulthood. Each bar represents a tertile of the number of years of parental home ownership. Results are adjusted for the standard control variables: age, sex, race, body mass index, and neuroticism. Parentheses enclose the sample size.

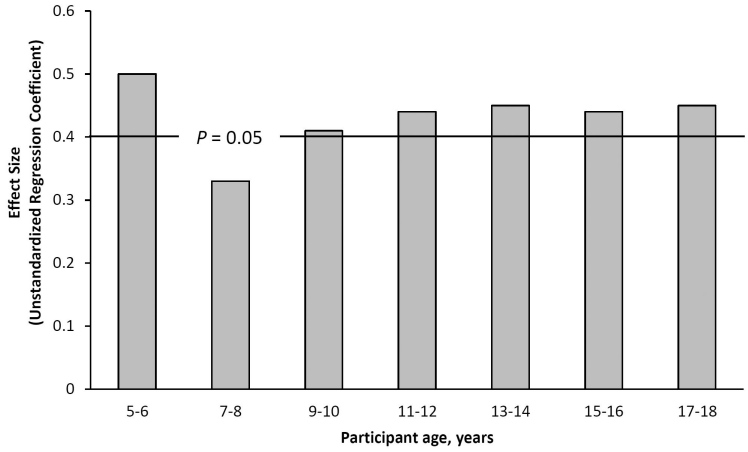


**Figure 2.**

Effect sizes (regression coefficients) for the association between participant's parental home ownership at different ages (2-year ranges from 5 to 18 years) and adult CD8+CD28− lymphocyte telomere length. All analyses include control for the standard covariates: age, sex, race, body mass index, and neuroticism.

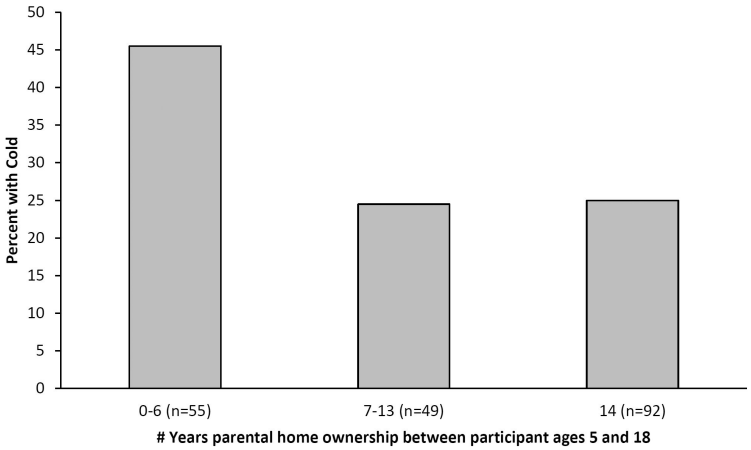


**Figure 3.**

Percentages of participants with clinical illness (colds) by the number of years of parental home ownership (from 5 through 18 years of age). Each bar represents a tertile of the number of years that participants' parents owned their home. (Parentheses enclose the sample size)

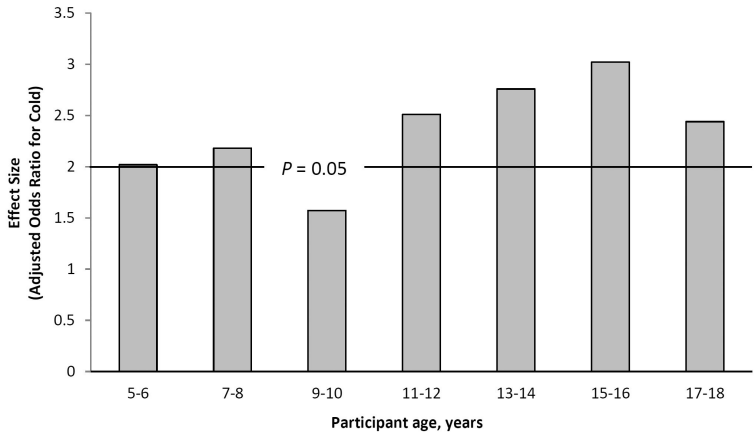


**Figure 4.**

Adjusted (for standard controls) effect sizes (odds ratios) for the association between parental home ownership and adult susceptibility to colds at different ages (2-year ranges from 5 to 18 years). Standard controls include age, sex, race, pre-challenge antibody, body mass index, season, and neuroticism.

## Table 1

Population Characteristics

| Characteristic | Total sample ($n$ = 196) | Sub-sample with $CD8^+CD28^-$ TL data ($n$ = 135) | Comparison statistic[a] | $p$ |
|---|---|---|---|---|
| Sex (female) | 83 (42.3%) | 56 (41.5%) | $X^2$ (1) = 0.16 | 0.69 |
| Age (years) | 29.8 (10.9) | 29.9 (11.0) | $z$ = 0.28 | 0.78 |
| Race (white) | 136 (69.4%) | 97 (71.9%) | $X^2$ (1) = 1.24 | 0.26 |
| Pre-challenge virus-specific Ab ≥4 | 37 (18.9%) | 24 (17.8%) | $X^2$ (1) = 0.33 | 0.57 |
| BMI ($kg/m^2$) | 25.7 (6.4) | 26.4 (5.6) | $z$ = 1.98 | 0.05 |
| Season of trial | | | $X^2$ (2) = 0.05 | 0.97 |
| Spring | 62 (31.6%) | 43 (31.9%) | | |
| Summer | 81 (41.3%) | 56 (41.5%) | | |
| Winter | 53 (27.0%) | 36 (26.7%) | | |
| Emotional stability (scale range, 0– 50) | 34.6 (7.6) | 34.6 (7.8) | $z$ = 0.07 | 0.95 |
| Adult SES | | | | |
| Educational Attainment | | | $X^2$ (3) = 0.87 | 0.83 |
| High school or less | 45 (23.0%) | 29 (21.5%) | | |
| Less than 2 years of college | 52 (26.5%) | 36 (26.7%) | | |
| 2 years of college + associate's degree | 47 (24.0%) | 32 (23.7%) | | |
| Bachelor's degree or higher | 52 (26.5%) | 38 (28.1%) | | |
| Current home owner | 15 (7.7%) | 9 (6.7%) | $X^2$ (1) = 0.65 | 0.42 |
| Ages 5 to 18 years | | | | |
| Number of years parent(s) owned home (possible range, 0–14) | 9.6 (5.4) | 9.8 (5.3) | $z$ = 1.18 | 0.24 |
| Average # of supervisory adults in the home | 1.8 (0.3) | 1.8 (0.3) | $z$ = 1.53 | 0.13 |
| Average # of children in the home | 2.7 (1.4) | 2.8 (1.6) | $z$ = 0.17 | 0.86 |
| Number of times family moved[b] (possible range, 0–6) | 1.9 (1.9) | 1.7 (1.5) | $z$ = 2.23 | 0.03 |
| Other childhood variables | | | | |
| Parents separated/divorced before participant was 19 years old | 82 (41.8%) | 50 (37.0%) | $X^2$ (1) = 4.18 | 0.04 |
| Mother's age when participant was born[c] | 27.3 (7.0) | 27.5 (6.5) | $z$ = 1.17 | 0.24 |

Mean (SD), $n$ (percent), TL = telomere length

[a] Comparison statistics were derived by assessing values obtained from the 135 participants with $CD8^+CD28^-$ TL length data relative to those obtained from the complete sample of 196 (i.e., 135 with TL data + 61 without TL data). Results of z tests (for continuous variables) and were adjusted for sample overlap by multiplying test values by a correction factor, $C = [(1 + n/N)/(1 - n/N)]^{1/2}$ as recommended by Hayes and Berry (2006). Likewise, results of chi-square analyses (for dichotomous and categorical variables) were multiplied by $C^2$ (Hayes & Berry, 2006).

[b] Assessed separately for ages 6 to 14 and ages 15 to 18, respectively. The value presented here represents the sum of these two assessments

[c] $n$ = 194 and $n$ = 133, respectively