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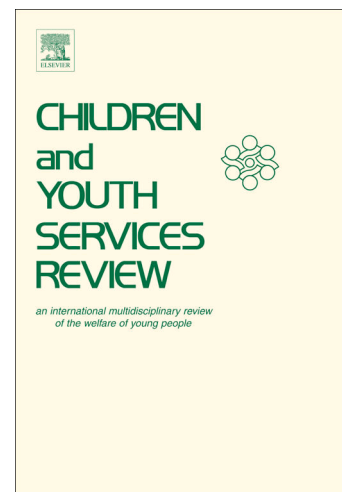
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Authors contributions:

Anne M. Koponen: Wrote the research plan and acquired funding for the follow-up until 2016. Participated in the planning of the data collection, analyzed the data, wrote the first draft and managed the writing of the manuscript as the first author.

Niina-Maria Nissinen: Data merging and curation, manuscript reviewing and revising.

Mika Gissler: Participated in conception of the original study and design, original study cohort generation and data collections until 2007 and 2008-2016, anonymized the original data, reviewed and revised the manuscript, data analysis supervision.

Hanna Kahila: Participated in conception of the original study and design, study cohort generation and data collections until 2007 and 2008-2016, reviewed and revised the manuscript.

Ilona Autti-Rämö: Participated in conception of the original study and design, study cohort generation and data collections until 2007 and 2008-2016, reviewed and revised the manuscript.

Taisto Sarkola: Participated in conception of the original study and design, study cohort generation and data collections until 2007 and 2008-2016, reviewed and revised the manuscript.

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Highlights

Prenatal substance exposure is related to out-of-home care during early childhood

Long-term and stable family-type care is associated with less psychiatric morbidity

Care instability is associated with psychiatric morbidity regardless of exposure

Abstract

A majority of youths with prenatal substance exposure (PSE) have experienced out-of-home care (OHC), but there is a lack of studies on its association with mental health in adolescence and adulthood. The main aim of this retrospective longitudinal cohort study was to explore whether type of OHC (family/institutional) and number of OHC placements are associated with mental and behavioral disorders among youth with PSE (n=393) and unexposed controls (n=147) after controlling for the effect of important confounding factors. Before these analyses, characteristics of OHC and factors associated with the age at entry to care were analyzed separately in both groups. Data from hospital medical records and nine registers were merged and analyzed using descriptive statistics, Pearson correlations and multivariate Cox regression models. Exposed youths entered OHC earlier in life, and the lifetime duration of OHC was longer with more placements and a higher proportion of family-type OHC. Despite these differences in OHC history, a high number of placements was associated with behavioral and emotional disorders with onset in childhood and adolescence (International Statistical Classification of Diseases ICD-10, F90-F98) among both the exposed and controls. Among the exposed, the number of placements and institutional care were also associated with later appearing mental and behavioral disorders (F10-F69). The results suggest that interventions to support placement stability and favor family-type care could be beneficial in the promotion of mental health among children and youth entering OHC.

Key words: Prenatal substance exposure; youth; adverse childhood experiences; out-of-home care; mental and behavioral disorders

1. Introduction

Most youths that have been in long-term out-of-home care (OHC) from early childhood come from high-risk backgrounds involving parental substance abuse, child physical and mental abuse and neglect of care (Oswald et al., 2010; Tarren-Sweeney, 2008b). When a safe and supportive environment cannot be assured with their biological parents, children are removed to OHC. Preadmission psychosocial experiences and experiences in care with repeated loss of significant caregivers and care by unfamiliar adults negate the opportunity for secure attachments and affect children's mental health and well-being (Gypen et al., 2017; Pecora et al., 2009; Rutter, 2000; Van IJzendoorn et al., 2020). Cumulative adversity causes toxic stress, which can lead to enduring brain dysfunction (Hart & Rubia, 2012; Miguel et al., 2019; Siegel 2001; Zeanah & Boris, 2000). Brain development is constantly modified by environmental experiences and suboptimal attachment experiences, especially during the sensitive periods of brain development in the first years of life, hinder neural integration and the mind's capacity to function as a well-integrated system (Alberry et al., 2021; Siegel, 2001). The younger the infant, the greater is the role of the primary caregiver in mediating environmental influences (Glaser, 2000).

The prevalence of mental health problems among children and youth in OHC is significant and they show complex psychopathology (Egelund & Lausten, 2009; Nygaard et al., 2020; Oswald et al., 2010; Tarren-Sweeney, 2008b; Vinnerljung & Sallnäs, 2008). Variance in OHC content related to timing, type, duration, and stability is reflected in the overall quality of OHC. Known OHC-related predictors of mental health problems include older age at entry into care (Tarren-Sweeney, 2008a; 2008b), placement instability (Gypen et al., 2017; Lewis et al., 2007; Stott, 2012; Tarren-Sweeney, 2008a; 2008b; Vinnerljung & Sallnäs, 2008), perceived placement insecurity, and intellectual disability (Tarren-Sweeney, 2008a; 2008b). Family-type OHC has been shown to be beneficial compared with institutional-type OHC, especially at the age of 6–24 months (Tarren-Sweeney, 2008b; Van IJzendoorn et al., 2020). Van IJzendoorn et al. (2020) found strong negative associations between institutional OHC and children's physical growth, cognition, and attention, and weaker negative associations with children's socioemotional development and mental health.

Previous studies on children in OHC are limited by a lack of information about prematurity and prenatal substance exposure (Nelson et al., 2011; Van IJzendoorn et al., 2020). Psychosocial experiences that precede the entry into OHC, experiences during OHC, prematurity and prenatal substance exposure can all increase the risk of neurodevelopmental and other mental and

behavioral disorders in adolescence and adulthood. Long-term follow-up studies accounting for multiple factors in combination are, thus, needed.

Children with prenatal substance exposure are particularly vulnerable to mental and behavioral disorders as a result of central nervous system dysfunction caused by alcohol and/or drugs and adverse social interactive experiences (Fisher et al., 2011; Irner, 2012; Lambert & Bauer, 2012; Streissguth et al., 1996). Prenatal alcohol exposure (PAE) and suboptimal attachment experiences both increase the risk of brain abnormalities (Gautam et al., 2015; Glaser, 2000; Hart & Rubia, 2012; Miguel et al., 2019; Nelson et al., 2011). Exposed infants typically are difficult to care for because of withdrawal symptoms, irritability, and feeding and sleeping problems (Steinhausen et al., 1982; Spohr & Steinhausen, 1984). As many mothers with substance abuse problems have a reduced capacity to interpret children's communicative signals and respond to them accurately, the regulatory capacity of the dyad is compromised (Atchison, 2007; Beeghly & Tronick, 1994; Flykt et al., 2021; Pajulo et al., 2001). Many exposed children face neglect of daily care, physical abuse and family violence, and the majority end up in OHC (Austin et al., 2021; Flannigan et al., 2021; Koponen et al., 2009; Sarkola et al., 2007).

A few studies have investigated associations between characteristics of OHC and mental and behavioral disorders among individuals with PAE or prenatal polysubstance exposure. Streissguth et al. (2004) showed that receiving a diagnosis under the Fetal Alcohol Spectrum Disorders (FASD) continuum and rearing in a good stable environment were the best protective factors against various problematic behaviors among children and adults with PAE. In the study by Fagerlund et al. (2011), length of time spent in residential care (care units with a maximum of 7 children and a minimum of 7 employees) was the most pervasive risk factor associated with behavioral problems among children and adolescents with FASD. Koponen et al. (2009; 2013) showed that placement at an early age in family foster care predicted better mental health among children with PAE. Nygaard et al. (2020) found an enhanced risk of mental health problems among youths with prenatal polysubstance exposure despite early placement in permanent foster or adoptive homes.

Out-of-home care in Finland

In Finland, the Child Welfare Act (2007) safeguards children's rights to a safe growth environment and favorable development. The local municipal authorities are responsible for organizing child welfare services. Maternity and child health care clinics, child daycare

centers and schools have a central role in providing preventive services to promote children's well-being and support parenting. OHC is only indicated if preventive measures have failed.

According to the Child Welfare Act children must be taken into care "if 1) *their health or development is seriously endangered by lack of care or other circumstances in which they are being brought up; or 2) they seriously endanger their health or development by abuse of intoxicants, by committing an illegal act other than a minor offense or by any other comparable behavior*". Substitute care may be arranged in the form of family care or institutional care or in some other way required by the child's needs. Family care is preferred when possible. When a place is chosen, particular attention must be paid to the child's needs, maintenance of close human relations, the continuation of the care, and the child's linguistic, cultural and religious background. Child welfare institutions include children's homes, correctional schools and other comparable child welfare institutions. A maximum number of seven children or young people may be cared for in a residential unit, and the unit must have a minimum of seven employees in care and upbringing work. OHC ends at the age of 18 years, but extended aftercare services were available for OHC youth until the age of 24 years at the time of the study. (Child Welfare Act, 2007; STM.)

The share of children in OHC has been continuously increasing in Finland since 1991 and is at a higher level compared with other Nordic countries (Kääriälä & Hiilamo, 2017; THL, 2021). In 2020, 1.6% of the population's 0–20-year-olds were placed outside the home (THL, 2021). The increase in OHC share has been associated with parental alcohol and other substance abuse coupled with economic hardship. At the same time, there have been continuous cuts in social services and income transfers (Hiilamo, 2017). The risk of intergenerational transmission of OHC has been shown to be high because the accumulated disadvantage experienced by parents with OHC history easily passes to the next generation (Wall-Wieler et al., 2018).

Research questions

The main aim of this retrospective longitudinal cohort study was to investigate whether type of OHC (family/institutional) and number of placements are associated with mental and behavioral disorders among youth with prenatal substance exposure (PSE, n=393) after controlling for the effect of important confounding factors (e.g. age at entry to care). A similar analysis was carried out among unexposed controls (n=147). Before these analyses, characteristics of OHC and factors associated with age at entry to care were analyzed separately

in both groups. We hypothesized that institutional OHC and a high number of placements are associated with mental and behavioral disorder outcomes among both the exposed and controls.

Methods

1.1. Data collection

Youths with OHC in the present retrospective longitudinal register-based study are part of a larger research cohort also including those without OHC. The original cohort consists of 615 exposed youths and 1787 unexposed matched controls aged 15-24 years in 2016 (anonymized). This study includes all 393 youths with PSE and at least one OHC placement, and all 147 unexposed control youths with at least one OHC placement. Thus, the current study sample includes the comparison of 64% of the original youths with PSE and 8% of the original non-PSE controls.

The original study cohort consisted of children with PSE born in 1992-2001 to mothers with a significant substance abuse problem identified by public health maternity clinic nurses in the Helsinki metropolitan area. Identification was based on a test score (≥ 8) on the Alcohol Use Disorders Identification Test (AUDIT), detected illegal drug abuse or nonmedical use of a central nervous system medication or opioid maintenance, and on evaluation of the mother's life situation. Identified women were referred for pregnancy follow-up to antenatal clinics at Helsinki University Hospital (HUS). The pregnancy follow-up included visits scheduled every 2-4 weeks according to patient needs. Patients were offered the service of an experienced multi-disciplinary addiction treatment team and offered easy access to addiction treatment and/or psychiatric care services. At each visit, substance use (i.e. alcohol, cannabis, amphetamine, heroin, buprenorphine, and other drugs) was monitored by voluntary urine toxicology screenings and self-reports. The majority of the exposed children were exposed to alcohol or alcohol and drugs (anonymized). A non-PSE control cohort matched for key characteristics of the PSE cohort was generated 3:1 from the Medical Birth Register according to the following criteria: no evidence of maternal substance abuse in any of the national health and social welfare registers at the time of the offspring's birth, and with maternal age, parity, number of fetuses, month of birth, and hospital of delivery individually matched for each PSE family. Mothers' mean age at the time of the child's birth was 27 years (SD 6.5, range 15-45 years).

Hospital medical records of substance-abusing mothers and their newborns were reviewed and linked with register data from multiple mandatory national health and social welfare registers from birth to 2016. Similar register data from the national registers were gathered for each

mother-child control dyad. The unique identification number assigned to each Finnish citizen at birth or immigration was used to link the data and after the linkage, identification numbers were concealed and replaced with study numbers. The data collection process and registers are described in detail in (anonymized).

The study was approved by the local ethical committee of HUS (Dnro 333/E8/02) and all register organizations, which provided data. No study subjects were contacted. All register linkages were performed by a statistical authority (Finnish Institute for Health and Welfare, THL) and the data were analyzed anonymously by researchers with research permission provided by the register keepers. According to Finnish law, informed consent is not required in register studies when study subjects are not contacted.

1.2. Variables and register sources

The variables used in the present study are listed below. These include variables on childhood adversities and characteristics of OHC considered important for children's neurocognitive and emotional development (Miguel et al., 2019; Shonkoff et al., 2009). The following national registers were used as sources of information: the Population Information System, Medical Birth Register, Care Register for Health Care (previously Hospital Discharge Register), Education Register, Register of Child Welfare, Cause of Death Register, Criminal Records Register, and Register of Social Assistance.

The primary ICD diagnoses of neurodevelopmental disorders (F80-F89 and F90-F98):

Disorders of psychological development (F80-F89) include disorders of speech, language, scholastic skills, and motor functions. Behavioral and emotional disorders with onset usually occurring in childhood and adolescence (F90-F98) include hyperkinetic disorders (ADHD) and disorders of conduct, emotions and social functioning.

The primary ICD diagnoses of mental and behavioral disorders with onset in

adolescence and adulthood (F10-F69) include mental and behavioral disorders due to psychoactive substance use; schizophrenia, schizotypal and delusional disorders; mood disorders; neurotic, stress-related and somatoform disorders; behavioral syndromes associated with physiological disturbances and physical factors, and disorders of adult personality and behavior.

The primary diagnoses were based on at least one inpatient episode (public and private hospitals, 1992-2016) or one outpatient care episode (public hospitals, 1998-2016) provided

with International Statistical Classification of Diseases and Related Health Problems ICD-10 codes F80-F89, F90-F98, F10-F69 (1996-2016) and the corresponding ICD-9 codes (1992-1995) based on the Hospital Discharge Register (1992-1993) and the Care Register for Health Care (1994-2016).

Youths' demographic background factors: **sex** (male, female) from the Medical Birth Register; **native language** (Finnish or Swedish, other) from the Population Information System; **marital status** (married, unmarried (single/divorced/widow)) from the Population Information System and **completed secondary education** (no, yes) from the Education Register.

FASD (no, yes): FAS (Fetal Alcohol Syndrome), PFAS (Partial Fetal Alcohol Syndrome), ARND (Alcohol Related Neurobehavioral Disorder), ARBD (Alcohol Related Birth Defect) from the Register of Congenital Malformations. At least one inpatient or outpatient care hospital episode with ICD-9 code 7607A or ICD-10 code Q86.0. FAS (dysmorphic) from the Hospital Discharge Register or Care Register for Health Care.

Neonatal Abstinence Syndrome (NAS), (no, yes): Prenatal hospital records as well as the Medical Birth Register, and Hospital Discharge Register or Care Register for Health Care including inpatient episodes and outpatient hospital care episodes with ICD-9 code 7795 or ICD-10 code P96.1.

Maternal smoking during pregnancy: Exposure to mother's daily smoking (no exposure or mother stopped smoking after the first trimester, mother smoked throughout pregnancy) from the Medical Birth Register.

Newborn health: **gestational weeks at delivery** (<37 weeks, ≥37 weeks); **Apgar score at one minute** (0-6, 7-10); **birth weight** (<2500 g, ≥2500 g) from the Medical Birth Register.

Out-of-home care: a) **age at the first placement**, b) **number of placements**, c) **number of years in OHC**, d) **proportion of lifetime in OHC**, e) **family-type OHC**=relative or friend family, foster family, professional foster family with family license, family support center, own home with parent/parents, f) **institutional OHC**=professional foster care with institution license, children's home, reform school, substance abuse center, institution for intellectually disabled, g) **proportion of lifetime in family-type care:** 1=50-100% of lifetime in OHC and placed only in an institution or in institution and family-type OHC, 2=<50% of lifetime in OHC and placed only in an institution or in institution and family-type of OHC, 3=<50 % of

lifetime in OHC and placed only in family-type OHC, 4=50-100% of lifetime in OHC and placed only in family-type of OHC. Information about OHC during 1992-2016 is based on the Register of Child Welfare, which includes data on children and youth subject to child welfare measures.

Maternal factors:

Mother's life situation at delivery: age (<25 years, ≥25 years); **marital status** (married, unmarried (single/divorced/widow)); **socioeconomic status** (high: self-employed/lower-level employee/upper-level employee, low: manual worker/student/pensioner/other) from the Medical Birth Register.

Sum of five maternal risk factors:

Primary diagnosis of mental or behavioral disorder (1987-2016): At least one outpatient (1998-2016) or inpatient care (1987-2016) episode with a primary diagnosis of mental or behavioral disorder: ICD-9 codes (1987-1995) 290 and 293-319, and ICD-10 codes (1996-2016) F00-F09 and F20-F99 from the Hospital Discharge Register or the Care Register for Health Care.

Diagnosis related to substance abuse problem (1987-2016): At least one outpatient (1998-2016) or inpatient care (1987-2016) episode with a primary or a secondary diagnosis or external cause of alcohol and/or drug-related abuse: ICD-9 (1987-1995) codes: 291-292, 303-305, 3570, 4255, 5353, 5710, 5711-5713, 6483, 6555, 9650, and 9696-9697 and ICD-10 (1996-2016) codes E24.4, F10-F16, F18-F19, G31.2, G40.5, G40.51, G40.52, G62.1, G72.1, I42.6, K29.2, K70, K85.2, K86, O35.4-O35.5, P04.4, R78.0-R78.5, T40, T43.6, T50.2-T50.3, T51, Z71.4, Z72.1-Z72.2, X45, and X69 from the Hospital Discharge Register or the Care Register for Health Care.

Mortality (no, yes; date of death) from the Cause of Death Register.

Criminal record (no sentence, at least one sentence during 1985-2018) from the Criminal Records Register.

Social assistance (no long-term social assistance, long-term social assistance (10-12 months during a one-year period) in 2002-2016 from the Register of Social Assistance. Social assistance is the last-resort financial assistance for individuals and families in order to guarantee a minimum standard of living.

1.3. Data analysis

Data from hospital medical records and nine registers were merged for this longitudinal register-based cohort study. Descriptive analyses using Pearson chi²-tests included baseline comparisons between the exposed/unexposed cohorts and the proportion of mental and behavioral disorders according to the OHC type (family care only, institution/institution+family care) and the number of OHC placements (1-2 placements, 3-9 placements). Factors associated with the age at the first placement, number of placements and amount of lifetime in OHC were analyzed using Pearson correlations.

Cox regression modeling was used in longitudinal univariate and multivariate analyses. In these analyses, only those who had received the diagnosis after their first placement were included. Sensitive analyses were carried out using the whole cohort. The follow-up started from birth and lasted until the first diagnosis of disorder in psychological development (F80-F89), behavioral or emotional disorder with onset in childhood and adolescence (F90-F98), or mental or behavioral disorders with onset in adolescence or adulthood (F10-F69), or death, or end of the follow-up in 2016. Crude and adjusted Hazard Ratios (aHRs) with 95% confidence intervals (CIs) are reported. The level of statistical significance was set at $p < 0.05$. Variables for multivariate Cox regression models were chosen based on previous studies, correlation analysis and on a theoretical and statistical basis. A sum score of five maternal risk factors (mental or behavioral disorder, diagnosed substance abuse problem, death, long-term social assistance, criminal record) was created to address multicollinearity.

The exposed and unexposed cohorts differed significantly regarding the proportion of OHC (exposed 64%, controls 8%), age at the first OHC placement and the proportion of lifetime in family-type of OHC. It is important to consider the association of these contextual factors with youth's mental and behavioral disorders, and therefore the analyses were carried out separately among the exposed and the controls. Because of the larger proportion of OHC and earlier OHC placement among the exposed, we had enough cases for more detailed analysis among them in Cox regression analyses. Among the exposed, we used two cut points for age at the first OHC episode: 3 years (<3 years, ≥ 3 years) and 7 years (<7 years, ≥ 7 years). Among the controls, only the latter cut point of 7 years was used. The years before school age, particularly the first years of life, are considered to be critical for postnatal brain development.

Among the exposed, the variable describing the proportion of the lifetime in family-type of care was divided into four classes: 1=50-100% of life in OHC with institution/institution+family care, 2=below 50% of life in OHC with institution/institution+family care, 3=below 50% of life in OHC with family care only, 4=50-100% of life in OHC with family care only. For comparison with controls, the division into two classes was also used: 1=OHC with institution/institution+family care, 2=OHC with family care only. Among controls, only the latter categorization was applied. SPSS version 25 was used in the data analyses.

2. Results

2.1. Cohort description

The sex distribution was similar for the exposed and unexposed cohorts. Sixty percent of the exposed and 51% of the controls were 18-24 years old in 2016 (range 15-24 years). In the control group, the proportion of youth speaking another language than Finnish or Swedish (the main official languages in Finland) as their native language was larger (8.2%) than among the exposed (0.3%). Mothers of the exposed had smoked more often throughout pregnancy than control mothers. The exposed offspring had slightly lower birth weight, but the difference did not reach statistical significance. Among the exposed, 10.2% had received a diagnosis under a FASD continuum and 9.7% had a Neonatal Abstinence Syndrome (NAS) diagnosis. (Table 1.) No significant differences between the exposed and the controls were found in gestational age and 1-minute Apgar-scores (data not shown).

The exposed and controls did not differ in the total prevalence of mental or behavioral disorders or in the prevalence of neurodevelopmental disorders (F80-F89, F90-F98). The controls were more often diagnosed with mental or behavioral disorders with onset in adolescence and adulthood (F10-F69). (Table 1.) Higher prevalence among the controls was seen in the subcategories of schizophrenia, schizotypal and delusional disorders and neurotic, stress-related and somatoform disorders ($p < 0.05$) but not in the other subcategories.

The median age of the first F80-F89 diagnosis was 7.0 years (interquartile range IQR 5.0 years) among the exposed and 6.0 years (IQR 4.5 years) among the controls. The corresponding figures regarding F90-98 diagnoses were 9.8 years (IQR 5.6 years) and 9.5 years (IQR 5.3 years) respectively, and regarding F10-F69 diagnoses 14.1 years (IQR 4.7 years) and 14.5 years (IQR 3.8 years), respectively.

No difference between the substance-using and control mothers was found in socioeconomic status at delivery ($p=0.662$) or prevalence of mental or behavioral disorders ($p=0.264$), but the substance-using mothers were older ($p<0.001$), more often unmarried ($p=0.007$) and had more risk factors regarding diagnosed substance abuse, criminality and long-term social assistance ($p<0.001$). Among the exposed 83.0%, and among the controls 46.3% had 2-5 maternal risks ($p<0.001$). In addition, a major difference was found in the death rate. (anonymized) Thirteen percent ($n=47$) of the exposed with no diagnosed FASD had lost their mother before reaching adult age. Among youths with a diagnosed FASD the rate was 35% ($n=14$). The corresponding rates regarding diagnosed NAS were 14.4% ($n=51$) and 26.3% ($n=10$), respectively. Of the controls, 1.4% ($n=2$) had lost their mother.

Table 1. Background factors and mental and behavioral disorders among exposed and control youths (% , n)

	Exposed, n=393 % (n)	Controls, n=147 % (n)	p-value
Sociodemographic background and maternal risks			
Sex			0.403
Male	50.4 (198)	54.4 (80)	
Female	49.6 (195)	45.6 (67)	
Age at the end of follow-up 2016			0.066
15-17 years	40.2 (158)	49.0 (72)	
18-24 years	59.8 (235)	51.0 (75)	
Native language			<0.001
Finnish or Swedish	99.7 (391)	91.8 (135)	
Other (child of immigrant parents)	0.3 (1)	8.2 (12)	
(Missing)	(1)	(0)	
Health and substance exposure			
Birth weight			0.055
<2500 g	13.5 (53)	7.5 (11)	
≥2500 g	86.5 (340)	92.5 (136)	
Mother's daily smoking throughout pregnancy			<0.001
Yes	82.4 (324)	42.2 (62)	
Fetal Alcohol Spectrum Disorder (FASD)			
Yes	10.2 (40)		
Neonatal Abstinence Syndrome (NAS)			
Yes	9.7 (38)		
<i>Neurodevelopmental or other mental or behavioral disorder with onset in adolescence or adulthood</i>			0.246
No mental or behavioral disorder	34.1 (134)	27.9 (41)	
Neurodevelopmental disorder only (F70-F99)	26.5 (104)	23.1 (34)	
Other mental or behavioral disorder only (F10-F69)	14.5 (57)	17.0 (25)	
Both disorders (F70-F99 + F10-F69)	24.9 (98)	32.0 (47)	
F80-F89 Disorders of psychological development			0.108
Yes	20.1 (79)	26.5 (39)	
F90-F98 Behavioral and emotional disorders with onset usually occurring in childhood and adolescence			0.530
Yes	46.6 (183)	43.5 (64)	
F10-F69 Any mental or behavioral disorder with onset in adolescence or adulthood			0.046
	39.4 (155)	49.0 (72)	

2.2. Characteristics of out-of-home care among the exposed and the control youths

The exposed youths were placed at a younger age than the controls. Half of the exposed were placed for the first time before the age of three and almost one-fifth before the age of six months. The corresponding figures among the controls were 15% and 3%. The first placement among the controls was typically at school age or teenage.

Almost half of the controls had only one placement while less than one-fifth of the exposed had one placement and half had three or more placements. Almost half of the exposed had been in OHC for at least 50% of their lifetime (controls 10.2%). The exposed were most typically placed in a children's home or a foster family, and the controls in a children's home. Only a minority had been in a family-type care all of their time in OHC (exposed 16.0%, controls 19.8%). This minority had the most stable OHC history with the smallest number of placements. (Table 2.)

Table 2. Characteristics of out-of-home care among the exposed and controls (% , n)

	Exposed, n=393 % (n)	Controls, n=147 % (n)	p-value
<i>Age at first out-of-home placement</i>			<0.001
<6 months	18.6 (73)	3.4 (5)	
6 months - 2 years	32.8 (129)	11.6 (17)	
3-6 years	24.2 (95)	19.0 (28)	
7-12 years	15.0 (59)	27.2 (40)	
13-17 years	9.4 (37)	38.8 (57)	
Mean (range)	4.1 (0-17)	9.2 (0-17)	
Median	2.0	10.0	
<i>Age at first out-of-home placement</i>			<0.001
<7 years	75.6 (297)	34.0 (50)	
≥7 years	24.4 (96)	66.0 (97)	
<i>Number of out-of-home placements</i>			<0.001
1	18.3 (72)	47.6 (70)	
2	31.6 (124)	26.5 (39)	
3	29.8 (117)	17.7 (26)	
4-9	20.4 (80)	8.2 (12)	
Mean (range)	2.7 (1-9)	1.9 (1-6)	
Median	3.0	2.0	
<i>Type of out-of-home placement*</i>			
Relative or friend family	5.1 (20)	5.4 (8)	0.869
Foster family	66.4 (261)	25.9 (38)	<0.001
Professional foster home (family license)	13.5 (53)	10.2 (15)	0.306
Professional foster home (institution license)	13.0 (51)	15.0 (22)	0.547
Children's home	80.4 (316)	72.1 (106)	0.038
Family support center	7.1 (28)	15.0 (22)	0.005
Reform school	4.8 (19)	8.8 (13)	0.079
Substance abuse center	2.5 (10)	2.7 (4)	0.909
Institution for intellectually disabled	1.0 (4)	0.7 (1)	0.586
Own home with parent/parents	12.7 (50)	13.6 (20)	0.786
Independent supported living	2.0 (8)	0.7 (1)	0.248
Other type of placement	10.4 (41)	8.8 (13)	0.584
<i>Number of years in out-of-home care</i>			<0.001

0-4	37.9 (149)	76.9 (113)	
5-9	13.2 (52)	12.9 (19)	
10-14	24.2 (95)	5.4 (8)	
15-18	20.6 (81)	4.1 (6)	
19-21	4.1 (16)	0.7 (1)	
Mean (range)	9.0 (0.0-20.9)	3.2 (0.0-19.3)	
Median	9.3	1.1	
<i>Proportion of a lifetime in out-of-home care %</i>			<0.001
<25	36.1 (142)	76.2 (112)	
25-49	15.0 (59)	13.6 (20)	
50-74	16.3 (64)	4.1 (6)	
75-100	32.6 (128)	6.1 (9)	
<i>Distribution of care type categories</i>			<0.001
Institution/institution+family 50-100%	41.0 (161)	8.8 (13)	
Institution/institution+family <50%	43.0 (169)	71.4 (105)	
Only family-type OHC <50%	8.1 (32)	18.4 (27)	
Only family-type OHC 50-100%	7.9 (31)	1.4 (2)	
<i>Proportion of 3-9 placements according to the type of out-of-home care</i>			
Institution/institution+family 50-100%	75.2 (121)	84.6 (11)	
Institution/institution+family <50%	43.8 (74)	24.7 (26)	
Only family-type OHC <50%	0 (0)	3.7 (1)	
Only family-type OHC 50-100%	6.4 (2)	0 (0)	

*A child may have many OHC places

2.3. Factors associated with age at first OHC placement, number of placements and amount of lifetime in OHC

Among the exposed, a diagnosis of FASD and NAS, maternal older age and several maternal risk factors were associated with placement at an earlier age and a higher proportion of a lifetime in OHC. NAS during infancy, mother's criminal record and long-term social assistance were associated with more OHC placements. (Table 3.)

Among the controls, maternal risk factors were associated with younger age at first OHC placement, more placements and more of the lifetime in OHC. In addition, low birth weight predicted younger age in OHC, maternal young age and daily smoking predicted more lifetime in OHC, and male sex predicted more OHC placements. Compared with the exposed, mothers' mental health problems for the controls were more strongly associated with the age at the first OHC placement and amount of lifetime in OHC. (Table 3.)

Table 3. Factors associated with age at first placement, number of placements and percentage of lifetime in OHC. Pearson correlation coefficients, exposed n=393, controls n=147.

	Age at first placement r (p-value)		Number of OHC placements r (p-value)		Percentage of lifetime in OHC r (p-value)	
	Exposed	Controls	Exposed	Controls	Exposed	Controls
Gender and health in infancy						
Sex: Male						
Female	-.03	.13	-.03	-.22**	-.04	-.13
Birth weight: ≥2500 g						
<2500 g	-.04	-.21***	-.02	-.02	.07	-.06
Mother smoked throughout pregnancy: No						
Yes	-.06	.03	.06	.09	.05	.18*
FASD: No						
Yes	-.16**		.02		.29***	
NAS: No						
Yes	-.18***		.11*		.20***	
Mother's life situation at delivery						
Age: <25 years						
≥25 years	-.15**	.01	.00	-.11	.17***	-.14*
Marital status: Married						
Not married	.04	.06	-.03	-.05	-.04	-.12
Socioeconomic status: Higher						
Lower	.04	.07	.10	-.12	.03	.01
Maternal risk factors						
Mental or behavioral disorder: No						
Yes	-.06	-.28***	-.05	.05	.01	.17*
Diagnosed substance abuse disorder: No						
Yes	-.12*	-.18*	.03	.22**	.10*	.14
Criminal record: No						
Yes	-.04	-.13	.13*	.13	.05	.17*
Death: No						
Yes	-.18***	.12	.00	.01	.22***	-.06
Long-term social assistance: No						
Yes	-.18***	-.18*	.17***	.12	.13**	.15
Sum of maternal risks	-.23***	-.30***	.09	.20*	.19***	.24**

*p<0.05, **p<0.01, ***p<0.001

2.4. Child mental and behavioral disorders in relation to type and number of OHC placements

Figures 1a-b show a clear pattern in the prevalence of all categories of mental and behavioral disorders in relation to the type of OHC and the number of OHC placements among both the exposed and the controls. The rates seem to be lower among youth with family-type care only, compared with institutional care, and lower among youth with fewer than three placements compared with those with three or more placements.

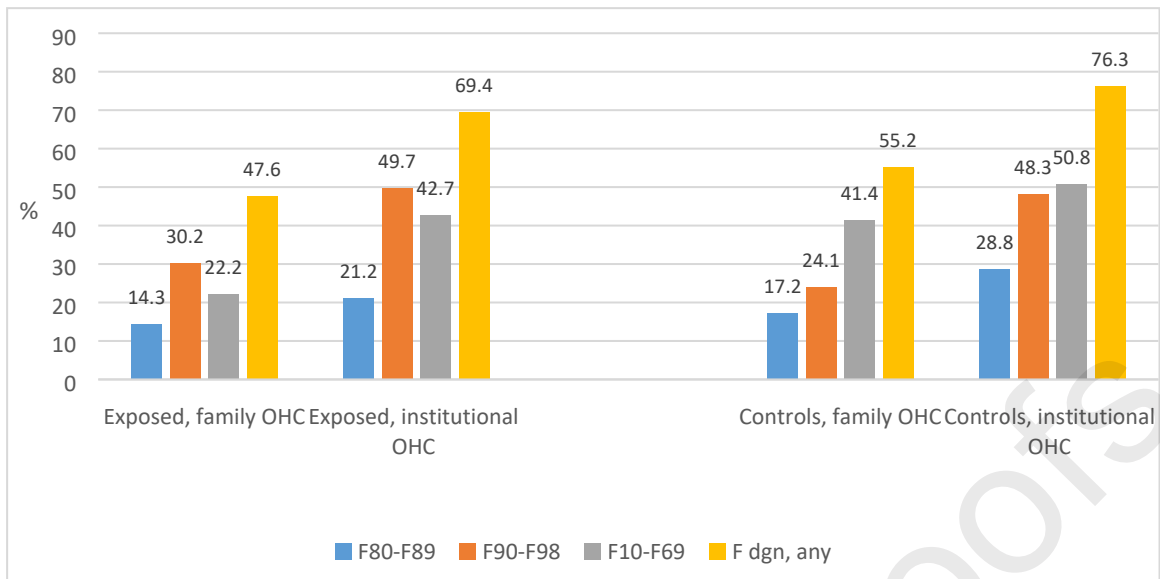


Figure 1a. Prevalence of mental and behavioral disorders in relation to the type of out-of-home care among exposed and control youths (%; exposed n=393, controls, n=147).

Difference between family-type OHC only/family+institutional OHC:

Exposed: F80-F89, $p=0.209$, F90-F98, $p=0.004$, F10-F69, $p=0.002$, F-dgn, any, $p<0.001$.

Controls: F80-F89, $p=0.206$, F90-F98, $p=0.019$, F10-F69, $p=0.361$, F-dgn, any, $p=0.023$.

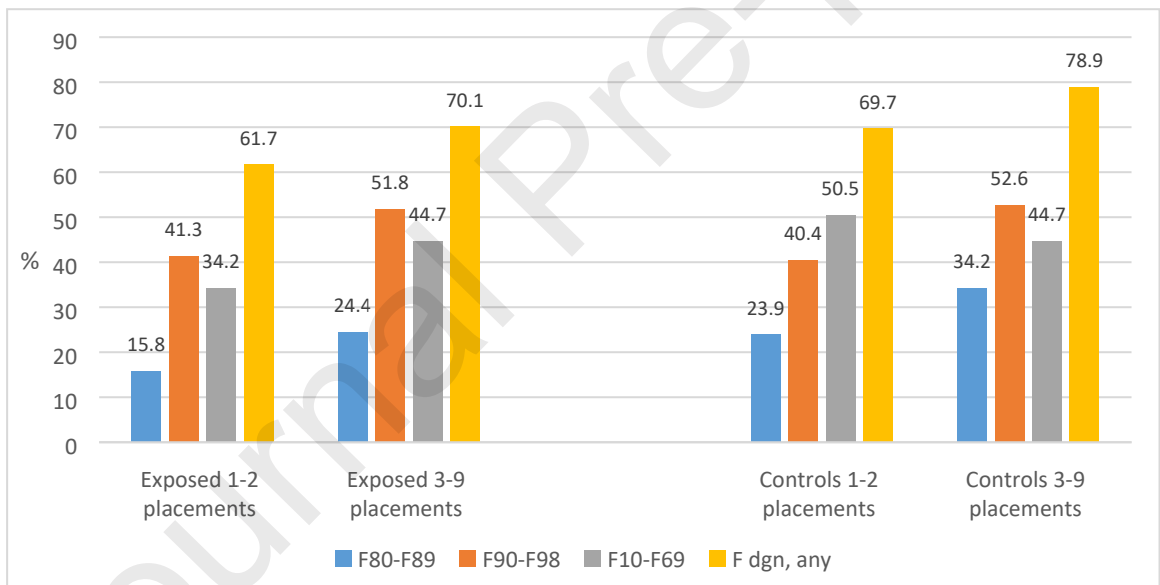


Figure 1b. Prevalence of mental and behavioral disorders in relation to number of out-of-home care placements among exposed and control youths (%; exposed n=393, controls n=147).

Difference between 1-2/3-9 OHC placements:

Exposed: F80-F89, $p=0.034$, F90-F98, $p=0.038$, F10-F69, $p=0.033$, F-dgn, any, $p=0.082$.

Controls: F80-F89, $p=0.213$, F90-F98, $p=0.189$, F10-F69, $p=0.543$, F-dgn, any, $p=0.275$.

2.5. Multivariate associations between OHC type, number of OHC placements, and mental and behavioral disorders among exposed youth

Behavioral and emotional disorders with onset in childhood and adolescence (F90-F98) were more common among the exposed with more of their lifetime in institutional OHC when compared with any other group with less time in institutional care. After adjustment of covariates, the risk was almost two times higher compared with youths with the highest proportion of their lifetime in family-type of care ($1/0.54=1.85$). When the four categories were dichotomized into two classes (1=institution/institution+family OHC, 2=family OHC only), the risk was similar. In addition, many placements, male sex and FASD were associated with the risk of F90-F98 diagnoses. (Table 4a, Figures 2a-b.)

Association between amount of lifetime in family care and mental and behavioral disorders with onset in adolescence and adulthood (F10-F69) was less clear. However, three or more placements seemed to increase the risk of F10-F69 diagnoses as well as female sex and first OHC placement after the age of two years. (Table 4b, Figures 2c-d.)

When the previous analyses were checked using the age of seven years ($<7, \geq 7$ years) as a cut point for the first placement, and separately using the whole cohort, the associations between the proportion of lifetime in family care, number of placements and diagnoses in F90-F98 and F10-F69 remained similar. The proportion of life in family care and the number of placements were not associated with the risk of disorders of psychological development (F80-F89). (Data not shown.)

Table 4a. Associations between proportion of life in family-type care, number of out-of-home care (OHC) placements, and behavioral and emotional disorders with onset in childhood and adolescence F90-F98 from birth to early adulthood among exposed youth. Cox regression hazard models, n=370.

	F90-F98			F90-F98	
	Model 1 HR (95% CI)	Model 2 aHR (95% CI)		Model 1 HR (95% CI) ¹	Model 2 aHR (95% CI) ¹
Type of care			Number of placements		
≥50% institution+family	1	1	1	1	1
<50% institution+family	0.41 (0.21-0.81)**	0.40 (0.20-0.79)**	2	3.30 (1.68-6.50)***	3.17 (1.59-6.31)***
<50% family OHC only	0.36 (0.17-0.74)**	0.43 (0.20-0.90)*	3	3.53 (1.79-6.94)***	3.20 (1.60-6.41)***
≥50% family OHC only	0.48 (0.34-0.67)***	0.54 (0.37-0.78)***	4-9	5.17 (2.60-10.28)***	5.11 (2.51-10.41)***
Sex: Female		1			1
Male		1.48 (1.07-2.04)*			1.59 (1.15-2.18)**
Birth weight: ≥2500 g		1			1
<2500 g		1.20 (0.74-1.93)			1.22 (0.74-1.99)
FASD: No		1			1
Yes		1.27 (0.77-2.08)			1.76 (1.06-2.92)*
NAS: No		1			1
Yes		1.53 (0.96-2.42)			1.33 (0.84-2.13)
Sum of maternal risks		1			1
0		2.59 (0.34-19.49)			1.99 (0.26-15.07)
1		2.51 (0.34-18.23)			1.72 (0.23-12.57)
Age at first placement		1			1
<3 years		1.01 (0.72-1.42)			1.08 (0.78-1.50)
≥3 years					

¹ Adjusted for birth year

*p<0.05, **p<0.01, ***p<0.001

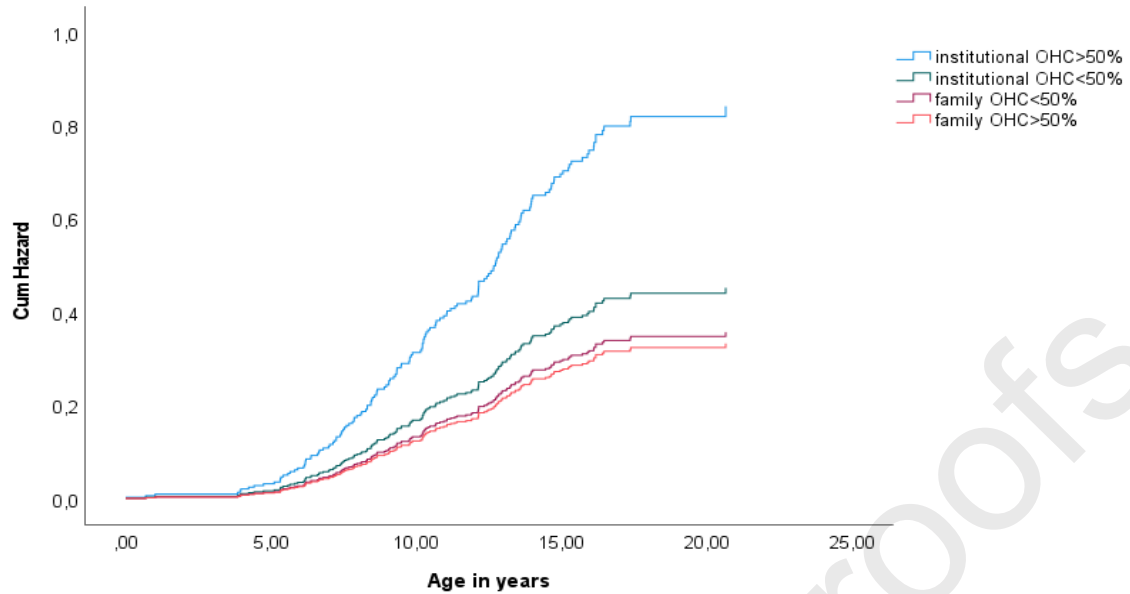


Figure 2a. Association between **proportion of life in family-type care** and behavioral and emotional disorders with onset in childhood and adolescence (F90-F98) from birth to early adulthood among exposed youth (n=370). Cox regression hazard model, adjusted for sex, birth weight, FASD, NAS, the sum of maternal risk factors, and age at first time in OHC.

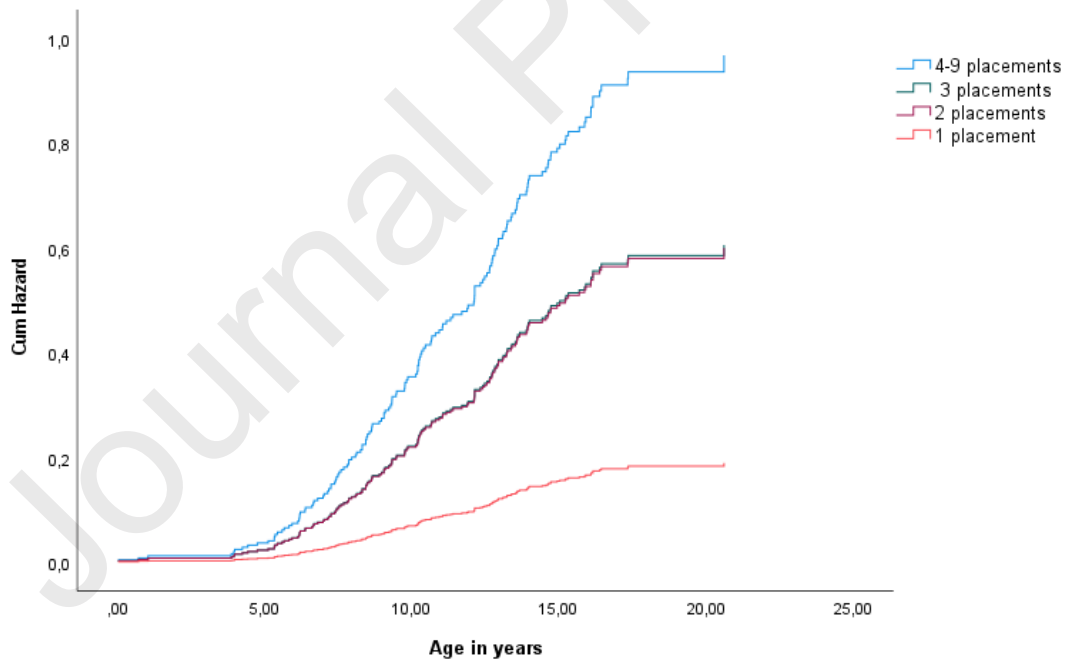


Figure 2b. Association between **number of out-of-home care placements** and behavioral and emotional disorders with onset in childhood and adolescence (F90-F98) from birth to early adulthood among exposed youth (n=370). Cox regression hazard model, adjusted for sex, birth weight, FASD, NAS, the sum of maternal risk factors, age at first time in OHC, and birth year.

Table 4b. Associations between proportion of life in family-type care, number of OHC placements, and mental and behavioral disorders with onset in adolescence and adulthood (F10-F69) among exposed youth. Cox regression hazard models, n=379.

	F10-F69			F10-F69	
	Model 1 HR (95% CI)	Model 2 aHR (95% CI)		Model 1 HR (95% CI) ¹	Model 2 aHR (95% CI) ¹
Type of care			Number of placements		
≥50% institution+family	1	1	1	1	1
<50% institution+family	0.30 (0.12-0.74)**	0.29 (0.11-0.72)**	2	1.38 (0.78-2.45)	1.56 (0.86-2.81)
<50% family care only	0.54 (0.25-1.18)	0.47 (0.20-1.08)	3	1.98 (1.14-3.43)*	2.33 (1.32-4.14)**
≥50% family care only	1.04 (0.74-1.47)	0.94 (0.64-1.39)	4-9	2.04 (1.15-3.63)*	2.51 (1.36-4.64)**
Sex: Female		1			1
Male		0.64 (0.45-0.90)*			0.65 (0.47-0.92)*
Birth weight: ≥2500 g		1			1
<2500 g		1.09 (0.66-1.78)			1.08 (0.66-1.78)
FASD: No		1			1
Yes		1.03 (0.59-1.81)			0.99 (0.57-1.72)
NAS: No		1			1
Yes		0.70 (0.35-1.39)			0.60 (0.30-1.20)
Sum of maternal risks					
0		1			1
1		1.20 (0.28-5.23)			1.17 (0.27-5.11)
2-5		1.63 (0.39-6.76)			1.48 (0.36-6.14)
Age at first placement					
<3 years		1			1
≥3 years		1.23 (0.85-1.78)			1.48 (1.04-2.12)*

¹ Adjusted for birth year

*p<0.05, **p<0.01

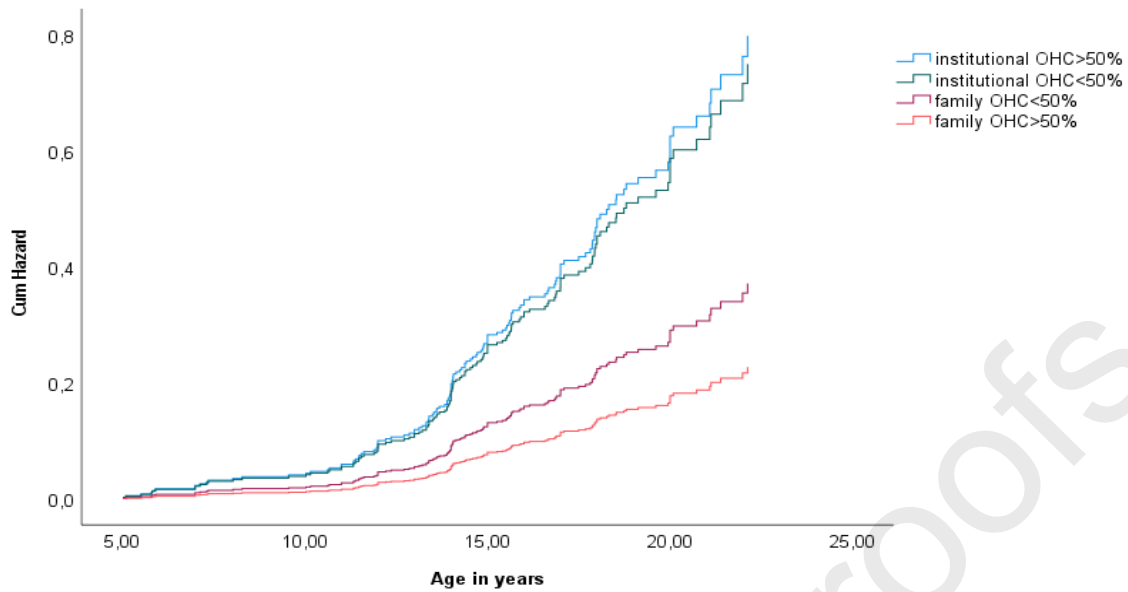


Figure 2c. Association between **proportion of life in family-type** care and mental and behavioral disorders with onset in adolescence and adulthood (F10-F69) from birth to early adulthood among exposed youth (n=379). Cox regression hazard model, adjusted for sex, birth weight, FASD, NAS, the sum of maternal risk factors, and age at first time in OHC.

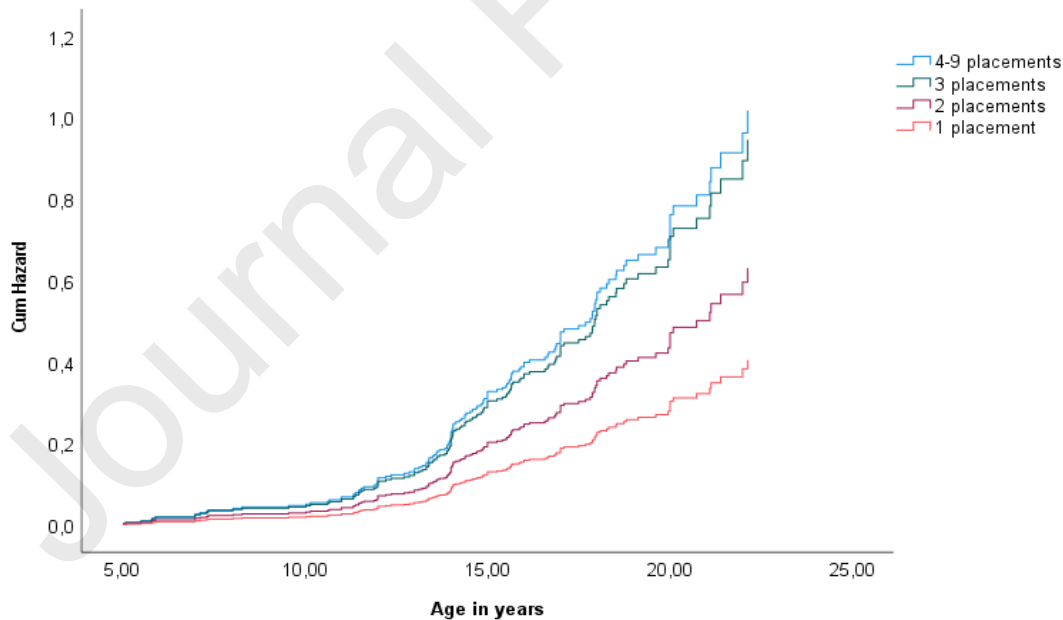


Figure 2d. Association between **number of placements** and mental and behavioral disorders with onset in adolescence and adulthood (F10-F69) from birth to early adulthood among exposed youth (n=379). Cox regression hazard model, adjusted for sex, birth weight, FASD, NAS, the sum of maternal risk factors, age at first time in OHC, and birth year.

2.6. Multivariate associations between type and number of placements and mental and behavioral disorders among unexposed controls

Among the unexposed controls, associations between the type and number of placements and mental and behavioral disorders were weaker than among the exposed. The only significant association was found between the number of placements and an increased risk of behavioral and emotional disorders with onset in childhood and adolescence (F90-F98). (Table 5, figures 3a-b.) The results were similar when the whole cohort was used. No associations were found between the type and number of placements, disorders of psychological development (F80-F89), and mental and behavioral disorders with onset in adolescence and adulthood (F10-F69). (Data not shown.)

Table 5. Association between type and number of placements, and behavioral and emotional disorders with onset in childhood and adolescence (F90-F98) from birth to early adulthood among unexposed controls. Cox regression hazard models, n=121.

	F90-F98			F90-F98	
	Model 1 HR (95% CI)	Model 2 aHR (95% CI)		Model 1 HR (95% CI) ¹	Model 2 aHR (95% CI) ¹
Type of care Institution/ Institution + family Family only	1 0.66 (0.29-1.50)	1 0.52 (0.23-1.20)	Number of placements 1 2 3 4-9	1 2.89 (1.23-6.76)* 3.10 (1.26-7.63)* 6.35 (2.20-18.26)***	1 2.30 (0.97-5.48) 2.78 (1.07-7.24)* 4.51 (1.46-13.98)**
Sex: Female Male		1 1.20 (0.62-2.34)	Sex: Female Male		1 1.26 (0.63-2.52)
Birth weight ≥2500 g <2500 g		1 0.37 (0.09-1.56)	Birth weight ≥2500 g <2500 g		1 0.40 (0.09-1.72)
Sum of maternal risks 0 1 2-5		1 1.39 (0.48-4.05) 1.74 (0.68-4.41)	Sum of maternal risks 0 1 2-5		1 1.49 (0.50-4.47) 1.79 (0.69-4.65)
Age at first placement <7 years 7-12 years ≥13 years		1 0.60 (0.28-1.28) 0.22 (0.09-0.57) **	Age at first placement <7 years 7-12 years ≥13 years		1 0.79 (0.35-1.79) 0.35 (0.13-0.94) *

¹ Adjusted for birth year

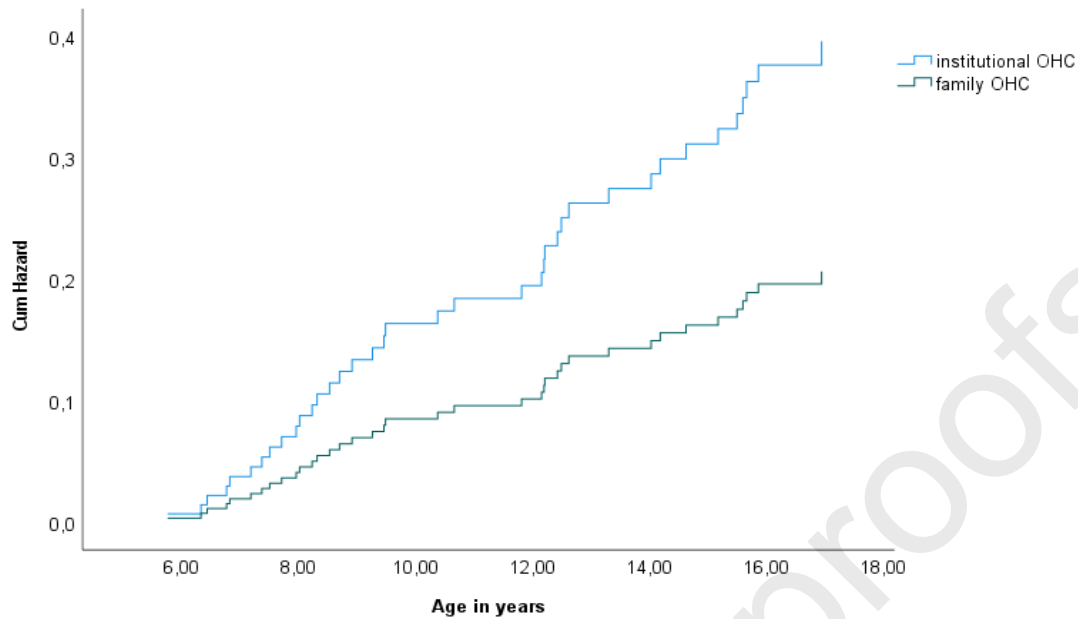


Figure 3a. Association between proportion of life in family-type of care and behavioral and emotional disorders with onset in childhood and adolescence (F90-F98) from birth to early adulthood among unexposed controls (n=121). Cox regression hazard model, adjusted for sex, birth weight, the sum of maternal risk factors, and age at first time in OHC.

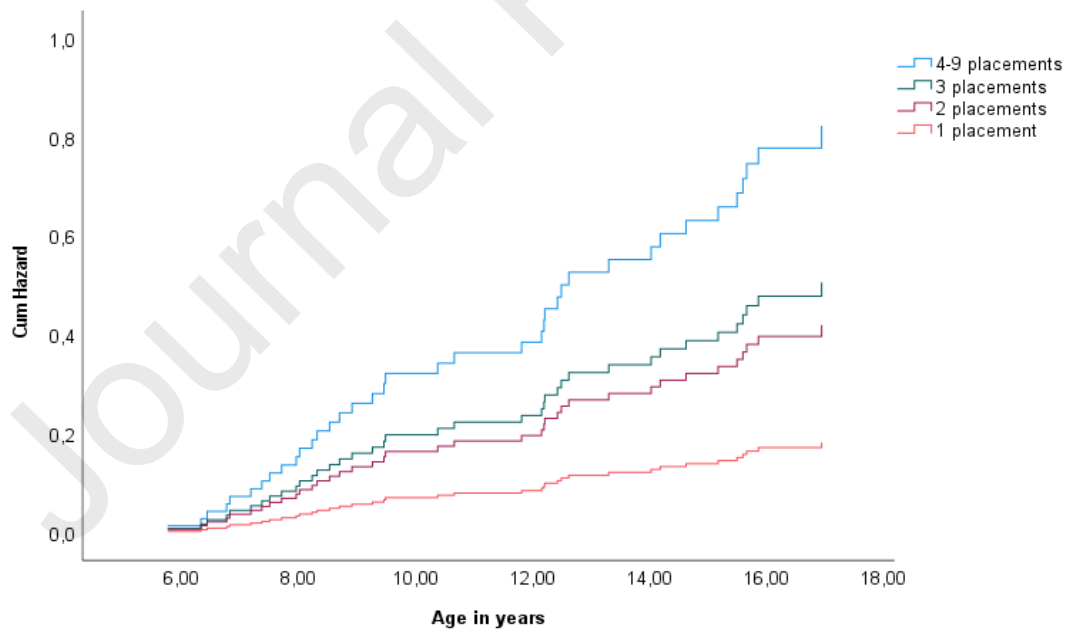


Figure 3b. Association between number of placements and behavioral and emotional disorders with onset in childhood and adolescence (F90-F98) from birth to early adulthood among the unexposed controls (n=121). Cox regression hazard model, adjusted for sex, birth weight, the sum of maternal risk factors, age at first time in OHC, and birth year.

3. Discussion

As the majority of youth with PSE have experienced OHC, it is important to study their OHC history and its association with mental health. If similar associations are found among unexposed controls, this gives additional understanding of the results. This study focused on characteristics of OHC, factors associated with timing, duration and number of OHC placements, and associations between the type and number of placements and mental and behavioral disorders among the exposed youth and controls. The results revealed that in both groups, maternal risk factors were associated with earlier entry into OHC, but a major difference existed in age at first placement, type and number of placements and the proportion of lifetime in OHC. Despite these differences, placement instability turned out to be strongly associated with a high risk of mental and behavioral disorders in both groups.

In accordance with our previous findings on this cohort (anonymized), the present study showed that severe and advanced maternal addiction problems anticipated early placement and long-term stay in OHC, as the highest proportion of a life in OHC was found among youths with diagnosed FASD or NAS, maternal death, and many maternal risk factors including older age. Most of the exposed children were placed for the first time before the age of three and a majority before school age. Infancy and early childhood is a critical time for the development of the brain and social skills, and placement at a young age and family-type of care have most likely protected the child from adverse experiences (e.g. physical abuse, neglect of care) possibly present in the biological home, which could have harmed the child's development (Glaser, 2020).

On the other hand, many placements and disruptions in attachment relationships are also detrimental for mental health (Siegel, 2001; Tarren-Sweeney, 2008a; Van IJzendoorn et al., 2020) and only a minority of the exposed had avoided these experiences. The results suggest that long-term family care was a protective factor and many placements a risk for behavioral and emotional disorders with onset in childhood and adolescence (F90-F98) and later appearing mental and behavioral disorders (F10-F69) among the exposed. These associations remained even after controlling for the effects of important confounding factors, such as a diagnosis under the FASD continuum, NAS, birth weight and age at first OHC placement. The results are in line with the studies by Streissguth et al. (2004), Fagerlund et al. (2011) and Koponen et al. (2009; 2013), which showed that placement stability and family care were associated with a lower risk of behavioral problems among individuals prenatally exposed to alcohol. A stable and nurturing home context affords children opportunities to secure attachment relationships

and stability in school settings, peer networks, health care providers, and access to community resources and activities (Leve et al., 2009).

Similarly, among the controls, those with several maternal risks had ended up in OHC (anonymized) and a high number of maternal risks was associated with earlier entry and longer duration of care as well as a high number of placements. The prevalence of maternal mental and behavioral disorders was as high as among the exposed. However, these disorders were diagnosed later than among mothers of the exposed (anonymized) and control youths were placed mostly at school age or teenage for the first time. In previous studies, older age at entry into OHC has been associated with children's poorer mental health as older age at entry often means poor pre-care of mental health and other problems in the family (Tarren-Sweeney, 2008a; 2008b). Thus, late interference to problems and lack of support may be one explanation for the high prevalence of mental and behavioral disorders among the controls. Our previous study (anonymized) found that maternal mental health problems were strongly associated with control youths' mental and behavioral disorders. The result is in line with studies among normative population, which have found a strong association between father's and especially mother's psychiatric morbidity and offspring's psychiatric diagnoses (Paananen et al., 2013; 2021) and disability pension due to mental disorders in young adulthood (Merikukka et al., 2018). According to Fisher et al. (2011), early adversities have an equal effect as PAE in the onset and growth of behavior dysregulation during adolescence.

Among the controls, a high number of placements was associated with behavioral and emotional disorders with onset in childhood and adolescence (F90-F98). The result is in line with studies among normative samples which show that placement instability is harmful to emotional development (Gypen et al., 2017; Rubin et al., 2007; Stott, 2012; Tarren-Sweeney, 2008a; 2008b; Van IJzendoorn et al., 2020; Vinnerljung & Sallnäs, 2008). However, institutional care and high number of placements were not associated with mental and behavioral disorders with onset in adolescence and adulthood (F10-F69) among the controls.

The results of the study partly supported our hypothesis by showing a strong relationship between placement instability and disorders which reflect emotion and behavior dysregulation (F90-F98). Youths in OHC had the highest number of maternal adversities (anonymized) and interruptions in attachment relationships. The results are in accordance with cumulative adversity and attachment models (Tarren-Sweeney 2018b) and with the view that PAE combined with early life stress may lead to more severe behavioral deficits, as suggested by

Alberry et al. (2021). A high prevalence of Attention-Deficit/Hyperactivity Disorder (ADHD) and deficits in emotion regulation and executive control, which are included in the F90-F98 category, has also been found among institutionalized children also in previous studies (Van IJzendoorn et al., 2020). In the study by Sariaslan et al. (2022), young adults placed in institutional care settings were more often diagnosed with a severe mental illness or depression compared with their siblings placed in foster care. Each additional placement episode increased the risk of these diagnoses. These associations remained even after careful adjustment for preplacement behavioral problems and other important confounders. However, it cannot be ruled out that in some cases a severe mental illness or depression may increase the risk of additional placements. Still, causes for placement breakdown are diverse and the child's behavior is only one cause among others (Kalland & Sinkkonen, 2001; Khoo & Skoog, 2014; Oosterman et al., 2007; Rock & al., 2015).

Strengths and limitations

The study is one of the first to investigate associations between OHC characteristics and mental and behavioral disorders among youth with PSE. The study addresses the need to take into account the effect of PSE and contextual factors in OHC studies. The quality of care is not the only factor affecting the outcomes of OHC. The major strength of the study is the unique and large data set with verified substance use during pregnancy. Longitudinal design, the matched control group and the combination of medical records and register data with multiple variables enabled us to study the combined effects of environmental adversities and PSE. Register data avoid bias caused by low response rate, recalling and subject loss. In Finland, health care is publicly funded and all Finnish citizens and permanent residents have access to it. The reporting to the national health and social welfare registers used in this study is mandatory and their good coverage, quality, and suitability for epidemiological research have been verified (Aro et al., 1990; Gissler & Haukka, 2004; Sund, 2012). Diagnoses are made by medical professionals and registered in national databases.

A high attendance (99.7%) at antenatal maternal services provided by health care center maternity clinics of health care centers (anonymized) made it possible to identify pregnant women with a substance misuse problem. Despite that, we estimate that only women with the most severe substance abuse problems were identified for the study, as the exposed cohort represents only 0.4% of all children born in the Helsinki metropolitan area in 1992-2001 (anonymized). Thus, the results may not reveal the effects of slight and/or occasional substance

use. Also, the control group may include mothers with light substance use, which has not been noticed and registered by health care professionals. The same problem exists in all studies on substance use during pregnancy (Behnke et al., 2013).

Most children and adolescents use child and school health services provided by the municipalities and everyone has an identical possibility to be referred to specialist health care when needed. We included all diagnoses from specialist health care but not diagnoses from primary health care because they were not available for the complete study period. Therefore, the prevalence of mental and behavioral disorders may be higher than found in this study. Another limitation is the lack of direct evidence of child abuse and neglect, because this information is not available from the registers. However, according to the study by Kalland & Sinkkonen (2001), most children in OHC have faced these adversities. An additional limitation is the lack of information on fathers and the quality of life in family and institutional care, which may vary greatly depending on the family situation or care arrangements in institutions. Finally, as many risk factors co-occur, we are able to show only associations, not causality, between OHC characteristics and mental and behavioral disorders. Exposed children's symptoms caused by PSE (Steinhausen et al., 1982; Spohr & Steinhausen, 1984) and earlier adverse attachment experiences complicate forming a secure attachment relationship with the new caregiver (Bowlby, 1969; Schofield & Beek, 2005). Thus, the child's behavior may be exhausting and lead to placement interruptions.

Implications for practice and policy

Information about the detrimental effects of alcohol and drugs on the fetus should be delivered widely in society. Low-threshold services for substance abuse problems and identification and monitoring of high-risk pregnancies are of the utmost importance. Multi-component age-appropriate interventions targeted at biological parents, foster parents, children and service systems have been proven to be beneficial for improving the well-being of foster children and their families (Leve et al., 2009; Olson & Montague, 2011; Petrenko, 2013; 2019). Accumulated knowledge based on these interventions, existing care models and studies has been integrated as a new theoretical framework by Reid et al. (2022) to guide support to children and families with FASD. This framework can be applied to care for all children with PSE and their families.

The theoretical framework of Reid et al. (2022) consists of four key components. *Strengthening the family social economy* pays attention to formal institutional (e.g., housing, health care, income), and informal (e.g., family, friends, and neighbors) support. A family's ability to access

both formal and informal support is strengthened. The goal is to empower caregivers to take advantage of opportunities when they arise. *Promoting hope* focuses on individual and family strengths, decreasing stigma and building positive self-identity. The goal is to help individuals with FASD to adjust to their diagnosis and unique neurodevelopmental profile and become independent actors in their own life. *Acknowledging family expertise* includes recognition of the knowledge, expertise, and lived experience of caregivers regarding FASD and the importance of strong therapeutic alliances between health care professionals and children, caregivers, and other family members. *Providing education and skill building* includes services and interventions to support children to develop their self-regulatory and adaptive skills, which are key areas of challenge among children with FASD (Reid et al., 2022).

Reid et al. (2022) state that specialist services for children with FASD and their families are significantly limited all over the world. The aim of the proposed care model is to increase awareness of FASD among health care professionals and integrate interventions and specialized services into existing systems of care. The family is seen as a critical unit to support children with FASD. Families often have the best expertise on FASD, and support services should be planned and provided in collaboration with them.

The family-directed approach by Reid et al. (2022) helps to strengthen the attachment relationship between the caregiver and child with PSE and decreases the risk of placement breakdowns. Previous studies have shown that relationship-focused interventions in early life, designed to help caregivers to be more sensitive and responsive to their children's emotions and needs, enhance the security of attachment and healthy regulation of children's behavior and stress responses. Early interventions take advantage of the plasticity of the brain (Olson & Monague, 2011) and play a role in shaping neural systems and effective stress management later in life (Fisher et al., 2006). At preschool age and beyond, positive behavior support and enhancing individual strengths are needed (Leve et al., 2012; Olson & Monague, 2011). In adolescence, individual therapy and interventions focusing on enhancing resilience and social and academic skills have provided positive outcomes (Leve et al., 2009; 2012).

According to Leve et al. (2009) the ability to mobilize support from close relationships, school and community is a key aspect of resilience. Without a stable home context, this may not be possible. Raising foster children and especially those with PSE may be very stressful, and caregivers need support and education in order to prevent placement interruptions (Leve et al., 2012; Olson & Monague, 2011). It is estimated that the association between placement

interruptions and behavior problems is bidirectional. Interventions targeted at decreasing children's behavior problems prevent placement interruptions, and a stable home environment decreases behavior problems (Leve et al., 2012).

Conclusion

The results revealed a great difference in OHC history between youths with and without PSE. Despite these differences, placement instability was similarly associated with disorders which reflect emotional and behavioral dysfunction both among the exposed and the controls. The results highlight the need for preventive child welfare services and interventions starting from the prenatal period in order to avoid detrimental effects of PSE and OHC. If this is not possible, interruptions in attachment relationships should be avoided. The personnel working with children taken into care should have expertise in rearing children who need special care.

Abbreviations

ADHD Attention-Deficit/Hyperactivity Disorder
ARBD Alcohol Related Birth Defect
ARND Alcohol Related Neurobehavioral Disorder
AUDIT Alcohol Use Disorders Identification Test
FAS Fetal Alcohol Syndrome
FASD Fetal Alcohol Spectrum Disorder
HUS Helsinki University Hospital
ICD International Statistical Classification of Diseases and Related Health Problems
NAS Neonatal Abstinence Syndrome
OHC Out-of-home care
PAE Prenatal Alcohol Exposure
PFAS Partial Fetal Alcohol Syndrome
PSE Prenatal Substance Exposure

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Niina-Maria Nissinen: Data merging and curation, manuscript reviewing and revising.

Mika Gissler: Participated in conception of the original study and design, original study cohort generation and data collections until 2007 and 2008-2016, anonymized the original data, reviewed and revised the manuscript, data analysis supervision.

Hanna Kahila: Participated in conception of the original study and design, study cohort generation and data collections until 2007 and 2008-2016, reviewed and revised the manuscript.

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Highlights

Prenatal substance exposure is related to out-of-home care during early childhood

Long-term and stable family-type care is associated with less psychiatric morbidity

Care instability is associated with psychiatric morbidity regardless of exposure

Journal Pre-proofs