The contribution of neighborhood socioeconomic disadvantage on depressive symptoms over the adult lifetime: a 32-year prospective cohort study

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Running head: Neighborhood and depression

Abstract
The association between socioeconomic disadvantage and increased risk of depressive symptoms in adulthood is well established. We tested A the contribution of early exposure to neighborhood socioeconomic disadvantage on later depressive symptoms throughout life, B the persistence of the potential association of early exposure with depressive symptoms, and C the contribution of other known risk factors to the association. Data were collected from a prospective, population-based Young Finns Study 32 year follow -up study that included participants aged 3 to 18 years at baseline 1980. Participants were followed up with repeated measurements of depressive symptoms between 1992 and 2012 N=2788 and linked to national grid data on neighborhood disadvantage via residential addresses. We examined the associations mixed models separately in 5-, 9-, 15-, and 20-year follow ups. Living in a disadvantaged neighborhood during childhood and adolescence was associated with a higher level of depressive symptoms in adulthood in all follow-up periods β 0.07, *P*-value 0.001 compared with others. Individual adulthood socioeconomic status mediated the associations. Living in a socioeconomically disadvantaged area during childhood and adolescence has long lasting negative association with mental health irrespective of family related risks, partially due to socioeconomic adversity later in life.

Key words: Area, neighborhood, mechanisms, depression, population, risk

List of abbreviations:

95% CI = 95% confidence interval
SD = standard deviation

Although the etiology of depression and depressive symptoms is multifactorial 1, adverse environmental exposures in early life are known to play a role 1-4. It is unclear whether early life experiences predict depression because they are linked to accumulation of risks over a lifetime. Alternatively, childhood and adolescence may be critical periods in life that have irreversible effects on mental health. One psychosocial risk that may have long-term effects on mental health outcomes is growing up in disadvantaged residential neighborhoods characterized by poverty, lack of employment opportunities, a high percentage of renters, and reduced economic prospects 5, which, in turn, are related to marginalization 6, 7 and low neighborhood integration.

Although many 7-22 but not all 23, previous studies have shown an association between neighborhood socioeconomic factors and depression, a recent meta-analysis did not reveal consistent support for such an association 24. This meta-analysis found an association between neighborhood socioeconomic disadvantage and later depression only in studies with short <5 years follow-up times but not in those with longer ones. Most of the studies included in the meta-analysis comprised older adults and only one study was based on participants <16 years at baseline 24.

Additionally, there are multiple other family-related psychosocial risks in childhood that potentially affect the development of depressive symptoms, including low parental socioeconomic status, parental mental health problems 16-20, parental alcohol use or antisocial behavior 20, 25, parental unhealthy diet 14, 26, 27, quality of emotional environment the degree acceptance and nurturance 28, and stressful life events 14, 29. Studies suggest that these family-related psychosocial risks confer increased risk of mental or physical health problems 16-22, 25-28 particularly when multiple risk factors accumulate 14, 30, 31.

Depressive symptoms and major depressive disorder have high risk of recurrence. Recurring episodes have been shown to predict a progressively increasing risk of subsequent episodes, particularly with onset in adolescence 32-35. Furthermore, although the initial onset of a depressive episode may be preceded by stressful life events, later recurrent episodes may be less closely related

to such distal stressors due to an individual's heightened sensitivity to environmental stressors of daily life 36, 37. Thus, factors that increase the risk of early depressive episodes may thus dramatically increase the risk of developing depression later in life 38, 39. Few studies using prospective data have examined the associations of childhood and adolescence neighborhood disadvantage with the development of later mental health problems 14, 15. Similarly, very few studies have considered the associations of other family-level risks with the development of depressive symptoms 12, 13 in addition to individual socioeconomic status. Understanding how childhood and adolescent risk factors predict change in risk factors over a lifetime is thus of growing scientific and public health relevance, potentially facilitating focused and timely prevention.

In the present study, we used data from the prospective Young Finns cohort study. We examined the association of long-term neighborhood disadvantage during childhood and adolescence with the development of depressive symptoms in adulthood using multiple follow-up times from 5 to 20 years. We also considered the associations of accumulated psychosocial adversities in childhood from multiple domains. We also tested the potential mediating effect of adulthood socioeconomic adversity using causal mediation models 40.

METHODS

Study design and participants

The Young Finns Study N=3596 is an ongoing five-center population-based cohort study of cardiometabolic risk factors and endpoints in Finnish children and adolescents 41. The first data-collection phase was between 15 September and 5 December 1980 ages 3-18 years. Subsequent data collections were conducted in 1983, 1986, 1989, 1992, 1997, 2001, 2007, and 2012.

In this analysis, we included participants with data on neighborhood socioeconomic disadvantage who attended the first examination in 1980 and provided data on depressive symptoms at least in one follow-up examination in 1992, 1997, 2001, 2007, and 2012 N = 2354. All participants provided written informed consent and the study was approved by the local ethics committees.

Measures

The exposure to multiple, not only individual, risk factors have been shown to have more serious developmental consequences and cumulative scores have recently become general in research on childhood psychosocial risks 42 - 46. Such models define binary risk factors risk versus no risk, which are then summed together to form a cumulative score. This approach has the advantage of being parsimonious, making no assumptions about the relative strengths of multiple risk factors or their collinearity, and enables testing of additive associations over a range of exposures 47. We built both the neighborhood socioeconomic disadvantage score and the childhood psychosocial risk score in a similar way, based on previous studies 14, 30, 31, 48, 49.

Neighborhood socioeconomic disadvantage

Annual data on neighborhood socioeconomic disadvantage were obtained from Statistics Finland. This national database assigns a neighborhood socioeconomic disadvantage score to each Finnish resident in 250-meter grids with 10 or more residents. The score for each grid is derived from the proportion of adults with primary education only, the unemployment rate, and the proportion of people living in rented housing. Each of the three variables were standardized as a Z score mean 0, standard deviation 1 48. The overall socioeconomic disadvantage score for each neighborhood is the mean value across all three Z scores, with the national mean being 0 and standard deviation being 1. A higher score indicates greater neighborhood socioeconomic disadvantage. Thus, each participant in our study was assigned a "neighborhood disadvantage" score based on the overall socioeconomic disadvantage score of his or her place of residence. We

calculated the participants' exposure to neighborhood socioeconomic disadvantage in childhood age 3 to 18 years by summing the annual residential time-weighted disadvantage Z scores at each address between the of age 3 and 18 years. Thus, each participant in our study was assigned a "neighborhood disadvantage" score based on the cumulative socioeconomic disadvantage score over his or her residential history in childhood. We used the national mean of 0 as cut-off for the distribution of the Z score to create two groups: low ≤national mean 0 and high >0 neighborhood disadvantage. We additionally used recent neighborhood socioeconomic disadvantage scores that were measured using a 5-year time-dependent cumulative disadvantage score prior to each measurement of depressive symptoms in adulthood.

Family-related psychosocial risks in childhood

As in previous studies 14, 30, 50, the following four separate risk childhood clusters were created: A socioeconomic, B psycho-emotional, C life events, and D parental lifestyle. These all were measured as parental reports in 1980. The risk domain components were summed together using the following procedure: 0=no risk, 1=risk. The cut-off points were defined based on theoretical and empirical knowledge as there are no clinically established thresholds for some of the risk factors 14. A total cumulative risk score was calculated by summing the separate risk domains together.

A. Socioeconomic risk cluster

The following four components were included: low education, manual occupation, low income lowest 25%, and unsteady employment history any of the following: periods of unemployment, long-term sickness absence, or parents on disability benefits 30. The cut-off point for the overall socioeconomic risk domain was ≥3.

B. Psycho-emotional risk factors

Psycho-emotional factors were mental health status, childrearing style, life satisfaction, and alcohol abuse. Mental health status was in inquired as: "Have you ever been diagnosed by a health

professional as having a mental health problem?" "yes"=1 point and "no"=0 points. Childrearing style and life satisfaction were measured using a 5-point scale derived from the Operation Family study 51; a response indicating dissatisfaction i.e. 4 or 5 on a 5-point scale with any of the three life roles was classified as high risk. Parental heavy alcohol use was measured as the frequency of heavy drinking occasions per year and the response "once a week" indicated high risk. The cut-off point for high-risk in the psycho-emotional domain was ≥1.

C. Stressful life events

Stressful life events included moving homes, change of school, divorce in the family, deaths of significant persons parents, siblings, and hospitalization or serious illness or both in the family. The presence of each event was assigned 1 point. The cut-off point for high risk was ≥1 events.

D. Parental lifestyle

Parental lifestyle behaviors included body mass index, levels of regular physical activity, and smoking status. The following cut-off points were used to classify a high-risk level for each category: mother or father or both is obese body mass index >30; mother or father or both is a current smoker; mother or father or both indicated no regular physical activity. The cut-off point for high risk was ≥3 risks.

E. Cumulative risk score

The cumulative risk score was created by adding together all the individual risk domains range 0 to 4. A detailed description of the construction of the childhood psychosocial risk score, including information on the basis of the cut-off points and risk domain compositions has been reported previously 14 and also in the Web Appendix Web Table 1 .

Depressive symptoms

Depressive symptoms were assessed in 1992 ages 15 to 30 years and in 1997, 2001, 2007, and 2012 using a modified version of Beck's Depression Inventory 51, 52. The participants were asked to rate 21 items e.g. "I often feel sad" on a 5-point scale ranging from totally disagree 1 to

totally agree 5. Cronbach's α of the scale ranged from 0.89 to 0.92. In the original version of the Beck's Depression Inventory, subjects are asked to choose between one of four alternative descriptions of 21 items, for instance: 0 I do not feel sad, 1 I feel sad, 2 I am sad all the time and I cannot snap out of it, 3 I am so sad or unhappy that I cannot stand it. In the present study, the participants were asked to rate the second original response option e.g., "I often feel sad" on a five-point Likert response option ranging from totally disagree 1 to totally agree 5. These second response options were selected because they more accurately measure depressive symptoms among the normal population 53. The means of the scores from the 21 items at each wave were used as the outcome in the analyses range 1 to 5.

Individual socioeconomic adversity in adulthood

Indicators of adulthood individual socioeconomic adversity were the length of the participant's highest education in years, mean income continuous variable, and unemployment during follow-up from 1992 to 2012 yes or no. Each indicator was standardized mean=0, standard deviation =1. The only exception was unemployment, which was coded as 1 for a history of unemployment and 0 otherwise. The overall score for adulthood individual socioeconomic status was the mean of the 3 indicators; a lower score indicates lower individual socioeconomic adversity.

Statistical analyses

The data for the main analyses were structured such that each participant contributed 1 to 5 person-observations to the dataset, depending on the number of study phases available for that individual. This study design allowed us to use all available data and permits considerations of the non-independence of repeated measurements person-observations on the same individual. The data were analyzed using multilevel linear regression, specifically the random-intercept model i.e. a mixed-effects model 54.

The analyses were conducted in the following steps. 1 We examined how depressive symptoms changed over time and whether the trajectories of depressive symptoms were different according to childhood neighborhood socioeconomic disadvantage groups using four different follow-up time intervals. We conducted four identical series of repeated mixed models with two, three, four, and finally all five measurement points: first baseline T0 and five-year follow up T5, second three time points T0, T5 and ten year follow-up T10, third, four time points T0, T5, T10 and fifteen-year follow up T15 and forth, five time points T0, T5, T10, T15 and twenty-year follow up T20. These models were adjusted for age, sex, and family-related psychosocial risk in childhood. We also examined the associations when adjusted for the most recent neighborhood disadvantage score the previous 5-year period in each data collection phase of depressive symptoms in adulthood. 2 We examined the potential causal mediating effect of adulthood socioeconomic adversity in the association between childhood neighborhood disadvantage and adulthood depressive symptoms using the approach developed by Imai and co-workers. This was based on the counterfactual framework and nonparametric identification based on the sequential ignorability assumption 40, 55-58. The effects were separated into natural direct effects, natural indirect effects, and total effects. The natural direct effect provides an estimate for the association between childhood neighborhood disadvantage and depressive symptoms in a scenario where the level of exposure to the mediator is similar among individuals exposed and not exposed to high childhood neighborhood disadvantage. The natural indirect effect refers to the excess risk of depressive symptoms among those exposed to high childhood neighborhood disadvantage due to their neighborhood disadvantage in adulthood. For total effect, both natural direct and indirect effects are considered to estimate the association between childhood neighborhood disadvantage and depressive symptoms. The proportion mediated of the total effect is given as percentages for the mediator.

Data analysis was performed with R 3.5.1 and the “lme4” package for multilevel regression procedure and “mediation” package for mediation analyses following the procedure for

implementing mediation function in multilevel data 58, 59. We used linear mixed modeling as we used continuous mean score depressive symptoms score as an outcome.

RESULTS

Characteristics of the study participants **Table 1** show that, on average, the level of depressive symptoms declined during follow-up **Figure 1**. There were no differences in these trends between the neighborhood disadvantage groups test of time interaction *P*=0.381. In the model adjusted for age and sex **Table 2**, exposure to childhood neighborhood disadvantage was associated with a higher level in depressive symptoms at the 5, 9, 15, and 20-year follow-up times β-coefficients 0.07, 0.08, 0.08, and 0.08; *P*-values 0.009, 0.001, <0.001, and <0.001, respectively **Figure 1**. The associations between neighborhood area disadvantage and depressive symptoms **Table 2 and 3** were somewhat attenuated when the models were additionally adjusted for family-related psychosocial risks in childhood. The attenuation was most evident during the first follow-up time. When the models were adjusted for neighborhood disadvantage in adulthood during the last 5 years preceding each measurement of depressive symptoms, the associations between childhood neighborhood disadvantage and depressive symptoms remained essentially the same **Table 2**.

To detect whether the relatively large age range in our cohort would affect our results, we divided the participants into two groups 3 to 9 years and 12 to 18 years and tested the area disadvantage-age group interaction on depressive symptoms in each follow-up phase. No interaction effects were statistically significant *P*-value range 0.13 to 0.26.

A total of 39% of the association between childhood neighborhood disadvantage and depressive symptoms was mediated through adulthood socioeconomic adversity Figure 2. There was no interaction between adulthood socioeconomic adversity the mediator and childhood neighborhood disadvantage the exposure in predicting depressive symptoms *P*=0.38.

In the additional analyses, we first imputed five different datasets using predictive mean, matching our imputation method and repeating the age- and sex-adjusted model with the longest

possible follow-up time. The results were very similar to those using complete cases data β range 0.06 to 0.08; all *P*-values <0.001 Web Table 2. We also examined the association between neighborhood disadvantage and depressive symptoms over the whole follow up including all measurement points using inverse probability censoring weights to weight the models for missingness. This analysis included all confounders and the results are reported in the Web Table 3. Overall, the results remained very similar, with a slight attenuation when neighborhood disadvantage during last 5 years was adjusted for. We also conducted the analyses using continuous neighborhood socioeconomic disadvantage score. Compared to the dichotomous score, the regression coefficients were slightly smaller range 0.05 to 0.06 but nevertheless significant *P*-value range 0.006 to 0.001. Finally, we repeated the analyses using continuous childhood cumulative psychosocial risk score, i.e., standardized sum score. These results were hardly any different compared to those based on the sum score of dichotomized individual risks Web Table 4.

DISCUSSION

In this prospective nationwide cohort study, we evaluated the association of cumulative neighborhood disadvantage in childhood and adolescence with the occurrence of depressive symptoms spanning a 20-year period from young adulthood to middle age. We observed that participants who lived in disadvantaged areas during childhood and adolescence were at increased risk of experiencing depressive symptoms in adulthood. This association was independent of the childhood family's socioeconomic position and other risks and more recent neighborhood disadvantage. This finding is in line with previous studies suggesting that childhood and adolescence may be critical periods for later development of depressive symptoms 16-22, 25-28. This finding points to a need for prevention efforts focusing on children's living circumstances as part of strategies to reduce the burden on depression in the population.

We also observed that the association between neighborhood disadvantage in early years and later depressive symptoms was mediated through the participants' own socioeconomic position

in adulthood. Thus, it seems that neighborhood disadvantage in childhood has an impact on obtained socioeconomic status in adulthood that in turn associates with long-term development of depressive symptoms, suggesting that adulthood socioeconomic status is probably one of the more immediate causal factors of depressive symptoms.

Previous studies have yielded mixed evidence on whether growing up in a disadvantaged residential neighborhood is associated with an increased risk of later depression. A meta-analysis performed by Richardson and others concluded that only studies with <5 years of follow up showed an association between disadvantaged neighborhoods and depression whereas studies with longer follow-up times did not 24. To the best of our knowledge, the present study is one of the first to use neighborhood information over a lifetime from early childhood to adolescence with multiple measures of depressive symptoms spanning 20 years.

The causality between neighborhood factors and health-related outcomes such as depression has recently been questioned 60, as the associations are not expected to be strong. However, most previous studies used shorter follow-up times or larger geographical areas when measuring neighborhood disadvantage than this study 61, 62. A recent twin study that demonstrated that neighborhood disadvantage increases the genetic risk of depression also supports this notion 63.

Our results offer insights to the role of environmental exposures in the development of depressive symptoms. Our results suggest that there may be an association of the childhood physical and social environment with depression that is mediated not only through the close family environment and social relations but also through other pathways. These include proximal and distal environments that increase the risk of depressive symptoms.

The strengths of our study are its prospective design and its exceptionally long follow-up period 41. We also used an objective measurement of neighborhood socioeconomic disadvantage that was categorized based on national means, repeat data five data collection phases on depressive symptoms, and various other risk factors. This was based on a denser 250 m estimation of

disadvantage than in most previous studies. We were also able to use multiple repeated measurement of neighborhood disadvantage in respondents' childhood and adolescent phases. There are some limitations that should be considered. This was an observational study and although we used a longitudinal design, the possibility to make causal inference based on the associations is limited. The sample size was acceptable but did not allow for an analysis of possible subgroup differences on the associations of neighborhood socioeconomic disadvantage, such as differences by sex, age groups, or larger area units. The measurement of neighborhood socioeconomic disadvantage included education, unemployment, and home ownership but did not consider other potentially important characteristics such as income and single-parent households.

The sample attrition was almost 40% between baseline and the last depressive symptoms measurements 32 years later. This is a relatively minor limitation because we used repeated measures mixed modeling that takes information from any data collection phase. Furthermore, although the differences between the baseline population and those reporting depressive symptoms at the last data collection phase were small in terms of demographic characteristics and neighborhood disadvantage, sample attrition may have led to an underestimation or overestimation of associations. The study was performed in a single country with a racially homogenous population; this may restrict the generalizability of the findings. Finland has relatively low levels of income inequality and wealth inequality and thus studies in less socioeconomically egalitarian societies are warranted. Depressive symptoms were measured using self-reports; diagnoses made by professionals using clinical interviews would have been preferable. However, the validity of the Beck's Depression Inventory -r has been shown to be good 53, 64, 65 and self-reported mental health problems have been shown to have similar developmental patterns as clinical measures 66. In our analyses, we did not consider clustering of individuals within neighborhoods. Before adulthood, the participants with data on neighborhood disadvantage had lived in 3060 different neighborhoods grids and moved on average 1.81 times range 1-15; the average total

population per grid was 207, and there were on average 0.91 participants per grid. In adulthood, they had lived in 9540 different grids and moved on average 7.03 times range 1-29; the average total population per grid was 175, and there were on average 0.29 participants per grid. Because individuals' moving histories were independent from the moving histories of the other participants, clustering of individuals within neighborhoods is extremely rare, thus spatial autocorrelation is an unlikely source of bias in these data. We were unable to calculate age-related neighborhood risk scores, but we do not consider that a serious limitation. The neighborhood disadvantage represents a general marker of environmental risks for all of the residents in that neighborhood.

Although there are multiple advantages in combining individual familial psychosocial risks into composites parsimony and lack of assumptions about relative strengths or collinearity, it is possible that different risk factors may be differentially important, and some may be collinear. Thus, future studies may additionally analyze the associations of multiple individual risks separately when analyzing associations between childhood psychosocial risks and health outcomes.

Further research using interventions or natural experiments is needed to examine whether improvements in both neighborhood and familial risk factors would decrease depressive symptoms and other mental health problems. For example, it would be important to examine if active policies prevent any area from becoming disadvantaged. Implementing such policies may be difficult, but one example is the spatial social mixing policy applied in some larger cities in the Nordic countries, which have been shown to be effective in preventing spatial social segregation 67. This means scattering municipal rental housing amongst other types of housing, thereby preventing the formation of large areas with primarily rented flats. It would be important to examine if such a mixing policy in neighborhood facilities may help prevent stress and a negative atmosphere in disadvantaged neighborhoods.

Our results suggest that neighborhood socioeconomic disadvantage is associated with later depressive symptoms and that the association is mediated through socioeconomic status later in life.

Thus, long-term political decisions aiming at preventing large differences in disadvantage between residential areas may be important to prevent long-term mental health problems.

REFERENCES

1. Kendler KS, Kessler RC, Walters EE, et al. Stressful life events, genetic liability, and onset of an episode of major depression in women. *Am J Psychiatry* 1995;1526:833-42.
2. Kendler KS, Kendler MD, Gatz M, et al. Personality and major depression. *Arch Gen Psychiatry* 2006;63:1113-20.
3. Kendler KS, Neale MC, Kessler RC, et al. Major depression and phobias: the genetic and environmental sources of comorbidity. *Psychol Med* 1993;232:361-71.
4. Kendler KS, Gardner CO, Prescott CA. Toward a comprehensive developmental model for major depression in women. *Am J Psychiatry* 2002;1597:1133-45.
5. Browning CR, Cagney KA. Neighborhood structural disadvantage, collective efficacy, and self-rated physical health in an urban setting. *J Health Soc Behav* 2002;434:383-99.
6. Ross CE, Jang SJ. Neighborhood disorder, fear, and mistrust: The buffering role of social ties with neighbors. *Am J Commun Psychol* 2000;284:401-20.
7. Ross CE, Mirowsky J. Neighborhood disadvantage, disorder, and health. *J Health Soc Behav* 2001;423:258-76.
8. Mair C, Roux AVD, Galea S. Are neighbourhood characteristics associated with depressive symptoms? A review of evidence. *J Epidemiol Community Health* 2008;6211:940-U21.
9. Silver E, Mulvey EP, Swanson JW. Neighborhood structural characteristics and mental disorder: Faris and Dunham revisited. *Soc Sci Med* 2002;558:1457-70.
10. Schneiders J, Drukker M, van der Ende J, et al. Neighbourhood socioeconomic disadvantage and behavioural problems from late childhood into early adolescence. *J Epidemiol Community Health* 2003;579:699-703.
11. Haines VA, Beggs JJ, Hurlbert JS. Neighborhood Disadvantage, Network Social Capital, and Depressive Symptoms. *J Health Soc Behav* 2011;521:58-73.
12. Ross CE. Neighborhood disadvantage and adult depression. *J Health Soc Behav* 2000;412:177-87.
13. Hybels CF, Blazer DG, Pieper CF, et al. Sociodemographic characteristics of the neighborhood and depressive symptoms in older adults: Using multilevel modeling in geriatric psychiatry. *Am J Ger Psychiatry* 2006;146:498-506.
14. Elovainio M, Pulkki-Raback L, Hakulinen C, et al. Childhood and adolescence risk factors and development of depressive symptoms: the 32-year prospective Young Finns follow-up study. *J Epidemiol Community Health* 2015;6911:1109-17.
15. Lemstra M, Neudorf C, D'Arcy C, et al. A systematic review of depressed mood and anxiety by SES in youth aged 10-15 years. *Can J Public Health* 2008;992:125-9.
16. Ramchandani PG, Murphy SE. Parental depression and the challenge of preventing mental illness in children. *Br J Psychiatry* 2013;2022:84-5.
17. Hay DF, Pawlby S, Waters CS, et al. Antepartum and postpartum exposure to maternal depression: different effects on different adolescent outcomes. *J Child Psychol Psychiatry* 2008;4910:1079-88.
18. Pawlby S, Hay D, Sharp D, et al. Antenatal depression and offspring psychopathology: the influence of childhood maltreatment. *Br J Psychiatry* 2011;1992:106-12.

19. Pawlby S, Sharp D, Hay D, et al. Postnatal depression and child outcome at 11 years: The importance of accurate diagnosis. *J Affect Disord* 2008;1071-3:241-5.
20. Sellers R, Collishaw S, Rice F, et al. Risk of psychopathology in adolescent offspring of mothers with psychopathology and recurrent depression. *Br J Psychiatry* 2013;2022:108-14.
21. Gluckman PD, Hanson MA, Spencer HG, et al. Environmental influences during development and their later consequences for health and disease: implications for the interpretation of empirical studies. *P Roy Soc B-Biol Sci* 2005;2721564:671-7.
22. Gluckman PD, Hanson MA, Beedle AS. Early life events and their consequences for later disease: A life history and evolutionary perspective. *Am J Hum Biol* 2007;191:1-19.
23. Goldstein RB, Lee AK, Haynie DL, et al. Neighbourhood disadvantage and depressive symptoms among adolescents followed into emerging adulthood. *J Epidemiol Community Health* 2019;737, 590-597.
24. Richardson R, Westley T, Gariepy G, et al. Neighborhood socioeconomic conditions and depression: a systematic review and meta-analysis. *Soc Psychiatry Psychiatr Epidemiol* 2015;5011:1641-56.
25. Mars B, Collishaw S, Smith D, et al. Offspring of parents with recurrent depression: Which features of parent depression index risk for offspring psychopathology? *J Affect Disord* 2012;1361-2:44-53.
26. Gale CR, Jiang B, Robinson SA, et al. Maternal diet during pregnancy and carotid intima-media thickness in children. *Arteriosclerosis Thrombosis and Vascular Biology* 2006;268:1877-82.
27. Gale CR, Robinson SM, Godfrey KM, et al. Oily fish intake during pregnancy - association with lower hyperactivity but not with higher full-scale IQ in offspring. *J Child Psychol Psychiatry* 2008;4910:1061-8.
28. Rutter M. Nature, nurture, and development: From evangelism through science toward policy and practice. *Child Development* 2002;731.
29. Kendler KS, Hettema JM, Butera F, et al. Life event dimensions of loss, humiliation, entrapment, and danger in the prediction of onsets of major depression and generalized anxiety. *Arch Gen Psychiatry* 2003;608:789-96.
30. Hakulinen C, Pulkki-Raback L, Elovainio M, et al. Childhood Psychosocial Cumulative Risks and Carotid Intima-Media Thickness in Adulthood: The Cardiovascular Risk in Young Finns Study. *Psychosom Med* 2016;782:171-81.
31. Pulkki-Råback L, Elovainio M, Hakulinen C, et al. Cumulative Effect of Psychosocial Factors in Youth on Ideal Cardiovascular Health in Adulthood. The Cardiovascular Risk in Young Finns Study. *Circulation* 2015;1313:245-53.
32. Association AP. *Diagnostic and statistical manual of mental disorders, 4th edition*. Washington, DC: APA; 2000.
33. Hermens ML, van Hout HP, Terluin B, et al. The prognosis of minor depression in the general population: a systematic review. *Gen Hosp Psychiatry* 2004;266:453-62.
34. Kessler RC, Zhao S, Blazer DG, et al. Prevalence, correlates, and course of minor depression and major depression in the National Comorbidity Survey. *J Affect Disord* 1997;451-2:19-30.
35. Burcusa SL, Iacono WG. Risk for recurrence in depression. *Clin Psychol Rev* 2007;278:959-85.
36. Monroe SM, Harkness KL. Life stress, the "kindling" hypothesis, and the recurrence of depression: considerations from a life stress perspective. *Psychol Rev* 2005;1122:417-45.

37. Kim-Cohen J, Caspi A, Moffitt TE, et al. Prior juvenile diagnoses in adults with mental disorder: developmental follow-back of a prospective-longitudinal cohort. *Arch Gen Psychiatry* 2003;607:709-17.
38. Colman I, Ataullahjan A. Life course perspectives on the epidemiology of depression. *Can J Psychiatry* 2010;5510:622-32.
39. Messer LC, Boone-Heinonen J, Mponwane L, et al. Developmental Programming: Priming Disease Susceptibility for Subsequent Generations. *Curr Epidemiol Rep* 2015;21:37-51.
40. Imai K, Keele L, Tingley D. A general approach to causal mediation analysis. *Psychol Methods* 2010;154:309-34.
41. Raitakari OT, Juonala M, Rönnemaa T, et al. Cohort profile: The Cardiovascular risk in young Finns study. *Int J Epidemiol* 2008; 376:1-7.
42. Dannefer D. Cumulative advantage/disadvantage and the life course: Cross-fertilizing age and social science theory. *J Gerontol B-Psychol* 2003;586:S327-S37.
43. DiPrete TA, Eirich GM. Cumulative advantage as a mechanism for inequality: A review of theoretical and empirical developments. *Ann Rev Sociology* 2006;321:271-97.
44. Schafer MH, Ferraro KF, Mustillo SA. Children of Misfortune: Early Adversity and Cumulative Inequality in Perceived Life Trajectories. *Am J Sociol* 2011;1164:1053-91.
45. Willson AE, Shuey KM, Elder GH. Cumulative advantage processes as mechanisms of inequality in life course health. *Am J Sociol* 2007;1126:1886-924.
46. Evans GW, Li DP, Whipple SS. Cumulative Risk and Child Development. *Psych Bulletin* 2013;1396:1342-96.
47. Brody GH, Yu TY, Chen YF, et al. Cumulative Socioeconomic Status Risk, Allostatic Load, and Adjustment: A Prospective Latent Profile Analysis With Contextual and Genetic Protective Factors. *Developmental Psychology* 2013;495:913-27.
48. Kivimaki M, Vahtera J, Tabak AG, et al. Neighbourhood socioeconomic disadvantage, risk factors, and diabetes from childhood to middle age in the Young Finns Study: a cohort study. *Lancet Pub Health* 2018;38:e365-e73.
49. Elovainio M, Pulkki-Raback L, Hakulinen C, et al. Psychosocial environment in childhood and body mass index growth over 32years. *Prev Med* 2017;972:50-5.
50. Hakulinen C, Pulkki-Raback L, Elovainio M, et al. Childhood Psychosocial Cumulative Risks and Carotid Intima-Media Thickness in Adulthood: The Cardiovascular Risk in Young Finns Study. *Psychosom Med* 2016;782:171-81.
51. Katainen S, Räikkönen K, Keskivaara P, et al. Maternal child-rearing attitudes and role satisfaction and children's temperament as antecedents of adolescent depressive tendencies: Follow-up study of 6- to 15-year-olds. *J Youth Adolesc* 1999;28 2:139-63.
52. Beck AT, Steer RA. Internal consistencies of the original and revised Beck Depression Inventory. *J Clin Psychol* 1984;406:1365-7.
53. Rosenstrom T, Jokela M, Hintsanen M, et al. Longitudinal course of depressive symptoms in adulthood: linear stochastic differential equation modeling. *Psychol Med* 2013;435:933-44.
54. Rabe-Hesketh S, Skrondal A. *Multilevel and longitudinal modeling using STATA*. New York: Stata Press; 2012.
55. Imai K, Keele L, Yamamoto T. Identification, Inference and Sensitivity Analysis for Causal Mediation Effects. *Stat Sci* 2010;251:51-71.
56. Imai K, Yamamoto T. Causal Inference with Differential Measurement Error: Nonparametric Identification and Sensitivity Analysis. *Am J Polit Sci* 2010;542:543-60.

57. Imai K, Keele L, Tingley D, et al. Unpacking the Black Box of Causality: Learning about Causal Mechanisms from Experimental and Observational Studies. *Am Polit Sci Rev* 2011;1054:765-89.
58. Tingley D, Yamamoto T, Hirose K, et al. mediation: R Package for Causal Mediation Analysis. *J Stat Software* 2014;595, 1-38.
59. Mediation- package https://cran.r-project.org/web/packages/mediation/ vignettes/mediation.pdf.
60. Oakes JM. Invited commentary: repeated measures, selection bias, and effect identification in neighborhood effect studies. *Am J Epidemiol* 2014;1808:785-7.
61. Airaksinen J, Hakulinen C, Elovainio M, et al. Neighborhood effects in depressive symptoms, social support, and mistrust: Longitudinal analysis with repeated measurements. *Soc Sci Med* 2015;136-137:10-6.
62. Jokela M. Are neighborhood health associations causal? A 10-year prospective cohort study with repeated measurements. *Am J Epidemiol* 2014;1808:776-84.
63. Strachan E, Duncan G, Horn E, et al. Neighborhood disadvantage and depression in adult twins: genetics and genexenvironment interaction. *Psychol Med* 2017;474:627-38.
64. Rosenstrom T, Jokela M, Hintsanen M, et al. Body-image dissatisfaction is strongly associated with chronic dysphoria. *J Affect Disord* 2013;1502:253-60.
65. Katainen S, Räikkönen K, Keltikangas-Järvinen L. Adolescent temperament, perceived social support, and depressive tendencies as predictors of depressive tendencies in young adulthood. *Europ J Person* 1999;133:183-207.
66. Jokela M, Singh-Manoux A, Shipley MJ, et al. Natural course of recurrent psychological distress in adulthood. *J Affect Disord* 2011;1303:454-61.
67. Vaattovaara M, Joutsiniemi A, Kortteinen M, et al. Experience of a preventive experiment: Spatial social mixing in post-world war II housing estates in Helsinki, Finland. In: Baldwin Hess T, Tammaru T, van Ham M, eds. *Housing Estates in Europe: Poverty, Ethnic Segregation and Policy Challenges*, 2018: 215-40.

Table 1. Sample characteristics of Young Finns study 1980, % or mean SD, N=2788 - 1974

Variables	Neighborhood disadvantage during childhood [a]						
	low			high			P-value
	MeanSD	No	%	MeanSD	No	%	
Sex							
Female		816	51.3		614	51.3	0.966
Male		776	48.7		582	48.7	
Age at baseline 1992, years	21.9 5			22 4.8			0.595
Neighborhood disadvantage during last 5 years at baseline 1992 high/low	-0.4 0.5			0.4 0.7			<0.001
Depressive symptoms at baseline 1992	2.1 0.6			2.2 0.6			0.018
Childhood psychosocial risks							
0		735	60.8		397	35.1	<0.001
1		377	31.2		255	40.3	
2		77	6.4		98	56.0	
3		20	1.6		15	42.9	
Adulthood socioeconomic adversity							<0.001
low		1387	91.4		819	77.0	
high		131	8.6		244	23.0	

[a]Note age 3 -18 years

Table 2. Association between childhood neighborhood disadvantage and development of depressive symptoms according to follow-up times mixed effects models.

Model and predictor	5-year follow up			9-year follow up			15-year follow up			20-year follow up		
	Estimates	*95% CI*	*P-value*	*Estimates*	*95% CI*	*P-value*	*Estimates*	*95% CI*	*P-value*	*Estimates*	*95% CI*	*P-value*
Model 1[a]												
Neighborhood disadvantage during childhood	0.07	0.02 to 0.12	0.009	0.08	0.03 to 0.13	0.001	0.08	0.04 to 0.13	<0.001	0.08	0.03 to 0.12	0.001
Age	-0.01	-0.01 to -0.00	0.002	-0.01	-0.01 to -0.01	<0.001	-0.01	-0.01 to -0.01	<0.001	-0.01	-0.01 to -0.01	<0.001
Male sex	-0.19	-0.24 to -0.14	<0.001	-0.19	-0.23 to -0.14	<0.001	-0.17	-0.21 to -0.12	<0.001	-0.15	-0.19 to -0.10	<0.001
Model 2[b]												
Neighborhood disadvantage during childhood	0.05	-0.01 to 0.11	0.100	0.06	0.00 to 0.11	0.049	0.06	0.01 to 0.12	0.026	0.06	0.00 to 0.11	0.044
Age	-0.01	-0.01 to -0.00	<0.001	-0.01	-0.01 to -0.01	<0.001	-0.01	-0.01 to -0.01	<0.001	-0.01	-0.01 to -0.01	<0.001
Male sex	-0.19	-0.25 to -0.13	<0.001	-0.19	-0.25 to -0.14	<0.001	-0.17	-0.23 to -0.12	<0.001	-0.15	-0.21 to -0.10	<0.001
Childhood psychosocial risks	0.07	0.03 to 0.11	0.001	0.07	0.03 to 0.11	<0.001	0.06	0.02 to 0.10	0.001	0.06	0.03 to 0.10	0.001
Model 3[c]												
Neighborhood disadvantage during childhood	0.04	-0.01 to 0.10	0.135	0.07	0.02 to 0.12	**0.010**	0.08	0.03 to 0.12	**0.002**	0.07	0.03 to 0.12	**0.002**
Age	-0.01	-0.01 to -0.00	**0.001**	-0.01	-0.01 to -0.01	**<0.001**	-0.01	-0.01 to -0.00	**<0.001**	-0.01	-0.01 to -0.00	**<0.001**
Male sex	-0.19	-0.24 to -0.14	**<0.001**	-0.18	-0.23 to -0.13	**<0.001**	-0.17	-0.21	**<0.001**	-0.15	-0.19	**<0.001**

								to -0.12			to -0.10	
Neighborhood disadvantage during last 5 years	0.05	0.01 to 0.08	**0.016**	0.03	0.00 to 0.06	**0.044**	0.02	-0.00 to 0.05	0.053	0.02	-0.00 to 0.04	0.061

a. Adjusted for age and sex
b. Adjusted for age, sex and childhood psychosocial risks
c. Adjusted for age, sex and neighborhood disadvantage during last 5 years

Table 3. Model characteristics

Model and years of follow-up	σ^2	τ_{00}	ICC	Observations	Marginal R^2	Conditional R^2
Model 1[a]						
5	0.16	0.24	0.61	3423	0.027	0.618
9	0.17	0.24	0.59	5010	0.030	0.599
15	0.18	0.25	0.58	6570	0.026	0.591
20	0.18	0.25	0.58	7897	0.022	0.590
Model 2[b]						
5	0.16	0.23	0.59	2481	0.034	0.603
9	0.17	0.23	0.57	3623	0.038	0.590
15	0.18	0.23	0.57	4748	0.030	0.585
20	0.18	0.24	0.57	5712	0.026	0.580
Model 3[c]						
5	0.16	0.24	0.61	3299	0.028	0.622
9	0.17	0.24	0.59	4817	0.030	0.598
15	0.18	0.25	0.58	6272	0.026	0.591
20	0.18	0.25	0.58	7493	0.022	0.589

a. Adjusted for age and sex
b. Adjusted for age, sex and childhood psychosocial risks
c. Adjusted for age, sex and neighborhood disadvantage during last 5 years

***Figure 1*: Depression in different ages by neighborhood disadvantage**

***Figure 2*: Mediation effect of own socioeconomic position in the association between neighborhood disadvantage in childhood and depressive symptoms**