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Cumulative risk over the early life course and its relation to academic achievement in childhood and early adolescence

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ABSTRACT

Early-life risk factors, such as family disruption, maltreatment, and poverty, can negatively impact children's scholastic abilities; however, most previous studies have relied on cross-sectional designs and retrospective measurement. This study investigated the relation between cumulative risk factors during the early life course and subsequent academic achievement in a cohort of children and adolescents. Data for this study were based on registry-data material from the LIFECOURSE study of 1151 children from the 2000 birth cohort in Reykjavik, Iceland, assembled in 2014–2016. Multiple lifetime risk factors, including maternal smoking during pregnancy, parent's disability status, being born to a young mother, number of children in the household, family income, number of visits to school nurses, and reports of maltreatment, were assessed. Latent class analysis and Analysis of Covariance (ANCOVA) were used to predict academic achievement in the 4th and 7th grades. Individuals with no risk factors reported the highest average academic achievement in the 4th ($M = 66$ points, $SD = 17$) and 7th grades ($M = 67$ points, $SD = 15$). There was a significant main effect for 4th-grade risk factors and academic achievement ($F[7, 1146] = 12.06$, $p < 0.001$) and a similar relationship between the risk factor profile and achievement scores in 7th grade ($F[7, 1146] = 15.08$, $p < 0.001$). Each additional risk factor was associated with a drop in academic achievement at both grade levels. We conclude that academic achievement declines in proportion to the number of risk factors in early life.

1. Introduction

During the last three decades studies have consistently shown that exposure to early-life risk factors, such as family disruption, maltreatment, and poverty, can negatively impact children's scholastic abilities and academic achievement (Gutman et al., 2002; Prelow and Loukas, 2003; Fantuzzo et al., 2010). Poor academic achievement can lead both parents and teachers to lower expectations of students' academic performance, which in turn can discourage children's further academic success (Entwisle, 1995). Moreover, poor academic performance during childhood and adolescence can increase the risks of a life course trajectory that can lead to antisocial behaviors, health-compromising behaviors, and greater odds of incarceration (Hirschi, 1969; Yoshikawa, 1995; McKinsey and Company, 2009).

There is growing evidence that the accumulation of only a few risk factors can contribute to poor adolescent outcomes. For example, a study of psychiatric disorders in children 10 years of age in the United Kingdom found that a single risk factor did not significantly increase the overall risk of developing a psychiatric disorder, but that two or more risk factors increased the risk for a psychiatric disorder fourfold (Rutter, 1979). Similarly, the Rochester Longitudinal Study revealed that the number of risk factors was related to concurrent behavior problems in school (Sameroff et al., 1987a), as well as mental health problems and lower academic outcomes (Sameroff et al., 1998). More recent studies have replicated the effect of multiple risk factors on various outcomes such as delinquency (Lanza et al., 2014), maltreatment (MacKenzie et al., 2011), and juvenile court petitions (Smokowski et al., 2004). Generally, these studies support the notion that the effects of the accumulation of risk factors exceed the effects of any single factor.

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Several studies have focused specifically on the impact of multiple risk factors on academic achievement. In a study among 7th-grade African American students, a high number of risk factors was associated with school absenteeism, lower mathematics test scores, and lower Grade Point Average (GPA) (Gutman et al., 2002) Similarly, another study showed that living in a single-parent household, maternal psychological distress, maternal education level, perceived financial strain, and neighborhood problems, were predictive of lower mathematics achievement scores as well as behavioral problems in a group of 10–14 year old economically disadvantaged Latino youth (Prelow and Loukas, 2003). A particularly noteworthy finding was that worse outcomes were associated with five risk factors and not with four or less risk factors.

While these findings highlight the cumulative impact of multiple risk factors on academic achievement and related outcomes, much of the research on multiple risk factors across the early life course and academic achievement has relied on cross-sectional designs with retrospective measurement and limited causal inference. Our study extends previous work in three major ways. First, we utilized comprehensive data from national government registry sources. Second, we employed a cohort design that allowed us to look at risk in relation to outcomes longitudinally, from pre-birth through the age of 13. Third, we employ a person-centered analytic approach to the data (Lanza et al., 2011) instead of the more commonly employed variable-centered methods that have been used to investigate the relationship between variables and to examine processes mutual to a group of people (Laursen and Hoff, 2006). Thus, the overarching goal of the present study was to address two questions: 1) Does increased number of risk factors across the early life course lead to lower academic achievement in 4th and 7th grade?; and 2) Does the risk-factor profile produce distinct underlying classes of participants that reveal different academic outcomes?

2. Method

This report is based on registry data from a 5-year cohort study being conducted by the Icelandic Center for Social Research and Analysis at Reykjavik University. Registry data were assembled in years 2014–2016. The data registries from which the data are derived include the Icelandic Primary Health Care Clinics, the Reykjavik Child Protection Agency (CPA), the Icelandic Directorate for Health (equivalent to the Surgeon General in the US and which oversees the entire health registry system in Iceland), the Statistical Bureau of Iceland, and the Educational Testing Institute of Iceland. The study was approved by the National Bioethics Committee of Iceland.

2.1. Sample and procedure

The sample comprised all 1151 adolescents (49% female) that were born and residing in the City of Reykjavik, the capital of Iceland, in the year 2000, and is derived from registry data that were made available for the study. Thus, for purposes of the present analysis, the study design is a registry-based, retrospective cohort study with children born and residing in Reykjavik in the year 2000. No prospective data were collected. The analyses examined all available data that had been collected over the period from the pregnancy of each participant's mother, through to the 7th grade (13 years) of the study participants.

2.2. Measures

Risk-factor variables and criteria of risk and non-risk were selected to be comparable to those used in other similar studies (Gutman et al., 2002; Prelow and Loukas, 2003; Fantuzzo et al., 2010; Entwisle, 1995; Hirschi, 1969; Yoshikawa, 1995; McKinsey and Company, 2009; Rutter, 1979; Sameroff et al., 1987a).

2.2.1. Prenatal information

The Primary Health Care Clinics of Iceland provided data with prenatal information. In Iceland, each expectant mother visits a national healthcare center for regular examinations where data on various mental and physical health and behaviors are collected. The following measures were abstracted for use in the current analyses:

Smoking status during pregnancy. During the first trimester mothers are screened for smoking status. Assigned codes were 1 = yes, smoker, and 0 = no, previous, or never smoker at the time of birth.

Mother's age. Participants of young mothers at the time of birth (age < 19) were identified in the risk category.

Number of children in the household. Participants of families with three or more children at the time of birth were identified in the risk category.

2.2.2. School health information

For health and well-being of school children, data were abstracted from the Primary Health Care Clinics, which oversee the work of school nurses in Iceland who routinely conduct health examinations on children at the age of six, nine, and 12 years, in addition to being available to children in case of need.

Visits to school nurses. Participants that scored in the top 85th percentile in number of visits were defined as belonging in the risk category (13 visits+ for 4th-grade students, 17+ visits for 7th-grade students).

Emotional well-being in school. During visits to school nurses in 4th grade children are screened for their emotional well-being at school for the current year (i.e., "How do you generally feel at school?"). Feeling bad at school were classified in the risk category.

2.2.3. Child maltreatment

Maltreatment data were abstracted from the records of the Reykjavik Child Protection Agency (CPA). Given that initial reporting of children to the CPA does usually not entail a need for intervention and that most case files are closed after a brief inspection, we defined maltreatment as 2+ reports in the CPA database from the age of 0–13 years.

2.2.4. Statistical bureau data

The Statistical Bureau of Iceland is the center for official statistics in Iceland. For the current analysis, the databank provided the following information:

Income. Income in the bottom 15th percentile (in Icelandic Kronur) when each participant was born and/or when he/she was 10 and 13 years of age was defined as a risk factor (14% at birth, at 10 and 13 years old).

Marital status. If parents were not married or in registered domestic partnership at the time of each participant's birth and/or when he/she was 10 and 13 years old it was coded as a risk factor.

Disability status. If either parent were registered as disabled at time of each participant's birth and/or when he/she was 10 and 13 years old it was defined as a risk factor.

2.2.5. Academic achievement

Data were assembled from the Educational Testing Institute, which oversees the universal standardized comparison exams for the national school system in Iceland. Every student in Iceland sits through standardized test in the Icelandic language and in mathematics in 4th and 7th grade. The purpose of the standardized exams is to determine whether students are meeting the national curriculum proficiency objectives. The grades of participants in the present study were normally distributed on a scale of 0–60, with an average score of 30 and a standard deviation of 10. For the purposes of our analyses, we created an academic achievement score by collapsing the test scores in Icelandic and Mathematics within 4th and 7th grades respectively ($r = 0.62$ for 4th graders and $r = 0.67$ for 7th graders).

Completion rates for registry data ranged from 86.8% to 100% with the exception of emotional well-being in school which had a completion rate of 64.3%.

2.3. Data analyses

Consistent with previous studies (Gutman et al., 2002; Sameroff et al., 1987b), each of the variables described above was transformed into a dichotomous variable and then summed into a cumulative risk scale. This approach was selected in order to explore the quantity of risk rather than assessing relative individual risk. For contextual understanding, the bivariate interrelations between risk factors and the outcomes are presented in Table 1.

For all the variables, participants were coded with 0 if no risk was present and with 1 if risk was present (e.g., age of mother was under 19 = 1; age of mother was over 19 = 0). In the case of continuous variables where objective categorical definitions of risk were not available, the presence of risk was defined according to either the lowest 15% or top 15% of the sample.

Separate risk variables were computed for 4th-grade and 7th-grade students; with 12 dichotomous indicators (maternal smoking, 2 + CPA reports, young mother, number of children in family, emotional well-being in school, parents marital status at birth and during grades 4/7, visits to school nurses in grades 1 to 4/1 to 7, family income at birth, family income at the age of 10/13, parent disability status at birth, parent disability status in 2010/2013). The risk index was then analyzed with ANCOVA and linear regression controlling for gender, using SPSS version 22. Missing data were handled with the automatic multiple imputation function of fully conditional specification. We independently analyzed 5 copies of the data, each with missing values suitably imputed. Imputations were conducted on all risk factors and outcome variables. For comparative purposes, we ran our analyses both with and without imputed missing data. The comparative analysis did not yield markedly different results; thus, our reported results include findings based on the imputed values for missing data.

Latent class analysis (LCA) using the poLCA software package in SPSS was used to assess the underlying risk factor profile of students in 7th grade given number of risk factors produced from the registry data. We concluded our analyses by employing ANOVA on the relationship between the latent classes and academic achievement. All aspects of this reporting are consistent with the STROBE statement reporting requirements for observational studies in epidemiology.

Table 1
Descriptive statistics for all study variables, LIFECOURSE study of children in Reykjavik, Iceland.

	Means (*SD*)	Range	n risk (%)
Risk variables			
Maltreatment records	0.33 (*0.71*)	0–3	109 (9.5)
Visits to school nurse	10.70 (*15.30*)	1–192	161 (14.0)
Emotional well-being at school	1.86 (*0.42*)	0–2	32 (1.5)
Maternal smoking	0.32 (*0.58*)	0–2	227 (15.2)
Number of children	0.92 (*0.94*)	0–5	72 (5.8)
Average age of mother	29.16 (*5.56*)	16–45	54 (4.5)
Income in ISK (at birth)	3480 (*3236*)[a]	0–52,440[a]	173 (14)
Income in ISK (4th grade)	8793 (*6171*)[a]	0–80,919[a]	173 (14)
Income in ISK (7th grade)	11,252 (*9971*)[a]	0–172,022[a]	173 (14)
Marital status (at birth)	1.65 (*0.48*)	1–2	405 (34.5)
Marital status (4th grade)	1.71 (*0.46*)	1–2	339 (29.0)
Marital status (7th grade)	1.69 (*0.46*)	1–2	353 (30.0)
Disability status (at birth)	0.04 (*0.19*)	0–2	42 (2.7)
Disability status (4th grade)	0.10 (*0.32*)	0–2	109 (7.3)
Disability status (7th grade)	0.15 (*0.39*)	0–2	160 (11.4)
Achievement variables			
4th grade	61.45 (*19.06*)	10–119	NA
7th grade	61.31 (*19.00*)	3–114	NA

[a] Numbers reported in thousands.

3. Results

On average, at the age of 10, participants had been exposed to one and a half risk factor during the course of their life (M = 1.52, *SD* = 1.50), with 32.4% of participants having no risk factor at that age, and 0.3% of participants accumulating seven risk factors over their life course. At 13 years, the average risk factor profile was similar, one and a half per individual participant (M = 1.53, *SD* = 1.52), with 32.0% of participants having no risk factor at this age, and 0.4% of the participants accumulating seven risk factors during their lifetime. No gender differences were found in the number of reported risk factors at either age. Means and standard deviations for risk factors and outcome variables are presented in Table 1.

Table 2 presents a Spearman's *rho* rank correlation matrix for all risk factor and outcome variables in the study. As shown, most risk factors were either relatively weekly or not at all correlated to the outcomes (*rho* ≥ 0.20). The inter-correlation between the risk factor variables that were a part of the same model (4th or 7th grade respectively) ranged from non-significant to the low .40s and was highest in the demographic variables.

3.1. Multiple risk factor analysis

The multiple risk factor index shows the results from the ANCOVA controlling for gender. The cumulative risk factor yielded a significant main effect for 4th grade academic achievement ($F\,[7, 1146] = 12.06$, $p < 0.001$), and gender ($F\,[1, 1146] = 4.76$, $p < 0.029$); similar results were found in the relationship between the risk factor profile and achievement scores in 7th grade, ($F\,[7, 1146] = 15.08$, $p < 0.001$) and for gender ($F\,[1, 1146] = 14.79$, $p < 0.001$).

As depicted in Fig. 1, each additional risk factor was associated with a drop in grades at both ages. Individuals with zero risk factors reported the highest average academic achievement scores in 4th grade (M = 66 points, *SD* = 17) and in 7th grade (M = 67 points, *SD* = 15). For each risk factor the linear regression analyses revealed an average drop of −3.24 and −3.54 points on the academic achievement scale in 4th and 7th grade, respectively ($p < 0.001$).

Additionally, to examine whether individuals with zero risk factors differed from individuals with at least one risk factor, we employed the Bonferroni post hoc test on all possible group comparisons. A significant difference was found between zero risk factors and all combinations of one or more additional risk factors in both 4th grade ($p < 0.001$) and in 7th grade ($p < 0.001$).

3.2. Latent class analysis

In identifying the optimal number of classes from our LCA we compared models with 2–6 classes using the Bayesian Information Criterion (BIC) and the Akaike Information Criterion (AIC) for model interpretation for the 7th grade data. The model which produced two risk classes had the optimal fit compared to the models with 3–6 risk classes ($G^2 = 208.10$, df = 492, BIC = 3498.72, AIC = 6210.65). Table 2 includes the proportional distribution to the high and low risk classes identified from the LCA.

After examining the risk factor profile based on the class identification we referred to Class 1 as *high-risk* and Class 2 as *low-risk*

Table 2
Correlations between risk factor and outcome variables.

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.	18.
1. Academic achievement 4th grade	1																	
2. Academic achievement 7th grade	0.80**	1																
3. 2 + CPA	−0.200*	−0.24**	1															
4. Young mother	−0.06*	−0.08**	0.08**	1														
5. Number of children	−0.08**	−0.11**	0.11**	−0.06	1													
6. Well-being in school	−0.10**	−0.13**	0.02	0.04	−0.04	1												
7. Maternal smoking	−0.14**	−0.17**	0.27**	0.17**	0.06*	−0.01	1											
8. Visit to school nurses in 4th grade	−0.11**	−0.12**	0.09**	0.04	−0.02	0.04	0.10**	1										
9. Visit to school nurses in 7th grade	−0.10**	−0.11**	0.09**	0.03	−0.01	0.04	0.10**	0.99**	1									
10. Marital status at birth	−0.12**	−0.11**	0.13**	0.12**	−0.03	−0.01	0.21**	0.04	0.04	1								
11. Total income at birth	−0.09**	−0.05	0.04	0.07*	0.01	−0.04	0.02	−0.05	−0.04	0.40**	1							
12. Disability status at birth	−0.05	−0.10**	0.25**	−0.02	0.07*	0.08**	0.14**	0.07*	0.07*	0.06*	−0.02	1						
13. Marital status 2010	−0.13**	−0.14**	0.26**	0.11**	0.01	−0.04	0.17**	0.03	0.03	0.35**	0.09**	0.04	1					
14. Total income 2010	−0.15**	−0.13**	0.12**	0.15**	0.02	0.02	0.14**	0.00	−0.01	0.15**	0.13**	0.01	0.42**	1				
15. Disability status 2010	−0.09**	−0.15**	0.29**	−0.02	0.06*	0.00	0.12**	0.07*	0.06	0.05	−0.04	0.33**	0.12**	−0.03	1			
16. Marital status 2013	−0.13**	−0.14**	0.26**	0.08**	0,02	−0.03	0.15**	0.01	0.01	0.30**	0.06*	0.03	0.83**	0.38**	0.11**	1		
17. Total income 2013	−0.11**	−0.13**	0.13**	0.14**	0,04***	0.00	0.16**	−0.01	−0.01	0.17**	0.10**	0.05	0.37**	0.52**	0.01	0.42**	1	
18. Disability status 2013	−0.15**	−0.21**	0.36**	0.02	0.06*	0.040	0.17**	0.07*	0.06*	0.09**	−0.03	0.30**	0.19**	0.07*	0.77**	0.17**	0.08**	1

* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

participants. The high-risk class included around 26% of the sample. Generally, it was more likely for study participants in the *high-risk* class to encompass a greater probability for each risk factor than their low-risk class counterparts. The high-risk class had significantly poorer academic achievement in 7th grade ($F\,[1, 1033] = 50.34$, $p < 0.001$), compared to the *low-risk* class (Table 3).

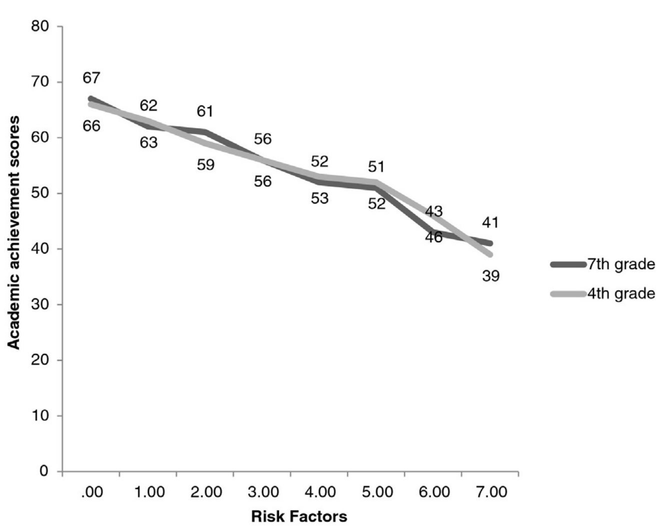

Fig. 1. Number of risk factors and academic achievement scores in 4th and 7th grade, LIFECOURSE study of children in Reykjavik, Iceland.

4. Discussion

Our results show that early life course exposure to an increased number of risk factors predicted lower grades in both 4th and 7th grades. A single risk factor significantly predicted lower achievement scores. Our LCA resulted in two distinct classes: a high-risk and low-risk class, with the high-risk class being more likely to be exposed to a greater number of risk factors and subsequent poorer academic scores.

Table 3
Identification of classes and risk factor probability by class, LIFECOURSE Study of children in Reykjavik, Iceland.

	High risk (Class 1) %	Low risk (Class 2) %
Proportion of sample	26.1	73.9
Gender		
Girls	47.9	49.5
Maltreatment		
Yes	33.5	1.2
School nurse visits		
85th percentile +	22.4	12.8
Maternal smoking during pregnancy		
Yes	44.0	11.5
Number of children		
≥3	9.7	4.9
Age of mother		
<19	12.1	1.5
Emotional well-being at school		
Bad	4.3	1.6
Family income in 7th grade		
15th percentile and below	46.2	2.9
Marital status in 7th grade		
Not married	23.4	15.2
Disability status in 7th grade		
Yes	34.3	6.6

Children exposed to several risk factors have been shown to be more likely to have a range of adverse developmental outcomes, such as higher rates of emotional and behavioral disorders (e.g., delinquency, drug and alcohol abuse), as well as educational underachievement (Gortmaker et al., 1990; Roeser et al., 1998; Webster-Stratton and Taylor, 2001), compared to those with few or no risk factors. Risk factors that have been linked to poor academic achievement are relatively consistent across studies. Multiple studies have concluded that greater number of children in one family is a predictor of poorer academic achievement for each of the children (Blake, 1989; Perez Sanchez et al., 2013; Soni, 2013). Likewise, children born to young mothers have been shown to be at increased risk for a range of unfavorable developmental outcomes, including lower academic achievement scores (Barratt, 1991; Levine et al., 2001; Woodward et al., 2001; Shaw et al., 2006). Other studies have assessed the relationship between maltreatment and academic outcomes (Eckenrode et al., 1993; Eckenrode et al., 1995; Brown et al., 1999; Coohey et al., 2011) and generally have found that maltreated children had poorer results when compared to children who had not experienced maltreatment.

The research is less consistent about the relationship between maternal smoking during pregnancy and childhood outcomes. In one review (Huizink and Mulder, 2006), maternal smoking was shown to be related to cognitive and neurobehavioral outcomes in children. On the other hand, a quasi-experimental study based on all births in Sweden between the years of 1983 and 1991 found that maternal smoking was related to poorer academic achievement in children when comparing unrelated individuals; however, when comparing siblings that were differentially exposed to maternal smoking, the results also suggested that maternal smoking did not lead to poorer academic achievement relative to exposure (D'Onofrio et al., 2010). Moreover, studies (Roeser et al., 1998) have shown that mental health problems negatively impact academic outcomes; as many as one in five children in school may have undiagnosed mental health problems (Puskar and Marie Bernardo, 2007). Children who frequently visit the school nurse are more likely to experience mental health problems and should be treated as a high-risk group (Rogers and Reese, 1965; Whitaker, 1968; Schneider et al., 1995).

Additionally, previous studies have been inconclusive as to whether the negative impact of risk factors shows a threshold effect, i.e., whether exposure to a certain number of risk factors must occur before change is observed in the outcomes, or whether the severity of negative consequences is additively related to the number of risk factors (Rutter, 1979; Appleyard et al., 2005). Our results suggest that each risk factor that is accumulated over the early life course adds to the additive negative impact on academic achievement in both 4th and 7th grade. Thus, exposure to a single risk factor over the early life course appears to result in poorer academic outcomes, as compared to no risk factors. Consistent with the broader work showing the impact of adverse childhood experiences on later well-being in adolescence (Balistreri and Alvira-Hammond, 2016), our findings also indicate that any and all exposure to risk factors appears to have impact on academic outcomes both in 4th and 7th grades, with that impact increasing additively with a greater number of risk factors, irrespective of grade. These findings thus suggest an onset of a pattern that may continue into adulthood (Forehand et al., 1998).

Finally, two methodologic issues, one of measurement, the other analytic, deserve comment. First, we used a binary approach to the coding of risk (i.e., 0 = no-risk, 1 = risk), in our study. By dichotomizing our measure of risk and using an arbitrary single cutoff value to designate risk versus no risk, we may have used an overly simplistic measure for our analytic purposes. From both theoretical and measurement perspectives, some risk variables may be inherently binary (e.g., maternal smoking), in which case such simplification is clearly justified, while other variables (e.g., number of visits to school nurses or emotional well-being) could be measured as a continuous-scale variable. Thus, while the approach we took constituted a necessary simplification, the underlying relationships between risks, time, and outcome are far more complex than our coding approach may imply. However, although potentially there may be other options for operationalizing risk, we believe our approach nevertheless was valid for the purposes of this study. Whatever approach is used, the concept of "risk" is best considered as gradually increasing. Second, few studies have identified classes in the area of multiple risk factors. However, in one study (Lanza et al., 2011) the primary goal was to compare several variable-centered and person-centered methods for modeling multiple risk factors. The authors concluded that it is most valuable to use person-centered models of analysis, such as LCA, to understand densities of prediction of multiple risk factors. By using a person-centered model of analysis, we identified the groups of individuals who are at the highest risk for poor outcomes later in life. This permitted us to show that the high-risk class was more likely to have been exposed to a greater number of risk factors. The risk factor with the highest probability in the high-risk class was history of maltreatment. Other important risk factors in the high-risk class were maternal smoking and emotional well-being in school. There was less difference between the classes in other variables.

4.1. Limitations

This study has several limitations. First, the results were derived from retrospective registry-based data and thus precluded us from collecting additional background and control variables for the analyses. Second, our list of risk factors used in the analyses is not exhaustive and is limited to those data obtained from the registry sources. For example, it is possible that other covariates, such as biological composition (e.g., genetic factors), or chronic stress, would have had an impact on the findings. Third, our coding approach for all risk-factor variables assumes that all children exposed to any one risk factor were at an equal level of risk for poor academic achievement outcome (a consistent and common challenge for research in this area). Fourth, we did not have access to data concerning younger siblings when assessing the number of siblings in the household at the time of birth. As a result, this variable only includes those numbers as they pertain to older siblings. Finally, the cohort sample studied was limited to individuals born in the City of Reykjavik.

5. Conclusions

Each risk factor that was accumulated over the early life course served as an additive predictor of poor academic outcomes for children in 4th and 7th grades. These findings point to the importance of early identification of at-risk children and the need to provide adequate support for them, especially for children exposed to multiple risk factors over the life course. Educational policy should emphasize for young and future parents the importance of the developmental impact of cumulative risk factors in the early life course of children, if they are to grow into successful adults. Finally, future studies might benefit from employing latent class analytic approaches to identify high-risk groups and the major contributing factors to their risk standing, including educational outcomes.

Conflict of interest statement

Authors disclose no conflicts of interest.

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