Effects of Parental Mental Illness on Common Child Health Outcomes

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Abstract

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Background: Serious mental illness (SMI), including major depression, bipolar disorder, and schizophrenia, in parents is a major public health concern. Parental mental illness can adversely affect the health and well-being of children. Prior studies have demonstrated associations between maternal depression and child physical health conditions, including infection and injury, which are leading causes of morbidity and mortality in young children worldwide. No prior studies conducted in Asia have investigated whether young children whose mothers or fathers have mental illness, especially serious mental illness, are at higher risk and injury and infection.

Objectives: Our aim was to compare the incidence of injury or common infectious diseases among young Taiwanese children whose parents were and were not affected by serious mental illness.

Methods: We used a retrospective cohort design and utilized data from several population-based databases in Taiwan, including the Maternal and Child Health Database, the Taiwan National Health Insurance Research Database, and birth and death certificate databases. To account for clustering of recurring outcomes within children and multiple children having the same parent, we employed generalized estimating equation Poisson models to estimate incidence rate ratios (IRR) of injury and common infectious disease occurring before age 5 among children exposed to parental SMI compared to unexposed children. We examined whether these associations were modified by parent socioeconomic status and age. We also assessed whether the associations differed by whether the mother or father or both parents were affected and by the timing of onset and type of SMI diagnosis.

Results: We identified 1,999,322 singletons born in 2004-2014 who had data from both parents (91% of all singleton deliveries). A higher percentage of children with parental SMI (61%) had any childhood injury compared to children without parental SMI (54%). Parental SMI was associated with a 14% (IRR 1.14, 95% confidence interval [CI] 1.13-1.15) and 49% (IRR 1.49, 95% CI: 1.42-1.57) higher risk of childhood injury and injury hospitalization, respectively. Parental SMI was also associated with a 4% (IRR 1.04, 95% CI: 1.03-1.05) higher risk of antibiotic-treated common infectious disease and a 31% (IRR 1.31, 95% CI: 1.29-1.33) higher risk of common infectious disease requiring hospitalization.

Associations between parental SMI and these child outcomes were stronger with increasing paternal or maternal age. Additionally, the risk of injury or common infectious disease requiring

hospitalization was greater among children with two SMI-affected parents than among those with SMI-affected mothers, only. Children with only SMI-affected mothers were at higher risk relative to those with only SMI-affected fathers. Additionally, risks were greater for children with parents affected by schizophrenia or bipolar disorder than for those whose parents had major depressive disorder. In general, associations with most outcomes were similar regardless of whether parents' SMI diagnoses pre-dated or occurred after the child's birth.

Conclusions: Our study of Taiwanese children found that parental SMI is associated with increased risk of childhood injury and of common infectious disease. These findings highlight the importance of effective treatment for parents with SMI. In addition, enhancing parenting skills, promoting home safety, and providing support for these vulnerable families, including crisis planning and mapping social and health care resources, may reduce morbidity risk in offspring during the preschool years.

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DEDICATION

This dissertation is dedicated to the memory of my grandmother, Rui-Yun Yeh.

Chapter 1. INTRSODUCTION: BACKGROUND, AIMS AND SIGNIFICANCE

Mental illness affects a person's cognition, mood and behavior and can impair family, social, and occupational function. In 2010, mental illness was the leading cause of years lived with disability (YLDs) worldwide, accounting for 22.9% of all YLDs.[1] Serious mental illnesses (SMI), such as schizophrenia and mood disorders (bipolar disorder and major depressive disorder), typically result in more substantial functional impairment and greater interference with major life activities.[2,3] Most psychiatric disorders are first recognized in adolescence or early adulthood and thus can impair functioning, including child-rearing, across the lifespan.[1]

Even among persons with the same specific SMI diagnosis, individual clinical courses vary greatly. Only a small proportion of individuals with schizophrenia recover completely. About 10-20% have a favorable course, and most remain chronically ill with exacerbations and remissions of positive symptoms (hallucinations, delusions and disorganized behavior). After an initial episode, 80% relapse within 5 years. Among patients receiving treatment, 16-23% experience a relapse within a year. Baseline functioning deteriorates with each relapse, and long-term sufferers usually require daily living support. Cognitive deficits, the core feature of schizophrenia, may not improve over time. Negative symptoms of schizophrenia, including flat affect, loss of interest, emotional and social withdrawal and attentional impairment, are persistent and cause significant social and occupational dysfunction.[2,3]

The course of major depressive disorder (MDD) is generally recurrent and episodic in nature, but with much variation among individuals. Some people remain symptom free for many years, whereas others never achieve remission. About 50% of patients exhibit depressive symptoms

before the first diagnosed episode. Two in five individuals with MDD recover within 3 months of onset, and four in five within 1 year. About 50-80% will have a recurrent episode, usually within 2-3 years; and 90% of individuals with ≥ 3 episodes will have another episode.[4] As illness progresses, depressive episodes occur more frequently and last longer. About 5-10% of patients with a MDD diagnosis have a manic episode 6-10 years after the first depressive episode (typically after having 2-4 depressive episodes). Major depression-related impairments in physical, social, and role functioning range from very mild which is not noticed by other people to complete incapacity to perform essential self-care tasks.[2,3] Residual cognitive and functional impairment may persist during inter-episodic intervals after the improvement of major symptoms.[5]

The first episode of bipolar disorder is usually a depressive episode (75% in women and 67% in men). Manic episodes tend to have a rapid onset (days or weeks). More than 90% of individuals with a single manic episode will have recurrent mood (manic or depressive) episodes, and 40-50% have a second mood episode within 2 years of the first. The interval between episodes often shortens over time and stabilizes at 6-9 months after 5 episodes. A minority (5-15%) of sufferers have rapid cycling bipolar disorder, experiencing >4 mood episodes within a year. Many individuals with bipolar disorder return to a fully functional level between episodes; however, 30% are chronically ill and show severe impairment in work, resulting in lower socioeconomic status (SES). Functional recovery lags considerably behind symptom resolution. Some individuals with bipolar disorder also have cognitive impairment even during euthymic (normal mood) periods.[2,3]

Overall, current treatments for psychiatric disorders generally focus on symptom resolution, and relatively little attention is given to functional improvement. Remission of schizophrenia and mood disorders is mainly defined by criteria for episode duration and symptom severity.[6,7]

However, functional impairment can occur globally as well as across family, interpersonal and occupation domains, and may persist even in the absence of symptoms.[2,3]

Individuals with psychiatric disorders, especially schizophrenia and mood disorders, have lower reproductive fitness,[8,9,18–23,10–17] partly because they are less likely to form relationships resulting in childbearing.[10,11,27,12,13,15,18,22,24–26] However, many of people with SMI become parents. In the U.S., the National Comorbidity Survey that employed a structured diagnostic interview in 1990s found that 67.2% and 75.5% of the women and men with severe and persistent mental illness, respectively, were parents.[28] Pregnancy and the postpartum period are a time when people are particularly vulnerable to episodes of psychiatric disorder.[29–32] It is estimated that 5-60% of women suffer from depressive symptoms during perinatal periods;[33–39] and that 5.6-12.7% and 5.0-9.6% MDD during pregnancy and postpartum, respectively.[40–43] Males may also be affected; a meta-analysis of 23 cohort studies and 19 cross-sectional studies generated an estimate of the period prevalence of perinatal paternal depression as 10.4% (95% CI: 8.5-12.7%).[44]

1.1 Effects of parental mental illness on early childhood health outcomes

Parental mental illness is a particularly important public health issue given its potential impact to both parents and child. Research on the influences of parental mental illness on child health has mainly centered on negative consequences of maternal depression for child cognitive/language development,[45–47] motor development,[48] and emotional health.[49–52] Limited evidence also suggests paternal mental illness affect child language development and emotional health.[53–57] The effects of parental mental illness on child physical health have been less well examined, although studies suggest potential associations. For example, the presence of maternal schizophrenia or mood disorders[49,58–60] or paternal schizophrenia before childbirth[61,62] are associated with several adverse

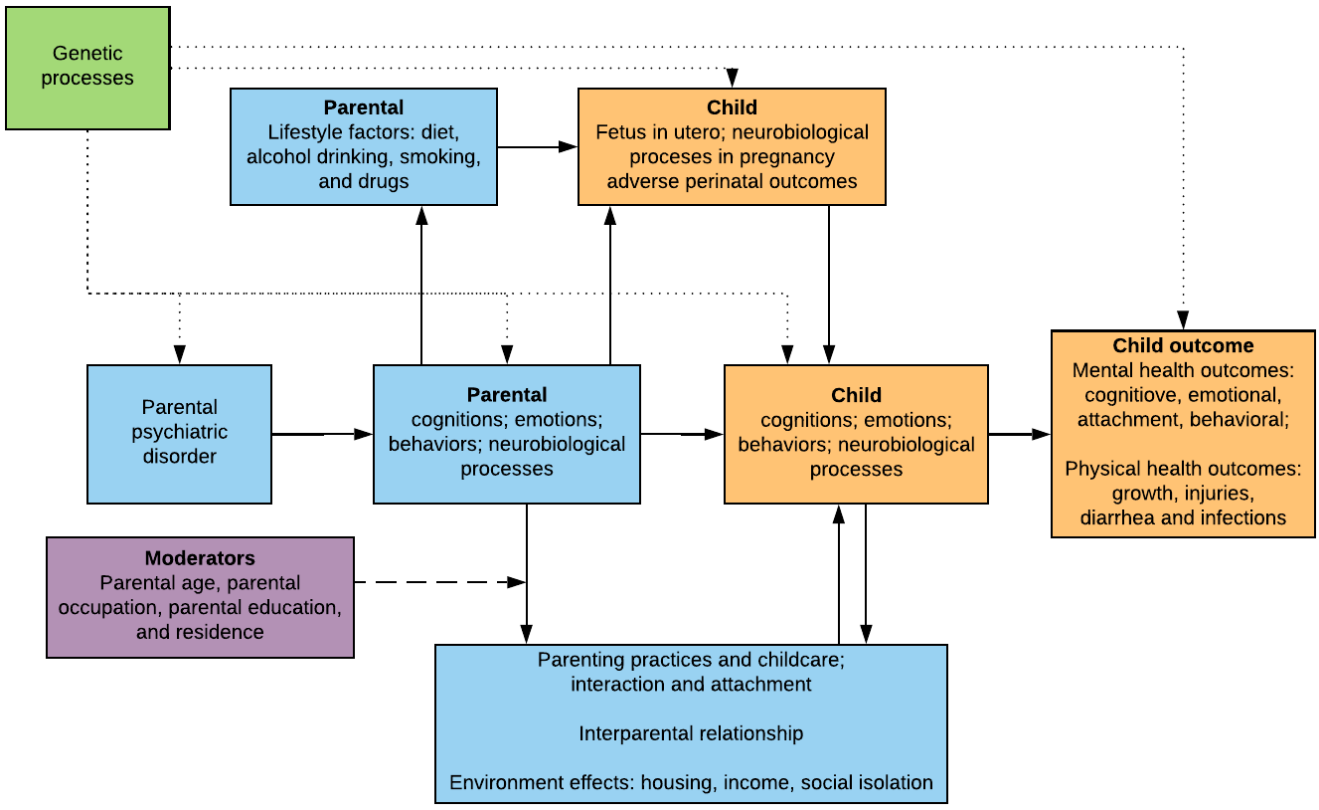
neonatal outcomes, including premature birth and low birthweight (LBW). Maternal depression was also found to be associated with poor infant growth in low- and middle-income countries[48,63,64] and child overweight in high-income countries.[65] In rural areas of low income countries, maternal depression has been associated with child febrile illness,[66] acute respiratory infection[67] and diarrhea.[67,68] Maternal depression has been linked to child injury.[69–73] Yet many of these studies used self-reported rating scales administered at a single point in time as the measurement of maternal depression, which could lead to exposure misclassification.[74,75] Self-report rating scales have high sensitivity and low specificity for diagnosis of depression and often misclassify people with transient distress as depressed. Additionally, the exposed groups studied were usually restricted to women with depression or depressive symptoms that manifested during the perinatal period and did not take into account symptoms at earlier other times in the parent's life.

Several population-based studies also indicate a probable link between parental mental illness and child mortality. In Taiwan, parental SMI and maternal postnatal depression, respectively, were associated with a 2.4 and 1.7 times greater childhood mortality before the age of 5 years.[76,77] In Denmark, children of parents with psychiatric admission had a 1.3-2.6 times greater risk of subsequent infant mortality (0-1 year);[78] a 2.3 times greater risk of sudden infant death syndrome;[78] and a 1.6 times greater risk of mortality between 1-4 years.[79] Children with two affected parents had a greater risk of mortality than those with one affected parent.[79] Two Swedish studies also reported that offspring of parents with schizophrenia had a two-fold greater risk of infant death.[60,62] These findings highlight the need to further evaluate the effects of parental SMI on child physical health, particularly among young children who rely most heavily on parent care.

1.2 PLAUSIBLE MECHANISMS FOR EFFECTS OF PARENTAL MENTAL DISORDERS ON CHILD PHYSICAL HEALTH OUTCOMES

Genetic, biological, behavioral and environmental factors have been proposed as plausible mechanisms for the association between parental mental disorders and offspring health[49] (Figure 1-1). Yet little research has been conducted to directly investigate the pathways between parental SMI and child physical health outcomes, including diarrhea, respiratory infection, and injury. In the following sections, we describe biological, parent behavioral, family and social factors that could serve as plausible pathways between parental SMI and child physical health outcomes.

Figure 1-1 Possible mechanisms underlying the association between parental psychiatric disorders and child health outcomes



Dotted lines: genetic processes; solid lines: direct effects; dashed lines: modifying effects
Orange colors: the child; blue colors: the parents; green colors: genetic factors; purple colors: effect modifiers. Figure was modified from Stein et al.[49]

1.2.1 *Biological factors originating in the antenatal phase*

Several studies have shown that infants of mothers with SMI[58,59,62,80–83] or of fathers with schizophrenia,[61,62] have an increased risk for LBW and for preterm birth. LBW and preterm birth are risk factors of airway disease, asthma, or recurrent infections.[84] Preterm infants are also more likely than full-term infants to have neurodevelopmental disabilities in childhood[84], which may increase risk of injury.[70,85] The causes of these adverse outcomes among infants of parents with SMI are likely multifactorial. First, psychiatric symptoms in pregnancy might have a direct physiologic impact. Depression is associated with dysregulation in the hypothalamic-pituitary-adrenal (HPA) axis, which can result in elevated maternal cortisol level and inflammatory response. This might further affect fetal growth and fetal immune system[86] and predispose offspring to intrauterine growth restriction and preterm birth. Yet little literature addresses the potential physiologic impact of maternal schizophrenia and bipolar disorder on fetal development during pregnancy.

Second, some pregnant women with SMI may be socioeconomically disadvantaged[58,59,61,62,87], which could lead to stress and unhealthy lifestyle behaviors, such as smoking, substance use[62,80,81,87,88], poor nutrition and inadequate prenatal care.[80,89,90] These factors are known to adversely affect fetal development.[84,87,91] Third, some researchers have suggested that these adverse outcomes may be related to maternal use of psychotropic medications.[58,87,92] Mood stabilizers, such as Valproate and Lithium, are associated with increased risks of malformations.[93,94] However, whether antidepressants and antipsychotics increase risks of preterm birth and LBW is controversial, as other studies did not find these associations.[88,95]

1.2.2 *Parent SMI-related illness factors during the early childhood period*

Several SMI-related illness factors can make parenting demands even more challenging for parents with SMI than unaffected parents. These factors include symptoms of SMI, cognitive and functional impairment, SMI-related illness coping, and comorbid substance abuse.

Symptoms and cognitive and functional impairment

Parenting requires a broad range of knowledge about personal and food hygiene and home-safety, as well as problem-solving abilities, including skills for child management, physical care, emergency response and stress coping.[96] Parenting is challenging, and few, if any, cultures provide universal positive parenting classes for adults and teens who are taking on this role for the first time.[97] Parenting is particularly challenging for parents with SMI, who may be under the influence of SMI-related symptoms and experience impairment in problem-solving abilities and functioning that further exacerbate the common challenges of parenting.

Illness coping

Parents may struggle to cope with their mental illness, leaving little time and energy to meet a child's needs and provide supervision. They may become overwhelmed by increased stress and family conflicts, further reducing coping capacity. A focus group study summarized that mothers with mental illness frequently faced challenges with daily parenting, managing mental illness and stigma, and retaining custody of and contact with their children.[98] These mothers desired to develop normal lives for themselves and their children, but had role strain in which maternal needs might conflict with children's needs.[98] The adverse effects of illness coping also occur among parents with serious physical illness and adverse life events. Children have a greater rate of hospital contact for injury during the first year after parent's cancer diagnosis;[99] and parental adverse life events are related to an increased likelihood of child traumatic brain injury.[100]

Comorbid substance use disorder

SMI may co-occur with alcohol and/or substance use disorder[101], influencing parents' responsiveness to a child's emotional and physical needs or level of supervision. Parental substance abuse/dependence disorder has been shown to increase risk of injury- or infection-related hospitalizations for chidren.[102] Furthermore, incarceration resulting from illicit substance use may more permanently disrupt the parent-child bond and expose children to a more alien and under-supervised environment.

1.2.3 *Family and social factors*

Evidence suggests that a child's characteristics may affect their parents' response and modify parental mental illness. For example, infant irritability or poor motor functioning are risk factors for postpartum depression.[103] Infants or children have difficult temperamental characteristics, or with disabilities place greater demands on their parents. In turn, parents' symptoms could also influence children's temperament. Parental mental illness also could affect the stability of the parents' relationship, resulting in marital disruption and single parenthood.[10,12,22,59,62,80,81,104] In these circumstances, another partner may not be available to compensate for caregiving.

SMI also affects social relationships. Parents with mental illness often have weak social networks and difficulty finding help for children in crisis.[105] Negative attitudes and stigmatization from the community may place these parents and their children in a socially isolated position.[106,107] Stigma may also hinder parents from seeking mental health treatment,[106] which could lead to a prolonged and severe course of mental illness. Overall, this places parents with SMI at a greater disadvantage of reaching ideal parenting capacity.

Social and physical environmental effects associated with mental illness, such as unemployment, reduced income, poor housing, social isolation, and disadvantaged

neighborhood,[57,104,108] may impact the adequacy of parenting environment and the family's economic and social capital. Children of low SES families are more likely to be exposed to polluted air and water, sources of infection, and unsanitary and crowded environments.[109,110] Due to poverty or financial difficulties, parents with mental illness may be unable to provide safety measures or devices throughout the household, thereby increasing the risk of avoidable childhood injury.[110] Finally, low-income neighborhoods, more characteristically likely to be the environments of children of parents with SMI, have more unsafe play areas, greater/faster street traffic, and fewer public services.[110] These characteristics additionally increase the risk of childhood injury.

1.3 Dissertation Aims

In Taiwan, respiratory and digestive system diseases are the most common reasons for ambulatory visits among children aged 0-5 in 2000 and 2009;[111] and unintentional injury and pneumonia have been among the five leading causes of death among children aged 1-4 since 2004.[112] Unintentional injury is also a leading cause of disabilities in children worldwide,[113] which can have long-term impact on children as well as parents. Parents often develop emotional distress and intense guilt following injury or illness to their children,[114–116] and family functioning can undergo additional stresses by the burden arising from the child's illness.[117] Parents with mental health problems are especially susceptible to these additional consequences of child illness.[116]

To date, there are no routine screening nor intervention programs to assess or address parental mental illness in Taiwan. To our knowledge, no studies have been conducted in Taiwan to examine the association between parental mental illness and physical health of young children. To fill this research gap, we conducted a population-based retrospective cohort study to investigate the associations between parental SMI (schizophrenia, bipolar disorder and major depressive disorder) and child injury and common infectious disease (diarrhea or respiratory infection) in children < 5

years in Taiwan. We also examined whether the associations between parental SMI and selected child outcomes differed by urbanicity levels of residence, by parental occupation, or by parental age. Finally, we assessed whether the associations between parent's SMI and child health outcomes varied according to different measurements of parent's SMI, including (1) number and identity of parent(s) with SMI, (2) timing of onset, and (3) type of SMI diagnosis.

We used Taiwan national data from the Maternal and Child Health Database (MCHD), the Taiwan National Health Insurance Research Database (NHIRD), and birth and death certificate data. The MCHD is comprised of children born in 2004-2014 and contains encrypted IDs of father, mother and child, allowing the parent-child linkage. The NHIRD covers claims data for inpatient and ambulatory services from 1998 to 2014. We also extracted parent-child pairs/triads from NHIRD and then formed the final study population by matching the parent-child pairs/triads in the NHIRD and/or the MCHD to the birth certificate data.

The findings from this project can help us better understand the associations between parental mental illness and child physical health. The results of our study may suggest ways that parents with mental illness could benefit from supportive services as they raise young children.

Chapter 2. METHODS

2.1 DATA SOURCES

We used four Taiwanese national databases to accomplish the aims of this study: the National Health Insurance Research Database (NHIRD), the birth certificate database, the death certificate database, and the maternal and child health database (MCHD). These databases were initially held by different government institutions. Since 2009, the Health and Welfare Data Science Center (hereafter referred to as the Data Center) in the Ministry of Health and Welfare has collected and maintained these databases for research purposes.

In Taiwan, every citizen is assigned a unique national identification number (national ID) at birth, and every foreign national holding a resident visa is issued a unique Alien Resident Certificate number (foreign ID). The Data Center used the same encryption algorithm to encrypt national ID and foreign ID in the above databases so that these databases could be linked to each other. These encrypted national ID and foreign ID will be heretofore referred to as ID unless specified otherwise. This study was approved by the Cathay General Hospital Institutional Review Board in October 2016 (CGH-P105047) and the Data Science Center in the Department of Statistics, Ministry of Health and Welfare, Taiwan in December 2016. IDs in the datasets used in the project were encrypted to protect patient privacy. Due to confidentiality concerns, researchers are not permitted to present findings with stratum-specific sample sizes of <3.

2.1.1 *National Health Insurance Research Database (NHIRD)*

The NHIRD was originally held by the National Health Insurance Administration (NHIA), Ministry of Health and Welfare. The NHIRD contains all records of diagnoses, procedures, prescriptions and treatments from medical facilities contracted with Taiwan's National Health

Insurance (NHI) program. The NHI Program is a government-run, single-payer system based on a public-contract model. Every Taiwanese citizen, foreign national working in Taiwan, and foreign national living in Taiwan for > 6 months must enroll in the NHI Program. Only those who lose their insurance eligibility can withdraw, for example, giving up Taiwanese citizenship, moving abroad for more than 6 months, going missing, or letting Alien Resident Certificate expire. Infants with Taiwanese citizenship can be covered by their mothers' or fathers' insurance for at most 60 days before joining the program (30 days before July 2010). Infants without Taiwanese citizenship (e.g. children of foreign employees) cannot be automatically covered by their parents' insurance and can only join the NHI after living in Taiwan for six months.[118] The NHI was established in March 1995, and the coverage rate was 92% by the end of 1995 and ≥ 99.9% in 2003.[119]

Taiwan's healthcare system consists of private and government-owned hospitals and outpatient clinics and other facilities. In July 2015, the NHI had contracted 20,631 (> 93%) medical institutions in Taiwan to provide healthcare services.[120] The NHI does not adopt a gatekeeper system, so the insured can choose any hospital or specialist without a referral. Overall, the NHI provides an inclusive package, including outpatient, inpatient, dental and emergency care, mental health services, physical and community rehabilitation, and preventive care. The funds for NHI are principally salary-based premiums.[118] Providers are paid by the NHIA mainly on a fee-for-service basis, and providers need to submit claims data to the NHIA in order to obtain reimbursement. The NHI has programs to improve accessibility, and these include:[121] (1) 100% subsidy of premium for low-income household and persons older than 70 years; (2) relief loans and installment plans for the near-poor or the temporarily unemployed; (3) co-payment exemptions for prenatal care and delivery, preventive care, medical services in remote areas and offshore

islands, low-income households, children younger than 3 years, and persons with catastrophic illness including serious mental illness.

The NHIA has established audit committees consisting of experts who regularly review a random sample of medical records to examine diagnoses, procedures, and prescriptions within the claims data and have implemented punitive measures for inconsistency between claims data and medical records. The NHIA regularly assembles data from insurance enrollment, contracted medical institutions, and claims data from the NHI Program to generate the NHIRD.

Five sub-databases of the NHIRD were used in this project (Table 2-1). Inmates and people who work in the military were excluded from the registry of beneficiaries database, the primary database used to identify the study cohort. The inpatient and ambulatory expenditures datasets can be linked with the registry of beneficiaries by ID number; these two expenditures datasets can be linked to the details of inpatient and ambulatory care orders by using the following set of key variables: date of fee, date of application, sequential number, encrypted hospital ID, application type and case type.

Table 2-1 Basic information of five NHIRD sub-databases used in this project

Sub-databases	**Years covered**	**Variables included**
Registry of beneficiaries	2000-2014	Insured's ID, date of birth and sex, whether the insured's ID is a national ID; enrollee's ID, sex, whether the enrollee's ID is a national ID, occupation type, amount of salary, location of company that an enrollee works for or residence of household, and the relationship between the insured and the enrollee
Inpatient expenditures by admission	1998-2014	ID, age, admission date, 5 diagnostic codes of International Classification Diseases (ICD), 2 ICD external causes of injury codes, 5 ICD procedure codes, specialty, duration of stay
Details of inpatient orders	2000-2014	Orders of examinations, procedures, and prescription drugs
Ambulatory care expenditures by visit	1998-2014	ID, age, visit date, 3 ICD diagnostic codes, 2 ICD procedure codes, specialty
Details of ambulatory care orders	2000-2014	Orders of examinations, procedures, and prescription drugs

2.1.2 *Birth certificate database*

The Taiwan national birth certificate database was originally held by the Health Promotion Administration, Ministry of Health and Welfare. Medical facilities in Taiwan must submit a birth certificate application form within 7 days after delivery for every livebirth and stillbirth of ≥ 20 weeks gestation or of ≥ 500 grams birthweight (regardless of parents' nationality) to both the Health Promotion Administration and the Department of Household Registration, Ministry of the Interior. Each birth certificate is to be issued for one livebirth or stillbirth. The birth certificate data is entered into the registry and a copy is provided to the parents.

The Taiwan national birth certificate database contains information on gestational age, birthweight, infant sex, infant birth date (month and year, only), infant's congenital malformations, stillbirth/livebirth status, singleton or twin/multiple gestation; maternal risk factors during pregnancy, mode of delivery, procedures or complications during delivery, mother's birthdate, mother's residence in the household registry and current residence (township), mother's original nationality (country of birth); father's birthdate, father's residence in the household registry, and father's original nationality. This database also includes mother's ID and whether the mother's ID is a national ID; but father's and child's IDs are unavailable. This database was comprised of all livebirths and reported stillbirths in 2004-2014 in Taiwan (n= 2,252,573).

2.1.3 *Death certificate database*

The death certificate database was originally held by the Ministry of Health and Welfare. The database contains encrypted ID, sex, date of death, place of death (hospital, clinic, house, etc.), type of death (natural, accident, or homicide), and an ICD9 diagnostic code and E-code for cause

of death (before 2008) or an ICD10 diagnostic code (after 2008). This database was comprised of all deaths occurring in 1998-2014 of Taiwan citizens (n=2,354,328).

2.1.4 *Maternal and child health database (MCHD)*

The MCHD provides the parent-child linkage for children with Taiwanese citizenship. Each record contains the IDs of each child and the child's parents. This database was developed by Dr. Chung-Yi Li and his team in the Department of Public Health, National Cheng Kung University, during 2015-2016 with the assistance from the Data Center. Dr. Li's group developed the MCHD mainly based on the birth registry held by the Department of Household Registration, supplementing with data from the NHIRD and the birth certificate database. The following paragraphs describe the process of Dr. Li's group's construction of the MCHD of 2004-2011.

In Taiwan, a parent with Taiwanese citizenship is required to register the newborn at a household registration office within 60 days after the child's birth (30 days before 2010). The Department of Household Registration has compiled this data into the birth registry. However, the recorded IDs for foreign parents are sequential numbers assigned by each county; while in the NHIRD and the birth certificate database, the record IDs for foreign parents are foreign IDs. In order to facilitate the linkage across databases, Dr. Li's team employed the following methods to replace the sequential numbers in the birth registry for foreign mothers.[122]

There are 1,558,796 and 1,603,794 children in the birth registry and birth certificate database of 2004-2011, respectively. As a first step, the team compared three common variables in these two datasets: mother's ID, child's birthdate (year/month), and child's birth order. This step yielded 1,405,762 (90.2%) matches. The unmatched records in the birth registry could have had mother's IDs that were sequential numbers so that these records could not been matched to birth certificate records. For these unmatched records, Dr. Li's group tried to find whether the father's ID in the

birth registry was associated with an insured's ID in the registry of beneficiaries and that the relationship variable to the insured was spousal relationship. If so, they compared the insured's birthdate (year and month) with the mother's birthdate in the birth registry. If these two values agreed, they used the insured's ID to replace the mother's ID in the birth registry. This step yielded 67,899 (4.4%) additional matches.

After the above procedures, 85,135 (5.5%) birth registry records remained unreplaced, which were then matched to the birth certificate records on five common variables: birthdates of child and the two parents (year and month), birth location, and gestational age. The research team started from matching on these five variables, then four, and down to one variable. If the result was a one-to-one match across key variables used, then the mother's ID in the birth certificate was used to replace that in the birth registry. This step yielded 81,763 (5.3%) matches. Finally, 3,372 (0.2%) birth registry records didn't match on even one variable. These mothers might have had their IDs recorded incorrectly or have given birth abroad. By contrast, 61,349 (3.8%) of the birth certificate records did not have a match in the birth registry. This could have resulted from stillbirths (17,237 stillbirths), non-Taiwanese children, errors in the recorded variables or errors of the matching process. The MCHD of 2004-2011 was constructed from the modified birth registry of Dr. Li's group work, containing IDs of child and parents. The database has been used to address research questions, on topics such as maternal mortality and maternal and child health.[123,124]

The MCHD used in this study comprised children with Taiwanese citizenship born in 2004-2014 (n=2,171,765) and was also developed by Dr. Li's team. The processes employed to develop this database were similar to those used by Dr. Li's team for development the MCHD of 2004-2011, except that the second strategy required at least three variables matched. The birth registry of 2004-2014 has 11,343 (0.5%) unmatched records.

2.2 LINKAGE BETWEEN DATABASES

2.2.1 *Linkages of other study relevant databases to the registry of beneficiaries of 2000-2014*

This section examines the linkages of the inpatient and ambulatory expenditures databases, the death certificate and birth certificate databases, and the MCHD to the registry of beneficiaries. The registry of beneficiaries of 2000-2014 comprised 29,817,508 unique IDs. Most IDs in the aforementioned databases (95.0-99.6%) could be linked to an ID in the registry of beneficiaries (Table 2-2). A small proportion (0.1-0.3%) of IDs in these databases that could be linked to the registry of beneficiaries had multiple birthdates recorded in the registry of beneficiaries.

Table 2-2 Linkage yield of matching the other study relevant databases to the registry of beneficiaries (2000-2014) using IDs

Database (year)	**Unique ID (N)**	**Linkable (N)**	**%**	**Unlinkable (N)**	**%**
Inpatient expenditures by admission (1998-2014)	14,398,640	14,333,327	99.55	65,313	0.45
Ambulatory care expenditures by visit (1998-2014)	29,483,715	28,005,082	94.98	1,478,633	5.02
Death certificate (1998-2014)	2,353,997	2,329,053	98.94	24,944	1.06
Birth certificate (2004-2014)					
Mother's ID	1,541,646	1,527,324	99.07	14,322	0.93
MCHD (2004-2014)					
Mother's ID	1,500,762	1,491,794	99.40	8,968	0.60
Father's ID	1,439,050	1,417,727	98.52	21,323	1.48
Child’s ID	2,171,731	2,138,166	98.45	33,565	1.55

The percentage (95.0%) of linkable IDs in the ambulatory care expenditures was lower relative to other databases. However, this database spanned from 1998 to 2014, therefore, the registry of beneficiaries which covered the years 2000 to 2014 might not have included the IDs of foreign workers who left Taiwan before 2000 or persons who died before 2000, who used the

outpatient services. The death certificate database included deaths that occurred from 1998 to 2014. In 1998 and 1999, there were 246,901 deaths, of which IDs should not have been identified in the registry of beneficiaries. However, the actual number of IDs in the death certificate database that could not be identified in the registry of beneficiaries was only 24,944. Therefore, some IDs of deceased persons might not have been removed immediately from the registry of beneficiaries during the earlier period of the NHI Program.

In the birth certificate database, 14,322 mother's IDs were not able be linked to the registry of beneficiaries database. The potential reasons for nonlinkages are listed as follows. (1) The mothers had not joined the NHI Program during 2000 to 2014. By regulations, foreign spouses are eligible to join the program when they have a job or stay in Taiwan for ≥ 6 months (≥4 months before 2012). After 2013, national mothers who have been abroad for ≥ 2 years also have to stay in Taiwan for ≥ 6 months to qualify for the NHI Program. Therefore, some mothers might not have been eligible when the child was born. (2) Some of the mothers' IDs were recorded incorrectly.

In the MCHD, 8,968 mother's IDs were not able to be linked to an ID in the registry of beneficiaries. However, 5,647 (63.0%) of these IDs existed in another database (5,636 in the birth certificate database, 9 in the death certificate database; and 1,580 and 1,695 in the inpatient and ambulatory care expenditures databases, respectively). For father's IDs, 21,323 were not able to be linked to the registry of beneficiaries. Among these IDs, 13,970 (65.5%) existed in another database (73 in the death certificate database; and 5,725 and 13,962 in the inpatient and ambulatory care expenditures databases, respectively). The reasons for the nonlinkages to the registry of beneficiaries could be that (1) the parents served in the military or were in prison during 2000-2014; (2) the parents had temporarily or never joined the NHI Program during 2000-2014; (3) some of these IDs were sequential numbers assigned by each county for foreign-born parents,

which had not been replaced in the MCHD; (4) some of these IDs were recorded incorrectly; or (5) very few parents might have changed their IDs.

In the MCHD, 33,565 child IDs were not able to be linked to the registry of beneficiaries. Among these unlinkable IDs, 18,398 (54.8%) existed in another database (3,932 in the death certificate database; and 5,634 and 14,640 in the inpatient and ambulatory care expenditures databases, respectively). The reasons of nonlinkages could be because: (1) the children were born near the end of 2014 and had not been enrolled formally, (2) the children were enrolled as a dependent of their parents who were in the military service or in prison, (3) the children died in the first few months of life, or (4) the children only temporarily or never joined the NHI Program during 2000 to 2014.

2.2.2 *Linkages between the birth certificate database, the MCHD, and the registry of beneficiaries using mother's IDs*

The Taiwanese birth certificate data for the study time period included 2,228,117 livebirth records (one record per infant), of which 9 records were missing mother's ID. The MCHD for the study time period included records for 2,171,731 children, among whom 11,301 were born before 2004. Therefore, the MCHD contained ~67,700 fewer records than the birth certificate database. (The MCHD also had ~63,000 fewer children reported by the Department of Household Registration.[125]) Therefore, some children probably weren't captured in the birth registry. In addition, the number of unique mother's IDs in the MCHD was 40,884 fewer than that in the birth certificate database (Table 2-2).

Most (95.0%) of the birth certificate records for the study time period had a mother's ID that could be linked to both the registry of beneficiaries and the MCHD (Table 2-3); 4.3% only to the registry of beneficiaries; 0.3% only the MCHD; and 0.4% unlinkable to both databases. Among

15,673 records with a mother's ID unlinkable to the registry of beneficiaries, 13,258 IDs were a national ID (defined by the variable ID_ROC_M); and among 105,459 mother's IDs that were unlinkable to the MCHD, 36,745 were a national ID.

Table 2-3 Linkage yield of matching records of livebirths in the birth certificate database to the registry of beneficiaries and the MCHD by using mother's IDs

National ID in the birth certificate#	Linkable to the registry of beneficiaries*	Linkable to the MCHD*	N	%
Y	L	L	2,005,090	89.99
Y	L	N	28,013	1.26
Y	N	L	4,526	0.2
Y	N	N	8,732	0.39
N	L	L	110,663	4.97
N	L	N	68,669	3.08
N	N	L	2,370	0.11
N	N	N	45	0
Missing ID			9	0
Sum			2,228,117	100

This table includes livebirths occurring in Taiwan regardless of citizenship.
Y national ID (defined by the variable ID_ROC_M with a value of 0), N: foreign ID (defined by the variable ID_ROC_M with a value of 1); * L: linkable, N: unlinkable.

The MCHD had 2,171,765 records (one record per child) in which 34 records were duplicated child's IDs, and 1,057 had a missing mother's ID. Most (96.3%) of the records had a mother's ID linkable to both the registry of beneficiaries and the birth certificate database (Table 2-4); 3.0% only to the registry of beneficiaries; 0.3% only the birth certificate; and 0.3% unlinkable to both databases. Among 65,562 records with a mother's ID linkable to the registry of beneficiaries but not the birth certificate, 62,249 were a national ID (defined by the variable ID_ROC). Therefore, in the MCHD, mother's IDs unlinkable to the birth certificate were primarily national IDs; while in the birth certificate, two-thirds of the mother's IDs unlinkable to the MCHD were foreign IDs.

For the 71,623 records in the MCHD with a mother's ID unlinkable to the birth certificate database, most (61,337 [85.6%]) either had a match in the birth certificate database, or the mother's

IDs had been replaced by an ID from the registry of beneficiaries or the birth certificate database (indicated by m_bhp=1, Table 2-4). These findings implied that most of the mother's IDs unlinkable to the birth certificate database were replaced by a different mother's ID from the registry of beneficiaries. Otherwise, these mother's IDs should have been able to be linked to the birth certificate database. Foreign-born parents could have multiple IDs within the registry of beneficiaries and the birth certificate database because their foreign IDs would be changed to national IDs after receiving citizenship. However, the algorithm used to develop the MCHD only retrieved a single ID from the registry of beneficiaries for these foreign mothers. This contributed to the nonlinkages between the MCHD and the birth certificate records.

Table 2-4 Linkage yield of matching records in the MCHD to the registry of beneficiaries and birth certificate records by using mother's IDs

Linkable to the registry of beneficiaries*	Linkable to the birth certificate *	m_bhp	National ID in the registry of beneficiaries#	N	%
L	L	1	Y	1,983,080	91.31
L	L	1	N	109,142	5.03
L	N	1	Y	58,002	2.67
L	N	1	N	3,313	0.15
L	N	0	Y	4,247	0.20
N	L	1	--	6,829	0.31
N	N	0	--	6,039	0.28
N	N	1	--	22	0.00
missing				1,057	0.05
Sum				2,171,731	100

The MCHD was comprised of children with Taiwanese citizenship registered in the birth registry of 2004-2014; and 34 records for duplicated child's IDs were removed from the table.
* L: linkable; N: unlinkable. # Y national ID defined by the variable ID_ROC with a value of 0), N: foreign ID (defined by the variable ID_ROC with a value of 1). m_bhp: 1 represents the following conditions: (1) a birth registry record had a match in the birth certificate database or (2) a mother's ID in the birth registry was replaced by an ID from the registry of beneficiaries or the birth certificate database. 0 indicates a record did not fulfill the above criteria.

2.2.3 *Overall linkages of IDs in the MCHD to the birth certificate and the registry of beneficiaries*

Most (89.6%) of the records in the MCHD had child's and parents' IDs that were linked to the registry of beneficiaries and the birth certificate (Table 2-5). The second largest group (n=82,151 [3.8%]) had missing father's IDs, which probably resulted from extra-marital births. According to the official figures,[125] 33,481 children born out of wedlock were acknowledged by their biological fathers; therefore, some of the missing father's IDs were retrievable from the registry of beneficiaries by using the relationship between the insured and the enrollee. As for the third largest group, 64,161 (2.9%) records had a mother's ID linkable to the registry of beneficiaries but not the birth certificate database. This group probably resulted from the above-mentioned issue related with the algorithm to develop the MCHD.

The fourth largest group (n=34,528 [1.6%]) had a father's ID unlinkable to the registry of beneficiaries. Among this group, 10,179 children had a father's ID that was the same as the mother's ID in the MCHD; and of these fathers' IDs, 72.4% were associated with ≥ 5 children. In addition, most of these father's IDs were associated with multiple mother's IDs. Therefore, we suspected that some of these unlinkable father's IDs were sequential numbers for foreigners assigned by counties. Identical sequential numbers were probably used by different counties, which caused the above phenomena. (The website of Department of Household Registration reported that 20,298 infants born in 2004-2014 had foreign-born fathers[125]). The fifth largest group (n=23,941 [1.1%]) had child's IDs unlinkable to the registry of beneficiaries. These children might have been born near the end of 2014, never joined the program during 2004-2014, or died in the first few months of life.

Totally, the MCHD had 1,057 (0.1%) and 86,780 (4.0%) records with a missing mother's and father's ID, respectively (Table 2-5). Overall, 13,960 (0.6%) and 127,772 (5.9%) children could

not have their maternal and paternal data, respectively, retrieved from the registry of beneficiaries; and 72,692 (3.4%) could not have their data retrieved from the birth certificate database using their mother's ID.

Table 2-5 Linkage yield of matching records in the MCHD to the registry of beneficiaries and birth certificate records using child's and parents' IDs

Child's ID*	enrol_c	Mother's ID*	enrol_m	birth_m	Father's ID*	enrol_f	N	%
Y	L	Y	L	L	Y	L	1,944,470	89.58
Y	L	Y	L	L			82,151	3.77
Y	L	Y	L		Y	L	64,161	2.93
Y	L	Y	L	L	Y		34,528	1.59
Y		Y	L	L	Y	L	23,941	1.10
Y		Y	L	L	Y		5,258	0.24
Y	L	Y		L	Y	L	4,929	0.22
Y	L	Y			Y	L	4,753	0.22
Y		Y	L	L			1,894	0.09
Y	L	Y					1,101	0.05
Y		Y		L	Y		1,002	0.05
Y	L	Y	L				852	0.04
Y		Y		L	Y	L	758	0.03
Y	L				Y	L	519	0.02
Y	L						486	0.02
Y		Y	L		Y	L	349	0.02
Y	L	Y	L		Y		112	0.01
Y		Y			Y	L	110	0.01
Y		Y					83	0
Y	L	Y		L			81	0
Y		Y	L				62	0
Y							45	0
Y	L	Y		L	Y		36	0
Y		Y	L		Y		27	0
Y		Y		L			25	0
Y	L	Y			Y		18	0
Y		Y			Y		7	0
Y					Y	L	3	0
Y	L/				Y		4	0
Sum							2,171,765	100.00

The MCHD is comprised of children with Taiwanese citizenship who had been registered in the birth registry of 2004-2014.

* Y: not missing, blank: missing. enrol_c, enrol_m, enrol_f: whether child's ID, mother's ID, father's ID, respectively, could be linked to an ID in the registry of beneficiaries; and birth_m: whether a mother's ID could be linked to the birth certificate database (L: linkable; blank: unlinkable).

2.3 RETRIEVAL OF CHILD-PARENT PAIRS FORM THE REGISTRY OF BENEFICIARIES

2.3.1 *Retrieval process*

This section describes the process of retrieving child-parent pairs from the registry of beneficiaries. According to the National Health Insurance Law, children and unemployed married persons must join the NHI Program as dependents of their parents and spouses, respectively, except in some uncommon circumstances. The registry of beneficiaries contains a variable "category of dependent" specifying the relationship between the insured and the enrollee. Accordingly, a child-parent (or spouse) relationship can be determined if a child (or a spouse) has been enrolled in the program as a dependent. Therefore, in the first step, we retrieved spouse and child-parent pairs from the registry of beneficiaries of 2000-2014 based on the values specified in the variable "category of dependent."

The official online data showed that 110,386 females and 8,013 males had changed their Taiwanese citizenship status in 2000-2014. Foreign-born parents could have multiple IDs in the registry of beneficiaries and the birth certificate database because their initial foreign IDs would be changed to national IDs after receiving citizenship. We used the following method to handle foreign-born parents with multiple IDs. Among the retrieved spouse and child-parent pairs, if an ID was associated with multiple IDs documented as spouse (or as father/mother) and all these IDs had the same birthdate, then these multiple IDs were considered to belong to the same person. We created a unique indicator for these multiple IDs. There were 172,958 female and 13,471 male indicators associated with multiple IDs. Most of these IDs that apparently belonged to the same person did not occur in the registry of beneficiaries for a given year. In the registry of beneficiaries, the sex is recorded as unknown (value: 9) for a foreign ID. We employed several pieces of information to help determine the sex for these IDs: the sex of the other person in the spouse pairs,

whether the ID existed as a mother's ID in the birth certificate database, and whether the ID was part of multiple IDs belonging to a same person.

Two different deterministic linkage methods were used to form complete mother-father-child triads. In the first method, the spouse pairs were first linked to the birth certificate to retrieve their children's birthdates by matching on mother's ID and father's birthdate (year/month). Then these matched records were linked to the child-parent pairs by matching on parent's ID and child's birthdate (year/month). The triads retrieved by this method would include children fulfilling all the following criteria: (1) having been enrolled as a dependent of either one of the parents, (2) whose mother also had been enrolled together with the father, (3) whose birth was recorded in the birth certificate database, and (4) the recorded child's and father's birthdates in the registry of beneficiaries were the same as those in the birth certificate database. In the second method, the father-child pairs and mother-child pairs in the registry of beneficiaries were matched on child's ID. These triads consist of children having been enrolled as a dependent of the mother and as a dependent of the father at different time points.

Among the retrieved child-parent pairs, if a child ID was associated with multiple mother's (or father's) IDs, and the birthdates of these parents' IDs were different, then the parent's IDs of the parent-child pairs that appeared later in the registry of beneficiaries were removed. The later-appearing parent's IDs could be stepparent's IDs. Finally, the parent-child pairs/triads of interest were restricted to children born between 2004-2014.

2.3.2 *Results of retrieval*

From the registry of beneficiaries, we retrieved 2,225,067 children with Taiwanese citizenship (defined by the variable ID_ROC with a value of 0) and born between 2004-2014. Among these children, 1,552 were not associated with any parent's ID, and 110,941 had multiple parents' IDs

(Table 2-6). In total, 2,348,413 parent-child pairs/triads were recovered from the registry of beneficiaries. About 45.2% of these pairs/triads were obtained by matching the spouse pairs, the parent-child pairs, and the birth certificate records; 10.0% were obtained by directly matching on child's IDs; and 41.3% only have either father or mother's IDs retrieved from the registry of beneficiaries (Table 2-7).

Table 2-6 Number of parent's IDs retrieved from the registry of beneficiaries for each child

Number of retrieved mother's IDs	Number of children	%	Number of retrieved father's IDs	Number of children	%
1	1,777,679	94.34	1	1,593,286	99.70
2	94,051	4.99	2	4,562	0.29
3	11,803	0.63	3	190	0.01
4	683	0.04	4	10	0.00
5	31	0.00	5	5	0.00
Sum	1,884,247	100.00	Sum	1,598,053	100.00

Table 2-7 Number of parent-child pairs/triads retrieved by each retrieval source

Sources of parent-child pairs/triads retrieved	N	%
Mother-father-child triads obtained by matching spouse and parent-child pairs and birth certificate	1,061,885	45.22
Mother-father-child triads obtained by matching on child's ID between father-child and mother-child pairs	234,518	9.99
Mother-child pairs only	629,350	26.80
Father-child pairs only	339,786	14.47
Mother-child pairs generated by using multiple IDs belonging to a same person	81,636	3.48
Father-child pairs generated by using multiple IDs belonging to a same person	1,238	0.05
Sum	2,348,413	100.00

2.3.3 *Comparing parent-child pairs between the MCHD and the registry of beneficiaries*

There were 2,282,532 children associated with at least one parent's ID in the MCHD and/or the registry of beneficiaries. Most of the child's IDs (2,112,714 [92.6%]) existed both in the MCHD and the registry of beneficiaries; and 59,017 (2.6%) and 110,801 (4.9%) only in the MCHD

and only in the registry of beneficiaries, respectively. Among the child's IDs only existing in the MCHD, 33,565 (56.9%) could not be linked to the registry of beneficiaries, and 11,301 (19.1%) were associated with a date of birth earlier than 2004. (The date of birth was retrieved from the registry of beneficiaries.) For the child's IDs only existing in the registry of beneficiaries, 38,185 (34.5%) had both mother's and father's IDs retrieved from the registry of beneficiaries, 38,105 (34.4%) only had mother's IDs, and 34,511 (31.1%) only had father's IDs.

The parent's IDs in the MCHD were compared with those in the registry of beneficiaries (Table 2-8). For child's IDs with a missing parent's ID in the MCHD, 610 and 25,870 had mother's and father's IDs, respectively, retrieved from the registry of beneficiaries. Among child's IDs in the MCHD, 78.1% had a single retrieved mother's ID agreeing with that in the MCHD; 4.7% had multiple retrieved mother's IDs of which one was the same as that in the MCHD; and only 0.4% had different mother's IDs. As for father's IDs, 68.4% of child's IDs had a single retrieved father's ID agreeing with that in the MCHD; 0.1% had multiple father's IDs of which one was the same as that in the MCHD; and only 0.5% had different father's IDs. Overall, parents' IDs retrieved from the registry of beneficiaries were highly concordant with parent's IDs in the MCHD were: 99.5% and 99.2% of the retrieved mother's and father's IDs were the same as those in the MCHD.

About 16.7% and 27.0% of child's IDs failed to retrieve a mother's ID and father's ID respectively, from the registry of beneficiaries. The percentage of the former was smaller than the latter, which was because a child was more likely to be enrolled as a dependent of the parent who had a lower salary. These percentages were lower than the estimates reported in previous research,[122,126] in which 59% and 49% of children could not be linked to their mothers and fathers, respectively. The lower percentages in the current study are probably because (1) the registry of beneficiaries used covered longer time periods, and (2) father's and child's birthdates and the birth

certificate records were also employed in forming mother-father-child triads. The latter strategy helped capture the mother-child relationship when both the child and the mother were enrolled as a dependent of the father.

Table 2-8 Results of comparing parents' IDs in the parent-child pairs between the MCHD and the registry of beneficiaries

Results of comparison		**Mother's ID**		**Father's ID**	
		Number of children	%	Number of children	%
ID is missing in both data sources		447	0.02	60,909	2.80
No ID retrieved from the registry of beneficiaries		363,327	16.73	585,470	26.96
Single ID retrieved from the registry of beneficiaries	ID is missing in the MCHD	552	0.03	25,718	1.18
	ID is different in two data sources	6,570	0.30	10,385	0.48
	ID is the same in two data sources	1,696,461	78.12	1,484,679	68.36
Multiple IDs retrieved from the registry of beneficiaries	ID is missing in the MCHD	58	0.00	152	0.01
	The retrieved IDs are different from that in the MCHD	3,063	0.14	1,307	0.06
	One of the retrieved IDs is the same as that in the MCHD	101,253	4.66	3,111	0.14
Sum		2,171,731	100.00	2,171,731	100.00

Table 2-9 summarizes the pattern of linkages of mother's ID stratified by comparison results. Among 12,887 children with a mother's ID in the MCHD unlinkable to the registry of beneficiaries, most of the single retrieved mother's IDs and half of the multiple retrieved IDs were foreign IDs. So, a substantial proportion of these unlinkable mother's IDs were sequential numbers of foreign mothers that had not been replaced. Among 101,253 children with multiple retrieved mother's IDs in which one of them was the same as that in the MCHD, most (94.8%) of the other retrieved mother's IDs denoted different nationality, i.e., the mother's ID in the MCHD was a national ID, and the other retrieved ID was a foreign ID. This indicated that the mother had undergone a status change from 2000-2014.

Table 2-9 Numbers of mother's IDs in the MCHD that were foreign ID and unlinkable to the registry of beneficiaries and the birth certificate database stratified by comparison results

Comparison result		N	ID in the MCHD			ID from the registry of beneficiaries
			Foreign ID*	Unlinkable to registry of beneficiaries	Unlinkable to birth certificate	Unlinkable to birth certificate
ID is missing in both data sources		447	--	--	--	--
No ID retrieved from the registry of beneficiaries		363,327	7,119	8,327	12,319	--
Single ID retrieved from the registry of beneficiaries	ID is missing in the MCHD	552	--	--	--	93
	ID is different in two data sources	6,570	946	1,986	2,535	3,526
	ID is the same in two data sources	1,696,461	80,363	0	482	473
Multiple IDs retrieved from the registry of beneficiaries	ID is missing in the MCHD	58	--	--	--	4#
	The retrieved IDs are different from that in the MCHD	3,063	107	2,574	2,655	168#
	One of the retrieved IDs is the same as that in the MCHD	101,253	23,925	0	53,644	910#
Sum		2,171,731	112,460	12,887	71,635	5,174

Number of children with multiple IDs in which none of them could be linked to the birth certificate
*Foreign ID: defined by the variable ID_ROC with a value of 1.

Among the 71,635 child's IDs with a mother's ID in the MCHD unlinkable to the birth certificate database, 57,528 (80.3%) of the retrieved mother's IDs were linked to the birth certificate database. This implies that some foreign-born mothers had their sequential number replaced by an ID that was not the one at the child's birth. Overall, using retrieved mother's IDs from the registry of beneficiaries could lower the number of children with a missing mother's ID or ID unlinkable to the registry of beneficiaries from 13,944 to 8,774 and a mother's ID unlinkable to the birth certificate database from 71,635 to 14,107.

As for father's IDs in the MCHD, the IDs linkable to the registry of beneficiaries were all national IDs. Among child's IDs with father's IDs in the MCHD unlinkable to the registry of beneficiaries, most of the father's IDs retrieved from the registry of beneficiaries were foreign IDs. Overall, using retrieved father's IDs from the registry of beneficiaries could lower the number of children with missing father's ID or a father's ID unlinkable to the registry of beneficiaries from 126,431 to 93,037 (Table 2-10).

Table 2-10 Numbers of father's IDs in the MCHD that were foreign ID and unlinkable to the registry of beneficiaries stratified by comparison results

Comparison result		N	ID in the MCHD	
			Unlinkable to registry of beneficiaries	Foreign ID*
ID is missing in both data sources		60,909	--	--
No ID retrieved from the registry of beneficiaries		585,470	32,128	0
Single ID retrieved from the registry of beneficiaries	ID is missing in the MCHD	25,718	--	--
	ID is different in two data sources	10,385	7,524	0
	ID is the same in two data sources	1,484,679	0	0
Multiple IDs retrieved from the registry of beneficiaries	ID is missing in the MCHD	152	--	--
	The retrieved IDs are different from that in the MCHD	1,307	0	0
	One of the retrieved IDs is the same as that in the MCHD	3,111	0	0
Sum		2,171,731	39,652	0

*Foreign ID: defined by the variable ID_ROC with a value of 1.

2.4 CONSTRUCTION OF STUDY POPULATION

This section describes the data sources for constructing the study population, the data linkage methods between parent-child pairs/triads and the birth certificate database, and the final linkages of the parent-child pairs/triads.

2.4.1 *Data sources*

Three data sources were used to construct the study population: the parent-child pairs/triads in the MCHD, the parent-child pairs/triads retrieved from the registry of beneficiaries, and the birth certificate database. Table 2-11 briefly describes characteristics of children in terms of birth years, health insurance enrollment, and nationality in each data source. The sample frame for the study population was children (1) with Taiwan citizenship, (2) born 2004-2014, and (3) included either in the MCHD or the registry of beneficiaries.

Table 2-11 Data sources for constructing the study population

The dark yellow color indicates children with Taiwan citizenship and born 2004-2014.

(1) Parent-child pairs/triads in the MCHD

<table>
<tr><td colspan="2">Children with Taiwan citizenship born between 2004-2014 and enrolled in the NHI program during 2004-2014
N=2,126,865</td><td rowspan="2">Children with Taiwan citizenship but not enrolled in the NHI program during 2004-2014
(unknown children's birthdates)

N=33,565</td><td rowspan="2">Children with Taiwan citizenship born before 2004

N=11,301</td></tr>
<tr><td>Children having been enrolled as a dependent of one of the parents
N=2,112,714</td><td>Children having not been enrolled as a dependent of one of the parents
N=14,151</td></tr>
</table>

Birthdates for child's and parent's IDs in the MCHD were extracted from the registry of beneficiaries.

(2) Parent-child pairs/triads retrieved from the registry of beneficiaries

<table>
<tr><td colspan="2">Children with Taiwan citizenship born during 2004-2014 who had been enrolled as a dependent of one of the parents in the NHI program.
N=2,223,515</td><td rowspan="2">Children (1) had Taiwan citizenship, (2) were born during 2004-2014, (3) had not been enrolled as a dependent of one of the parents in the NHI program, and (4) were not included in the MCHD.
N=1,552</td></tr>
<tr><td>Child's IDs included in the MCHD
N=2,112,714</td><td>Child's IDs not included in the MCHD
N=110,801</td></tr>
</table>

(3) Birth certificate

<table>
<tr><td>Live-born infants with Taiwan citizenship born in 2004-2014

N=2,225,131</td><td>Live-born infants without Taiwan citizenship#
N=2,977</td><td>Stillbirths

N=24,456</td></tr>
</table>

defined by two variables in the birth certificate: 1. mother's ID was foreign ID (the variable ID_ROC_M), and 2. father's original nationality was non-Taiwanese

2.4.2 *Data linkage methods*

Exact deterministic linkage was used to match records between the parent-child pairs/triads in the MCHD and/or the registry of beneficiaries and the birth certificate database. We first performed the linking by matching on mother's ID, child's birthdate, child sex, and father's birthdate; and then by matching on mother's ID, child's birthdate, child sex for the remaining unmatched records. For child's IDs in the MCHD that could not retrieve their birthdates from the registry of beneficiaries (n=33,565), we first used mother's ID and father's birthdate as the key variables to link the data. For the remaining unmatched records, the child's birth year was estimated from the variables "visit date" and "age" in the inpatient and ambulatory care expenditure datasets; and child's death year was estimated from the variable "date of death" in the death certificate database. Then we used mother's ID, child's birth year (or death year), and/or father's birthdate as the key variables.

For child's IDs existing in the MCHD, if their father's IDs in the MCHD were missing or could not be linked to the registry of beneficiaries, the birthdates of the father's IDs retrieved from the registry of beneficiaries were employed in the above matching process. Similarly, if child's IDs could not be matched to birth certificate records by using their mother's IDs in the MCHD, the retrieved mother's ID from the registry of beneficiaries was used as the key variable.

In the linking process, if the following two conditions were met, then the records were considered unmatched: (1) if a child's ID was matched to different birth events, or (2) the number of child's IDs in a birth event was larger than that of records in a birth event. These two conditions mostly occurred in the situation when children's birthdates were missing, and mother's ID and father's birthdate were used as the key variables.

2.4.3 *Results of matching parent-child pairs/triads to birth certificate records*

Table 2-12 provides numbers of parent-child pairs/triads matched to a birth certificate record in each matching step. Most (90.8%) of the matched records were obtained by matching on mother's ID, child's birthdate, child sex, and father's birthdate. For the records matched on mother's ID, child's birthdate and child sex, 98.6% were missing father's birthdate in either the birth certificate or the registry of beneficiaries. Overall, 96.8% of parent-child pairs/triads had a matched birth certificate record; and 98.7% of livebirth records in the birth certificate database had a matched parent-child pairs/triad.

Table 2-12 Number of parent-child pairs/triads in the MCHD and/or the registry of beneficiaries matched to a birth certificate record by key variables

Key variables used in matching	**Child's ID existing both in the registry of beneficiaries and the MCHD**	**Child's ID only existing in the MCHD**	**Child's ID only existing in the registry of beneficiaries**
Child's birthdate retrieved from the registry of beneficiaries			
Mother's ID, child's birthdate, child sex, and father's birthdate	1,959,172	5,443	31,053
Mother's ID, child's birthdate, child sex	143,299	8,439	23,277
Child's birthdate unknown			
Mother's ID and father's birthdate		17,655	
Mother's ID, child's birth year*, father's birthdate		3,876	
Mother's ID, child's death year*, father's birthdate		200	
Mother's ID, child's birth year*		5,841	
Mother's ID, child's death year*		563	
Sum of matched records	**2,102,471**	**42,017**	**54,330**
Unmatched records	**10,243**	**5,699**	**56,471**

*The child's birth year was estimated from the visit date and age variable in the inpatient/outpatient data; and child's death year the date of death in the death certificate.

Table 2-13 lists numbers of matched records in the MCHD by group as well as father's birthdates or mother's IDs retrieved from the registry of beneficiaries that were used to obtain a matched record. (The group assignment is specified in Table 2-5). In Group 1, when the mother's IDs in the MCHD were used in the linking process, 9,459 mother-father-child triads could not be linked to a birth certificate record even when these mother's IDs existed in the birth certificate database. So, another 6,422 triads were matched by using the mother's IDs retrieved from the registry of beneficiaries. This was due to the issue of multiple IDs owned by foreign-born mothers. For example, a mother could have her foreign ID registered in the birth certificate for the first child and her national ID registered for the second child. If the MCHD developers selected her national ID number, using this ID could not have achieved a matched birth certificate record for the first child even when this ID could be linked to the birth certificate database.

Table 2-13 Number of MCHD records matched to a birth certificate record by group and number of matches by using mother's ID or father's birthdate retrieved from the registry of beneficiaries

Group	N#	Matched records	%	Matched by using retrieved mother's ID*	Matched by using retrieved father's birthdate*
1	1,940,664	1,937,627	99.84	6,422	
2	81,569	81,420	99.82	18	24,678
3	58,574	53,155	90.75	53,155	
4	34,453	34,412	99.88	4	8,770
5	23,941	21,197	88.55	22	
Other	21,229	16,677	78.56	4,760	19
Sum	**2,160,430**	**2,144,488**	**99.26**	**64,381**	**33,467**

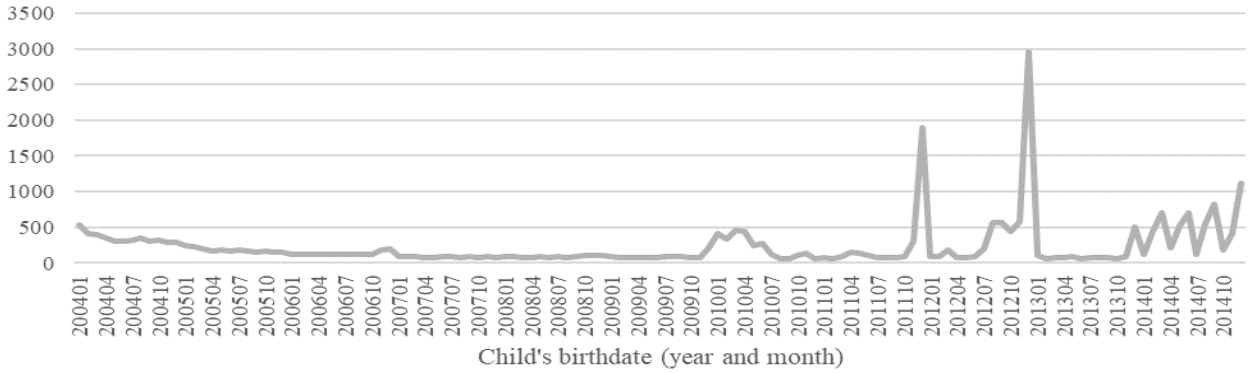
Group assignment is specified in Table 2-5.
Children born before 2004 had been removed from each group.
* Number of records in which a mother's ID (father's birthdate) in the parent-child pairs retrieved from the registry of beneficiaries was used to obtain a matched record.

In Group 3, the mother's IDs in the MCHD could not be linked to the birth certificate database, and thus 90.8% of the triads were matched by using the retrieved mother's IDs. Among the 21,197

matched records in Group 5 in which a child's birthdate could not be retrieved from the registry of beneficiaries, 43.8% had a child's birthdate between 2004 and 2013 in the birth certificate database, 10.2% between Jan. 2014 and Oct. 2014, and 46.0% had a child's birthdate between Nov. 2014 and Dec. 2014. Therefore, approximately half of the children who were born in Nov. or Dec 2014, could be assumed to have been covered under their parent's insurance. Overall, 99.3% of the child's IDs in the MCHD were matched to a birth certificate record.

Among the child's IDs in the MCHD, the main factors causing nonlinkages were mother's IDs unlinkable to birth certificate records (n=7,903 [49.6%]) and missing child's birthdates (n=5,034 [31.6%]). By contrast, for the child's IDs retrieved from the registry of beneficiaries, the main reasons causing nonlinkages were missing mother's IDs (n=34,517) and mother's IDs that were unlinkable to the birth certificate database (n=17,074). In the birth certificate database, 0.8% and 7.2% of records with national and foreign mother's IDs, respectively, were unmatched. Calendar time also seems to have had effects on matching (Figure 2-1). Approximately 5,000 children born in Dec 2012 or Dec 2013 were unmatched, which might be due to administrative errors in registering newborns born around the end of calendar year; and children born in 2014 could have not yet been enrolled in the NHI Program or registered in the birth registry.

Figure 2-1 Number of unmatched records in the birth certificate database by child's birthdate



2.4.4 *Linkages between parent-child pairs/triads in the MCHD and/or the registry of beneficiaries and birth certificate records*

Among the parent-child pairs/triads with a matched birth certificate record, if a child's ID was associated with multiple father's (or mother's) IDs that had different birthdates, we only kept the father's (or mother's) IDs that had the same birthdate as that in the birth certificate record. If the multiple mother's IDs had the same birthdate, but these IDs co-existed in more than 30 datasets of the registry of beneficiaries, we also only kept the mother's IDs that existed in the birth certificate. In total, there were 2,272,783 unique child's IDs, 1,535,873 unique mother's IDs, and 1,493,683 unique father's IDs. Table 2-14 summarizes number of parent's IDs retrieved from the MCHD and/or the registry of beneficiaries for each child after the above processes. Very few children had multiple father's IDs, and most (98.4%) of the children with multiple mother's IDs were ultimately found to involve foreign-born mothers.

Table 2-14 Final number of parent's IDs retrieved from the MCHD and/or the registry of beneficiaries for each child

Number of mother's IDs	**Number of children**	**%**	**Number of father's IDs**	**Number of children**	**%**
1	2,125,027	95.02	1	2,169,843	99.82
2	97,452	4.36	2	3,754	0.17
3	13,169	0.59	3	184	0.01
4	713	0.03	4	11	0.00
5	18	0.00	5	4	0.00
Sum	2,236,379	100.00	Sum	2,173,796	100.00

Most (90.7%) of the parent-child pairs/triads had child's and parents' IDs that were linked to the registry of beneficiaries and a matched birth record (Table 2-15). The second largest group had a missing father's ID, of which 74.5% had a missing father's birthdate on the birth certificate records. This indicates that most of these children were likely born outside marriage. The third largest group among the matched records had a father ID unlinkable to the registry of beneficiaries.

In this group, 94.7% had a father's birthdate recorded on the birth certificate. This implies that these children were born within marriage; and these fathers could have served in the military, been in prison, been a non-Taiwan national, or temporarily or never been enrolled in the NHI Program.

Table 2-15 Linkage between parent-child pairs/triads exited in the MCHD and/or the registry of beneficiaries and birth certificate records

Matched birth record*	Child's ID#	link_c%	Mother's ID#	link_m%	Father's ID#	link_f%	N	%
Y	Y	L	Y	L	Y	L	2,060,420	90.72
Y	Y	L	Y	L			79,637	3.51
Y	Y	L	Y	L	Y		25,598	1.13
Y	Y		Y	L	Y	L	21,262	0.94
Y	Y	L	Y		Y	L	4,998	0.22
Y	Y		Y	L	Y		4,689	0.21
Y	Y		Y		Y		952	0.04
Y	Y		Y		Y	L	732	0.03
Y	Y		Y	L			487	0.02
Y	Y	L	Y		Y		23	0.00
Y	Y		Y				13	0.00
Y	Y	L	Y				7	0.00
	Y	L			Y	L	34,710	1.53
	Y	L	Y	L			15,562	0.69
	Y	L	Y	L	Y	L	15,398	0.68
	Y		Y	L	Y	L	3,018	0.13
	Y		Y	L			1,469	0.06
	Y	L	Y		Y	L	1,154	0.05
	Y		Y	L	Y		599	0.03
	Y		Y		Y	L	135	0.01
	Y		Y				95	0.00
	Y	L					85	0.00
	Y		Y		Y		58	0.00
	Y						45	0.00
	Y	L	Y	L	Y		38	0.00
	Y	L	Y				35	0.00
	Y				Y	L	9	0.00
	Y	L/			Y		3	0.00
Sum							2,271,231	100.00

* Whether a child-parent pair/triad had a matched birth certificate record (Y: yes; N: no)
# Whether a child's ID, mother's ID and father's ID existed in the MCHD and/or the registry of beneficiaries. (Y: yes; blank: no)
% link_c, link_m, link_f: whether child's ID, mother's ID, father's ID, respectively, could be linked to the registry of beneficiaries (L: yes; blank: no)
Children without any parent's IDs (n=1,552) were not listed in the above table.

2.4.5 *Final study population*

The study population was restricted to children with complete health data for themselves and their parents as well as data from the birth certificate (n=2,060,420 the top row in Table 2-15). In addition, we further limited the study cohort to singleton births (n=1,999,322) for the following reasons: (1) For the same-sex multiples, it was difficult to assign birthweight because there was no indicator of birth order for each child's ID in the MCHD and/or the registry of beneficiaries; (2) Multiples have the same birthdate, therefore, it was challenging to retrieve health service data of the early months of child age that could have been under parent's insurance coverage, since child's birthdate was used as a key variable; and (3) Singletons and multiples tend to vary in characteristics and outcomes. For example, twins/multiples have been shown to have greater risk of infant mortality[127], pneumonia[128], and injury[129]. The final study population consisted of 1,999,322 children, 1,396,277 mothers, and 1,401,863 fathers.

2.5 RETRIEVING CHILD'S HEALTH RECORDS UNDER THE PARENTS' COVERAGE

Infants with Taiwanese citizenship can be covered by their parents' insurance for 60 days before joining the NHI program. In this situation, the infants' claims data are associated with their parent's ID, instead of the infant's ID. The following method was adopted to retrieve infants' inpatient/outpatient data under their parents' coverage. We first used parents' ID, ICD-9-CM diagnosis code for newborns and neonates (760-779), coverage indicator (copayment code: 902 and 903), and the age variable ("0-14 days","15-28 days","29 days-less than one year") to retrieve records that belonged to infants. Then, if the visit/admission date of a record was between 30 days prior to and 90 days after the child's birthdate, the child's ID was assigned to that record. We used a slightly longer interval because some children couldn't have their birthdate retrieved from the registry of beneficiaries, and the birthdates retrieved from the birth certificate only have the year

and month components. Table 2-16 summarizes numbers of records retrieved from parent's claims data and records finally assigned with a child's ID (separated for singletons and multiples). For singleton births, most of the records were successfully assigned to a child's ID (Table 2-16).

Table 2-16 Numbers of records retrieved from parents' data and assigned with a child's ID

Data sources		Records retrieved from parent's ID	Records matched to child's ID	
			Singletons	Multiples*
Ambulatory care expenditures by visit	Father	52,495	49,880	2,590
	Mother	3,106,795	2,982,993	155,200
Inpatient expenditures by admission	Father	10,560	10,140	757
	Mother	442,607	409,284	57,528

*Figures for multiples were inflated because the records could not be assigned exactly to a child's ID.

2.6 MEASURES

2.6.1 *Exposure variables*

The exposure of interest was parental SMI, including schizophrenia, bipolar disorder and MDD. We first retrieved all inpatient and outpatient records in the NHIRD with a psychiatric diagnosis (ICD-9-CM: 290-319) by using the father's and mother's ID as the key variables. For children with multiple parent's IDs, we evaluated the time sequence of appearance of these IDs in the retrieved records. For example, between records of different dates of visit that were associated with the same parent ID, we examined whether there was any record that was associated with another parent ID. There were few such records associated with out-of-order appearance of parent's IDs (106 maternal records and 15 paternal records).

We then identified all records with SMI with the visit date in the period from 6 years prior to childbirth to 5 years following childbirth, using ICD-9-CM codes (Table 2-17). A disorder was defined by a diagnosis made at least once by a psychiatrist or twice by a non-psychiatrist physician.

The hierarchy of diagnosis was determined by the conventional diagnostic hierarchy (schizophrenia > bipolar disorder > MDD) and sources of diagnosis (psychiatrist> non-psychiatric physician). For example, one diagnosis of bipolar disorder from a non-psychiatric physician and two diagnoses of MDD from a psychiatrist would lead to a classification of MDD. But one diagnosis of bipolar disorder from a psychiatrist would lead to a diagnosis of bipolar disorder.

Table 2-17 Definitions of exposure variables: parent's serious mental illness (SMI)

Variable	Type	Classification of variable
Primary analyses *(1)* Parental SMI	Binary	SMI includes schizophrenia, bipolar disorder and major depressive disorder (MDD). ICD-9-CM codes: schizophrenia: 295, 297, 298.3, 298.4, 298.9; bipolar disorder: 296.00-296.16, 296.40- 296.81, 296.89-296.99, 298.1, 648.4; and MDD: 296.20-296.36, 296.82, 298.0 The value of SMI was positive after the date of onset for maternal or paternal SMI, whichever came first.
Secondary analyses *(2)* Parent(s) with SMI	Categorical	Four mutually exclusive categories: none, maternal, paternal, and both. If only one parent had SMI, the value was "maternal" or "paternal" after the date of onset for maternal or paternal SMI, respectively. If both parents had SMI, the value was changed to "both" after the date when both parents had SMI.
(3) Time of onset of maternal/paternal SMI	Categorical	Three mutually exclusive categories: none, before childbirth, and after childbirth. This variable was created separately for maternal and paternal SMI. If the date of onset occurred prior to childbirth, the value was "before childbirth"; otherwise, the value was "after childbirth" from the date of onset.
(4) Type of diagnosis for maternal/paternal SMI	Categorical	Four mutually exclusive categories: none, schizophrenia, bipolar disorder, and MDD. This variable was created separately for maternal and paternal SMI. The value was assigned with a certain diagnosis after the date of onset.

The *date of onset* was defined as the date of the first recorded visit with a code for a SMI. We derived four time-dependent exposure variables from the maternal/paternal diagnosis and the date of onset (Table 2-17). For the primary analyses, the exposure variable was presence of SMI of either parent (binary). If the onset of parental SMI was prior to the child's birth, the child was

classified as exposed from birth to 5 years. Otherwise, the child was considered unexposed until the date of onset of parental SMI. For secondary analyses, we expanded the exposure variable in three ways. We compared child health outcomes for exposure groups based on (1) number and identity of parent(s) with SMI: none, maternal only, paternal only, and both; (2) timing of onset of maternal/paternal SMI: none, before childbirth, and after childbirth, and (3) diagnosis for maternal/paternal SMI: none, schizophrenia, bipolar disorder, and MDD.

2.6.2 *Outcomes of interest*

The outcomes of interest were health care encounters for injury, and common infectious disease (diarrhea or respiratory infection) occurring in children < 5 years (measured by ICD-9-CM codes, see Table 2-18). We identified children's outpatient/inpatient records containing these ICD-9 codes. Since a child may seek medical care multiple times for the same problem, we generated episodes of illness excluding repeat visits with the same diagnostic category within a period of time. Compared to number of episodes, number of clinic visits would be more likely to be influenced by parent's healthcare-seeking behavior, doctor's practicing habits, and types and severity of illnesses.

A single injury event comprised all successive visits of the same injury type[130] in which an interval between two visits was < 90 days. A single injury event could include several injury types. To account for multiple injury types resulting from a single event, a new injury type recorded within 7 days of an initial injury event was considered as the same injury event when creating overall injury events.[130] A 90-day interval was used in this project rather than the 180-day interval adopted in other studies[130,131] because young children usually recovery quickly relative to older children and adults[132]. For example, most healing of child fractures is evident within 3 months.[133,134] S-Figure 1 presents distributions of the interval between two claims by injury types.

The frequencies of new claims per week after 12 weeks (about 90 days) also became relatively stable for most injury types. For each injury event, we created variables indicating whether inpatient services or emergency department had been utilized as well as whether a surgery or procedure had been performed (measured from ICD9-CM procedure codes). Emergency room visit was defined as a record associated with a value of emergency medicine in the variable department type (FUNC_TYPE). We also estimated number of care visits related to each event. For the inpatient records containing injury diagnosis codes, we also retrieved external causes of injury codes (ICD-9-CM E-codes, see Table 2-18).

Episodes of common infectious disease were identified by screening all outpatient/inpatient records after delivery through 5 years of life, excluding successive visits after an initial visit with between-visit intervals of < 14 days. This interval was decided based on the clinical courses of these diseases.[135–137] We also created a variable indicating whether antibiotics were prescribed during an episode. To create this variable, we retrieved details of inpatient/ambulatory care orders associated with records of diarrhea or respiratory infection. Each medication covered by the NHI has a drug code that can be mapped to an Anatomical Therapeutic Chemical (ATC) code. We identified ATC codes of antibiotics and converted them to NHI drug codes. Finally, we screened details of care orders of all episodes in order to ascertain the presence of drug codes of antibiotics. For each episode of common infectious disease, we also created variables indicating whether inpatient or emergency department services had been utilized during that episode. In addition, we estimated number of care visits for each episode. Visits on the same day were counted once.

To account for differential parent healthcare-seeking behavior, we also evaluated child outcomes requiring hospitalization, as well as antibiotics-treated common infectious disease.

Differences in help-seeking behavior would be less likely to affect help-seeking for more severe illnesses, such as those resulting in hospitalization.

Table 2-18 ICD-9-CM codes used to define outcomes of interest

Variable	Diagnosis codes
Episodes of child common infectious disease	**ICD-9-CM codes** Diarrhea: 001-009, 5589, 78791 Respiratory infection: 460-466; 480-488
Events of child injury	**ICD-9-CM codes** Injury: 800-999, excluding 905–909.9 (late effects), 958–958.8 (traumatic complications), and 995–999.9 (complications of medical care) Injury types[130] Fracture skull vault/base: 800-801.9 Fracture skull (apart from vault/base): 802-804.9 Intracranial Injury: 850-854.1 Nerve and spinal cord: 950-957.9 Burns: 940-949.9 Fracture neck and trunk: 805-809.9 Fracture upper limb: 810-818.9 Fracture lower limb: 820-827.9, 829-829.9 Multiple fractures of limbs: 819-819.1, 828-828.1 Internal trauma: 860-869.1 Vascular injury: 900-904.9 Crush injury: 925-929.9 Open wounds: 870-897.9 Superficial injuries and contusion: 910-924.9 Dislocations, strains, and sprains: 830-848.9 Foreign body: 930-939.9 Poisoning: 960-989.9
Categories of external cause of Injury	**ICD-9-CM E codes** Activity: E001- E030 Transport accidents: E800- E849 Accidental poisoning: E850- E869 Complications of surgical or medical care: E870- E879, E930- E949 Accidental falls: E880- E888 Accidents caused by fire and flames: E890- E899 Accidents due to natural and environmental factors: E900- E909 Accidents caused by submersion, suffocation, and foreign bodies: E910- E915 Accident caused by hot substance or corrosive material: E924 Other accidents: E916- E923, E925- E928 Late effects of accidental injury: E929- E929 Suicide and self-inflicted injury: E950- E959 Homicide and injury purposely inflicted by other persons: E960- E969 Undetermined: E980- E989

We also considered appendicitis occurring before the age of 5 years as a negative control outcome[138] that we used to detect uncontrolled confounding and potential bias. This outcome is conceptually less influenced by our hypothesized pathways through which parental SMI could affect common infectious disease and injury. If there is a large unexpected association between the negative control outcome and parental SMI, it might suggest inadequately controlled confounding or surveillance bias exists in our primary study associations. We identified child's outpatient and inpatient records containing relevant ICD-9-CM diagnostic codes (appendicitis: 540-542) and only considered the first event. The earliest date of diagnosis recorded was used as the date of diagnosis.

Healthcare-seeking behavior

We used prenatal and well-child visits to evaluate differences in parent's healthcare-seeking behavior between children with and without parental SMI. The NHI Program offers 10 free prenatal visits; and 7 (8 before 2011) free well-child visits from 0 to 5 years: 4 visits by the age of 1, 2 at the ages of 1-2, 1 at the ages of 2-3, 1 at the ages of 3-4, and 1 at the ages of 4-6.

For prenatal visits, we identified records in the ambulatory care expenditures for visits from 2003-2014 that were associated with "sequential numbers of visit" 41-60 (2003) or IC41-IC60 (2004-2014). For each mother, visits on the same day were counted once. Gestational week and child's birthdate were retrieved from the birth certificate and registry of beneficiaries, respectively, to estimate mother's pregnancy start date. Finally, we only kept the records with a visit date within the time period from 3 weeks prior to the pregnancy start date to the child's birthdate. For well-child visits, we identified records in the ambulatory care expenditures for visits from 2004-2014 associated with "sequential numbers of visit" IC11-IC19 or IC71-IC79. We then used child's birthdates to eliminate records that occurred after the age of 5 years.

Because children in the study population had different follow-up times due to administrative censoring, we only included children born before 2010 (N=1,126,253) when evaluating preventive health care utilization. (Those born after 2010 were excluded from these analyses.) We then calculated numbers of prenatal and well-child visits for each child and obtained the timing of the third and fifth well-child visit.

2.6.3 *Important covariates*

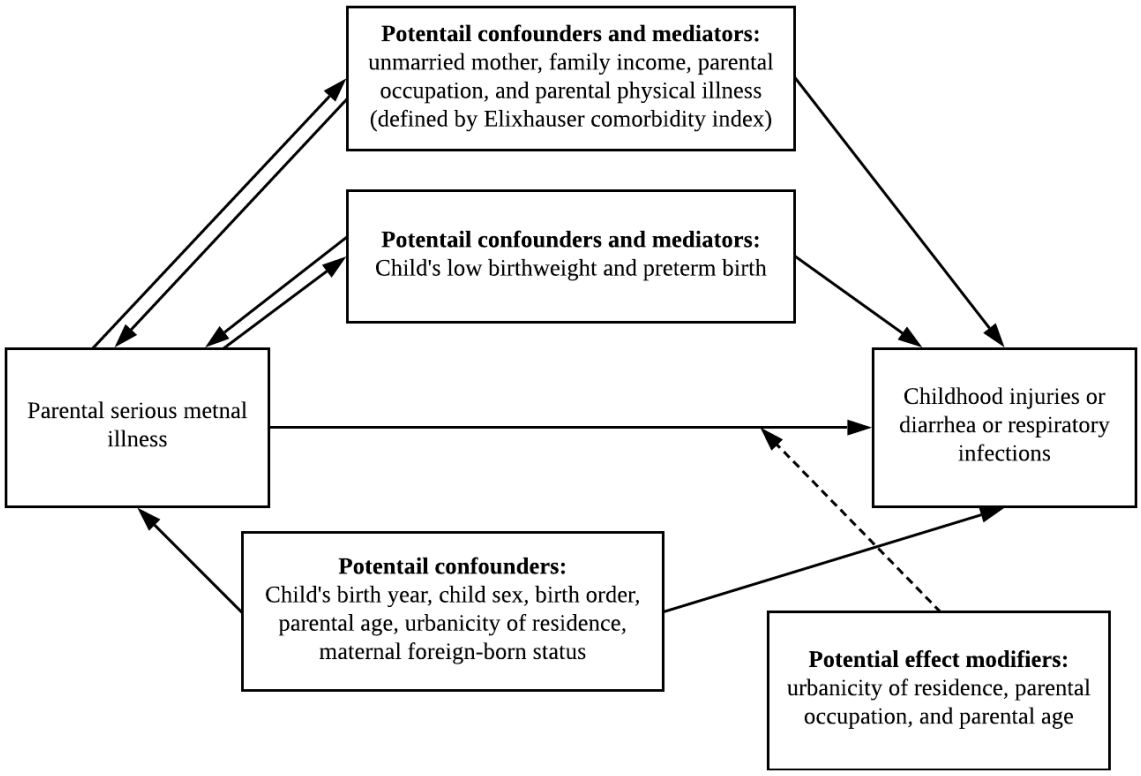
Important covariates were all measured at child's birth (Figure 2-2). Potential effect modifiers included urbanicity of residence[139–141], parental occupation[142–145] and parental age at child's birth.[146,147] Potential confounders considered included birth year[148–156], child sex[31,38,162,70,130,142,157–161], birth order[70,128,163–165], parental age at child's birth[142,146,147,166,167], unmarried mother[168–170], maternal foreign-born status[166,171–174], urbanicity of residence[139,142,182–188,143,175–181], family income[70,128,143,166,185,186], parental occupation[142,145,189–192], parental physical illness (defined by Elixhauser comorbidity index)[193–198], LBW and preterm birth,[129,199] and, for specific secondary analyses, another parent's SMI prior to childbirth.[32,44,200,201] Potential mediators included unmarried mother[168,169], family income[70,128,143,185,186,191,202], parental occupation[191,202], parental physical illness[99,193–196], LBW and preterm birth.[58,59,203,61,62,80–83,129,199] S-Table 1 summarizes the associations between important covariates and exposures or outcomes of interest. The following paragraphs describe how these covariates were measured from the databases.

Children's characteristics

Birth year and child sex were determined by child's birthdate and sex recorded in the registry of beneficiaries. For child's IDs unlinkable to the registry of beneficiaries, we used child's birthdate and sex recorded in the birth certificate if available. We created three categories for the variable birth year: 2004-2007, 2008-2010, and 2011-2013. Birthweight and gestational age were

retrieved from the birth certificate. LBW was defined as a birthweight of < 2,500 grams, and preterm birth as < 37 weeks of gestation. Birth order was measured by using the sequence in the mother-child pairs in the MCHD and/or the registry of beneficiaries of 2000-2014. For children without mother's IDs, the birth order was defined by the sequence in the father-child pairs. Three categories (1, 2, 3+) were generated for this variable.

Figure 2-2 Causal diagram hypothesized for confounders, mediators and effect modifiers



Children's health

In the sensitivity analyses, we excluded children with complex chronic conditions,[204] which consisted of congenital abnormalities, to reduce reverse causality bias. Children with complex chronic conditions may be more prone to injury or common infectious disease; and these child complex chronic conditions may lead to parental SMI. Thus, it would appear that parental SMI is

associated with an increased risk of child injury or common infectious disease. We identified these children by using outpatient/inpatient records containing relevant ICD-9 codes (S-Table 3).

Parental demographic characteristics

Maternal and paternal ages at birth were calculated from parent's birthdate and child's birthdate recorded in the registry of beneficiaries. For parent's IDs unlinkable to the registry of beneficiaries, we used parent's birthdate recorded in the birth certificate, if available. For descriptive and stratified analyses, we divided maternal age into the following categories: <20, 20–24, 25–29, 30–34, 35-39 and 40+ years; and father age: <25, 25–29, 30–34, 35-39, 40-44 and 45+ years. For multivariable analyses, we created two continuous parental age variables that were centered at the means (33 and 30 years for father and mother, respectively).

Unmarried mother was defined by missing or unknown father's household location in the birth certificate. Maternal foreign-born status was determined by the variables: mother's original and current nationality in the birth certificate records, as well as whether a mother had a foreign ID in the registry of beneficiaries. If any of these variables indicated a non-Taiwan national status, we considered the mother as foreign-born.

Socio-economic status

This project used four SES indicators: urbanicity of residence, family income, and maternal and paternal occupation types. All these SES indicators were measured by using the information recorded around the time of child's birth. Mother's current residence in the birth certificate was used as the proxy of residence. Urbanicity of residence was defined with an index derived by the cluster analysis of the five variables measured for each township in 2005: population density (persons per square kilometer), proportion of people with educational levels of college or above, proportion of people > 65 years, proportion of agricultural workers, and number of physicians per

100,000 people.[205] The variable has seven categories with cluster 1 representing highest urbanicity and cluster 7 least urbanicity.

Family income and occupation type were constructed from two variables in the registry of beneficiaries: salary (salary bands) and characteristics of the company or institution through which an enrollee joined the NHI Program. We first attempted to retrieve the data belonging to an enrollee (the father/ mother) recorded in the year of the child's birth by using enrollee's ID as the key variable. (For children born in 2011-2014, we tried to retrieve data of the birth month first). If there were no data in that year, we collected data recorded in the following year. And if using the enrollee's ID failed to retrieve a relevant record, insured's ID was taken as the key variable to retrieve data belonging to a dependent. The above algorithm generated few duplicate maternal or paternal records in terms of child's ID. For these duplicate records, we chose to keep the records by the following priorities: being retrieved by using enrollee's ID as the key variable, associated with a mother's ID that was the same as that in the birth certificate (for maternal records), and with a time point closer to the child's birth month and year. In total, 12,589 maternal records and 2,499 paternal records were removed. Table 2-19 summarizes numbers of records retrieved by each combination of key variable and time point.

Table 2-19 Numbers of parent records of the registry of beneficiaries retrieved by each combination of key variable and time point relative to the child's birth

Key variable	Time point of data	Maternal data	%	Paternal data	%
Enrollee's ID *	The year of childbirth	1,654,697	75.14	1,980,166	94.30
	The following year	97,125	4.41	51,759	2.46
Insured's ID *	The year of childbirth	436,081	19.80	63,553	3.03
	The following year	14,184	0.64	4,295	0.20
Sum		**2,202,087**		**2,099,773**	
Missing data		**34,292**		**74,023**	

*Enrollee's ID (ID1): the person who paid for the premium; Insured's ID (ID): the person covered by an insurance policy.
This table included all the children retrieved from the MCHD and/or the registry of beneficiaries, regardless of whether they were included in the final study population.

Finally, 34,292 (1.5%) and 74,023 (3.4%) children with non-missing mother's and father's IDs could not have their parent's data retrieved using the above algorithm. We searched all the available records in the registry of beneficiaries and obtained the data from the year (/month) that was nearest to the child's birthdate. Additional 21,254 and 38,954 maternal and paternal records were found in other time points. However, the numbers of days between the child's birthdate and the year of retrieval were large (S-Figure 2). Therefore, we decided to consider these data missing.

The accuracy of salary recorded in the registry of beneficiaries would vary depending on occupation type.[206] Generally, the salary would be more accurate for civil servants, teachers, and employees of public institutions than enrollees with other occupations. For instance, in 2005, for low-paid employees working for private companies, the registered salary was estimated to be 30% below the actual salary.[206] As for farmers and fishermen, the NHI denotes a single salary amount for this group. For unemployed people enrolled through a Township/District Office and people from low-income families, the registered value is the health insurance fee, instead of salary.

If a parent was enrolled as a dependent or unemployed, we assumed the salary to be zero. Monthly family income was then calculated as the sum of parents' salary. To handle the issues that salaries were recorded as salary bands and that some occupation types had no recorded salaries, we divided monthly family income into five income groupings according to quintiles in each birth year (S-Table 2). If one of the parents' occupation was the low-income household, and the other had missing occupation type or also belonged to the low-income household, the family income was directly classified as the lowest income group.

Maternal and paternal occupation types were classified according to the characteristics of company or institution through which an enrollee joined the NHI Program. The occupation type was divided into the following categories: (1) civil servants and teachers; (2) employees of

enterprises or institutions, employers and professionals; (3) union members, foreign crew members, farmers, and fishermen, (4) dependents; (5) the unemployed without a working spouse and low-income households. The fourth and fifth categories represent an unemployment status with a difference in whether the insured had a working spouse or parent. In the NHI, if married people are unemployed, they must be enrolled as a dependent of the spouse. If unemployed people cannot be enrolled as a dependent, then they must join the program through a Township/District Office. The low income household status in Taiwan is approved by a local government on the basis of average monthly income for each person in the household, as well as value of movable property and real estate.[207]

Parental physical illness

We used the Elixhauser comorbidity index (EI) as a measurement for parental physical illness. The EI is comprised of 31 comorbidities defined using ICD-9-CM codes.[208] This diagnosis-based index has been evaluated for its ability to predict several outcomes, such as 1-year mortality, long-term care admissions, hospitalizations, physician visits or health care expenditures.[209–211] The EI tends to have better performance in predicting mortality and health care utilization compared with other diagnosis-based indices, such as Charlson Comorbidity Index.[209] The EI contains several psychiatric disorders, including depression, psychoses, alcohol abuse, and drug abuse.[212] In this project, we removed these 4 comorbidity groups reflecting psychiatric disorders given their overlap or expected collinearity with our exposure of interest.

We first identified all outpatient/inpatient data associated with parent IDs that contained ICD-9 diagnostic codes for the comorbidity groups from 13 months before to 1 month after the child's birthdate. For children with multiple parent's IDs, we evaluated the time sequence of appearance of these IDs in the retrieved records. Few records were associated with out-of-order appearance of

parent's IDs (12 maternal records and 23 paternal records). We then excluded outpatient diagnostic codes that were reported < 3 times or that all appeared in the same month to avoid counting comorbid disorders due to miscodes. Finally, we used the claims data in the 12 months preceding the child's birthdate to generate EI. The original index does not have a scoring system, so we computed the score by summing individual categories (the presence or absence of a comorbidity). The score was further stratified into three groups (0, 1, >1).

Another parent's SMI was defined by the previously described method. For this covariate, we only considered SMI that occurred prior to childbirth. In addition, this variable was used in the second and third sets of the secondary analyses.

Child and parental deaths

Child and parental deaths were retrieved from the death certificate database. The death certificate database of 1998-2014 contained 2,353,997 unique IDs. A tiny proportion (0.01%) of these IDs could have been assigned to different persons. Among child's IDs, 11,778 could be linked to a death record. However, 18 records contained a date of death 30 days prior to the child's birthdate; so, we considered these 18 death records invalid. Another 1,347 records had a date of death 15 days earlier or later than the birthdate. This arose because these children didn't have a birthdate retrieved from the registry of beneficiaries, and their birthdates were instead retrieved from the birth certificate database, which only have the birth year and month. For these children, we corrected the child's birthdates according to the death date.

For mother's IDs, 4,083 death records were retrieved, among which 28 records with a date of death 16 days earlier than any of the birthdates of the mother's children. For father's IDs, 13,416 death records were retrieved, among which 79 records had a date of death 300 days earlier than any of the birthdates of the father's children. We considered these 28 maternal and 79 paternal

death records invalid. Finally, we generated the censored variable that was defined as any parent or child in the parent-child pairs/triad who died in the first five years of life.

2.6.4 *Missing data*

Among the study population, 23,964 (1.2%) children had missing paternal occupation and salary, 4,482 (0.2%) missing maternal and paternal occupation and salary, 4,037 (0.2%) missing both parents' occupation data, and 14 children missing either birthplace or paternal age (Table 2-20). Overall, 98.4% of children do not have any missing data in these variables. Because the proportion of missing data is relatively small, we used listwise deletion (complete-case analysis) to handle missing data in multiple regression analyses.

Table 2-20 Missing data of child's birthweight, gestational age and parental demographics among children in the study population

BW	GA	Birthplace	Maternal occupation/ salary	Paternal occupation/ salary	Family income	Maternal age	Paternal age	Number of children	%
X	X	X	X	X	X	X	X	1,966,825	98.4
X	X	X	X		X	X	X	23,964	1.2
X	X	X		X	X	X	X	4,482	0.2
X	X	X				X	X	4,037	0.2
X	X		X	X	X	X	X	9	0.0
X	X	X/	X/	X	X	X	X/	5	0.0
Sum								1,999,322	100.0

Abbreviation: BW: birthweight; GA: gestational age; X: non-missing

2.7 STATISTICAL ANALYSES

All analyses were carried out using SAS version 9.4 software package.

2.7.1 *Descriptive analyses*

Child and parental characteristics and SES were summarized for the study population stratified by whether a child had been exposed to parental SMI during the first five years of life. Continuous variables were described using mean and standard deviation, and categorical variables using frequency and percentage. We reported proportions of childhood injury or illness episodes in which inpatient services, emergency department, and surgery/procedure (or antibiotics) had been utilized. Children were followed-up from birth to date of death, 5th birthday, or December 31, 2014 (end of study period), whichever came first. In this project, we considered children and parents as having continuous enrollment in the NHI Program, since numbers and days of enrollment gaps for children and parents in the study population were very small (S-Figure 3).

Parental SMI was considered as a non-recurrent event. The prevalence of parental SMI when a child was born was calculated by dividing the number of children with parental SMI at birth by the number of children in the study population. Its incidence rates (IRs) in each year of the child's life were calculated by dividing the number of new onset events by the total of person-years at risk. Child injury and common infectious disease were considered as recurrent events. IRs of these child outcomes at a given age were calculated by dividing the number of events by the total follow-up time in that age. We calculated the absolute differences in IRs of child outcomes by subtracting the rates in the unexposed periods from those in the exposed periods. In the exploratory data analysis, we found that fitting the Poisson distribution to the number of episodes of injury or common infectious disease at each age yielded an apparently good visual agreement between observed data and expected values from the Poisson distribution (S-Figure 4). Therefore, we obtained unadjusted incidence rate ratios (IRRs) of these child outcomes and the associated 95% confidence intervals (CIs) by using Poisson regression. We also evaluated prevalence estimates

and IRs of parental SMI as well as IRs of child outcomes during the first five years of life stratified by covariates. Mann-Kendall trend test was used to detect monotonic trends in IRs of child outcomes across levels of a covariate.

For healthcare-seeking behavior, we assessed whether children of parents with and without SMI had different numbers of prenatal and well-child visits and compared the median time to attend the third and fifth well-child visits for these two groups. Finally, we estimated the Pearson correlation coefficients between number of preventive care visits and number of child outcomes.

2.7.2 *Multivariable analyses*

Generalized estimating equation (GEE) Poisson models were employed to estimate adjusted IRRs of outcomes in the exposed periods compared to the unexposed periods. In this project, children have different follow-up periods because of time-varying exposures and deaths. For children with any parent who died during the follow-up period, the observation-time was censored at the parent's date of death. Log-linear Poisson regression was therefore used to account for the varying follow-up time during which the children were exposed or unexposed.

GEE models account for multiple children of the same parent and recurrent events within children. In perfectly nested clusters, GEE models only require clustering on the top-level cluster.[213] Therefore, GEE models accounting for within-family clustering (multiple children per mother) were used for data analysis. GEE models are a marginal model, modelling population average parameters as a function of covariates. These models are based on quasi-likelihood estimation and do not specify the full likelihood of the data. A generalized linear model is used to estimate regression coefficients and a working correlation matrix accounts for within-subject correlation of outcomes. The regression coefficients are refit iteratively with estimated correlation. The within-subject correlation structure is treated as a nuisance parameter in GEE.[214–216] We chose

the independent correlation structure to guard against biased regression estimates that could be induced by time-dependent variables. Robust standard errors were used to ensure a valid estimate with a mis-specified correlation structure, and overdispersion provided that the number of clusters was large in this study.[217–219] Wald-based CIs were calculated for these regression coefficients using robust standard errors.

In the primary analyses, parental SMI was modeled as a time-dependent variable. The value of this variable was changed to be positive after the date of onset for maternal or paternal SMI, whichever came first, and then remained positive for the remainder of the follow-up period. After the onset of parental SMI, the effect of parental SMI on child outcomes was assumed to remain constant. The models included the interaction terms for parental SMI and child age of exposure (five age groups) for the child injury outcomes but not for the outcomes of child common infectious disease based on significance of the interaction term.

Based on the results of descriptive analyses and our knowledge of the existing literature, we developed several GEE Poisson models including precision variables and different potential confounders. The base model (model 1) included birth year (three-levels), child sex, and child age at injury or infection occurrence (five age groups). In model 2, we added birth order (three-levels: 1, 2, 3+), maternal and paternal ages at child's birth (continuous variables centered at the mean), foreign-born mother, and urbanicity of residence (seven-levels). In model 3, we added unmarried mother, family income (five-levels), maternal and paternal occupations (five-levels), and maternal and paternal physical illness (defined by Elixhauser comorbidity indices; three-levels: 0, 1, >1). In model 4, we added child's LBW and preterm birth. Unmarried mother, family income, parental occupation, parental physical illness, child's LBW and preterm birth could be confounders or mediators on the causal pathway between parental SMI and child's injury, therefore, controlling

for these variables could yield models that are over-adjusted and bias the risk estimates towards the null. So, our modeling strategy was to start with adjusting for covariates that could be confounders and would not be mediators and then to add covariates that have increasing possibility of mediating effects in regression adjustments.

To evaluate potential effect modifiers (urbanicity of residence, parental occupation, and parental age), we included interaction terms between exposure and these variables (separately) in regression models and also performed stratified analyses for these variables. Based on significance of the interaction term, we presented the stratified GEE Poisson regression by maternal and paternal ages separately (six-levels).

2.7.3 *Sensitivity analyses*

A set of sensitivity analysis excluded children with complex chronic conditions[204] to reduce reverse causality bias. Another two sets of sensitivity analyses excluded children with any parent having multiple IDs and with any parent who died during study follow-up.

2.7.4 *Secondary analyses*

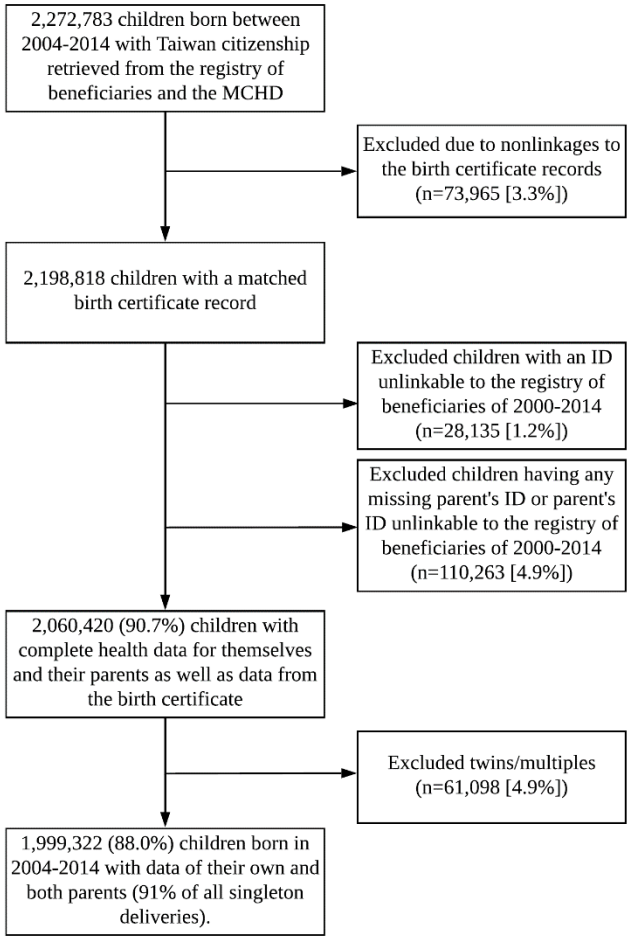
We also performed three sets of secondary analyses, in which the exposure variable was time dependent. The first set of secondary analyses included the exposure variable representing which parent(s) had SMI. The next set of secondary analyses, performed separately for maternal and paternal SMI, included the exposure variable representing SMI with onset prior to or following the child's birth. The final set of secondary analyses, also performed separately for maternal and paternal SMI, included expanding the exposure variable to denote the specific SMI diagnosis.

Chapter 3. RESULTS

3.1 CHARACTERISTICS OF CHILDREN EXCLUDED AND CHILDREN INCLUDED IN THE STUDY POPULATION

Among the 2,272,783 children born between 2004-2014 with Taiwan citizenship retrieved from the MCHD and/or the registry of beneficiaries, 273,461 (12.0%, see Figure 3-1) were excluded from the study population due to (1) nonlinkages to the birth certificate records (3.3%), (2) lack of information for the child (1.2%), (3) lack of information for both parents (4.9%), or (4) twins/multiples (2.7%).

Figure 3-1 Flow chart of study population selection



Children who were excluded from the study population were more likely to born in 2011-2014 than other children in the study population (S-Table 4). Children born in the later cohort had a shorter duration of enrollment in the NHI Program, which lowered the probability of capturing the father-child relationship from the registry of beneficiaries. The excluded children were more likely to be born prematurely and have LBW, a higher birth order, or complex chronic conditions, which probably resulted from the exclusion of twins/multiples. Children without a matched birth record tended to be born to a foreign mother (9,572 [26.5%]); whereas children with a matched birth certificate record but not included in the study population were less likely to have a foreign-born mother (13,772 [6.9%]) than children in the study population (194,634 [9.7%]). Families of children who were excluded from the study population tended to have lower income. This was partly because a larger proportion of these children only had single parent data from the registry of beneficiaries and their parents were more likely to be unemployed. Overall, these children's parents were slightly more likely to be older and have physical illness compared to the parents of children in the study population. A relatively larger proportion of the excluded children with a matched birth certificate record died in the first five years of life (4,899 [2.5%]) than children in the study population (5,943 [0.3%]). This could be because twins/multiples were more prone to health-related risks, or because of difficulty in linking parent-child data when early childhood death resulted in shorter duration of enrollment in the NHI Program.

The study population consisted of 1,999,322 parents-child triads. Of these children, 1,042,334 (52.1%) were male, and 90,917 (4.6%) had at least one parent diagnosed with SMI in the period from 6 years prior to childbirth to 5 years following childbirth (Table 3-1). A total of 16,910 (0.9%) were censored during the first five years of life due to child's or parent's death. Children born after

2010 did not have a complete five years of follow-up and consequently had a shorter time span for detecting parental SMI. As a result, children with parental SMI were more likely to born in the earlier birth cohorts than children without parents with SMI (Table 3-1). Children of parents with SMI were also more likely to be born prematurely, or have LBW or complex chronic conditions (Table 3-1). Parents with SMI were more likely to be unmarried or younger than 25 or older than 39 years at the time of childbirth, or to have lower family income or an occupation type as union members, famers, and fishermen, or unemployment. Parents with SMI also tended to have more comorbid physical illness. Parents and children in the parental SMI group were more likely to die within 5 years after delivery.

Table 3-1 Characteristics of children in the study population with and without parental serious mental illness (SMI), 2004-2014

	Without parental SMI		**With parental SMI[&]**	
	N	**%**	**N**	**%**
Birth year				
2004-2007	729,402	38.22	38,928	42.82
2008-2010	479,135	25.11	25,772	28.35
2011-2014	699,868	36.67	26,217	28.84
Children's characteristics				
Males	994,867	52.13	47,467	52.21
Low birthweight	110,559	5.79	6,632	7.29
Preterm birth	130,665	6.85	8,037	8.84
Birth order				
1	1,072,561	56.20	52,391	57.63
2	674,324	35.33	29,456	32.40
≥3	161,520	8.46	9,070	9.98
Complex chronic conditions	125,915	6.60	7,074	7.78
Parent characteristics				
Paternal age at birth (years)[#]				
<25	94,571	4.96	7,258	7.98
25–29	417,283	21.87	20,909	23.00
30–34	735,014	38.51	30,776	33.85
35-39	458,213	24.01	20,656	22.72
40-44	151,636	7.95	7,925	8.72
≥45	51,688	2.71	3,392	3.73

	Without parental SMI		With parental SMI[&]	
	N	%	N	%
Maternal age at birth (years)				
<20	32,922	1.73	2,698	2.97
20–24	246,731	12.93	15,932	17.52
25–29	641,563	33.62	29,919	32.91
30–34	700,385	36.70	28,837	31.72
35-39	252,208	13.22	11,653	12.82
≥40	34,596	1.81	1,878	2.07
Unmarried mother	57,817	3.03	6,201	6.82
Foreign-born mother	185,647	9.73	8,987	9.88
Socio-economic status				
Urbanicity of residence[#]				
1 (highest urbanicity)	386,906	20.27	17,893	19.68
2	614,705	32.21	31,058	34.16
3	451,840	23.68	20,072	22.08
4	273,886	14.35	13,184	14.50
5	31,564	1.65	1,605	1.77
6	65,763	3.45	3,336	3.67
7	83,728	4.39	3,769	4.15
Family income[#]				
High	388,932	20.42	12,705	14.02
Upper-middle	386,837	20.31	14,277	15.75
Middle	408,749	21.46	18,468	20.37
Lower-middle	383,910	20.16	20,825	22.98
Low	336,216	17.65	24,366	26.88
Paternal occupation[#]				
Civil servants and teachers	107,339	5.70	4,654	5.20
Employees, employers and professionals	1,426,958	75.83	60,672	67.74
Union members, farmers and fishermen	103,146	5.48	5,938	6.63
The unemployed and low-income household	183,438	9.75	14,439	16.12
Dependents	60,868	3.23	3,869	4.32
Maternal occupation[#]				
Civil servants and teachers	104,635	5.51	3,900	4.31
Employees, employers and professionals	1,205,308	63.42	47,920	53.01
Union members, farmers and fishermen	65,657	3.45	3,484	3.85
The unemployed and low-income household	123,605	6.50	11,871	13.13
Dependents	401,194	21.11	23,225	25.69
Parental physical illness				
Paternal Elixhauser index				
0	1,789,075	93.75	82,394	90.63
1	93,049	4.88	6,257	6.88
>1	26,281	1.38	2,266	2.49
Maternal Elixhauser index				
0	1,826,250	95.70	85,397	93.93
1	73,553	3.85	4,717	5.19
>1	8,602	0.45	803	0.88
Death occurred in the first five years of life				
Paternal death	7,699	0.40	1,024	1.13
Maternal death	2,071	0.11	394	0.43
Child's death	5,506	0.29	437	0.48

	Without parental SMI		With parental SMI[&]	
	N	%	N	%
Censored during the follow-up periods	15,086	0.79	1,824	2.01

#Data were complete for all variables except the following: Paternal age (N=1, 1 without parental SMI, 0 with parental SMI); Urbanicity of residence (N=13, 13 with, 0 without); Family income (N= 4,037, 3,716 with, 276 without); Paternal occupation (N= 28,001, 26,656 with, 1,345 without); Maternal occupation (N= 8,523, 8,006 with, 517 without).
& At least one parent with SMI in the period from 6 years prior to childbirth to 5 years following childbirth.

3.2 PARENT SERIOUS MENTAL ILLNESS

Among the children with Taiwanese citizenship born in 2004-2014, 38,939 (1.7%) had fathers with SMI diagnosed in the period from 6 years prior to their birth to 5 years following their birth. (Parents could have >1 type of SMI diagnosis.) Among children with paternal SMI, 10,471 (26.9%) had fathers with schizophrenia, 9,859 (25.3%) with bipolar disorder, and 18,609 (47.8%) with MDD. Of the 66,595 children with maternal SMI, 10,131 (15.2%) had mothers with schizophrenia, 15,536 (23.3%) with bipolar disorder, and 40,928 (61.5%) with MDD. Overall, 94.1% of parental psychiatric categories were determined by using the diagnosis made by a psychiatrist (S-Table 5). By using the pre-specified algorithms to define type of diagnosis, most of the parents had a single SMI diagnosis. Only 812 parents with multiple children had been defined by the algorithms to have different diagnoses across their children (S-Table 6). About a half of the changes of diagnosis were between MDD and bipolar disorder (n=440): 169 parents received the diagnosis of bipolar disorder before MDD, and 271 received the diagnosis of MDD before bipolar disorder.

The presence of maternal SMI was associated with whether or not a mother-father-child triad could be identified (S-Table 7). Among 79,637 mother-child pairs having a matched birth certificate record and a missing father's ID, 6.1% had maternal SMI, which was much greater than the mother-father-child triads with a matched birth certificate record (2.9%). The former group

had a large proportion (74.5%) of missing father's birthdate on the birth certificate, which is a proxy of unmarried mother. Other groups with a matched birth record that had a greater percentage of maternal SMI were mother-child pairs with unlinkable father's and child's IDs (4.3%), or with an unlinkable child's ID and a missing father's ID (8.6%). However, among mother-child pairs without a matched birth record, the percentage of mothers with SMI were not greater than for the mother-father-child triads with a matched birth record. Finally, among the groups without a matched birth record, complete mother-father-child triads and mother-father-child triads with an unlinkable mother's ID had a greater proportion of paternal SMI (2.8% and 4.1%, respectively) than the complete mother-father-child triads with a matched birth record (1.8%).

Table 3-2 summarizes prevalence (diagnosis made before a child's birth) and IRs (diagnosis in the first five years of life) of parental SMI. Children with a matched birth record but excluded from the study population were more likely to have prevalent or incident maternal SMI. However, they were less likely to have paternal SMI than were children included in the study. Children without a matched birth record had lower prevalence of maternal SMI and lower IR of paternal or maternal SMI.

In the study population, we found 36,389 (1.8%) children with paternal SMI and 57,509 (2.9%) with maternal SMI (Table 3-3). There were 2,981 (0.1%) children for whom both parents had SMI. Of children with one or both parents with SMI, 57,074 (62.8%) had the illness diagnosed before the birth and 33,843 (37.2%) after birth. Of children with paternal SMI, 23,721 (65.2%) had the SMI diagnosed before the birth and 12,668 (34.8%) after birth. The IR increased from 1.49 per 1,000 person-years at age 0-1 years to 1.86 at age 4-5 years (Table 3-4). Of children with maternal SMI, 34,522 (60.0%) had the SMI diagnosed before the birth and 22,987 (40.0%) after

birth. The IR was greatest in the first year (3.17 per 1,000 person-year) but approximately 3 per 1,000 person-year across the first five years of life.

Table 3-2 Prevalence and incidence of parent's serious mental illness, stratified by whether a child was included in the study population and matched to a birth certificate record

	N*	Prevalent cases[&]	% (95% CI)	Incident cases[&]	Person-years^	Rate[#] (95% CI)
Parental SMI						
Study population	1,999,322	57,074	2.85 (2.83-2.88)	33,837	7,421,442.7	4.56 (4.51-4.61)
Matched[@]	199,476	6,419	3.22 (3.14-3.30)	3,416	624,502.4	5.47 (5.29-5.66)
Unmatched[@]	66,864	1,059	1.58 (1.49-1.68)	584	263,768.8	2.21 (2.04-2.40)
Paternal SMI						
Study population	1,999,322	23,721	1.19 (1.17-1.20)	12,665	7,602,030.0	1.67 (1.64-1.70)
Matched[@]	109,234	1,031	0.94 (0.89-1.00)	531	346,344.5	1.53 (1.41-1.67)
Unmatched[@]	51,284	666	1.30 (1.20-1.40)	318	200,157.0	1.59 (1.42-1.77)
Maternal SMI						
Study population	1,999,322	34,525	1.73 (1.71-1.75)	22,981	7,550,948.5	3.04 (3.00-3.08)
Matched[@]	195,369	5,429	2.78 (2.71-2.85)	2,969	616,728.0	4.81 (4.64-4.99)
Unmatched[@]	30,998	394	1.27 (1.15-1.40)	291	137,274.6	2.12 (1.89-2.38)

Abbreviation: SMI: serious mental illness; CI: confidence intervals
@Matched: children with a matched birth certificate record but not included in the study population; unmatched: children without a matched birth record.
* Number of children with non-missing parent/paternal/maternal data in the NHIRD.
&Prevalent cases: the parent(s) had received a diagnosis before the child was born. Incident cases: the parent(s) received a diagnosis in the first 5 years of life.
^Censored when the children or the parent of interest died. Otherwise, a person was assumed to have continuous enrollment.
#per 1,000 person-years.

Table 3-3 Number of children in the study population with parent's serious mental illness (SMI) by diagnosis

	Paternal diagnosis			
Maternal diagnosis	Schizophrenia	Bipolar disorder	Major depressive disorder	No SMI
Schizophrenia	239	95	137	8,090
Bipolar disorder	143	403	309	12,386
Major depressive disorder	269	410	976	34,052
No SMI	9,140	8,350	15,918	1,908,405

Time frame of parent SMI diagnosis: from 6 years prior to childbirth to 5 years following childbirth.

Table 3-4 Incidence rates of parent's serious mental illness among children in the study population stratified by child age (from 0 to 4 years)

Child age (years)	Incident cases[&]	Person-years^	Incidence rate[#] (95% CI)
Parental SMI			
0-1	8,396	1,850,303.21	4.54 (4.44-4.64)
1-2	7,089	1,671,184.42	4.24 (4.14-4.34)
2-3	6,914	1,479,750.10	4.67 (4.56-4.78)
3-4	6,039	1,290,894.49	4.68 (4.56-4.80)
4-5	5,399	1,129,310.51	4.78 (4.66-4.91)
Paternal SMI			
0-1	2,818	1,885,278.49	1.49 (1.44-1.55)
1-2	2,716	1,707,700.78	1.59 (1.53-1.65)
2-3	2,622	1,516,683.89	1.73 (1.66-1.80)
3-4	2,338	1,327,492.91	1.76 (1.69-1.83)
4-5	2,171	1,164,873.93	1.86 (1.79-1.94)
Maternal SMI			
0-1	5,950	1,874,131.38	3.17 (3.10-3.26)
1-2	4,761	1,696,622.82	2.81 (2.73-2.89)
2-3	4,658	1,506,170.14	3.09 (3.01-3.18)
3-4	4,049	1,317,717.98	3.07 (2.98-3.17)
4-5	3,563	1,156,306.18	3.08 (2.98-3.18)

Abbreviation: SMI: serous mental illness; CI: Confidence intervals
&Incident cases: the parent(s) received a diagnosis after the child was born.
^Censored when the children or the parent of interest died. #per 1,000 person-years

S-Table 9 and S-Table 10 presents associations between covariates and parental SMI present before childbirth and between covariates and parental SMI onset in the first five years of life, respectively. Compared to the later birth cohorts, the earlier cohorts had lower prevalence estimates and greater IRs of parental SMI. The prevalence and IRs of parental SMI were greater among children with the following characteristics: LBW, preterm birth, child's complex chronic conditions, or being born to unmarried mother. In addition, prevalence and IRs of parental SMI were also associated with lower family income, lower parental occupation class, or parental physical illness. The prevalence of parental SMI was greater among first-born children and those of 3+ birth order than among second-born children. By contrast, the IR increased with increasing birth order. The prevalence and IRs of parental SMI were greater among younger and older parents, suggesting a U-shaped relationship between parental age and SMI. The only exception was

maternal SMI, where prevalence increased with advancing maternal age. Among children born to foreign mothers, fathers were more likely to have SMI at birth or during the follow-up period.

Child death and parental death in the first five years of life were associated with parental SMI. Relative to children without paternal death, the RR of parental SMI present before childbirth among children with paternal death was 2.20 (95% CI: 2.02-2.38); and the IRRs of parental SMI onset after childbirth were 5.42 (95% CI: 4.96-5.93). Relative to children without maternal death, the RR of parental SMI present before childbirth among children with maternal death was 3.15 (95% CI: 2.78-3.57); and the IRRs of parental SMI onset after childbirth were 7.27 (95% CI: 6.26-8.44). Compared to children who survived to age 5 years, children who died before age 5 had a greater probability of having prevalent parental SMI (RR 1.19, 95% CI: 1.04-1.36) and incident parental SMI (IRR 10.68, 95% CI: 9.39-12.13). As a result, children that were censored during the follow-up period were also more likely to have prevalent and incident parental SMI.

3.3 EARLY CHILDHOOD INJURY

3.3.1 *Descriptive analyses*

Among the children born in 2004-2014, 1,189,886 (52.4%) had a total of 2,190,890 injury events in the first five years of life (Table 3-5), consisting of 3,665,520 outpatient/inpatient visits. Of the children with any injury, 570,983 (48.0%) had > 1 injury events. There were 32,125 (1.4%) children who were hospitalized due to injury. The most common injuries (Table 3-5) were superficial injuries and contusion (accounting for 49.5% of all injury events), open wounds (27.3%), foreign body (7.7%), burns (6.5%), intracranial injury (5.6%), dislocations, strains, and sprains (5.3%) and poisoning (4.2%). The percentage of episodes utilizing inpatient services, emergency department services or surgery/procedures varied with injury type (Table 3-5). Fracture skull vault/base and internal trauma had the highest percentages of hospitalization (50.5% and 35.4%, respectively) and of surgery/procedures (21.3% and 20.1%, respectively). Fractures of skull, neck and trunk and limbs also had relatively high percentages of hospitalization (11.5-19.9%) and surgery/procedures (9.3-15.8%).

When accounting individual hospitalization, 33,889 hospitalizations were associated with injury ICD-9 diagnostic codes, among which 24,130 (71.2%) had ICD-9 E codes reported. The most common reported external causes of injury were accidental falls (6,888; 28.6%), other accidents (5,329, 22.1%), transport accidents (4,266; 17.5%), accident caused by hot substance or corrosive material (4,162; 17.2%), accidental poisoning (1,700; 7.1%), accidents caused by submersion, suffocation, and foreign bodies (1,394; 5.8%), and homicide and injury purposely inflicted by other persons (271; 1.1%).

Table 3-5 Injury events in the first 5 years of life among children with Taiwanese citizenship born in 2004-2014 by injury types

	Episodes	Children*	%*	Hospitalization	%#	ED	%#	Surgery/procedures	%#
Overall episodes	***2,190,890***	***1189886***	***52.4***	***33,046***	***1.5***	***556,900***	***25.4***	***58,161***	***2.7***
Fracture skull vault/base	2,795	2,728	0.1	1,411	50.5	958	34.3	595	21.3
Fracture skull (apart from vault/base)	3,468	3,417	0.2	690	19.9	1,047	30.2	398	11.5
Intracranial Injury	123,771	115,900	5.1	4,756	3.8	55,215	44.6	4,803	3.9
Nerve and spinal cord	2,466	2,099	0.1	237	9.6	121	4.9	243	9.9
Burns	141,807	132,717	5.8	7,040	5.0	41,295	29.1	6,051	4.3
Fracture neck and trunk	784	750	0.0	127	16.2	126	16.1	73	9.3
Fracture upper limb	41,475	39,114	1.7	4,762	11.5	11,633	28.0	6,563	15.8
Fracture lower limb	12,130	11,287	0.5	1,558	12.8	3,094	25.5	1,915	15.8
Multiple fractures of limbs	120	115	0.0	1	0.8	21	17.5	9	7.5
Internal trauma	1,755	1,687	0.1	622	35.4	469	26.7	352	20.1
Vascular injury	1,842	1,750	0.1	105	5.7	617	33.5	86	4.7
Crush injury	33,602	32,766	1.4	616	1.8	11,410	34.0	1,377	4.1
Open wounds	597,343	483,244	21.3	5,286	0.9	235,457	39.4	26,163	4.4
Superficial injuries and contusion	1,085,217	764,896	33.7	5,688	0.5	220,466	20.3	10,901	1.0
Dislocations, strains, and sprains	116,105	105,888	4.7	385	0.3	22,894	19.7	4,965	4.3
Foreign body	168,150	155,344	6.8	2,159	1.3	30,725	18.3	2,958	1.8
Poisoning	91,337	75,556	3.3	2,762	3.0	7,506	8.2	532	0.6

*Children refers to number of children who had been injured during the study follow-up. Those with >1 injuries of the same type were counted once. Denominator was the number of children with Taiwan citizenship born in 2004-2014 (N=2,272,783) and whose ID existed in the registry of beneficiaries and/or the MCHD.

Hospitalization and ED refer to a child had utilized inpatient or emergency department services during an episode. Surgery/procedures refers to surgery or procedure had been performed. Denominator was number of episodes of each category.

Table 3-6 summarizes IRs of injury events among the study population and among children with and without a matched birth certificate record. When estimating these IRs, children were assumed to be continuously enrolled until the end of the follow-up period or death. The IRs among children excluded from the study population (IR 240.9 [95% CI: 239.7-242.1] per 1,000 person-years for children with a matched record and IR 141.8 [95% CI: 140.4-143.2] for those without a matched record) were lower than that in the study population (IR 257.6 [95% CI: 257.2-257.9]).

Table 3-6 Incidence rates of childhood injury events in the first five years of life, stratified by whether a child was included in the study population or matched to a birth certificate record

	Children* (N)	Episodes (n)	Person-years^	Incidence rate# (95% CI)
Study population	1,999,322	1,993,821	7,741,026.33	257.6 (257.2-257.9)
Matched@	199,496	157,855	655,272.85	240.9 (239.7-242.1)
Unmatched@	73,965	39,214	276,499.52	141.8 (140.4-143.2)

Abbreviation: CI: Confidence intervals
@Matched: children with a matched birth certificate record but not included in the study population; unmatched: children without a matched birth record. The matched group could have a slightly inflated incidence rate because the records in the first 90 days of life could not be assigned exactly to a child's ID.
* Number of children with Taiwanese citizenship born in 2004-2014.
^Censored when the child died. Otherwise, a person was assumed to have continuous enrollment.
#per 1,000 person-years

In the study population, 1,082,064 (54.1%) children had a total of 1,993,821 injury events in the first 5 years of life, consisting of 3,340,554 inpatient/ambulatory care visits. Children with parental SMI had slightly greater percentage (61.0%) of having at least one injury event than those without parental SMI (53.8%). Children aged 0-1 years had the lowest IRs of injury events: 164.1 (95% CI: 163.6-164.7) per 1,000 person-years in the unexposed periods and 198.2 (95% CI: 194.7-201.9) in the exposed periods (Table 3-7). The highest IRs occurred at age 1-2 years: 343.5 (95% CI: 342.6-344.4) and 393.0 (95% CI: 388.1-398.0), respectively, for the unexposed and exposed periods. The IRs in the exposed periods were greater than those in the unexposed periods through the first five years of life. The unadjusted IRR of any child injury for the exposed periods relative to the unexposed periods decreased gradually from 1.21 (95% CI: 1.19-1.23) at age 0-1 years to 1.12 (95% CI: 1.1-1.14) at age 4-5 years. When actual healthcare visits were counted instead of injury events, the estimates of unadjusted IRRs were similar to above (S-Table 11).

S-Table 12 provides IRs of child injury in the exposed and unexposed periods for each injury type. Compared with the unexposed periods, children exposed to parental SMI were more likely to have intracranial injury (unadjusted IRR 1.21-1.50), burns (IRR 1.17-1.27), crush injury (IRR 1.17-1.37), open wounds (IRR 1.12-1.28), superficial injuries and contusion (IRR 1.11-1.18), or

poisoning (IRR 1.11-1.29). The exposed periods were also associated with a slightly greater risk for dislocations, strains, and sprains (IRR 1.01-1.19) and foreign body (IRR 1.05-1.23). For other injury types, such as fracture of skull, nerve and spinal cord, fracture of neck and trunk, fracture of limbs, internal trauma, and vascular injury, the numbers of events were small, which often resulted in wide 95% CIs containing null.

Table 3-7 Incidence rates of childhood injury events among children in the study population stratified by child age and by exposure to parental serious mental illness

Age (years)	Unexposed periods			Exposed periods			Rate difference (95% CI)	Unadjusted IRR (95% CI)
	Events	PY	Rate# (95% CI)	Events	PY	Rate# (95% CI)		
0-1	303,917	1,851,678.8	164.1 (163.6-164.7)	11,651	58,779.4	198.2 (194.7-201.9)	34.1 (30.4-37.7)	1.21 (1.19-1.23)
1-2	575,065	1,674,054.6	343.5 (342.6-344.4)	23,878	60,756.6	393.0 (388.1-398.0)	49.5 (44.4-54.6)	1.14 (1.13-1.16)
2-3	462,823	1,484,076.9	311.9 (311.0-312.8)	21,734	60,980.9	356.4 (351.7-361.2)	44.6 (39.7-49.4)	1.14 (1.13-1.16)
3-4	320,376	1,296,586.6	247.1 (246.2-248.0)	16,822	59,903.7	280.8 (276.6-285.1)	33.7 (29.4-38.1)	1.14 (1.12-1.15)
4-5	243,671	1,136,196.1	214.5 (213.6-215.3)	13,884	58,012.8	239.3 (235.4-243.3)	24.9 (20.8-28.9)	1.12 (1.10-1.14)

Abbreviation: PY: person-years; CI: Confidence intervals; IRR: incidence rate ratio.
#Incidence rate: per 1,000 person-years. Censored when the child died. Otherwise, a person was assumed to have continuous enrollment.

As for injury hospitalization, 29,392 (1.5%) injury events were associated with inpatient care among children in the study population. The IRs of injury hospitalization were lowest at age 4-5 years: 2.91 (95% CI: 2.81-3.01) per 1,000 person-years in the unexposed periods and 3.63 (95% CI: 3.17-4.16) in the exposed periods (Table 3-8). The IRs were highest at age 1-2 years: 5.24 (95% CI: 5.13-5.35) and 8.31 (95% CI: 7.61-9.07), respectively, in the unexposed and exposed periods. The IRs of injury hospitalization in the exposed periods were slightly greater than those in the unexposed periods. The unadjusted IRR decreased gradually from 1.62 (95% CI: 1.43-1.82) at age 0-1 years to 1.25 (95% CI: 1.08-1.44) at age 4-5.

Table 3-8 Incidence rates of injury hospitalization among children in the study population, stratified by child age and by exposure to parental serious mental illness

Age	Unexposed periods		Exposed periods		Rate difference	Unadjusted IRR
(years)	Events	Rate# (95% CI)	Events	Rate# (95% CI)	(95% CI)	(95% CI)
0-1	5,544	3.00 (2.92-3.08)	284	4.84 (4.31-5.44)	1.85 (1.28-2.42)	1.62 (1.43-1.82)
1-2	8,751	5.24 (5.13-5.35)	502	8.31 (7.61-9.07)	3.07 (2.34-3.81)	1.59 (1.45-1.74)
2-3	5,932	4.01 (3.91-4.11)	357	5.91 (5.33-6.55)	1.90 (1.28-2.52)	1.47 (1.32-1.64)
3-4	4,231	3.28 (3.18-3.38)	299	5.06 (4.52-5.66)	1.78 (1.20-2.36)	1.54 (1.37-1.74)
4-5	3,285	2.91 (2.81-3.01)	207	3.63 (3.17-4.16)	0.72 (0.22-1.23)	1.25 (1.08-1.44)

Abbreviation: CI: Confidence intervals.
Incidence rate: per 1,000 person-years. Censored when the child or any parent died.

S-Table 13 and S-Table 14 describe associations between covariates and medically attended injury events and between covariates and injury hospitalization occurring in the first five years of life, respectively. Risks of any medically attended injury event for children in the later birth cohorts were greater (unadjusted IRR 1.06, 95% CI: 1.06-1.06 in 2008-2010; and IRR 1.07, 95% CI: 1.07-1.07 in 2011-2014) compared to the earliest birth cohort of 2004-2007. Boys were more likely to be injured (IRR 1.18, 95% CI: 1.18-1.19) than girls. Higher birth-order children had a lower probability of having any injury (IRR 0.93 [95% CI: 0.93-0.93] and IRR 0.95 [95% CI: 0.95-0.96] for second-born children and for those of 3+ birth order, respectively) than first-born children. Children who had a complex chronic illness (IRR 1.09, 95% CI: 1.08-1.10) were at a greater risk of any injury. Paternal and maternal ages were both inversely associated with childhood injury risk; and Mann-Kendall test indicated a monotonic decreasing trend (p value: 0.005) in the IR of any injury over parental age. Compared to children with fathers aged 30-34 years, children with fathers aged <25 or age ≥45 years had IRRs of 1.10 (95% CI: 1.09-1.11) and 0.91 (95% CI: 0.90-0.92), respectively. Results were similar with respect to maternal age.

Children of unmarried mother (IRR 1.02, 95% CI: 1.02-1.03) or children with parental physical illness (IRR 1.08-1.14) were more likely to have injury. In contrast, children of foreign-

born mothers were less likely to have injury (IRR 0.89, 95% CI: 0.89-0.89). Urbanicity of residence was associated with childhood injury risk, with degrees of urbanicity negatively correlated with risk (p value of Mann-Kendall test: 0.004). The IRR for the lowest urbanicity level was 1.25 (95% CI: 1.24-1.26) compared to the highest level. Compared to children from the highest income families, children from lower-income families were more likely to incur injury (IRR 1.05-1.10). Compared to children with parental occupation of employees, employers and professionals, those with parental occupation of union members, farmers and fishermen were also more likely to be injured (IRR 1.08 [95% CI: 1.07-1.08] and IRR 1.14 [95% CI: 1.13-1.14] for paternal and maternal occupation, respectively) Finally, for children who died or whose parent(s) died during the follow-up, the IRRs of injury were very close to null value and with 95% CIs including null.

In contrast to the risk of having any medically attended injury, risk of injury hospitalization was about 15-20% lower for children in the later birth cohorts. LBW (unadjusted IRR 1.28, 95% CI: 1.22-1.34), preterm birth (IRR 1.28, 95% CI: 1.23-1.33), and higher birth order (IRR 1.10, 95% CI: 1.08-1.13 for second-born children and IRR 1.47, 95% CI: 1.41-1.52 for those of 3+ birth order), foreign-born mothers (IRR 1.26, 95% CI: 1.22-1.30) were associated with injury hospitalization. Several child and parental characteristics were associated with an even greater risk of injury hospitalization than that of any injury, including being male (IRR 1.30, 95% CI: 1.18-1.19), having complex chronic illness (IRR 1.64, 95% CI: 1.59-1.71), being born to an unmarried mother (IRR 1.61, 95% CI: 1.53-1.69), or parental physical illness (IRR 1.13-1.57). Paternal and maternal ages were both inversely associated with risk of injury hospitalization. The only exception was that risk for children with paternal age of 40-44 year and >45 years was 6% (IRR 1.06, 95% CI: 1.02-1.11) and 23% (IRR 1.23, 95% CI: 1.15-1.32), respectively, greater than those

with paternal age 30-34. Mann-Kendall test indicated a monotonic decreasing trend in IRs of injury hospitalization over maternal age (p value: 0.04) but not paternal age (p value: 0.57). Urbanicity of residence and family income were both negatively associated with risk of injury hospitalization (P values of Mann-Kendall trend test were 0.002 for urbanicity of residence and 0.01 for family income). For children whose parent(s) died during the follow-up, the IRRs of injury hospitalization were markedly elevated relative to children whose parents did not die (IRR 1.82 [95% CI: 1.55-2.14] and IRR 3.27 [95% CI: 2.60-4.11] for paternal and maternal death, respectively). Finally, compared to children did not die during the follow-up, children who died were at greater risk of injury hospitalization (IRR 15.85 [95% CI: 14.16-17.74]). In summary, the risk of injury hospitalization was markedly increased for children with several characteristics indicative of disadvantage or other risk factors, including LBW, preterm birth, unmarried mother, foreign-born mother, lower urbanicity of residence, younger parent age, lower-income family, lower parental occupation class, or parental physical illness.

3.3.2 *Multivariable analyses*

Table 3-9 presents the adjusted IRRs for the association between parental SMI and early childhood injury. For any medically attended injury event, children with parental SMI had a 14% (adjusted IRR [aIRR] 1.14, 95% CI: 1.13-1.15) greater rate of injury compared with unexposed children after adjusting for birth year, child sex, child age, birth order, parental ages, foreign-born mother, and urbanicity of residence. The aIRR did not change after further adjusting for unmarried mother, family income, parental occupation, parental physical illness, LBW and preterm birth. The associations between parental SMI and any injury event exhibited a tendency to weaken over time during the first five years of life (Table 3-9).

Table 3-9 Childhood injury in relation to having any parent with serious mental illness

	Adjusted incidence rate ratio (95% Confidence intervals)			
Child age (years)	**Model 1**	**Model 2**	**Model 3**	**Model 4**
Any injury				
0-5	***1.15 (1.14- 1.16)***	***1.14 (1.13- 1.15)***	***1.14 (1.13- 1.14)***	***1.14 (1.13- 1.15)***
0-1	1.21 (1.18- 1.23)	1.20 (1.18-1.23)	1.20 (1.17-1.22)	1.20 (1.17-1.22)
1-2	1.14 (1.13- 1.16)	1.14 (1.13-1.16)	1.13 (1.12-1.15)	1.13 (1.12-1.15)
2-3	1.14 (1.13- 1.16)	1.14 (1.12-1.16)	1.13 (1.12-1.15)	1.13 (1.12-1.15)
3-4	1.13 (1.12- 1.15)	1.13 (1.11-1.15)	1.12 (1.11-1.14)	1.12 (1.11-1.14)
4-5	1.12 (1.10- 1.14)	1.11 (1.09-1.13)	1.10 (1.08-1.13)	1.10 (1.09-1.13)
Injury hospitalization				
0-5	***1.51 (1.43- 1.59)***	***1.49 (1.42- 1.57)***	***1.40 (1.33- 1.48)***	***1.40 (1.33- 1.47)***
0-1	1.62 (1.44-1.83)	1.61 (1.43-1.82)	1.50 (1.33-1.69)	1.49 (1.32-1.69)
1-2	1.59 (1.45-1.74)	1.57 (1.41-1.72)	1.48 (1.35-1.62)	1.47 (1.34-1.62)
2-3	1.48 (1.32-1.64)	1.45 (1.31-1.62)	1.37 (1.23-1.53)	1.37 (1.23-1.53)
3-4	1.54 (1.37-1.74)	1.52 (1.35-1.71)	1.44 (1.28-1.62)	1.43 (1.27-1.62)
4-5	1.25 (1.08-1.44)	1.23 (1.06-1.42)	1.16 (1.00-1.35)	1.16 (1.00-1.34)

Model 1: adjusted for birth year and child sex. Child age was also adjusted in estimating IRR for ages 0-5.
Model 2: adjusted for the above variables and birth order, maternal and paternal ages, foreign-born mother, and urbanicity of residence.
Model 3: adjusted for the above variables and unmarried mother, family income, maternal and paternal occupations, and maternal and paternal Elixhauser indexes.
Model 4: adjusted for the above variables and child's LBW and preterm birth.

Parental SMI was associated with greater risk of injury hospitalization than that of any injury. Children of parents with SMI had a 49% (aIRR 1.49, 95% CI: 1.42-1.57) greater rate of injury hospitalization during the 5-year follow-up compared with unexposed children after adjusting for birth year, child sex, child age, birth order, parental ages, foreign-born mother, and urbanicity of residence (Table 3-9). When unmarried mother, family income, parental occupation, and parental physical illness were further adjusted, the aIRR decreased to 1.40 (95% CI: 1.33-1.48). The association between parental SMI and injury hospitalization weakened with child age from aIRR 1.61 (95% CI: 1.43-1.82) at age 0-1 years to 1.23 (95% CI: 1.06-1.42) at age 4-5 (Table 3-9).

3.3.3 *Sensitivity analyses*

S-Table 15 summarizes numbers of children and any injury event excluded in the sensitivity analyses, including those excluding: 1. children with complex chronic conditions; 2. excluding

children with a parent having multiple IDs; and 3. excluding children with a parental death before age 5 years. The percentages of episodes excluded from the analyses were slightly greater in the exposed periods compared to the unexposed period. However, the aIRRs obtained from these sensitivity analyses were similar to those of the primary analyses (S-Table 16).

3.3.4 *Stratified analyses*

When stratified on urbanicity of residence (S-Table 17) or parental occupation (S-Table 18), the stratified regressions did not show any noticeable pattern of changes of aIRR across strata. The coefficients for interaction terms between parental SMI and urbanicity of residence or parental occupation all had wide 95% CIs containing null and a large p-value (>0.05). When models were stratified on paternal and maternal ages separately, the results suggested these two variables modified the associations of parental SMI and child injury. When we took the approach of adding additional interaction terms, both the interaction term between parental SMI and paternal or maternal age (as well as the main effects) reached a p-value <.0001.

Paternal and maternal ages had a moderate correlation in the study population (Pearson r: 0.60, 95% CI: 0.60-0.60). Consequently, it would be difficult to interpret their interaction terms with parental SMI when both parental ages were entered to a multivariable regression. Therefore, we presented results from the stratified models (Table 3-10). The associations between parental SMI and any child injury in the older parental age groups were stronger than the younger age groups. The association was smallest among fathers aged < 25 years (aIRR 1.10, 95% CI: 1.07-1.13) and largest among fathers aged ≥45 years (aIRR 1.22, 95% CI: 1.16-1.28). Similarly, the association was smallest among mothers aged < 20 years (aIRR 1.09, 95% CI: 1.04-1.14) and largest among mothers aged ≥ 40 years (aIRR 1.17, 95% CI: 1.10-1.25). When inspecting the IRs of any injury events at < 5 years, the IRs for exposed and unexposed periods both decreased with

parental age (S-Table 13). But the rate of decrease was slower in the exposed period, which produced the pattern of effect modification. Parental age, especially paternal age, even more markedly modified the effect of parental SMI on injury hospitalization (Table 3-10).

Table 3-10 Stratified analyses for the associations between parental serious mental illness and early childhood injury by parental age

	Adjusted incidence rate ratio (95% confidence intervals)					
Any injury						
Child age	**Paternal age #**					
(years)	**<25**	**25-29**	**30-34**	**35-39**	**40-44**	**≥45**
0-5	***1.10 (1.07-1.13)***	***1.10 (1.08-1.12)***	***1.16 (1.14-1.17)***	***1.16 (1.14-1.18)***	***1.19 (1.16-1.23)***	***1.22 (1.16-1.28)***
0-1	1.24 (1.16-1.33)	1.15 (1.11-1.20)	1.20 (1.17-1.24)	1.24 (1.19-1.29)	1.22 (1.14-1.30)	1.28 (1.15-1.41)
1-2	1.09 (1.03-1.14)	1.10 (1.07-1.13)	1.17 (1.14-1.19)	1.15 (1.12-1.19)	1.17 (1.12-1.23)	1.16 (1.07-1.25)
2-3	1.08 (1.03-1.13)	1.11 (1.08-1.14)	1.14 (1.12-1.17)	1.14 (1.11-1.18)	1.20 (1.14-1.26)	1.31 (1.21-1.41)
3-4	1.05 (0.99-1.11)	1.08 (1.05-1.12)	1.15 (1.12-1.18)	1.14 (1.10-1.18)	1.19 (1.13-1.26)	1.27 (1.16-1.38)
4-5	1.09 (1.03-1.16)	1.07 (1.03-1.11)	1.12 (1.08-1.15)	1.13 (1.09-1.18)	1.19 (1.12-1.27)	1.11 (1.00-1.22)
	Maternal age #					
	<20	**20-24**	**25-29**	**30-34**	**35-39**	**≥40**
0-5	***1.09 (1.04-1.14)***	***1.10 (1.08-1.12)***	***1.14 (1.12-1.16)***	***1.16 (1.14-1.18)***	***1.18 (1.15-1.23)***	***1.17 (1.10-1.25)***
0-1	1.20 (1.06-1.35)	1.20 (1.15-1.26)	1.19 (1.15-1.23)	1.21 (1.18-1.25)	1.21 (1.15-1.28)	1.24 (1.09-1.42)
1-2	1.06 (0.97-1.15)	1.11 (1.08-1.15)	1.13 (1.11-1.16)	1.16 (1.13-1.19)	1.17 (1.13-1.22)	1.08 (0.97-1.19)
2-3	1.09 (1.01-1.19)	1.11 (1.07-1.15)	1.14 (1.11-1.17)	1.15 (1.12-1.18)	1.17 (1.12-1.22)	1.15 (1.03-1.28)
3-4	1.07 (0.98-1.17)	1.06 (1.02-1.10)	1.15 (1.12-1.18)	1.14 (1.11-1.17)	1.17 (1.11-1.23)	1.26 (1.11-1.42)
4-5	1.07 (0.97-1.18)	1.05 (1.01-1.10)	1.10 (1.07-1.14)	1.14 (1.11-1.18)	1.19 (1.13-1.25)	1.24 (1.08-1.42)
Injury hospitalization						
	Paternal age #					
	<25	**25-29**	**30-34**	**35-39**	**40-44**	**≥45**
0-5	***1.24 (1.05-1.47)***	***1.43 (1.29-1.59)***	***1.47 (1.34-1.61)***	***1.52 (1.36-1.70)***	***1.69 (1.43-2.01)***	***1.69 (1.33-2.16)***
0-1	1.47 (0.99-2.17)	1.93 (1.53-2.44)	1.50 (1.21-1.86)	1.28 (0.97-1.70)	1.79 (1.18-2.70)	1.89 (1.13-3.14)
1-2	1.24 (0.88-1.76)	1.50 (1.25-1.81)	1.55 (1.32-1.83)	1.62 (1.33-1.96)	1.62 (1.20-2.19)	2.30 (1.55-3.40)
2-3	0.98 (0.68-1.40)	1.29 (1.03-1.61)	1.62 (1.34-1.94)	1.61 (1.28-2.03)	1.77 (1.27-2.47)	0.72 (0.34-1.54)
3-4	1.41 (0.98-2.03)	1.43 (1.13-1.81)	1.43 (1.15-1.77)	1.66 (1.29-2.14)	1.64 (1.08-2.48)	1.73 (1.00-3.00)
4-5	1.25 (0.84-1.87)	1.02 (0.75-1.38)	1.12 (0.86-1.46)	1.33 (0.98-1.81)	1.67 (1.04-2.70)	1.70 (0.91-3.18)
	Maternal age #					
	<20	**20-24**	**25-29**	**30-34**	**35-39**	**≥40**
0-5	***1.26 (0.99-1.61)***	***1.40 (1.26-1.57)***	***1.54 (1.42-1.68)***	***1.48 (1.34-1.63)***	***1.56 (1.32-1.83)***	***1.36 (0.92-2.01)***
0-1	1.47 (0.81-2.67)	1.64 (1.25-2.15)	1.68 (1.36-2.06)	1.50 (1.19-1.88)	1.61 (1.14-2.28)	1.62 (0.71-3.69)
1-2	1.00 (0.60-1.68)	1.51 (1.24-1.84)	1.63 (1.40-1.90)	1.61 (1.35-1.90)	1.57 (1.18-2.09)	1.49 (0.79-2.82)
2-3	1.25 (0.75-2.08)	1.40 (1.13-1.74)	1.36 (1.13-1.65)	1.38 (1.11-1.72)	2.09 (1.54-2.82)	1.44 (0.58-3.56)
3-4	1.57 (0.93-2.65)	1.26 (0.98-1.62)	1.68 (1.39-2.04)	1.65 (1.31-2.07)	1.17 (0.76-1.79)	1.13 (0.35-3.62)
4-5	1.15 (0.62-2.13)	1.19 (0.89-1.61)	1.34 (1.06-1.68)	1.15 (0.86-1.55)	1.12 (0.63-2.02)	0.76 (0.19-3.14)

adjusted for birth year, child sex, birth order, maternal age (or paternal age), foreign-born mother, and urbanicity of residence. Child age was also adjusted in estimating IRR for ages 0-5.

3.3.5 *Secondary analyses*

The first set of secondary analyses involved expanding the binary exposure variable to denote which parent(s) had SMI: none, maternal, paternal, and both. Generally, children with both parents with SMI were more likely to have injury than children with an affected mother, only, who in turn had a greater risk than children with an affected father, only. Relative to children whose parents have no SMI diagnosis, the aIRR of any injury at < 5 years for children with both parents having a diagnosis of SMI was greater (aIRR 1.25, 95% CI: 1.19-1.31) than for children with maternal SMI only (aIRR 1.15, 95% CI: 1.14-1.17), which, in turn, was higher than children with paternal SMI only aIRR (1.12, 95% CI: 1.10-1.13). We conducted three pairwise comparisons of the exposure groups without adjustment for multiple comparisons. Compared to children with both parents having a diagnosis of SMI, the aIRRs were smaller for those with maternal SMI only (aIRR 0.92, 95% CI: 0.88-0.97) and for those with paternal SMI only (aIRR 0.89, 95% CI: 0.85-0.94). Compared to children with maternal SMI only, the aIRR was smaller for those with paternal SMI only (aIRR 0.97, 95% CI: 0.95-0.98). When stratified by child's age group, this trend became less consistent because of overlapping 95% CIs (S-Figure 5 and S-Table 19).

For injury hospitalization at <5 years (S-Figure 6 and S-Table 20), the aIRR point estimate for children with two parents diagnosed with SMI was greater (aIRR 1.85, 95% CI: 1.38-2.48) than that for those with maternal SMI only (aIRR 1.58, 95% CI: 1.48-1.68) or for those with paternal SMI only (aIRR 1.34, 95% CI: 1.23-1.46). In pairwise comparison, the aIRR (0.72, 95% CI: 0.53-0.98) was smaller for children with paternal SMI only compared to those with both parents having SMI. The aIRR (0.85, 95% CI: 0.77-0.95) was also smaller for children paternal SMI only compared to those with maternal SMI only. However, when comparing the risk

associated with maternal SMI to that with both parents having SMI, the 95% CIs included null (aIRR 0.85, 95% CI: 0.63-1.15).

The next set of analyses classified the exposure as SMI onset before childbirth and SMI onset after childbirth. For paternal SMI, the aIRR of any childhood injury for onset before childbirth (aIRR 1.12, 95% CI: 1.10-1.14) was of similar magnitude compared to onset after childbirth (aIRR 1.12, 95% CI: 1.10-1.14). For maternal SMI, the aIRRs were also similar for onset before (aIRR 1.16, 95% CI: 1.14-1.17) or after birth (aIRR 1.15, 95% CI: 1.14-1.17). The aIRRs for injury hospitalization were also similar between illness onset before and after childbirth (S-Table 20).

In the final set of secondary analyses, we examined exposures classified by parent SMI diagnosis, specifically: no SMI, schizophrenia, bipolar disorder, and MDD including parents with >1 disorder in each relevant analysis. Overall, the aIRRs associated with parental diagnosis of schizophrenia or bipolar disorder tended to be greater than parental diagnosis of MDD. Relative to children whose fathers were absent an SMI diagnosis, the aIRR for any childhood injury among children with fathers who were diagnosed with: 1. schizophrenia was 1.13 (95% CI: 1.11-1.16); 2. bipolar disorder was 1.15 (95% CI: 1.12-1.17); and 3. MDD was 1.10 (95% CI: 1.08-1.12). In pairwise comparisons of paternal diagnosis, the aIRRs for schizophrenia compared to bipolar disorder, for schizophrenia compared to MDD, and for bipolar disorder compared to MDD were 0.99 (95% CI: 0.96-1.02), 1.03 (95% CI: 1.00-1.06), and 1.04 (95% CI: 1.01-1.08), respectively.

Relative to children whose mothers were absent an SMI diagnosis, the aIRR for any childhood injury among children with mothers who were diagnosed with: 1. schizophrenia was 1.17 (95% CI: 1.14-1.20); 2. bipolar disorder was 1.17 (95% CI: 1.15-1.20); and 3. MDD was 1.15 (95% CI: 1.13-1.16). In pairwise comparisons of maternal diagnosis, the aIRRs for schizophrenia compared to bipolar disorder, for schizophrenia compared to MDD, and for bipolar disorder compared to

MDD were 1.00 (95% CI: 0.97-1.03), 1.02 (95% CI: 0.99-1.05), and 1.02 (95% CI: 1.00-1.05), respectively.

For injury hospitalization, the aIRR associated with paternal schizophrenia was 1.47 (95% CI: 1.29-1.68), paternal bipolar disorder 1.60 (95% CI: 1.41-1.83) and paternal major depressive disorder 1.22 (95% CI: 1.09-1.37). In pairwise comparisons of paternal diagnosis, the aIRRs for schizophrenia compared to bipolar disorder, for schizophrenia compared to MDD, and for bipolar disorder compared to MDD were 0.91 (95% CI: 0.76-1.09), 1.19 (95% CI: 1.00-1.41), and 1.31 (95% CI: 1.10-1.56), respectively. For maternal SMI, the aIRR associated with schizophrenia was 1.99 (95% CI: 1.75-2.26); bipolar disorder 1.70 (95% CI: 1.52-1.90); MDD 1.41 (95% CI: 1.31-1.52). In pairwise comparisons of maternal diagnosis, the aIRRs for schizophrenia compared to bipolar disorder, for schizophrenia compared to MDD, and for bipolar disorder compared to MDD were 1.17 (95% CI: 0.99-1.39), 1.41 (95% CI: 1.22-1.63), and 1.20 (95% CI: 1.05-1.37), respectively.

3.4 EARLY CHILDHOOD COMMON INFECTIOUS DISEASE

3.4.1 *Descriptive analyses*

During the study follow-up, 2,156,446 (94.9%) children had a total of 46,275,689 episodes of diarrhea or respiratory infection (referred to as common infectious disease, Table 3-11) in the first five years of life, consisting of 126,444,920 outpatient/inpatient visits. Of the children with any episode, 2,091,191 (97.0%) had >1 episode. There were 644,823 (28.4%) children who were hospitalized due to common infectious disease. Among common infectious disease, 2.4% and 4.2% involved inpatient and emergency department services, respectively; and 17.6% had been treated with antibiotics (Table 3-11). When counting diarrhea or respiratory infection separately, there were more episodes of respiratory infection than diarrhea. Diarrhea had a slightly greater percentage of inpatient or emergency department services utilization than respiratory infection, but a lower percentage of antibiotic treatment (Table 3-11).

Table 3-11 Episodes of common infectious disease in the first 5 years of life among children with Taiwanese citizenship born in 2004-2014

	Episodes	**Children***	**%***	**Hospitalization**	**%#**	**ED**		**Antibiotics**	**%#**
Overall	***46,283,625***	***2,156,446***	***94.9***	***1,129,647***	***2.4***	***1,942,323***	***4.2***	***8,138,760***	***17.6***
Diarrhea	7,898,299	1,818,926	80.0	386,351	4.9	447,257	5.7	670,334	8.5
Respiratory infection	44,848,383	2,149,942	94.6	931,629	2.1	1,659,946	3.7	7,970,264	17.8

*Children refers to number of children who had an episode during the follow-up period. Those with >1 episodes of the same category were counted only once. Denominator was the number of children with Taiwan citizenship born after 2004 (N=2,272,783) and existed in the registry of beneficiaries and/or the MCHD.

Hospitalization and ED refer to a child had utilized inpatient or emergency room services during an episode. Antibiotics refers to antibiotics had been prescribed during an episode. Denominator was the number of episodes of each category.

Table 3-12 summarizes IRs of common infectious disease among the study population and among children with and without a matched birth certificate record. When estimating IRs, children

were assumed to be continuously enrolled until the end of the follow-up period or death. The IRs among children excluded from the study population (IR 4.88 [95% CI: 4.87-4.88] per person-years for children with a matched record and IR 2.72 [95% CI: 2.71-2.72] for those without a matched record) were lower than that in the study population (IR 5.47 [95% CI: 5.47-5.47]).

Table 3-12 Incidence rates of common infectious disease in the first 5 years of life, stratified by whether a child was included in the study population and matched to a birth certificate record

	Children* (N)	Episodes (n)	Person-years^	Incidence rate# (95% CI)
Study population	1,999,322	42,327,561	7,741,026.33	5.47 (5.47-5.47)
Matched@	199,496	3,197,054	655,272.85	4.88 (4.87-4.88)
Unmatched@	73,965	751,074	276,499.52	2.72 (2.71-2.72)

Abbreviation: CI: Confidence interval
@Matched: children with a matched birth certificate record but not included in the study population; unmatched: children without a matched birth record. The matched group could have a slightly inflated incidence rate because the records in the first 90 days of life could not be assigned exactly to a child's ID.
* Number of children with Taiwanese citizenship born in 2004-2014.
^Censored when the child died. Otherwise, a person was assumed to have continuous enrollment.
#per person-years

In the study population, 1,928,281 (96.4%) children had a total of 42,327,561 episodes of common infectious disease at < 5 years, which involved 115,847,882 outpatient/inpatient visits. Children with parental SMI had slightly greater percentage (97.8%) of having common infectious disease than those without parental SMI (96.4%). Children aged 0-1 years had the lowest IRs: 4.42 (95% CI: 4.41-4.42) per person-year in the unexposed periods and 4.55 (95% CI: 4.53-4.57) in the exposed periods (Table 3-13). The highest IRs occurred at age 4-5 years: 6.11 (95% CI: 6.10-6.11) and 6.10 (95% CI: 6.08-6.12) per person-year for the unexposed and exposed periods, respectively. The differences in IRs between the exposed and unexposed periods were negligible. The unadjusted IRR across child age for common infectious disease during the exposed period relative to the unexposed periods were approximately 1.0 (Table 3-13). When actual healthcare visits were counted instead of illness episodes, the estimates of unadjusted IRRs were similar (S-Table 21).

S-Table 22 summarizes IRs for diarrhea and respiratory infection separately. Compared with children unexposed to parental SMI, exposed children were slightly more likely to have diarrhea (unadjusted IRR 1.03-1.14). The IRRs of respiratory infection were very close to the null value.

Table 3-13 Incidence rates of common infectious disease among children in the study population stratified by child age and exposure to parental serious mental illness

Age	Unexposed periods		Exposed periods		Rate difference	Unadjusted IRR
(years)	Events	Rate (95% CI)	Events	Rate (95% CI)	(95% CI)	(95% CI)
Any episode#						
0-1	8,178,200	4.42 (4.41-4.42)	267,551	4.55 (4.53-4.57)	0.14 (0.12-0.15)	1.03 (1.03-1.03)
1-2	9,703,178	5.80 (5.79-5.80)	350,578	5.77 (5.75-5.79)	-0.03 (-0.05--0.01)	1.00 (0.99-1.00)
2-3	8,365,611	5.64 (5.63-5.64)	344,883	5.66 (5.64-5.67)	0.02 (-0.00-0.04)	1.00 (1.00-1.00)
3-4	7,478,409	5.77 (5.76-5.77)	347,579	5.80 (5.78-5.82)	0.03 (0.01-0.05)	1.01 (1.00-1.01)
4-5	6,937,566	6.11 (6.10-6.11)	354,006	6.10 (6.08-6.12)	-0.003 (-0.02-0.02)	1.00 (1.00-1.00)
Used antibiotics&						
0-1	1,289,696	697 (696-698)	42,742	729 (722-736)	32 (25-39)	1.05 (1.04-1.06)
1-2	1,726,189	1033 (1031-1035)	64,164	1062 (1054-1070)	29 (21-37)	1.03 (1.02-1.04)
2-3	1,481,691	1001 (1000-1003)	63,523	1051 (1043-1060)	50 (42-58)	1.05 (1.04-1.06)
3-4	1,343,745	1041 (1039-1043)	64,430	1090 (1081-1098)	49 (40-58)	1.05 (1.04-1.06)
4-5	1,262,868	1118 (1116-1120)	65,773	1154 (1145-1163)	36 (27-45)	1.03 (1.02-1.04)
Hospitalized&						
0-1	286,547	155 (154-155)	11,805	201 (198-205)	46 (43-50)	1.30 (1.28-1.32)
1-2	263,891	158 (157-159)	12,371	205 (201-208)	47 (43-51)	1.30 (1.27-1.32)
2-3	177,992	120 (120-121)	9,895	164 (161-167)	44 (40-47)	1.36 (1.33-1.39)
3-4	132,569	103 (102-103)	8,132	138 (135-141)	35 (32-38)	1.34 (1.31-1.37)
4-5	106,098	94 (93-95)	7,004	123 (120-126)	29 (26-32)	1.31 (1.28-1.34)

#per 1,000 person-years Censored when the child died. Otherwise, a person was assumed to have continuous enrollment.
#Incidence rate: per person-year. & Incidence rate: per 1,000 person-years. Censored when the child died. Otherwise, a person was assumed to have continuous enrollment.

There was a total of 7,404,821 (17%) episodes of common infectious disease treated with antibiotics. The IRs of antibiotic-treated infection were lowest at age 0-1 years: 697 per 1,000 person-years (95% CI: 696-698) in the unexposed period and 729 (95% CI: 722-736) in the exposed period. The IRs gradually increased with child age to 1,118 (95% CI: 1,116-1,120) in the unexposed periods and 1,154 (95% CI: 1,145-1,163) in the exposed periods at age 4-5 years (Table 3-13). The unadjusted IRRs of antibiotic-treated infection were between 1.03-1.05. There were

1,016,304 (2%) episodes of common infectious disease that resulted in hospitalization. The IRs of hospitalized infection, by contrast, were highest at age 1-2 years: 158 per 1,000 person-years (95% CI: 157-159) in the unexposed periods and 205 (95% CI: 201-208) in the exposed periods; gradually decreased to 94 (95% 93-95) and 123 (95% 120-126) in the unexposed and exposed periods, respectively, at age 4-5 years (Table 3-13). The unadjusted IRRs of hospitalized infection were between 1.30-1.36 (greater than those of antibiotic-treated episodes).

S-Table 23, S-Table 24 and S-Table 25 presents associations between covariates and (1) childhood common infectious disease (overall infection), (2) antibiotic-treated infection and (3) hospitalized infection occurring before age 5 years, respectively. The risk of overall infection for children in the later birth cohorts was slightly lower (unadjusted IRR 0.99 [95% CI: 0.99-0.99] in 2008-2010; and 0.89 [95% CI: 0.89-0.89] in 2011-2014) compared to the earliest birth cohort of 2004-2007. Boys had greater risk of having overall infection (IRR 1.04, 95% CI: 1.04-1.04) than girls. Higher birth-order children had a greater probability of overall infection (IRR 1.08 [95% CI: 1.08-1.09] and 1.04 [95% CI: 1.04-1.05] for second-born children and for those of 3+ birth order, respectively) than first-born children. Having complex chronic illness (IRR 1.05, 95% CI: 1.05-1.06) was associated with slightly greater risk. Being born to unmarried mothers (IRR 0.92, 95% CI: 0.91-0.92) or foreign mothers (0.90, 0.90-0.91) was associated with a lower risk of overall infections. Paternal and maternal ages were both inversely associated with risk of overall infection. Compared to children with paternal age of 30-34 years, the IRRs were 1.01 (95% CI: 1.01-1.01) and 0.86 (95% CI: 0.86-0.86) for those with paternal age <25 or age ≥45 years, respectively. Results were similar with respect to maternal age. The only exception was that risk for children with maternal age of <20 years was 2% (95% CI: 0.97-0.98) smaller than those with maternal age

30-34. Mann-Kendall test indicated a monotonic decreasing trend in IRs over paternal age (p value: 0.01) but not maternal age (p value: 0.19).

Urbanicity of residence was associated with risk of overall infection, with degrees of urbanicity negatively correlated with risk (p value of Mann-Kendall trend test: 0.002). The IRR for the lowest urbanicity level was 1.13 (95% CI: 1.13-1.13) compared to the highest urbanicity. Children from lower-income families were slightly more likely to have overall infection (IRR 1.03-1.05) compared to those from the highest income families. The only exception was the lowest income group (IRR 0.96, 95% CI: 0.95-0.96). However, there was not enough evidence to support a monotonic trend over the family income groups (p value of Mann-Kendall test: 0.62). Children with parental occupation of union members, farmers and fishermen were more likely to have overall infections (IRR 1.05, 95% CI: 1.05-1.05) compared to children with parental occupation of employees, employers and professionals. Other occupation categories, on the contrary, were associated with a lower risk. Children with parental physical illness were slightly more likely to be have overall infection than children without (IRR 1.01-1.03). Finally, for children who died or whose parent(s) died during the follow-up, the IRRs were all less than 1 (0.82-0.94) than those who did not died or without parental death.

Most of the associations between covariates and antibiotic-treated infection were similar to the patterns of the overall infections. However, some covariates were associated with an greater risk of antibiotic-treated infection than that of overall infection, including being male (IRR 1.10, 95% CI: 1.10-1.11), having higher birth order (IRR 1.14 [95% CI: 1.14-1.14] for second-born children and 1.11 [95% CI: 1.10-1.11] for those of 3+ birth order), having complex chronic illness (IRR 1.25, 95% CI: 1.25-1.25), lower urbanicity of residence (IRR 1.04-1.30), or parental occupation as union members, farmers and fishermen (IRR 1.12 [95% CI: 1.12-1.13] and 1.14

[95% CI: 1.14-1.15] for paternal and maternal occupation, respectively). LBW (IRR 1.02, 95% CI: 1.02-1.02) and preterm birth (1.07, 1.07-1.08) were associated with a slightly greater risk of antibiotic-treated infection.

The excess risk of hospitalized infection were elevated for the following characteristics: being males (IRR 1.19, 95% CI: 1.19-1.20), being of LBW (IRR 1.36, 95% CI: 1.35-1.37), being of preterm birth (IRR 1.41, 95% CI: 1.4-1.42), and having complex chronic illness (IRR 2.00, 95% CI: 1.98-2.01). The excess risk also increased for having a parent with physical illness (IRR 1.16-1.61), being among the subset of our study cohort having experienced child or parental death (IRR 1.28-5.97), residence in a lower urbanicity region (greater rurality, IRR 1.15-1.99) and being from a family with lower income (IRR 1.18-1.43). The Mann-Kendall test indicated monotonic trends over urbanicity of residence (p value: 0.002) and family income (p value: 0.0143). Paternal and maternal ages were both inversely associated with risk of hospitalized infection. The only exception was that children with paternal age ≥45 were associated with a slightly greater risk (IRR 1.03, 95% CI: 1.01-1.04) compared with those with paternal age of 30-34. The Mann-Kendall test suggested a monotonic trend in IRs over maternal age (p value: 0.005) but not paternal age (p value: 0.19). For parental occupation, except for civil servants and teachers, all other occupation types had a greater risk of hospitalized infection compared to the occupation of employees, employers and professionals. Children of unmarried mothers (IRR 1.16, 95% CI: 1.15-1.17) or foreign-born mothers (1.12, 1.11-1.12) experienced a greater risk of hospitalized infection, which were reversed from the patterns of overall infection and antibiotic-treated infection.

3.4.2 *Multivariable analyses*

Children with parental SMI had a slightly greater risk of having any health service contact for childhood common infectious disease (aIRR 1.01 [95% CI: 1.01-1.01], Table 3-14) compared with

unexposed children after adjusting for birth year, child sex, child age, birth order, parental ages, foreign-born mother, and urbanicity of residence. The results did not change with further adjustment for unmarried mother, family income, parental occupation and physical illness, child's LBW and preterm birth. Parental SMI was associated with greater risk of antibiotic-treated infection or of hospitalized infection than that of any common infectious disease. Children with parental SMI had a 4% (aIRR 1.04 [95% CI: 1.03-1.05]) and 31% (aIRR 1.31 [95% CI: 1.29-1.33]) greater rate of antibiotic-treated infection and hospitalized infection, respectively, compared with unexposed children (Table 3-14). When unmarried mother, family income, parental occupation and physical illness, child's LBW and preterm birth were also adjusted, the IRR of hospitalized infection was slightly decreased to 1.27 (95% CI: 1.25-1.29).

Table 3-14 Childhood common infectious disease in relation to having any parent with serious mental illness

	Adjusted incidence rate ratio (95% Confidence intervals)			
	Model 1	**Model 2**	**Model 3**	**Model 4**
Overall infections	1.01 (1.01-1.01)	1.01 (1.01-1.01)	1.02 (1.01-1.02)	1.02 (1.01-1.02)
Used antibiotics	1.04 (1.04-1.05)	1.04 (1.03-1.05)	1.05 (1.04-1.06)	1.05 (1.04-1.06)
Hospitalized	1.32 (1.30-1.34)	1.31 (1.29-1.33)	1.27 (1.25-1.29)	1.27 (1.25-1.29)

Model 1: adjusted for birth year, child sex, and child age.
Model 2: adjusted for the above variables and birth order, maternal and paternal ages, foreign-born mother, and urbanicity of residence.
Model 3: adjusted for the above variables and unmarried mother, family income, maternal and paternal occupations, and maternal and paternal Elixhauser indexes.
Model 4: adjusted for the above variables and child's LBW and preterm birth.

3.4.3 *Sensitivity analyses*

The percentages of episodes excluded from the sensitivity analyses were slightly greater in the exposed periods than the unexposed periods (S-Table 15). However, the aIRRs obtained from the sensitivity analyses were similar to those of the primary analyses (S-Table 26).

3.4.4 *Stratified analyses*

When stratified on urbanicity of residence or parental occupations, the stratified models did not show any notable patterns of differences in aIRR for common infectious disease across strata. The coefficients of interaction terms between parental SMI and urbanicity of residence were negligible despite being highly significant ($p < 0.0001$). Most of the coefficients for interaction terms between parental SMI and parental occupation were associated with wide 95% CIs containing null. When models were stratified on paternal and maternal ages separately, the results suggested parental ages slightly modified the weak (very close to null) associations between parental SMI and overall infections (Table 3-15). This pattern became more obvious for hospitalized infection. The association between parental SMI and hospitalized infection was stronger for children with older parents than for those with younger parents (Table 3-15).

Table 3-15 Stratified analysis of associations between parental serious mental illness and early childhood common infectious disease by parental age

	Adjusted incidence rate ratio (95% confidence intervals)					
Overall infections						
Paternal age[#]	<25	25–29	30–34	35-39	40-44	≥45
	1.00 (0.99-1.00)	1.00 (1.00-1.01)	1.01 (1.01-1.02)	1.02 (1.01-1.02)	1.03 (1.02-1.04)	1.03 (1.02-1.05)
Maternal age[#]	<20	20–24	25–29	30–34	35-39	≥40
	1.01 (0.99-1.02)	1.01 (1.00-1.02)	1.01 (1.00-1.01)	1.02 (1.01-1.02)	1.03 (1.02-1.04)	1.03 (1.01-1.05)
Hospitalized						
Paternal age[#]	<25	25–29	30–34	35-39	40-44	≥45
	1.13 (1.07-1.19)	1.29 (1.25-1.33)	1.34 (1.30-1.37)	1.34 (1.30-1.38)	1.37 (1.30-1.45)	1.36 (1.25-1.48)
Maternal age[#]	<20	20–24	25–29	30–34	35-39	≥40
	1.16 (1.06-1.27)	1.22 (1.18-1.27)	1.33 (1.30-1.36)	1.33 (1.29-1.36)	1.41 (1.35-1.47)	1.46 (1.30-1.63)

adjusted for birth year, child sex, birth order, maternal age (/paternal age), foreign-born mother, and urbanicity of residence

3.4.5 *Secondary analyses*

Three set of secondary analyses were performed to evaluate associations between parental SMI and any childhood common infectious disease. The first set of analyses evaluated which parent(s) had a SMI: no SMI, maternal, paternal, or both. The next set of analyses classified the exposure as SMI onset before childbirth and SMI onset after childbirth. The final set of analyses classified the exposure by parent diagnosis: none, schizophrenia, bipolar disorder, and MDD. In these analyses, the associations between exposure and any common infectious disease were very close to null (S-Table 27).

We also assessed associations between parental SMI and hospitalized infections in secondary analyses (S-Figure 7 and S-Table 28). In the first set of analyses, relative to children with no parental SMI, the aIRR of hospitalized infections for children with both parents having been diagnosed with SMI was greater (aIRR 1.51, 95% CI: 1.37-1.65) than children with only maternal SMI (aIRR 1.39, 95% CI:1.36-1.42), or with only paternal SMI (aIRR 1.17, 95% CI:1.14-1.21). We conducted pairwise comparisons of the exposure groups without adjustment for multiple comparisons. Compared to children with both parents having SMI, the aIRRs were slightly smaller for those with only maternal SMI (aIRR 0.92, 95% CI: 0.84-1.02) and for those with only paternal SMI (aIRR 0.78, 95% CI:0.71-0.86). Compared to children with only maternal SMI, the aIRR was smaller for those with only paternal SMI (aIRR 0.84, 95% CI: 0.82-0.87).

In the next set of secondary analyses, the aIRR for paternal SMI onset before childbirth (aIRR 1.18, 95% CI: 1.15-1.21) was of similar magnitude as for onset after childbirth (aIRR 1.23, 95% CI: 1.19-1.28). For maternal SMI, the aIRRs were also similar for onset before (aIRR 1.43, 95% CI: 1.40-1.46) or after birth (aIRR 1.36, 95% CI: 1.33-1.40).

In the final set of analyses, the point estimate of aIRRs of hospitalized infections associated with schizophrenia or bipolar disorder tended to be greater than that of MDD. For paternal SMI, relative to no SMI, the aIRR in relation to schizophrenia was 1.24 (95% CI: 1.19-1.29); bipolar disorder was 1.24 (95% CI: 1.18-1.29); MDD was 1.16 (95% CI: 1.12-1.20). In pairwise comparisons of paternal diagnosis, the aIRRs for schizophrenia compared to bipolar disorder, for schizophrenia compared to MDD, and for bipolar disorder compared to MDD were 1.00 (95% CI: 0.94-1.06), 1.07 (95% CI: 1.01-1.12), and 1.07 (95% CI: 1.01-1.13), respectively. For maternal SMI, relative to no SMI, the aIRR associated with schizophrenia was 1.42 (95% CI: 1.34-1.49); bipolar disorder was 1.45 (95% CI: 1.40-1.50); and MDD was 1.38 (95% CI: 1.35-1.41). In pairwise comparisons of maternal diagnosis, the aIRRs for schizophrenia compared to bipolar disorder, for schizophrenia compared to MDD, and for bipolar disorder compared to MDD were 0.98 (95% CI: 0.92-1.04), 1.03 (95% CI: 0.98-1.08), and 1.05 (95% CI: 1.01-1.10), respectively.

3.5 NEGATIVE CONTROL OUTCOME- CHILD APPENDICITIS

3.5.1 *Descriptive analyses*

During the study follow-up, 4,218 (0.19%) children born in 2004-2014 received an appendicitis diagnosis. Table 3-16 summarizes IRs of appendicitis among the study population and among children with and without a matched birth certificate record. When estimating IRs, children were assumed to be continuously enrolled until the end of the follow-up period or death. Children without a matched birth certificate record had a lower IR than those in the study.

Table 3-16 Incidence rates of appendicitis in the first 5 years of life, stratified by whether a child was included in the study population and matched to a birth certificate record

	Children* (N)	**Episodes (n)**	**Person-years^**	**Incidence rate# (95% CI)**
Study population	1,999,322	3,862	7,732,793.87	0.50 (0.48-0.52)
Matched@	199,496	303	654,651.54	0.46 (0.41-0.52)
Unmatched@	73,965	53	276,407.48	0.19 (0.15-0.25)

Abbreviation: CI: Confidence interval
@Matched: children with a matched birth certificate record but not included in the study population; unmatched: children without a matched birth record. The matched group could have a slightly inflated incidence rate because the records in the first 90 days of life could not be assigned exactly to a child's ID.
^Censored when the children died. Otherwise, a person was assumed to have continuous enrollment.
#per 1,000 person-years

In the study population, 3,862 (0.19%) children received a diagnosis of appendicitis at < 5 years. Children of age 0-1 years had the lowest IRs: 0.33 (95% CI: 0.30-0.35) per 1000 person-years in the unexposed periods and 0.32 (95% CI: 0.21-0.51) in the exposed periods. The highest IRs occurred at age 4-5 years: 0.69 (95% CI: 0.65-0.74) and 0.76 (95% CI: 0.57-1.02), respectively, for the unexposed and exposed periods. The differences in IRs between the exposed and unexposed periods were negligible. The unadjusted IRRs varied across age groups, and the associated 95% CIs were wide due to very few events (Table 3-17).

Table 3-17 Incidence rates of appendicitis among children in the study population, stratified by child age and exposure to parental serious mental illness

Age (years)	Unexposed periods			Exposed periods			Rate difference (95% CI)	Unadjusted IRR (95% CI)
	Events	PY	Rate# (95% CI*)	Events	PY	Rate# (95% CI)		
0-1	605	1,851,358.90	0.33 (0.30-0.35)	19	58,769.96	0.32 (0.21-0.51)	0.003 (-0.15-0.14)	0.99 (0.63-1.56)
1-2	876	1,673,063.75	0.52 (0.49-0.56)	41	60,716.89	0.68 (0.50-0.92)	0.15 (-0.06-0.36)	1.29 (0.94-1.76)
2-3	745	1,482,403.64	0.50 (0.47-0.54)	22	60,905.23	0.36 (0.24-0.55)	-0.14 (-0.30-0.01)	0.72 (0.47-1.10)
3-4	681	1,294,434.51	0.53 (0.49-0.57)	42	59,789.19	0.70 (0.52-0.95)	0.18 (-0.04-0.39)	1.34 (0.98-1.82)
4-5	787	1,133,506.23	0.69 (0.65-0.74)	44	57,845.57	0.76 (0.57-1.02)	0.07 (-0.16-0.30)	1.10 (0.81-1.48)

Abbreviation: PY: person-years; CI: Confidence intervals; IRR: incidence rate ratio.
Incidence rate: per 1,000 person-years. Censored when the child died. Otherwise, a person was assumed to have continuous enrollment

S-Table 29 describes associations between covariates and appendicitis occurring at < 5 years. Risks of appendicitis for children in the later birth cohorts were lower (unadjusted IRR 0.67 [95% CI: 0.62-0.72] in 2008-2010; and 0.49 [95% CI: 0.44-0.54] in 2011-2014) compared to the earliest birth cohort of 2004-2007. Boys had a greater risk of having appendicitis (IRR 1.23, 95% CI: 1.15-1.31) than girls. Children of 3+ birth order had a greater probability of having appendicitis (IRR 1.12, 95% CI: 1.00-1.25) than first-born children. LBW (IRR 1.26, 95% CI: 1.12-1.43), preterm birth (IRR 1.32, 95% CI: 1.18-1.48), or complex chronic conditions (IRR 1.92, 95% CI: 1.75-2.11) was also associated with a greater risk of appendicitis. Paternal and maternal ages were both inversely associated with the appendicitis risk. Children of foreign-born mothers were less likely to receive a diagnosis of appendicitis (IRR 0.88, 95% CI: 0.79-0.98). Compared to the highest urbanicity, lower urbanicity levels were associated with greater risks of appendicitis (IRR 1.48-2.50). Children from lower-income families had a greater risk of appendicitis (IRR 1.25-1.49) than those from the highest income families. Compared to children with parental occupation of employees, employers and professional, those with parental occupation of union members, farmers

and fishermen were also more likely to have appendicitis (IRR 1.14 [95% CI: 1.00-1.29] and 1.42 [95% CI: 1.23-1.63] for paternal and maternal occupation, respectively).

3.5.2 *Multivariable analyses*

Children with parental SMI had an 10% (aIRR 1.10, 95% CI: 0.94-1.28) greater rate of appendicitis compared with unexposed children after adjusting for birth year, child sex and age, birth order, parental ages, foreign-born mother and urbanicity of residence (Table 3-18). If we further adjusted for unmarried mother, family income, parental occupation and physical illness, child's LBW and preterm birth, the IRR was slightly decreased to 1.08 (95% CI: 0.92-1.27). For the sensitivity analyses, the exclusion of children without complex chronic conditions or children with a parent having multiple IDs led to small decreases in the magnitude of aIRRs but did not change study conclusions (S-Table 30). The results of excluding children with parental death before age 5 years were similar to that of the primary analyses. All of the associated 95% CIs from these sensitivity analyses included null. In sum, these analyses did not provide enough evidence to support that exposed children had a greater risk of appendicitis than unexposed children.

Table 3-18 Childhood appendicitis in relation to having any parent with serious mental illness

Adjusted incidence rate ratio (95% Confidence intervals)			
Model 1	**Model 2**	**Model 3**	**Model 4**
1.10 (0.94-1.29)	1.10 (0.94-1.28)	1.09 (0.93-1.27)	1.08 (0.92-1.27)

Model 1: adjusted for birth year, child sex, and child age.
Model 2: adjusted for the above variables and birth order, maternal and paternal ages, foreign-born mother, and urbanicity of residence.
Model 3: adjusted for the above variables and unmarried mother, family income, maternal and paternal occupations, and maternal and paternal Elixhauser indexes
Model 4: adjusted for the above variables and child's LBW and preterm birth

3.6 PREVENTIVE HEALTH CARE UTILIZATION

The difference in healthcare seeking behavior, in terms of level of prenatal care and number of well-child visits, was negligible between children of parents with and without SMI. Among 1,126,253 children in the study population born before 2010, the mean numbers of prenatal and well-child visits were slightly fewer in the children with parental SMI (8.09 and 5.70, respectively) compared to children without (8.17 and 5.80, respectively). The median time of the third and the fifth well-child visits were also similar between two groups (Table 3-19).

Table 3-19 Utilization of preventive health services among children in the study population born in 2004-2009

	Without parental SMI* (N=1,068,926)			**With parental SMI* (N=57,327)**		
	Mean	**SD**		**Mean**	**SD**	
Prenatal visits (n)	8.17	2.47		8.09	2.50	
Well-child visits (n)	5.80	2.21		5.70	2.24	
	Median	**IQR**	**Missing (%)**	**Median**	**IQR**	**Missing (%)**
Days to the 3rd well-child visit	229	186-376	92,621 (8.6)	240	186-382	5,377 (9.4)
Days to the 5th well-child visit	552	386-759	256,152 (24.0)	553	389-771	14,822 (25.6)
Correlation between number of injury events and	**Pearson r**	**95% CI**		**Pearson r**	**95% CI**	
Number of prenatal visits	0.04	0.04-0.04		0.03	0.02-0.07	
Number of well-child visits	0.08	0.08-0.08		0.08	0.07-0.09	
Correlation between number of episodes of common infectious disease and						
Number of prenatal visits	0.10	0.09-0.10		0.10	0.09-0.11	
Number of well-child visits	0.23	0.23-0.23		0.25	0.24-0.26	

Abbreviation: SMI: serious mental illness; SD: standard deviation; IQR: interquartile range; CI: confidence intervals

*At least one parent with SMI in the period from 6 years prior to childbirth to 5 years following childbirth.

Among exposed children, the correlations between number of child injury events and that of prenatal visits and between injury events and well-child visits were very close to zero (Pearson r 0.03 and 0.08, respectively). The correlation between number of common infectious disease episodes and that of prenatal visits was also negligible (Pearson r 0.10). However, there was a

weak correlation (Pearson r 0.25) between number of well-child visits and that of common infectious disease episodes. Similar patterns were seen among unexposed children. In summary, common infectious disease was weakly associated with healthcare-seeking behaviors of both SMI affected and unaffected parents regarding healthcare visits for child health.

Chapter 4. DISCUSSION

4.1 EARLY CHILDHOOD INJURY

4.1.1 *Principal findings*

A slightly greater percentage (61.0%) of children with parental SMI had any childhood injury than for children without parental SMI (53.8%). The IRs of any childhood injury and injury hospitalization were 14% and 49%, respectively, greater in the exposed periods. The association between parental SMI and child injury was modified by parental age. The excess risk increased from 10% for fathers aged < 25 years to 22% for fathers ≥45 years. Similarly, the excess risk increased from 9% for mothers < 20 years to 17% for mothers ≥40 years. Parental age, especially paternal age, modified the association between parental SMI and injury hospitalization even more strikingly. Young children with two parents with SMI were more likely to have injury or injury hospitalization than children with an affected mother, only, who in turn had greater risk than children with an affected father, only. As for specific parental SMI diagnosis, risk of injury or injury hospitalization associated with parental diagnoses of schizophrenia or bipolar disorder tended to be greater than for a parental diagnosis of MDD. The risk was similar between parental SMI onset before and after childbirth. Finally, there was not enough evidence to support risk of childhood appendicitis, a negative control outcome, being greater in the exposed periods than unexposed periods. In addition, children with and without parental SMI had nearly identical number of prenatal and well-child visits. Overall, these two findings provided some indirect evidence to suggest that the associations between parental SMI and child injury were neither meaningfully biased by unmeasured or residual cofounding nor driven mostly by differential healthcare seeking behaviors.

4.1.2 *Interpretation in context of previous studies*

Incidence rates of injury

The IRs of childhood injury among children aged 0-5 years were similar to a Canadian study[130] that analyzed the data of children born in 1985-1987 who were registered with the Alberta Health Care Insurance Plan. Most of the IRs of specific injury type in our study were slightly lower than the Canadian study. The only exception was superficial injuries and contusion, of which the IRs were about 25-80 events per 1,000 person-years greater in our study than in the Canadian study. The IRs of specific injury types varied according to child ages, reflecting child growth and developmental status, which was also consistent with previous studies.[130] Since infants and toddlers have a disproportionately large head and weaker neck, they are more susceptible to brain injury in a falling or transport accident. In our study, several injury types, including burn, open wounds, superficial injury and contusions, dislocations, strains, and sprains, foreign body and poisoning, demonstrated a dramatic rise in incidences about the ages of one and two. During this period, toddlers have a rapid increase in motor development and develop curiosity about the environment without mastery of muscle coordination or appreciation of physical consequences, both of which contribute to the risks of these injury types.

Risk factors of injury

Several of the risk factors for childhood injury reported in previous research were observed in this study, including being male[70,130,142,143,159,220]; having older siblings[70,221]; being from a low-income areas[142,222]; being from a family of lower SES[70,142,143,187,223,224]; having a parent occupied as a farmer[145]; having a parent with physical illness[99]; of teenage parenthood[220], of single parenthood status[170]; or being born LBW or of preterm birth.[129,199] Several socioeconomic factors are interrelated, such as low family income, single parenthood, and teenage parenthood,

influencing parents' ability to provide material resources, safeguarding and supervision for their young children. Literature also shows that parental SES, including education levels, occupational status, and family income influences child health and development.[225,226]

Covariate adjustment

Studies across different cultures and contexts have shown that disadvantaged SES is associated with mental illness.[191] Two competing hypotheses have been proposed to explain this association: social causation and social selection. The social causation hypothesis argues that living with low SES is more harmful to health than living with high SES due to differences in essential needs for life maintenance and well-being across a multitude of domains including adequacy of the most basic needs including nutrition, shelter, basic medical care, social support, safety, and restorative time.[202] For example, occupational status influences health through social standing, prestige and occupational hazards; and income, a proxy of material resources, can influence health, for example, through the affordability of food, housing, and health care, and the psychological burden of being poor.[227]

In contrast, the social selection hypothesis posits that differences in SES result from differences in health status; people in poor health are less able to achieve favorable social status.[202] For example, health influencing education, occupational status, and income through the ability to invest in education or a career.[227] Current literature suggests that the association between low SES and depression is due mostly to social causation, in which the disadvantaged SES increases the risk of depression;[191,228] whereas for persons with schizophrenia, the decline in SES could be mainly a consequence of their illness (social selection).[191,228] Nonetheless, more research is still needed to tease out the causal direction of these relationships as several longitudinal studies

reported that both social causation and social selection contributed to the associations between low SES and mental illness.[229]

Evidence indicates bidirectional relationships between mental illness and chronic physical illness.[193–196] Development of mental illness in patients with chronic physical illness, such as diabetes, Alzheimer's disease, epilepsy, stroke, and cancer, may be due to the associated psychological stress and underlying biological processes.[195] Presence of mental illness noticeably worsens prognosis of physical illness because of poor compliance with treatment and impaired cognitive function associated with mental illness.[195] Mental illness has also been shown to be a risk factor for various physical illnesses, including obesity, coronary heart disease, cerebrovascular disease, diabetes, respiratory tract diseases and cancer.[193,196] Comorbidity mechanisms consist of disparities in healthcare, psychotropic medications, lifestyle, and psychiatric symptoms.[194] Furthermore, a person's SES also influences the comorbidity of physical and mental illness. A Scottish study showed that the prevalence of the physical-mental illness comorbidity were doubled in the most deprived versus the most affluent areas.[230]

Research also suggests parental mental illness is associated with single parenthood. Even before onset of illness, persons with schizophrenia have a lower probability of having a history of stable relationship or marriage.[12,25,26] People with mental illness also have a lower marriage rate and a higher divorce rate than the general population.[10,12,22,104] Single, separated or divorced women are at a greater risk of depression.[168,169] Therefore, single parenthood could be the risk factor or consequence of parental mental illness.

In our study, the prevalent estimates and IRs of parental SMI were associated with lower family income, lower parental occupation class, parental physical illness or unmarried mother. For children of parents with SMI onset after childbirth, these variables could be confounders, since

they could independently increase risk of parental SMI and childhood injury. By contrast, for children of parents with SMI onset before childbirth, these variables could be mediators in the causal pathway. Therefore, control of these variables could result in over-adjustment. On the other hand, if these variables could influence the severity, persistence, and recurrence of mental illness[106], then adjusting for these variables is still necessary for children of parents with SMI onset before childbirth. Our results showed that the magnitude of the association between parental SMI and any childhood injury scarcely changed after adjusting for several SES variables and parental physical illness. However, the risk of injury hospitalization associated with parental SMI decreased from 49% greater to 40% greater. This suggested that parental SES and parental physical illness might account for part of the association between parental SMI and childhood injury hospitalization by either acting as confounders or mediators.

LBW and preterm birth are risk factors for injury hospitalization.[129,199] Several studies have demonstrated that infants of parents with SMI have increased risk of adverse birth outcomes, including LBW or preterm birth.[58,59,61,62,80–83] Moreover, mothers of preterm infants have been found to be at a greater risk of depression than mothers of term infants.[203] This bidirectional association between parental SMI and LBW/preterm birth was also evident in our study. We, therefore, surmise that LBW and preterm birth could be confounders or mediators in the causal pathway between parental SMI and child injury. In addition, there might be unmeasured factors associated with LBW/preterm birth and child health outcomes. Therefore, adjusting for these two variables might induce collider stratification bias. Nevertheless, the associations between parental SMI and childhood injury remained similar after adjusting for LBW and preterm birth, suggesting that the mediator or confounding effects of these two variables were inconsequential in our study.

Associations between parental serious mental illness and child injury

Most previous studies assessed the associations between maternal depression and specific types of child injury.[71,220,231,232] Using the Clinical Practice Research Datalink (CPRD) and Hospital Episode Statistics (HES) in England, Baker et al.[231] reported maternal depressive episodes were associated with an increased risk of child poisoning (IRR 1.52, 95% CI: 1.31-1.76), child burns (IRR 1.31, 95% CI: 1.15-1.48), child fractures (IRR 1.15, 95% CI: 1.03-1.28) or injury hospitalization (IRR 1.25, 95% CI: 0.95-1.65) before the age 5 after adjusting for calendar year, region and socioeconomic deprivation. Orton et al[71] analyzed data of the Health Improvement Network (THIN) database, another primary care database in the UK. They estimated maternal perinatal depression to be a risk factor of first occurrences of childhood thermal injury (OR 1.16, 95% CI: 1.02-1.32) and poisoning (OR 1.45, 95% CI:1.24-1.70) after adjusting for child sex, child age, birth order, age of mother at birth, household composition, alcohol consumption, and Townsend Score.[71] However, perinatal depression was not a risk factor for child fracture.[71] By using THIN databases, Tyrrell et al[232] also reported perinatal depression to be a risk factor for first medicinal poisoning event (OR 1.54, 95% CI: 1.26-1.88) before age 5 years after adjusting for similar covariates as Orton et al[71]. Using a larger mother-child cohort in which maternal depression was measured by a self-rating scale at 21 months after childbirth, O'Connor et al[220] found that maternal depression was associated with an increased odds of burns/scalds among children aged 15–24 months (OR 1.29, 95% CI: 1.01-1.64) after adjusting for child sex, family type, education, psychosocial stress, and maternal life history risk.[220]

Our estimates of the associations between parental SMI and specific childhood injury types were slightly lower than those in previous studies (S-Table 12). One potential cause for our more conservative estimates is that our study population excluded children without complete parent data

in the NHRID. Consequently, a large proportion of children with single parents who might be more disadvantaged and influenced by parental SMI were not included in our study population. Another alternative explanation is that our study sample was more inclusive of the general population due to almost universal coverage of health insurance and more complete follow-up. In addition, our exposure measurement might be more accurate since most of parental psychiatric categories were determined by using the diagnosis made by a psychiatrist instead of primary care physician. Finally, there are some differences in study design between our study and the studies of Tyrrell et al,[232] Orton et al,[71] and O'Connor et al.[220] For example, we considered child injury as recurrent events while other authors only analyzed data of the first injury event. In addition, they reported risk estimates as odds ratios, which, given the commonality of the outcome will provide an inflated risk estimate than the risk ratio.[233]

4.2 EARLY CHILDHOOD COMMON INFECTIOUS DISEASE

4.2.1 *Principal findings*

Our results showed that difference in the IRs of any common infectious disease in early childhood was negligible between the periods in which children were exposed and unexposed to parental SMI. The IRs of antibiotic-treated infection and hospitalized infection were 4% and 31% greater during parent SMI-exposed periods relative to parental SMI-unexposed periods. The association between parental SMI and hospitalized infection was modified by parental age. The excess risk increased from 13% for fathers aged < 25 years to 36% for fathers ≥45 years. Similarly, the excess risk increased from 16% for mothers < 20 years to 46% for mothers ≥40 years. The risk of hospitalized infection among children with two parents with SMI was greater than for children with SMI affected mothers only, which was greater than those with SMI affected fathers only. As for specific parental SMI diagnosis, the excess risk specific to diagnosis of schizophrenia or bipolar

disorder tended to be greater than that for diagnosis of MDD. Lastly, the excess risk of hospitalized infection was similar for children with parental SMI onset before and after childbirth.

4.2.2 *Interpretation in context of previous studies*

Risk factors of common infectious disease

Several of the risk factors of childhood common infectious disease reported in previous research were also found in this study, including being male;[160–162,165,234] of higher birth order;[165] from deprived areas;[188] and from families of lower SES.[128,165,235,236] In our study, after adjusting for socioeconomic variables and parental physical illness, the magnitude of association between parental SMI and any common infectious disease was only minimally diminished. The risk of hospitalized infection decreased from 31% greater to 27% greater. The association remained similar after further adjusting LBW or preterm birth.

Associations between parental SMI and child common infectious disease

There were no directly comparable prior studies addressing the relationship between parental SMI and childhood common infectious disease. But several studies examined the separate associations between perinatal maternal depression and early childhood diarrhea[67,68,237] and respiratory infection[66,67,237] in rural areas of Pakistan and the United Kingdom. Rahman et al[238] reported that children of mothers with perinatal depression had a greater risk of diarrhea (OR 2.4, 95% CI: 1.7-3.3) compared with unaffected children. By using a large cohort in the United Kingdom, Ban et al[237] also found that children with perinatal maternal depression had an increased risk of childhood gastrointestinal infection (IRR 1.40, 95% CI: 1.37-1.42) and lower respiratory tract infection (IRR 1.27, 95% CI: 1.22-1.32, respectively) compared to unexposed children. By using self-rating scales, several studies also reported associations between maternal depressive

symptoms and child physical health outcomes, including febrile illness[66], antibiotic use[220] and use of medicine for diarrhea.[220]

In our study, parental SMI was not associated with a greater risk of having any health service contact for childhood common infectious disease. Parental SMI was only associated with a slightly greater risk of antibiotic-treated infection (IRR 1.04, 95% CI: 1.03-1.05) and a 31% greater risk of hospitalized infection (IRR 1.31, 95% CI: 1.29-1.33). The difference in estimates between our study and these previous studies might be due to differences in definition and measurement of exposures and outcomes or different contextual background.

Current literature shows that the increased risk of infection associated with mental illness is not only restricted to offspring of the affected parents. People with depression have been found to have a greater risk of a wide range of infections requiring hospitalization in Danish health database (IRR 1.61, 95% CI: 1.49–1.74).[239] The increased risk was observed not only during the first year after depression onset but remained increased during follow-up of > 11 years. Seminog et al.[240] also reported that the RR of pneumococcal disease for people hospitalized with schizophrenia, bipolar disorder, depression or anxiety was 2.3 (95% CI: 2.2-2.4), 2.3 (95% CI: 2.2-2.3), 2.1 (95% CI: 2.0-2.1) and 2.2 (95% CI: 2.1-2.2), respectively, relative to the comparison cohort.

Consistent with the idea that mental illness affects the immune system, an increased risk of infectious disease has been demonstrated among people who suffer from mental illness.[239,240] Some research suggests the maternal depression during pregnancy causes dysregulation in the HPA axis, which may affect the fetal HPA axis and immune system and later development.[86] Researchers have proposed that this pathway might partially explain the association between parental SMI and child common infectious disease. But our results showed that not only maternal SMI, but also paternal SMI increased the risk of hospitalized infection. Therefore, this pathway

was unable to account for all the findings. Moreover, studies show that contact with symptomatic family members is a risk factor of child diarrhea[236] or respiratory infections.[241] Furthermore, prevalence of smoking is greater in people with mental illness than the general population[242], and passive smoking is a risk factor for childhood respiratory tract infections.[234] Thus, the general increase in risk of hospitalized infection among the affected persons or their offspring has a number of plausible pathways.

4.3 General interpretation of study findings

4.3.1 *Risk of adverse childhood outcomes over time*

We observed that the increased risk of injury among children with parental SMI decreased gradually as the children aged, especially for injury hospitalization. The association between parental SMI and childhood injury was strongest in the first year of life. Entering new parenthood and providing constant care for a newborn is highly demanding both physically and mentally. Parents with SMI may suffer from worsening symptoms or a relapse episode during this period.[243–245] This may make them more vulnerable in ways that affect their caregiving and supervision of their newborn. Research also suggests that fathers' depressive symptoms were more strongly related to challenges in parenting younger children than older children.[246] In the current literature about child injury, Schwebel et al.[72] also found severe, chronic maternal depression predicted risk of child injury at ages 0-3 years but not at ages 3 to grade 1. As children mature, they require less intensive supervision and safeguarding. However, we did not find a similar pattern of reduction in excess risk of childhood common infectious disease with child age. This may indicate the required level of supervision and caregiving would vary with different dimensions of child health outcomes.

4.3.2 *Difference between overall and severe childhood outcomes*

The association between parental SMI and child health differed between minor and severe adverse child health outcomes. For any childhood injury, parental SMI was associated with 14% greater risk; while for injury hospitalization, the excess risk was increased to 49%. For overall common infectious disease, parental SMI was associated with negligible excess risk; while for hospitalized infection, the excess risk was increased to 31%. Several illness factors may influence the ability of parents with SMI to detect early signs of their children's health problems. These illness factors include symptoms of mental illness, cognitive and functional impairments, illness coping and role constraints. Some evidence suggests that adults with SMI have challenges recognizing their own physical illness states. Studies have shown that persons with schizophrenia or bipolar disorder have a markedly elevated 30-day mortality after infection, which might be due to treatment delays.[247] It is also possible that their children are exposed to greater risk of severe form of illness. For childhood injury, type of injury could also partly explain the difference in the degree of associations. The risks of a variety of injury types were greater among children exposed to parental SMI than unexposed children (S-Table 12). However, the increased risk was more pronounced for intracranial injury, burns, crush injury, and poisoning. These four injury types had a relatively greater proportion of hospitalization compared to other injury types.

Several covariates also exhibit differential risk between minor and severe child health outcomes. For example, the IR of injury hospitalization was markedly increased among children with markers of disadvantage, including living in areas with lower degrees of urbanization, having an unmarried mother, with parental physical illness, a lower-income family, or having a parent with a lower occupation class. In addition, several covariates, such as foreign-born mother, LBW and preterm birth, were positively associated with childhood injury hospitalization but negatively

associated with any medically-attended childhood injury. This pattern of different degree and direction of association also appeared in childhood common infectious disease.

One contributing factor to this pattern is that parents with low SES may use less outpatient care and more inpatient care for the same severity of illness or injury than families with high SES. Parents with low SES, parents with physical illness, and single parents may be constrained by their own poverty, illness, demands from work and less able to seek outpatient care when their children encounter minor illness or injury.[248] Parents with SMI tend to have lower SES and could be influenced by the effects of low SES. If this is true, then the greater excess incidence of illness and injury for children with parental SMI when outcomes were child health events treated in inpatient services may partially reflect differences in service utilization patterns instead of or in addition to severity of illness/injury. Another contributing factor is that low SES may be associated with greater disease severity and consequences when a child is ill as a consequence of treatment delays, caregiver burden, or environmental factors, which have been found in several studies focused on injury[222,249–251] and infectious intestinal disease.[252] As for foreign-born mothers, our data indicated they were more likely to be in families of lower income (data not shown). Additionally, foreign mothers may experience language barriers that impair access to health care services. Finally, people living in areas of lower degree of urbanization may have less access to health care and encounter less safe environments, which could contribute to disparities in health outcomes.

4.3.3 *Effect modification of urbanicity of residence and parental occupation and age*

In this project, we evaluated whether urbanicity of residence, parental occupation, and parental age modified the associations between parental SMI and adverse child outcomes.

Urbanicity of residence

Urbanicity of residence is a neighborhood-level SES indicator, which could affect health through physical, social, or service environments.[140,141] Several studies have shown that neighborhood SES is associated with SMI. For instance, risk of schizophrenia is greater in urban compared with rural areas[176–179]; and more advanced urbanicity is associated with a greater risk for MDD.[176,180] Risk of infectious disease and injury may be affected by characteristics of the surrounding environment.[224] Living in a rural residence is a risk factor for recurrent non-accidental traumatic events.[187] Studies also find an increase in the risk of unintentional injury among children living in low-income areas.[142,222] Economically deprived areas have been linked to greater incidence of pneumonia in children.[188]

The variable urbanicity of residence used in this project captured general information on neighborhood characteristics reflecting variability in population density, education levels, economic activities, characteristics of social networks, and health care resources. The indicator may also be associated with community attitudes toward mental illness. The index was found to be associated with different health care utilization patterns among persons with schizophrenia.[175] Lower level of urbanization defined by this index was also associated with greater risk for neonatal, infant and under-five mortality.[139] Our findings indicated that degree of urbanicity was positively associated with prevalence of maternal SMI, only; but it did not have a linear relationship with prevalence or incidence of paternal SMI, or incidence of maternal SMI. Degree of urbanicity was negatively associated with incidence of childhood injury or common infectious disease.

In addition to the direct effects of urbanicity on health, neighborhood SES has been found to modify the effects of interventions or family characteristics on child health outcomes.[253–255] However, our results did not support urbanicity of residence as a modifier of the association

between parental SMI and childhood injury or common infectious disease. Fang et al[139] used this index to show that the association between parental education and childhood mortality due to various causes of death, including injury and poisoning, before age 5 was modified by urbanicity of residence. They used place of birth recorded in the Taiwan Birth Registry to define urbanicity of residence; while we used mother's current residence recorded in the birth certificate. We considered mother's current residence to more accurately reflect where the child lived because some mothers could have decided to give birth in a hospital or clinic located in another city or township than the place she lived. Nonetheless, the major difference between our study and the study of Fang et al. was that their study focused on the outcome of child death and education as the primary exposure. The contextual characteristics of neighborhood might have greater influence on the association between parental education and childhood mortality than on the association between parental SMI and childhood injury or common infectious disease.

Parental occupation

Occupation type is related to prestige, social standing and influence, social networks, intellect, and material resources.[256] Studies have found strong relationships between occupation type (e.g., manual vs. non-manual labor) and diverse health indicators after controlling for income and education.[140] Occupation is related to income, so it can influence child health through material resources and access to health services. In addition, occupation type captures some aspects of education such as possession of knowledge and problem-solving skills. Parents with higher occupational status may be more receptive to health education messages and better able to communicate and access appropriate health services than parents with lower occupational status.[256] Finally, this variable also includes unemployment status and low income household, both of which are strongly associated with SMI[191,192], child diarrhea[236] or child injury.[142]

In our study, compared to the category of employees, employers, and professionals, the prevalence estimates and IRs of parental SMI were greater among the following three categories: (1) union members, farmers and fishermen, (2) the unemployed and low-income households, and (3) dependents. Children of a parent whose occupation was civil servants and teachers had the lowest prevalence and incidence of parental SMI. Children with a parent whose occupation was union members, farmers and fishermen were more likely to be injured or have common infectious disease compared to children with a parent whose occupation was employees, employers and professional. For child outcomes requiring hospitalization, all other parental occupation types except civil servants and teachers had a greater risk compared with parental occupation of employees, employers and professionals. Similar to our results, Hong et al.[145] also reported that risk of injury-related death was greatest for Korean children with a parent working in a manual job, followed by the unemployed and those working in a non-manual job. Among the specific type of paternal occupation, working as a famer was associated with the greatest risk and being an administrator the lowest risk.[145]

Few studies evaluated how parental occupation modifies the relationship between parental SMI and childhood injury. We chose parental occupation as a potential modifier instead of family income because occupation may fluctuate less than family income[256] and may have less misclassification.[206] We expected that parents with higher occupational status might have better knowledge and capacity of handling parenting problems and that they might be more able to buffer the effects of mental illness if they became ill. However, our results did not provide enough evidence to indicate that parental occupation modified the relationship between parental SMI and childhood injury or common infectious disease.

Parental age

The prevalence and IR of parental SMI were greater among children of the younger and older parents, suggesting a U-shaped relationship between parental age and SMI. The only exception was maternal SMI, of which prevalence increased uniformly with advancing maternal age. For child outcomes, paternal and maternal ages were both inversely associated with risk of injury or of common infectious disease. Our findings indicated that parental age modified the association between parental SMI and child injury, as well as the association between parental SMI and child hospitalized infection. The associations between parental SMI and selected child outcomes in the older parental age groups were stronger than those in the younger age groups. We also note that the actual IR of child injury or common infectious disease in the exposed and unexposed periods decreased with parental age (S-Table 13, S-Table 14, S-Table 23- S-Table 25). Thus, the strongest associations between parental SMI and child health outcomes were seen in the parental age groups with the lowest occurrence of child health outcomes.

Several factors could contribute to the effect modification by parental age. It is plausible that older parents were more likely to have improved economic circumstances and parenting capacity than younger parents. By contrast, younger parents, especially teenaged parents, have been found to have difficulties in their parenting roles with less supportive and more detached parenting behavior.[146,147] Furthermore, teenaged parenthood has been linked to an increased risk for parent's SMI[257], child mental illness[258] or child injury.[71,259] The risk factors related to early transition into parenthood, including SES of the original family and conduct behaviors could also influence parenting capacity.[147] Therefore, being young parents, regardless of whether the parents have mental illness, markedly increased the risk of adverse child health outcomes. On the other hand, the acquisition of parenting skills among parents with SMI as they age may be less pronounced,

relative to unaffected parents. This could result in a slower reduction in the IRs of adverse child outcomes as parents with SMI age.

4.3.4 *Secondary models*

Which parent(s) had mental illness

The risk of childhood injury among children with two parents with SMI was greater than those with an affected mother only, which was in turn greater than those with an affected father only. This pattern of differential risk has been found in the relationship between parental SMI and child mortality in which children with two affected parents had a greater risk than those with one affected parent.[79] Prior studies have also shown that the risks of adverse child outcomes associated with maternal SMI are greater than the risks with paternal SMI, including outcomes of disruptive caregiving for children in Denmark[260] and early childhood mortality in Taiwan.[76] The different risk between maternal and paternal SMI may be because mothers take on a disproportionate share of childcare responsibilities, and fathers are less able to compensate for caregiving when mothers are ill. Another reason could be that children with parental SMI have a greater probability of living with a single mother, and they are also more likely to live with their affected mother than with their affected father as shown in a Danish study.[261] Under these circumstances, if the mother is ill, there is no other parent to step in.

Nonetheless, our findings showed that paternal SMI was also associated with an increased risk of adverse child outcomes. Most of the current literature addresses how maternal mental illness, especially maternal depression, impacts children, and paternal mental illness has received little attention. Our findings provided evidence that not only maternal SMI, but also paternal SMI influences child health. Fathers' health plays an important role in a family. Coping with mental

illness could be overwhelming, which may affect the parenting of both the ill and well parent and the overall functioning and health of the family.

Timing of onset of mental illness

The risks of childhood injury and hospitalized infection were similar between parental SMI onset before and after childbirth. This could have several different interpretations. While we anticipated that parental SMI onset after childbirth might have a stronger effect on child health, the effect could have been attenuated due to misclassification of onset time by using administrative health data. An alternative explanation is that functional impairment or residual symptoms of SMI had been less improved by current treatment models, which could have a long-term impact on parenting ability. A meta-analytic review estimated the effect sizes of maternal disengaged behavior to be similar for both current and lifetime maternal depression, supporting the idea of continued parenting difficulties.[5] As a result, mental illness onset before and after childbirth could have a similar magnitude of parenting challenges.

Different types of SMI diagnosis

By classifying SMI into different diagnoses, we found that the risk specific to schizophrenia or bipolar disorder tended to be greater than to MDD. This pattern could be because these disorders are associated with a different degree of parenting challenges. Previous studies also suggest that specific SMI diagnoses could have different impacts on family functioning.[260,261] For example, Danish children of parents with schizophrenia had the greatest risk of being placed in out-of-home care[260] and encountering family dissolution,[261] compared to children with parents with bipolar disorder and MDD.

4.3.5 *Negative control outcomes*

To examine uncontrolled confounding and potential bias, we used childhood appendicitis as a negative control outcome. Our expectation was that childhood appendicitis would be less likely influenced by our hypothesized pathways; and finding a positive association between parental SMI and appendicitis would indicate our findings about main outcomes were confounded or biased. The disadvantage of choosing childhood appendicitis as a negative control was that it was a rare outcome and rarely diagnosed among young children. Consequently, our analyses yielded inconclusive results for appendicitis with relatively wide CIs. Nonetheless, the estimate of risk of childhood appendicitis was about 10% greater in the exposed periods; and under our model specifications, the effect of parental SMI could range from lowering the risk of appendicitis 6% to increasing the risk 28%. If the upper limit of the 95% CIs was considered, then the findings from our primary analyses could result at least partially from unmeasured/residual confounding or detection bias. However, it is unlikely that any remaining confounding or detection bias would explain the excess risk of the more severe child outcomes.

4.3.6 *Parents' healthcare seeking behaviors*

SMI could influence a parent's healthcare-seeking behavior for the child's illness, which could lead to an under- or over-estimated association between parental SMI and child health outcomes. We took two strategies to reduce the influence of parent's healthcare-seeking behavior. The first was counting childhood illness experience as numbers of episodes instead of clinic visits. The former would be less likely to be influenced by care-seeking behavior. Nevertheless, we found that counting illness as episodes and as clinic visits yielded very similar results (S-Table 11 and S-Table 21). The second strategy was to consider outcomes as those with hospitalization or antibiotic use, which would also be less affected by care-seeking behavior. Our results suggested that

different estimates between any child outcomes and hospitalized outcomes could be largely driven by varying severity of illness between children of parents with and without SMI.

Finally, we assessed the utilization patterns for preventive services for children with and without parental SMI. We assumed that parents with greater levels of healthcare-seeking behavior would uptake a greater number of preventive health visits and attend to them earlier in pregnancy or the child's life. The results indicated that differences in prenatal and well-child visits between two groups were small. In addition, number of well-child visits almost had no correlation with number of childhood injury events (Pearson r 0.08); and the correlation between well-child visits and common infectious disease was weak (Pearson r 0.23). In summary, it was unlikely that our results were markedly biased by parent healthcare-seeking behaviors.

4.3.7 *Representativeness of study population and generalizability of results*

Since our study population only included singleton children having parents' and child's IDs existing in the registry of beneficiaries, twins/multiples and children with only one parent's data were excluded. Consequently, our study results might not be generalizable to non-singletons. In addition, although the study population included 64,018 children born out-of-wedlock, another 62,203 out-of-wedlock children with a matched birth record were excluded. Most children in the latter group only had one parent's data, suggesting they were probably raised by single parents. Moreover, this group had greater percentage of maternal SMI. We also found that the excluded children were more likely to from lower-income families and their parents were more likely to be unemployed. Therefore, mothers with SMI who were excluded from the study population could have less social support, family income or resources and encounter more difficulties in parenting. As a result, our results could be an underestimation of the associations between parental SMI and adverse child outcomes.

Children and their parents who were excluded from our study population were more likely to have shorter enrollment time and greater number of enrollment gaps (S-Table 8). Children excluded also had lower IRs of selected child outcomes than the study population. When estimating IRs of child outcomes, children were assumed to be continuously enrolled until the end of the follow-up period or death. Therefore, the IRs for the excluded children could be underestimated. Similarly, children excluded had lower prevalent and IR of paternal SMI. This could be because fathers of these excluded children were more likely to have shorter enrollment time and missing IDs, which decreased the likelihood of capturing an exposure diagnosis. However, adding these excluded children into the study population requires intensive computation and additional assumptions. For example, we have to consider the actual enrollment time and exclude the enrollment gaps when calculating person-time at risk. Additionally, we have to assume that the probabilities of capturing child outcomes were similar between time periods of enrollment and non-enrollment in the NHI Program. This could be a false assumption since people would be more likely to participate in a health insurance program when they are less healthy.

4.4 STRENGTHS AND LIMITATIONS

4.4.1 *Strengths*

This project used a national health insurance database with a high coverage rate (> 99%) of the population in Taiwan that contained extensive information on diagnoses and treatments occurring in emergency room, inpatient and outpatient settings. The number of enrollment gaps and the length of gaps were small in the study population (S-Table 8). By using this database, we were able to capture different types of injury or common infectious disease treated in a variety of settings. Furthermore, this NHI Program offers affordable access to health care and has strategies aimed at removing financial barriers for low-income households. This would be an advantage for

a study of mental illness, since having health insurance facilitates access to mental health care,[262] which would reduce selection bias. Using these prospectively recorded data decreased the possibility of recall bias, nonresponse bias, and social desirability bias associated with self-reported data in questionnaire studies. Furthermore, we were able to collect and adjust for several important covariates that had minimal missing data (Table 2-20), such as birth order, birthweight, gestational age, unmarried mother, foreign-born mother, family income, and parental physical illness. Moreover, our analyses allowed child outcomes to be analyzed as repeated events instead of being restricted to the first events. Since some children with particular characteristics would be more susceptible to recurrent injury or common infectious disease, restricting outcomes to the first events could have generated biased results.[263]

Finally, we retrieved and formed the parent-child pairs/triads from several databases. The parents' IDs retrieved from the registry of beneficiaries were highly concordant with parents' IDs in the MCHD. In addition, most of the parent-child pairs/triads in the MCHD and/or the registry of beneficiaries and livebirth certificate records could be matched to each other. Moreover, very few children had multiple father's IDs retrieved by our procedures (Table 2-14), and almost of the children with multiple mother's IDs were classified as having a foreign-born mother. Overall, our procedures of forming child-parent linkage and matching them to the birth certificate records increased the data completeness for parent and child data.

4.4.2 *Misclassification and underestimation of parental SMI*

Misclassification of SMI diagnosis

Although ICD-9 codes are used across facilities within the Taiwan NHI to designate psychiatric diagnoses, the diagnostic codes may be inaccurate when assigned by less experienced or non-psychiatric physicians. However, studies conducted in other countries suggest that there is

high agreement between recorded mental health symptoms/history and discharge diagnoses on inpatient records.[264–267] The positive predictive value for schizophrenia, bipolar disorder, and MDD ranged from 81 to 95%.[264–267] A few studies reported good concordance on diagnosis of schizophrenia between interviews or recorded symptoms and diagnoses on psychiatric outpatient records, with the positive predictive values ranging from 87 to 98%.[268,269] In this study, we attempted to improve the accuracy of diagnosis by prioritizing the diagnosis made by a psychiatrist and requiring a diagnosis to appear twice if made by a non-psychiatrist physician. Most of maternal and paternal psychiatric diagnoses (94.1%) were made by a psychiatrist (S-Table 5). And only a few parents with multiple children were assigned different diagnoses between the birth of one child and the birth(s) of subsequent child(ren) (S-Table 6).

Underestimation of parental SMI

The NHI Program provides access to mental health care to all citizens. However, there is neither routine mental health screening in clinic visits nor community-based mental health screening programs in Taiwan. Therefore, there could be high levels of undetected and untreated mental disorders in the Taiwanese population, resulting in underestimation of mental disorders in the general population.[166,180] The degree of underestimation would be related to the severity of the illness. For example, the prevalence estimates of schizophrenia and bipolar disorder were similar in the NHIRD and community studies conducted in Taiwan,[166] but the prevalence of MDD was lower in the NHIRD compared to the community studies.[166,180]

It is difficult to directly compare our estimates of prevalence and IRs of parental SMI to other studies due to different research purposes, selection criteria, and measurement of mental illness. Most of the published studies selected parents with the first live-born child and estimated prevalence or incidence of inpatient admission or outpatient visits in the perinatal or postpartum

periods.[29,31,270,271] For example, by using data from Danish Psychiatric Central Register, Munk-Olsen et al.[29] reported the incidence of the first admission due to schizophrenia, bipolar disorder, and unipolar depressive disorder among primiparous mothers to be about 0.9 per 1,000 person-years in the first postpartum year, which compares with our estimation of 3.17 per 1,000 person-years for maternal SMI. Using data from Kaiser Permanente Northwest, Dietz et al.[270] reported 8.7%, 6.9%, and 10.4% of mothers with a livebirth experienced depression in the period of 39 weeks before pregnancy, during pregnancy, and 39 weeks after pregnancy, respectively. Among the mothers with depression, 20.6% were diagnosed to have MDD, which was slightly greater than the prevalence of MDD in our study.

Under-diagnosis of psychiatric disorder may affect effect size estimates of parental SMI on child outcomes. If the under-diagnosis of parental SMI is non-differential, not related to child outcomes, it would bias an existing association towards the null.[272] The study findings may be biased insofar as treatment seekers differ from persons with SMI who do not seek treatment. Parents who truly have SMI would be more likely to be diagnosed if they are higher treatment seekers. Then, if parents with SMI also seek more medical care for their children, this would artificially inflate our risk estimates. However, we counted childhood illness experience as numbers of episodes instead of clinic visits, which could reduce the influence of parent's healthcare-seeking behavior. Nonetheless, the results were similar between counting illness as episodes and as clinic visits. Therefore, it is less likely that our results were largely due to differential misclassification.

Misclassification of timing of onset

Timing of onset of mental illness might have been misclassified, since prodromal symptoms could occur months or years prior to a diagnosable disorder,[273–275] and people might not seek care

(and be diagnosed) until years after the onset of symptoms or disorder. The median duration of untreated psychosis has been reported to be 9.4 weeks[25] and 4 months[182] in the UK. The World Mental Health Survey Initiative conducted in 15 countries reported median delay to be 1-14 years for mood disorders.[276,277] Predictors of delay include living in low income countries, being of older age, having an earlier age of onset, having no severity indicators, and being male.[276–278] Alternatively, availability and acceptability of mental health services, community awareness, and clinician practice and referral patterns influence time to diagnosis, as well as incidence and prevalence estimates of psychiatric disorders. Studies analyzing health data have suggested incidence of treated psychiatric disorders has increased over the past two decades in several countries, including Taiwan;[148–155,279] and age at diagnosis has been declining.[149,150,152,154] Since the NHI Program provides affordable access to health care and has strategies aimed at removing financial barriers for low-income households, these conditions might be favorable towards decreasing delays to diagnosis.

When children whose parents had SMI were erroneously classified as unexposed, the person-time and events in the exposed group would be wrongly attributed to the unexposed group. Effects of this misclassification depend on whether the effect of parental SMI on child outcomes is constant over time. When the effect of parental SMI is constant over time regardless of the length of illness, the child events and accompanying person-time in the exposed periods among children with parents who had delays in diagnosis would be attributed to the non-exposed period. Consequently, the risk of adverse child outcomes in the unexposed period would be falsely inflated, and the IRR of child outcome associated with parental SMI would be then underestimated. Alternatively, suppose that parents with a longer duration of illness have larger effects than parents with a short duration of illness. In this scenario, the risk of child outcomes among children of

parents with a longer duration of illness would be assigned as the risk among children of parents with a shorter duration. This would result in an overestimation of the association between parental SMI and child outcomes, if we falsely assumed the effect of parental SMI is constant. On the contrary, if new-onset illness yields larger effects than chronic illness, then the results would be an underestimation.

Lack of data on severity and functional impairment of mental illness

The NHIRD did not contain detailed description of symptoms/signs of illness or level of functioning; therefore, it was not possible to assess and take into account symptom severity, functional impairment, and course of mental illness. In terms of the bias resulting from modeling the course of mental illness, if we wrongly assumed that the effects of parental SMI on child outcomes continued after first occurrence of diagnosis, the actual effects of mental illness would be attenuated.

4.4.3 *Misclassification of child outcomes*

Childhood injury and common infectious disease were defined by ICD-9 codes. Although the NHIRD has collected diagnostic codes, medical procedures and examinations, and prescriptions, it does not contain detailed descriptions of symptoms/signs and results of medical examination, for example, laboratory and imaging reports. These data can help determine the course and severity of a child's illness and injury as well as the accuracy of diagnosis. Canadian studies have assessed the accuracy of ICD-9 codes of respiratory infection[280] and childhood injury[281] in claims data. In Taiwan, research has assessed the accuracy of ICD-9 codes of aortic aneurysm,[282] acute stroke,[283] diabetes,[284] and pneumonia[285] in the NHIRD, with the positive predictive values ranging from 74.6 to 93.5%. However, to our knowledge, no studies have evaluated the accuracy of ICD codes for childhood diarrhea, respiratory infection, and injury in the NHIRD. But the audit committees of

Taiwan NHI regularly examine a random sample of medical records to ensure consistency with claims data, which might help reduce coding error. Based on the Canadian studies,[280,281] we expected that using ICD codes in the NHIRD to capture the child outcomes would have a lower sensitivity and a high specificity.

4.4.4 *Misclassification and absence of important covariates*

Birth order was measured from the available mother-child pairs in the MCHD and/or the registry of beneficiaries of 2000-2014 rather than parity; so, a small proportion of children could have been assigned with an incorrect birth order if their siblings were not linked to the mother. Unmarried mother was used as the proxy of single parenthood; however, the marital status could have changed after the child's birth, or their parents could have cohabited. Neither could we identify if children were living with their parents during the follow-up period. Nevertheless, a study reported that among children < six years old in Taiwan, 94.4% lived with either one of their parents and 80.3% lived with both parents.[206] We also used mother's residence in the birth certificate as the proxy of residence; which could be different from the child's usual residence. The original salary variable in the registry of beneficiaries had been shown to have varying degrees of misclassification by occupational type.[206] Moreover, in order to handle several issues related with the coding of this variable, we created a categorical variable for family income instead of using it as a continuous variable. Categorizing this variable would have generated potential misclassification of relevant income information and residual confounding. Several important covariates were measured at the time point of a child's birth and considered as a time-fixed covariate in the regression models, including urbanicity of residence, family income, parental occupation, parental physical illness and spouse's mental illness. But the values for these variables could have changed over the follow-up period and contributed to misclassification. We were

unable to measure protective factors, such as social support[44,245,286] or effective treatment, that might moderate the associations between parental SMI and child health outcomes. Finally, the databases we used did not have several important variables, like parents' education,[30] smoking,[30,31,270] and history of domestic violence.[40] Nonetheless, occupation and income are associated with education; and we adjusted for these variables in some models, such that the potential confounding effect of parental education could be partially removed.

4.5 CONCLUSIONS

Our findings show that children < 5 years old whose parents have SMI, especially those with two affected parents or parents with schizophrenia or bipolar disorder, are at increased risk of selected adverse health outcomes, including childhood injury and common infectious disease requiring hospitalization. These findings highlight the importance of treatment and intervention for SMI among parents and of providing support to affected families who are caring for infants and young children. Effective management of parents' mental illness may have beneficial effects for both the parents' well-being and child health.[287,288] Evidence also suggests that home visit programs improve maternal depression symptoms[287,289] and child injury.[290] In addition, reducing stigma toward mental illness, enhancing parenting skills, home safety interventions, improving mother-father work sharing, and providing support to vulnerable families during the postpartum period, including crisis plans and mapping social and health care resources, may reduce morbidity risk in offspring during the preschool years.[291,292] Future mixed methods studies that elucidate caregiving challenges and needs among parents with serious mental illness are needed to inform planning of services to these parents and their families.

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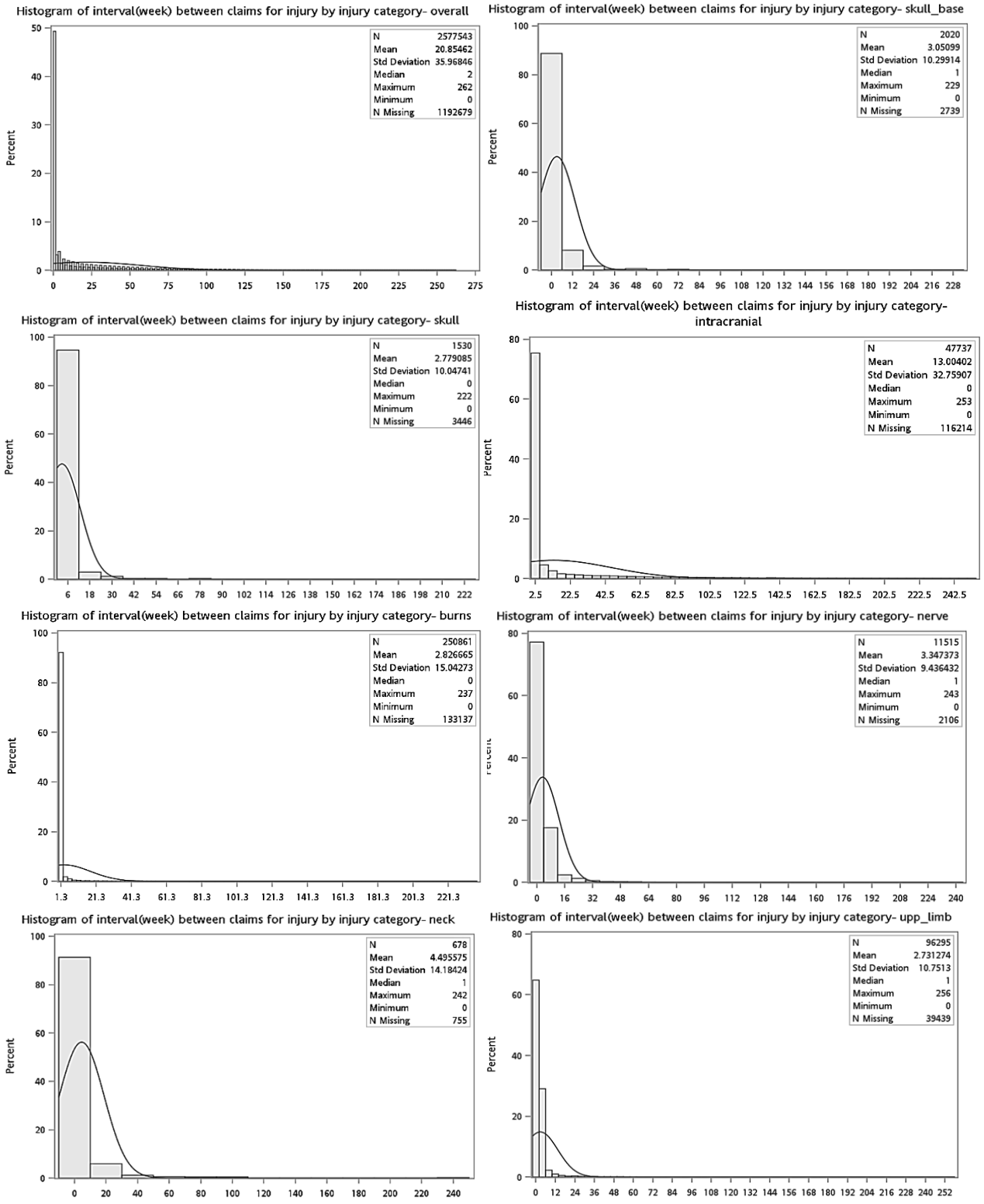
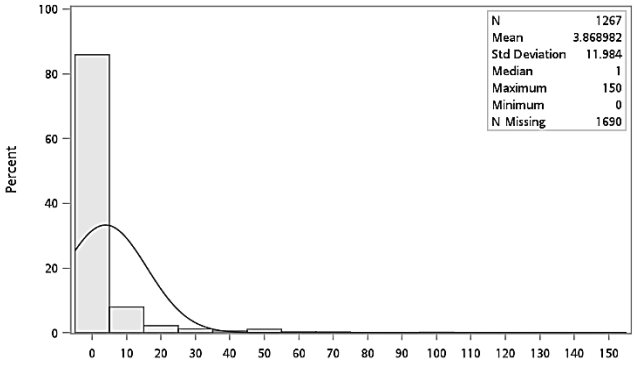
APPENDIX I: Supplemental figures

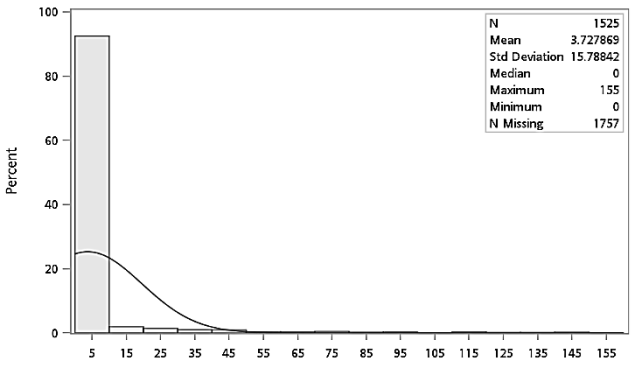
S-Figure 1 Interval between two clinical visits (in week) by injury type



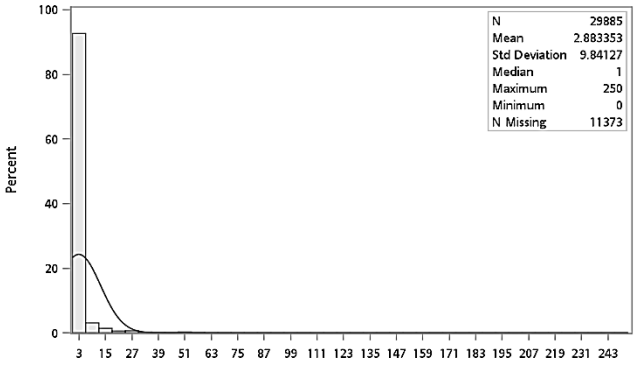
Histogram of interval(week) between claims for injury by injury category- internal



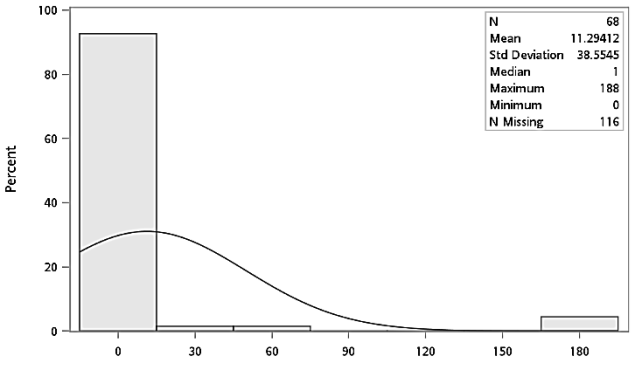
Histogram of interval(week) between claims for injury by injury category- vascular



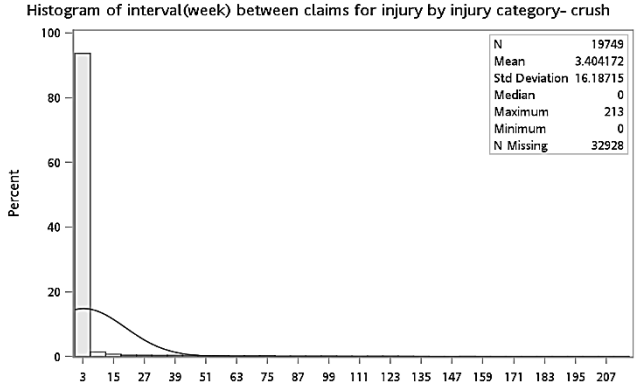
Histogram of interval(week) between claims for injury by injury category- low_limb



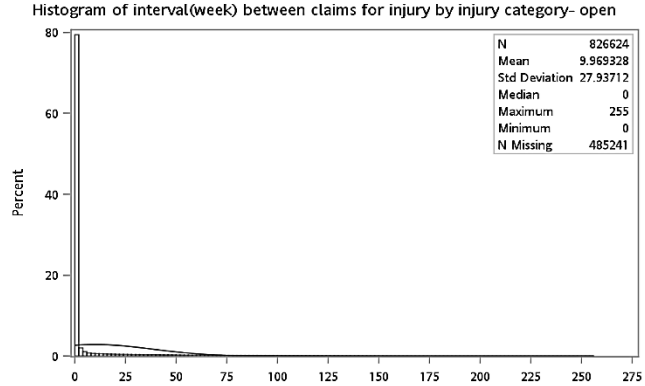
Histogram of interval(week) between claims for injury by injury category- mul_limb



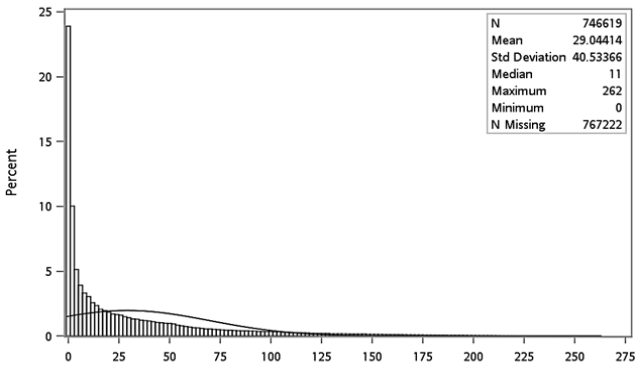
Histogram of interval(week) between claims for injury by injury category- crush



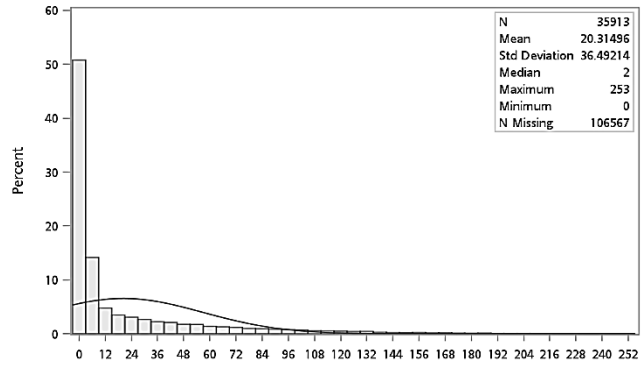
Histogram of interval(week) between claims for injury by injury category- open

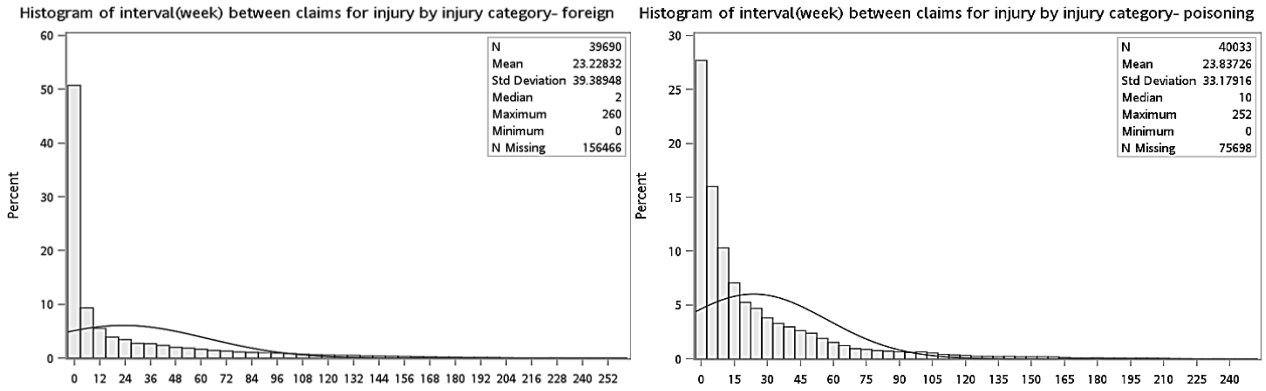


Histogram of interval(week) between claims for injury by injury category- superficial

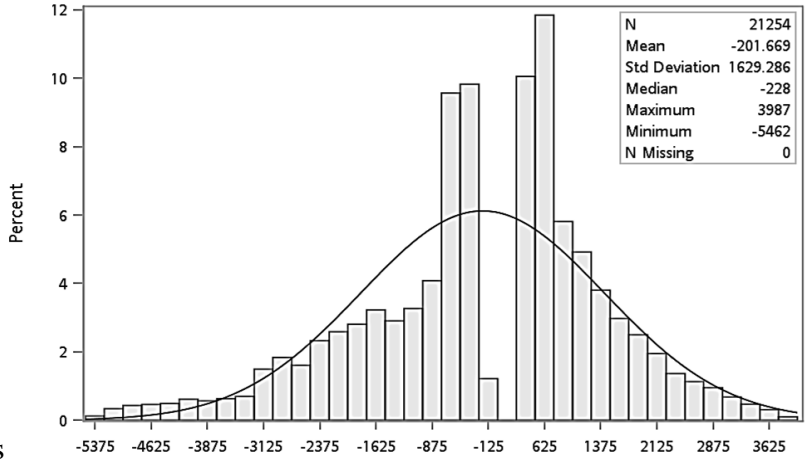


Histogram of interval(week) between claims for injury by injury category- sprains

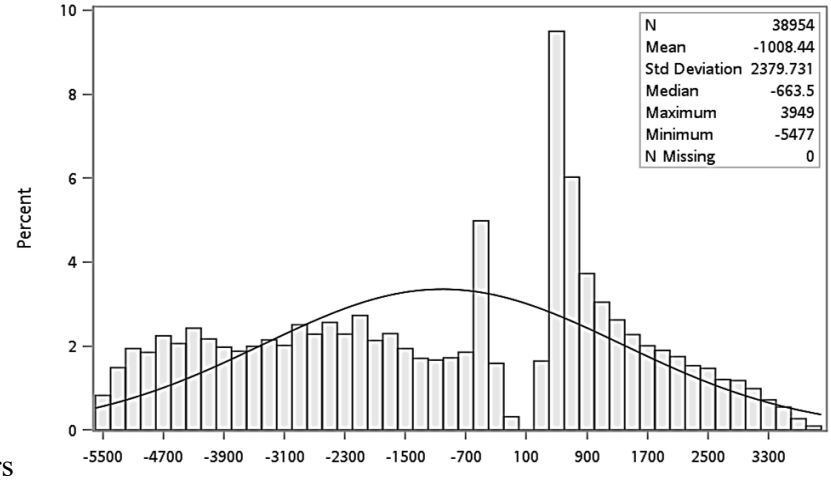




S-Figure 2 Difference in days between the data retrieval (year /month) and child's birthdate

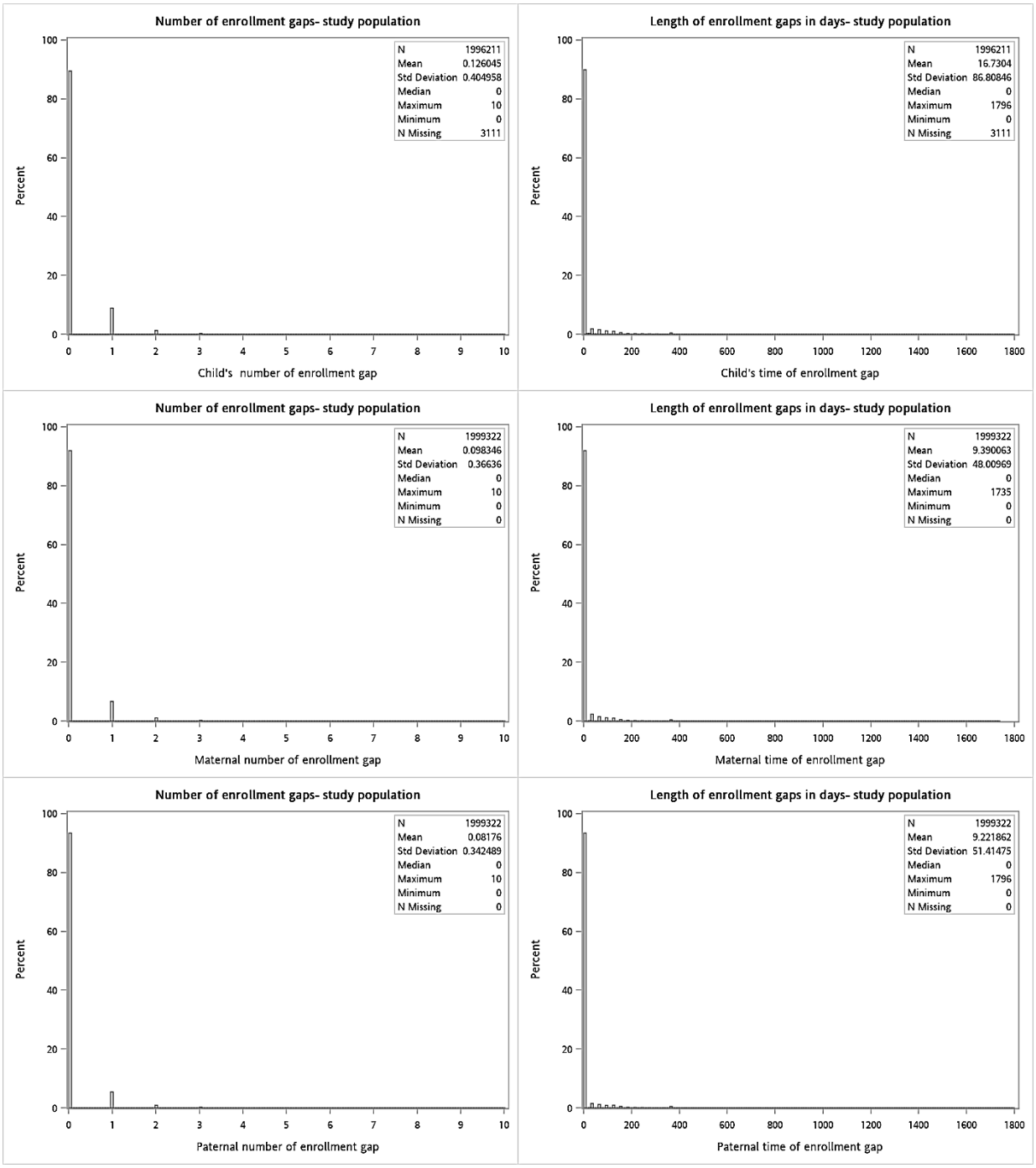


Mothers



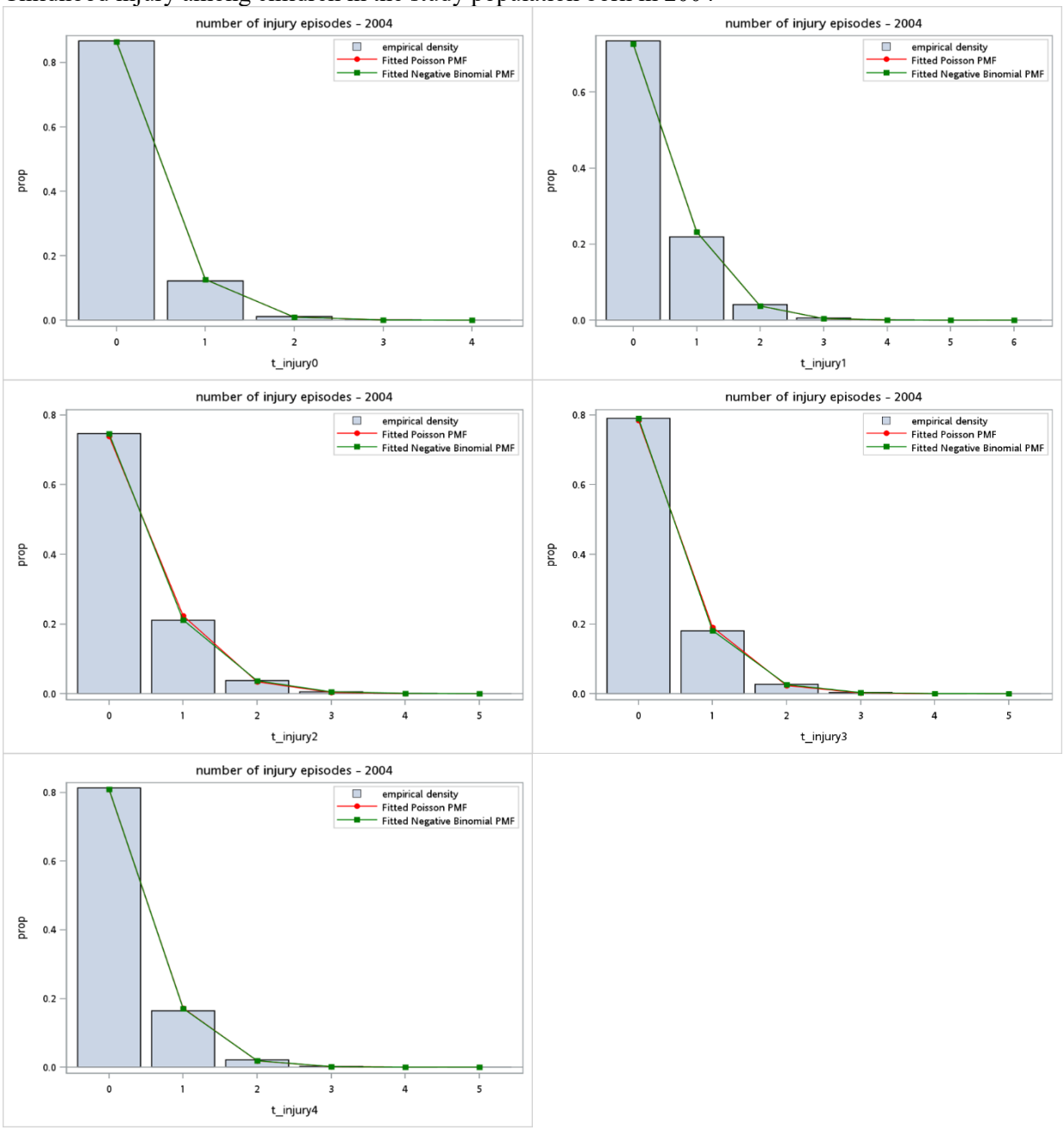
Fathers

S-Figure 3 Numbers and days of enrollment gaps for children and parents in the study population



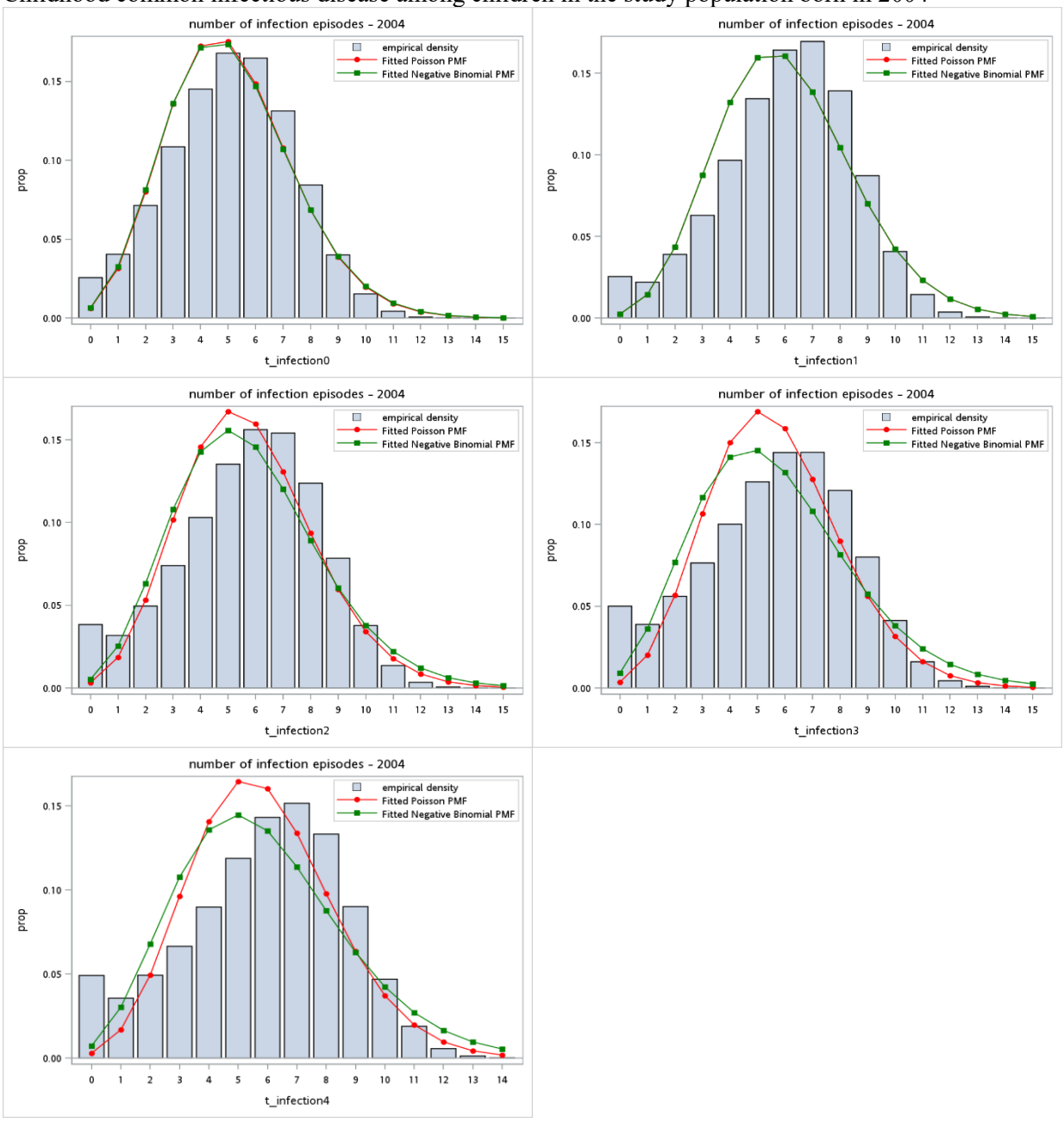
S-Figure 4 Observed number of injury events and expected values from a Passion distribution and a negative binomial distribution in each child age

Childhood injury among children in the study population born in 2004



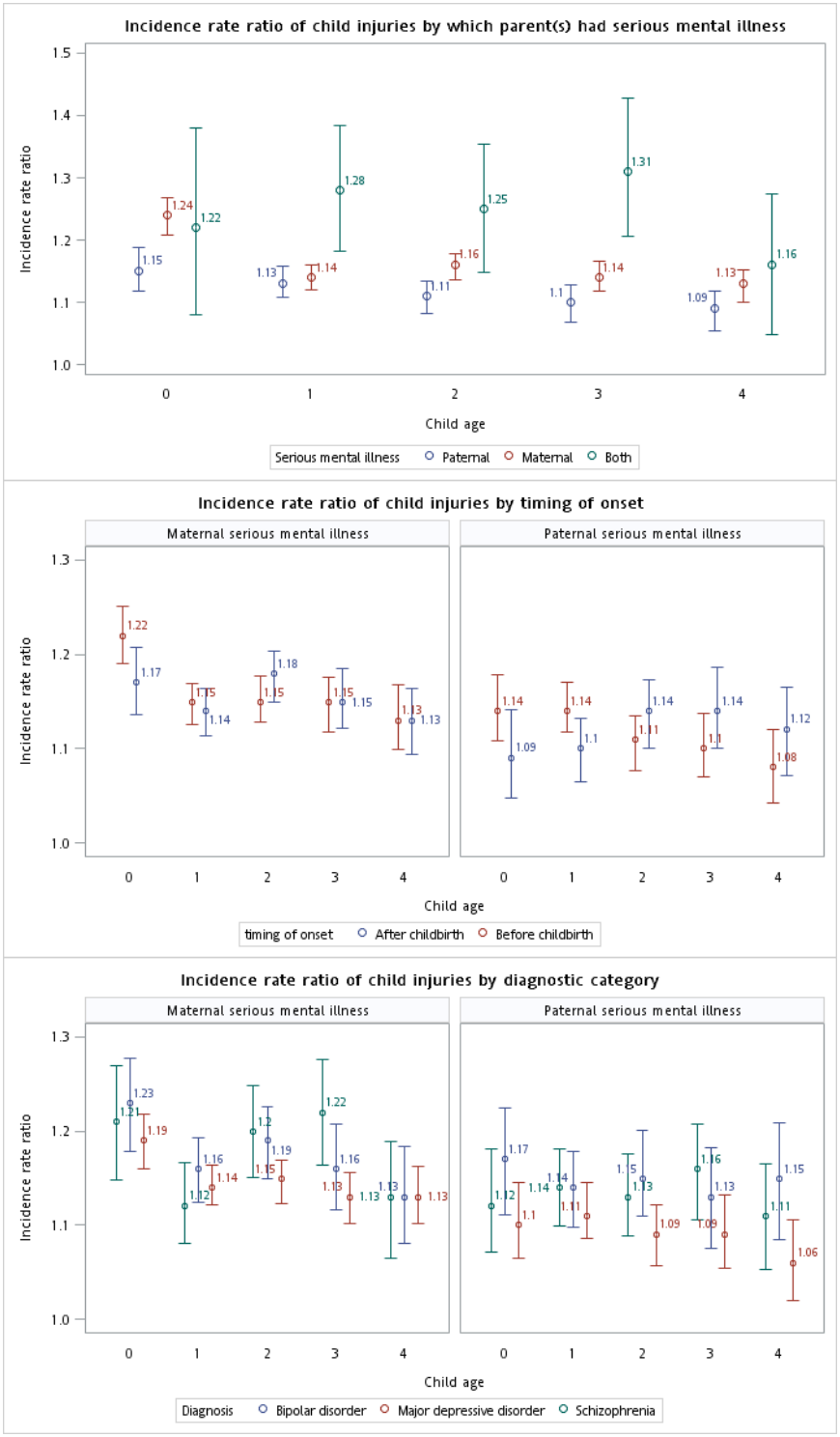
t_injury1-t_injury 4: number of injury events occurred at child age 0 years- at child age 4 years. The patterns were similar among children born in other birth years.

Childhood common infectious disease among children in the study population born in 2004



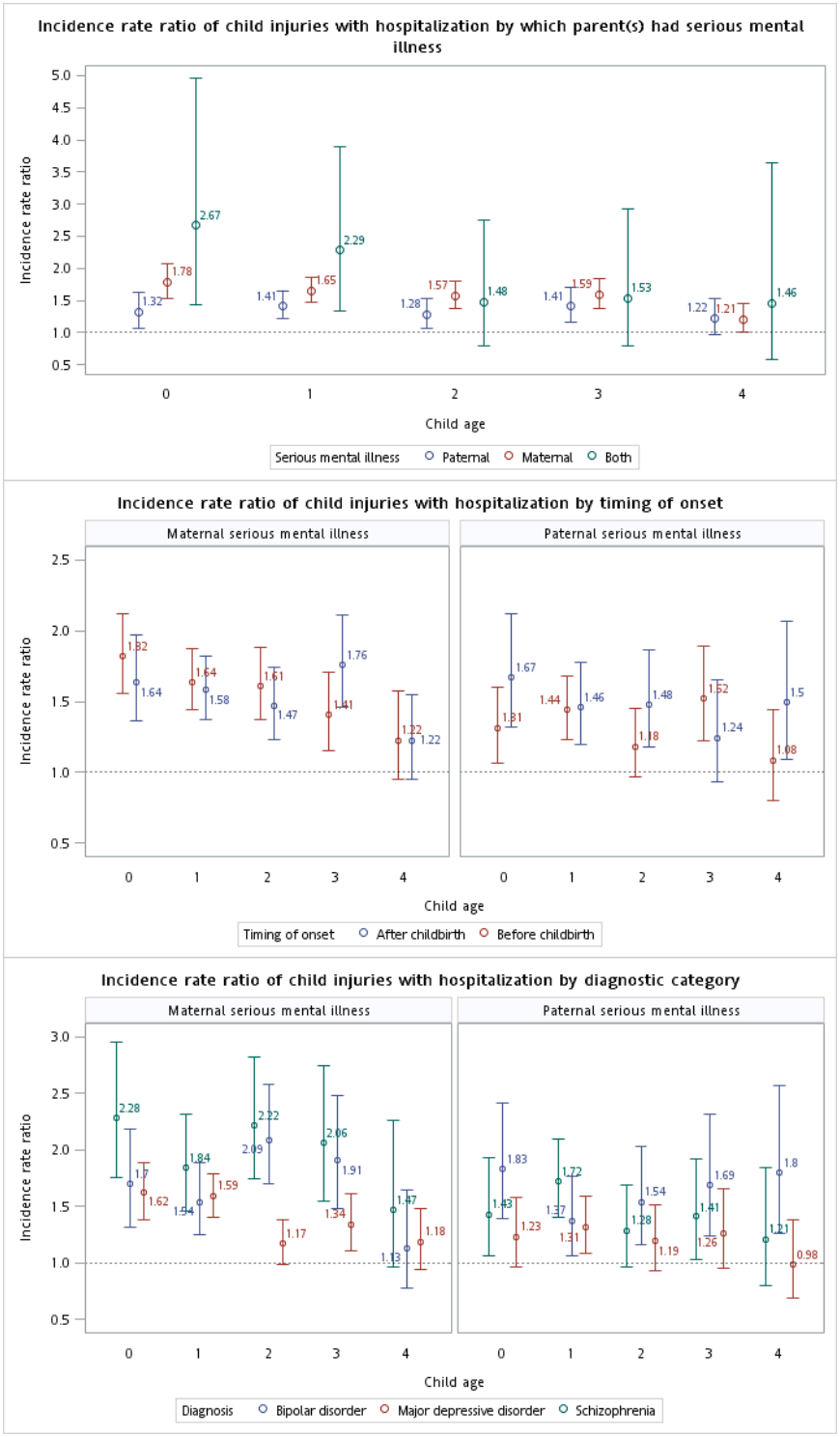
t_infection1-t_infection 4: number of episodes of common infectious disease occurred at child age 0 years- at child age 4 years. The patterns were similar among children born in other birth years.

S-Figure 5 Associations between parent's serious mental illness and any early childhood injury events in the secondary analyses, stratified by child age



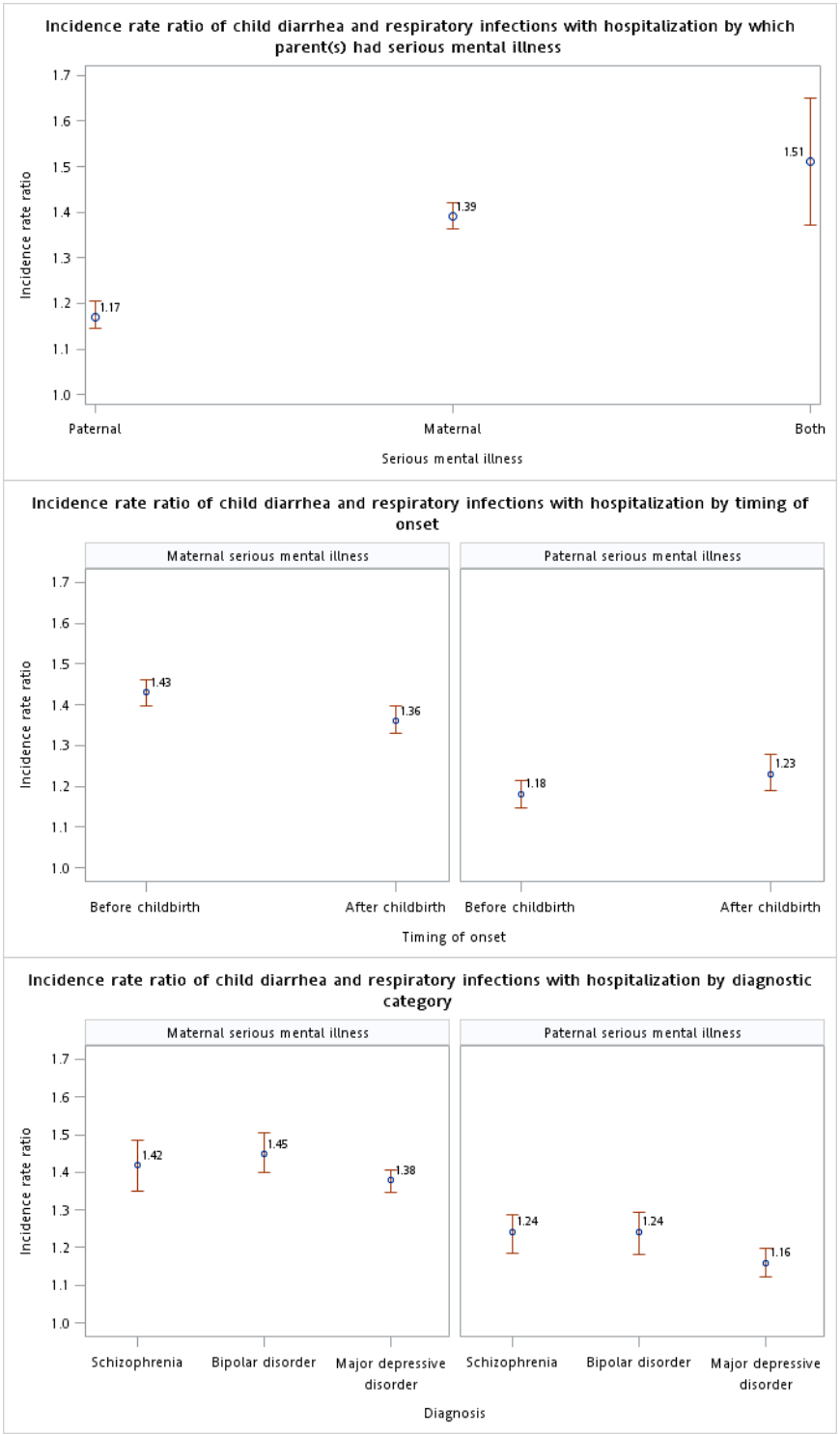
Models were adjusted for birth year, child sex, birth order, paternal and maternal ages, foreign-born mother, and urbanicity of residence.

S-Figure 6 Associations between parent's serious mental illness and early childhood injury hospitalization in the secondary analyses, stratified by child age



Models were adjusted for birth year, child sex, birth order, paternal and maternal ages, foreign-born mother, and urbanicity of residence.

S-Figure 7 Associations between parent's serious mental illness and child common infectious disease with hospitalization in the secondary analyses, stratified by child age



Models were adjusted for birth year, child sex, child age, birth order, paternal and maternal ages, foreign-born mother, and urbanicity of residence.

APPENDIX II: Supplemental tables

S-Table 1 Associations between potential confounders and the exposure and outcomes of interest

Variable	Association with exposures (parental mental illness)	Association with outcomes of interest (offspring physical health)
Birth year	Calendar year was associated with utilization of health care in Taiwan; and results from research using the NHIRD also suggested that incident cases of treated psychiatric disorder had been increasing over time.[153] In addition, secular events could be related to psychiatric disorders via stress (e.g. financial crisis in 2008). For instance, stock price index was found to be associated with psychiatric inpatient admission in Taiwan.[156]	Some unmeasured secular events may be related to child health (e.g. changes in overall population health or environmental factors; and outbreaks of communicable diseases).
Child sex	Chinese families usually favor boys, which can increase the stress of couples if they only have girls. Having a girl baby was shown to have new mothers experienced antipathy and criticism from their husbands and mother-in-laws.[38,157] A study in China also reported that women who gave birth to a female infant were more likely to have postpartum depression compared with those giving birth to a male infant.[158]	Male and female children may have different susceptibility to physical illness and injury. Physiological and behavior factors may generate different infectious disease incidences between girls and boys.[160–162] Boys also have a greater risk of injury compared with girls.[70,130,142,159]
Birth order	Having more children may be associated with more life stress, which may be a risk factor of psychiatric disorders. Primiparity was associated postpartum depression and postpartum psychosis/mania among mothers with bipolar I disorder.[164]	Number of children might be related to parent's time available for each child, parenting skills and home environment. The presence of siblings has been associated with respiratory syncytial virus infection in children.[128,163,165] Having older siblings was a risk factor for hospital-attended injury.[70]
Parent age	In the general population, the older age groups have greater prevalence of psychiatric disorders relative to the younger groups.[166,167]	Parental age may be related to childcare quality or child health condition; for example, younger parental age was shown to be related to greater use of discipline and lower nurturing behavior.[146,147] Parenting style is related to children's safety.[142]

Variable	Association with exposures (parental mental illness)	Association with outcomes of interest (offspring physical health)
Urbanicity of residence	Residence may be associated with levels of mental health service utilization, which could be influenced by the willingness to seek mental health care and the intensity of medical facilities and specialists. A recent study analyzing data of the NHIRD suggested an urban-rural inequity in psychiatric service utilization for patients with psychosis.[175] On the other hand, residence may represent some unmeasured factors related to stress. Several studies[176–179] have demonstrated an increased risk of schizophrenia in urban compared with rural areas. More advanced urbanicity was also associated with a greater risk for major depression.[176,180] However, a study analyzing the NHIRD of year 2000 reported no association between urbanicity and psychiatric disorders.[166]	Similarly, urbanicity may influence utilizations of healthcare and resources that support childcare. In Taiwan, children who were born in areas with lower levels of urbanization experienced greater risk for neonatal, infant and under-five mortality.[139] In a US study, living in a rural residence was a risk factor for a recurrent non-accidental traumatic event.[187] Studies also find an increase in the risk of unintentional injury among children living in low-income areas.[142,222] But a Canada study found that childhood injury was more common in children living in urban centers.[143] A deprived area was also found to be related to greater incidence of pneumonia in children.[188]
Maternal foreign-born status	Foreign-born women usually get married with a husband with lower income, which may increase life stress as well as the difficulties of acculturation. These mothers may have a language barrier that impair access to health care services. For example, in the NHIRD, native Taiwanese had greater risk of psychiatric disorders compared to non-Taiwanese.[166] This finding may have reflected a barrier to accessing health services since another Taiwanese study showed that immigrant mothers had high rates of psychological distress.[171] European studies also showed that immigrants had a high incidence rates of schizophrenia compared with the host population.[172–174]	Foreign-born mothers may have less time and family and social support in childcare.
Unmarried mother	Being a single mother is a risk factor for perinatal depression.[168,169]	Single parenthood is related to an increased risk of child injury.[170]
Family income	In the NHIRD, there was a dose-response relationship between insurance premium, which is determined based on salary, and psychiatric disorders. Lower salary was associated with greater odds of psychiatric disorder in terms of prevalence,[166] and greater incidences of bipolar disorder and schizophrenia.[185,186]	Financial problems and lower family income have been shown to be risk factors for child injury.[70,143] Similarly, family resources also influences risk of children respiratory infection.[128]

Variable	Association with exposures (parental mental illness)	Association with outcomes of interest (offspring physical health)
Occupational type	Unemployment is a risk factor for poor mental helath.[189–192] Occupational types may be related to stress (e.g. job loading, competition or dissatisfaction or unfulfillment), and it could be associated with awareness of illness and attitude toward utilization of mental health services.	Occupational types is often related to education, which is further associated with disease awareness, parenting skills, and safeguard procedures.[142] Unemployment status and low income household are both strongly associated with child diarrhea[236] and injury.[142] Children with a parent working in a manual job has the greatest risk of injury-related death, followed by children with unemployed parents and those working in a non-manual job.[145]
Parental physical illness	Current evidence suggests the bidirectional relationship between psychiatric disorders and chronic physical illness.[193–196] Development of psychiatric disorders in patients with chronic physical illness might be due to psychological stress, disability, and underlying biological process.[195] Psychiatric disorders have been shown to a risk factor in a variety of physical illnesses,[193,196] with the potential contributing factors being psychotropic medications, lifestyle, psychiatric symptoms, and disparities in the health care.[194]	Limited evidence shows physical illnesses can have impact on role disability.[197] A study conducted in South Africa found that children in families affected by AIDS-illness are at greater risk of child abuse.[198] In addition, parents with physical illness may be preoccupied by illness coping, leaving little time and energy to meet their children's need and provide supervision. For example, children had a greater rate of hospital contact for injury during the first year after parental cancer diagnosis.[99]
Low birthweight and preterm birth	Several studies have demonstrated that parents with mental illness are at an increased risk for adverse perinatal outcomes, including LBW, preterm birth, and small for gestational age.[58,59,61,62,80–83] On the other hand, mothers of preterm infants were at greater risk of depression than mothers of term infants.[203]	Low birthweight and preterm birth are risk factors of child injury.[129,199]
Spouse's (maternal/ paternal) serious mental illness	Spouse's mental illness is a source of life stress. Studies reported a positive relationship between maternal and parental mental illness.[32,44,200,201]	Spouse's mental illness may influence child health directly or indirectly (e.g. time and attention for childcare and home environment).

S-Table 2 Cutoff points for monthly family income (New Taiwanese Dollars) for each birth year among the study population

Birth year	Quintile1	Quintile2	Quintile3	Quintile4	Quintile5
2004	19,200	34,800	45,800	68,500	263,400
2005	19,200	35,700	48,000	71,000	263,400
2006	19,200	37,500	49,800	72,680	263,400
2007	21,000	41,100	53,580	76,400	263,400
2008	21,000	42,000	54,300	77,200	263,400
2009	22,800	42,000	57,000	80,200	313,700
2010	22,800	42,000	57,400	81,800	364,000
2011	30,300	43,800	60,600	84,000	364,000
2012	33,300	43,980	60,800	83,900	364,000
2013	33,300	45,800	63,100	87,600	364,000
2014	33,300	46,800	63,800	87,800	364,000
Overall	21,900	42,000	55,940	79,400	364,000

S-Table 3 ICD-9-CM diagnostic codes of child complex chronic conditions

Category	Subcategories	ICD-9-CM Codes
Neuromuscular	Brain and spinal cord malformations	740.0- 742.9
	Mental retardation	318.0- 318.2
	Central nervous system degeneration and disease	330.0- 330.9, 334.0- 334.2, 335.0- 335.9
	Infantile cerebral palsy	343.0- 343.9
	Muscular dystrophies and myopathies	359.0- 359.3
Cardiovascular	Heart and great vessel malformations	745.0- 747.4
	Cardiomyopathies	425.0- 425.4, 429.1
	Conduction disorders	426.0- 427.4
	Dysrhythmias	427.6- 427.9
Respiratory	Respiratory malformations	748.0- 748.9
	Chronic respiratory disease	770.7
	Cystic fibrosis	277.0
Renal	Congenital anomalies	753.0- 753.9
	Chronic renal failure	585
Gastrointestinal	Congenital anomalies	750.3, 751.1- 751.3, 751.6- 751.9
	Chronic liver disease and cirrhosis	571.4- 571.9
	Inflammatory bowel disease	555.0- 556.9
Hematologic or immunologic	Sickle cell disease	282.5- 282.6
	Hereditary anemias	282.0- 282.4
	Hereditary immunodeficiency	279.00- 279.9, 288.1- 288.2, 446.1
	Acquired immunodeficiency	0420- 0421

Category	Subcategories	ICD-9-CM Codes
Metabolic	Amino acid metabolism	270.0- 270.9
	Carbohydrate metabolism	271.0- 271.9
	Lipid metabolism	272.0- 272.9
	Storage disorders	277.3, 277.5
	Other metabolic disorders	275.0- 275.3, 277.2, 277.4
Other congenital or genetic defect	Chromosomal anomalies	758.0- 758.9
	Bone and joint anomalies	259.4, 737.3, 756.0- 756.5
	Diaphragm and abdominal wall	553.3, 756.6- 756.7
	Other congenital anomalies	759.7- 759.9
Malignancy	Malignant neoplasms	140.0- 208.9, 235.0- 239.9

This table was adapted from Feudtner et al.[204]

S-Table 4 Characteristics of children of the study population and children excluded from the study population, 2004-2014

	Children included the study population		Children excluded from the study population			
			With a matched birth record		Without a matched birth record	
	N	%	N	%	N	%
Birth year						
Missing					*5,427*	
2004-2007	768,330	38.43	56,126	28.13	27,700	40.42
2008-2010	504,907	25.25	45,823	22.97	18,155	26.49
2011-2014	726,085	36.32	97,547	48.90	22,683	33.10
Children's characteristics						
Child sex						
Missing			*2*		*5,427*	
Female	956,988	47.87	96,379	48.31	33,266	48.54
Males	1,042,334	52.13	103,115	51.69	35,272	51.46
Low birthweight						
Missing					*73,965*	
No	1,882,131	94.14	141,499*	70.93		
Yes	117,191	5.86	57,997*	29.07		
Preterm birth						
Missing					*73,965*	
No	1,860,620	93.06	142,806	71.58		
Yes	138,702	6.94	56,690	28.42		
Birth order						
Missing					*1,684*	
1	1,124,952	56.27	103,123	51.69	47,323	65.47
2	703,780	35.20	68,486	34.33	19,648	27.18
>=3	170,590	8.53	27,887	13.98	5,310	7.35
Complex chronic conditions						
Missing			*10,144*		*4,918*	
No	1,866,333	93.35	169,773	89.66	67,106	97.19
Yes	132,989	6.65	19,579	10.34	1,941	2.81

	Children included the study population		Children excluded from the study population			
			With a matched birth record		Without a matched birth record	
	N	%	N	%	N	%
Parent characteristics						
Paternal age						
Missing			*81,562*		*22,704*	
<25	101,829	5.09	4,654	3.95	1,058	2.06
25-29	438,192	21.92	21,995	18.65	6,931	13.52
30-34	765,790	38.30	44,832	38.01	17,296	33.74
35-39	478,869	23.95	32,091	27.21	14,115	27.54
40-44	159,561	7.98	10,450	8.86	7,009	13.67
>=45	55,081	2.75	3,912	3.32	4,852	9.47
Maternal age						
Missing					*42,967*	
<20	35,620	1.78	8,211	4.12	411	1.33
20-24	262,663	13.14	21,648	10.85	4,306	13.89
25-29	671,482	33.59	53,453	26.79	8,126	26.21
30-34	729,222	36.47	73,900	37.04	11,773	37.98
35-39	263,861	13.20	35,951	18.02	5,351	17.26
>=40	36,474	1.82	6,333	3.17	1,031	3.33
Unmarried mother						
Missing					*73,965*	
No	1,935,304	96.80	137,293	68.82		
Yes	64,018	3.20	62,203	31.18		
Foreign-born mother						
Missing					*37,830*	
No	1,804,688	90.26	185,724	93.10	26,563	73.51
Yes	194,634	9.74	13,772	6.90	9,572	26.49
Socio-economic status						
Urbanicity of residence						
Missing	*13*		*22*		*73,965*	
1 (highest urbanicity)	404,799	20.25	42,751	21.43		
2	645,763	32.30	67,635	33.91		
3	471,912	23.60	44,413	22.27		
4	287,070	14.36	25,868	12.97		
5	33,169	1.66	2,659	1.33		
6	69,099	3.46	7,208	3.61		
7	87,497	4.38	8,940	4.48		
Family income						
Missing	*4,037*		*9,530*		*9,724*	
High	360,582	18.07	20,804	10.95	3,680	5.73
Upper-middle	404,735	20.28	17,995	9.47	4,658	7.25
Middle	427,217	21.41	22,819	12.01	7,151	11.13
Lower-middle	401,114	20.10	35,185	18.52	13,959	21.73
Low	401,637	20.13	93,163	49.04	34,793	54.16

	Children included the study population		Children excluded from the study population			
			With a matched birth record		Without a matched birth record	
	N	%	N	%	N	%
Paternal occupation						
Missing	*28,001*		*120,617*		*24,496*	
Civil servants and teachers	111,993	5.68	5,529	7.01	1,856	3.75
Employees, employers and professionals	1,487,630	75.46	59,838	75.86	31,483	63.64
Union members, farmers and fishermen	109,084	5.53	3,681	4.67	3,135	6.34
The unemployed and low-income households	197,877	10.04	7,542	9.56	12,174	24.61
Dependents	64,737	3.28	2,289	2.90	821	1.66
Maternal occupation						
Missing	*8,523*		*15,245*		*47,016*	
Civil servants and teachers	108,535	5.45	9,429	5.12	1,232	4.57
Employees, employers and professionals	1,253,228	62.95	106,205	57.64	10,691	39.67
Union members, farmers and fishermen	69,141	3.47	5,799	3.15	343	1.27
The unemployed and low-income households	135,476	6.81	44,171	23.97	7,505	27.85
Dependents	424,419	21.32	18,647	10.12	7,178	26.64
Parental physical illness						
Paternal Elixhauser index						
Missing			*90,262*		*19,286*	
0	1,871,469	93.61	101,459	92.88	51,488	94.16
1	99,306	4.97	5,955	5.45	2,340	4.28
>1	28,547	1.43	1,820	1.67	851	1.56
Maternal Elixhauser index						
Missing			*4,127*		*37,853*	
0	1,911,647	95.61	183,384	93.87	35,668	98.77
1	78,270	3.91	10,664	5.46	390	1.08
>1	9,405	0.47	1,321	0.68	54	0.15
Death occurred in the first five years of life						
Paternal death						
No	1,990,599	99.56	199,111	99.81	73,698	99.64
Yes	8,723	0.44	385	0.19	267	0.36
Maternal death						
No	1,996,857	99.88	199,139	99.82	73,940	99.97
Yes	2,465	0.12	357	0.18	25	0.03
Child's death						
No	1,993,379	99.70	194,597	97.54	73,849	99.84
Yes	5,943	0.30	4,899	2.46	116	0.16

*For the same-sex multiples, it was difficult to assign birthweight because the MCHD and the registry of beneficiaries had no indicator of birth order for each child's ID. So, birthweight for same-sex twins/triplets was assigned with the mean of their birthweights.

S-Table 5 Number of children with Taiwanese citizenship born in 2004-2014 who had parental serious mental illness stratified by diagnosis and specialties

		Maternal SMI		Paternal SMI	
Diagnostic categories	**Specialties**	**Number of children**	**%**	**Number of children**	**%**
Schizophrenia	Psychiatrists	9,850	97.2	10,124	96.7
	Other specialties	281	2.8	347	3.3
Bipolar disorder	Psychiatrists	13,933	89.7	8,547	86.7
	Other specialties	1,603	10.3	1,312	13.3
Major depressive disorder	Psychiatrists	39,328	96.1	17,518	94.1
	Other specialties	1,600	3.9	1,091	5.9

Abbreviation: SMI: serious mental illness.
Time frame of making a diagnostic category: from 6 years prior to childbirth to 5 years following childbirth.

S-Table 6 Number of parents receiving different diagnosis across their children who had Taiwanese citizenship and were born in 2004-2014

Diagnosis 1	**Diagnosis 2**	**Diagnosis 3**	**Mothers (N)**	**Fathers (N)**
No diagnosis	Bipolar disorder		1,521	924
No diagnosis	Bipolar disorder	Major depression	16	3
No diagnosis	Bipolar disorder	Schizophrenia	5	4
No diagnosis	Major depression		4,767	2,189
No diagnosis	Major depression	Schizophrenia	8	4
No diagnosis	Schizophrenia		878	786
Bipolar disorder	Major depression		284	137
Bipolar disorder	Schizophrenia		95	90
Major depression	Schizophrenia		114	52
Sum			7,688	4,189

Time frame of making a diagnostic category: from 6 years prior to childbirth to 5 years following childbirth. The sequence of diagnoses was not presented in the chronological order.

S-Table 7 Number of children with Taiwanese citizenship born in 2004-2014 who had parental serious mental illness (SMI), stratified by pattern of linkages

Matched birth record*	Child's ID#	link_c %	Mother's ID#	link_m %	Father's ID#	link_f %	N	Maternal SMI&	%@	Paternal SMI&	%@
Y	Y	L	Y	L	Y	L	2,060,420	59,519	2.89	37,448	1.82
Y	Y	L	Y	L			79,637	4,874	6.12		
Y	Y	L	Y	L	Y		25,598	700	2.73	112	0.44
Y	Y		Y	L	Y	L	21,262	537	2.53	259	1.22
Y	Y	L	Y		Y	L	4,998	10	0.20	80	1.60
Y	Y		Y	L	Y		4,689	200	4.27	38	0.81
Y	Y		Y		Y		952	18	1.89	4	0.42
Y	Y		Y		Y	L	732	10	1.37	12	1.64
Y	Y		Y	L			487	42	8.62		
Y	Y	L	Y		Y		23				
Y	Y		Y				13				
Y	Y	L	Y				7				
	Y	L			Y	L	34,710			506	1.46
	Y	L	Y	L			15,562	379	2.44		
	Y	L	Y	L	Y	L	15,398	302	1.96	430	2.79
	Y		Y	L	Y	L	3,018				
	Y		Y	L			1,469				
	Y	L	Y		Y	L	1,154			47	4.07
	Y		Y	L	Y		599				
	Y		Y		Y	L	135				
	Y		Y				95				
	Y	L					85				
	Y		Y		Y		58				
	Y						45				
	Y	L	Y	L	Y		38	3	7.89		
	Y	L	Y				35				
	Y				Y	L	9				
	Y	L/			Y		3				
Sum							2,271,231	66,596	2.93	38,937	1.71

* Whether a parent-child pair/triad has a matched birth certificate record (Y: yes; N: no)
# Whether a child's ID, mother's ID and father's ID exists in the MCHD and/or the registry of beneficiaries. (Y: yes; blank: no)
% link_c, link_m, link_f: whether child's ID, mother's ID, father's ID, respectively, could be linked to the registry of beneficiaries (L: yes; blank: no)
& Time frame of making a diagnostic category: from 6 years prior to childbirth to 5 years following childbirth. Three cells with number < 3 were not reported in the table.
@ denominator: number of children in each row. Children without any parent's IDs (n=1,552) were not listed in the above table.

S-Table 8 Length of enrollment and enrollment gaps for children and parents, stratified by whether a child was included in the study population and matched to the birth certificate

	Groups[@]	Non-missing (n)	Missing[#] n	Missing[#] %	Mean	SD*
Child's enrollment						
Enrollment time (days)	Study population	1,999,322	0	0	1,364.9	580.9
	Matched	171,361	28,135	14.10	1,199.8	605.5
	Unmatched	66,985	6,980	9.43	1,004.0	633.6
Number of enrollment gaps	Study population	1,999,322	0	0	0.13	0.40
	Matched	171,361	28,135	14.10	0.20	0.51
	Unmatched	66,985	6,980	9.43	0.75	0.80
Total days of gaps	Study population	1,999,322	0	0	16.7	86.7
	Matched	171,361	28,135	14.10	44.3	174.7
	Unmatched	66,985	6,980	9.43	322.8	451.0
Paternal enrollment						
Enrollment time (days)	Study population	1,999,296	26	0.00	1,356.7	587.4
	Matched	88,090	111,406	55.84	989.5	763.9
	Unmatched	54,424	19,541	26.42	1,250.8	634.1
Number of enrollment gap	Study population	1,999,322	0	0.00	0.08	0.34
	Matched	88,090	111,406	55.84	0.05	0.29
	Unmatched	54,424	19,541	26.42	0.16	0.54
Total days of gaps	Study population	1,999,322	0	0.00	9.2	51.4
	Matched	88,090	111,406	55.84	6.8	50.8
	Unmatched	54,424	19,541	26.42	34.2	137.0
Maternal enrollment						
Enrollment time (days)	Study population	1,999,299	0	0.00	1,368.4	576.5
	Matched	192,940	6,556	3.29	1,091.7	687.6
	Unmatched	36,083	37,882	51.22	1,147.0	707.8
Number of enrollment gap	Study population	1,999,322	0	0.00	0.10	0.37
	Matched	192,940	6,556	3.29	0.11	0.41
	Unmatched	36,083	37,882	51.22	0.28	0.71
Total days of gaps	Study population	1,999,322	0	0.00	9.4	48.0
	Matched	192,940	6,556	3.29	15.8	83.9
	Unmatched	36,083	37,882	51.22	64.1	188.1

@Matched: children with a matched birth certificate record but not included in the study population; unmatched: children without a matched birth record.
*SD: standard deviation
missing: an ID unlinkable to the registry of beneficiaries.

S-Table 9 Associations between parent's serious mental illness present before childbirth and covariates among children in the study population

	Parental SMI			Maternal SMI			Paternal SMI		
	n[&]	%	RR	n[&]	%	RR	n[&]	%	RR
Birth year									
2004-2007	20,755	2.7	ref	11,895	1.55	ref	9,275	1.21	ref
2008-2010	15,650	3.1	1.15	9,641	1.91	1.23	6,331	1.25	1.03
2011-2014	20,669	2.85	1.06	12,989	1.79	1.15	8,115	1.12	0.93
Children's characteristics									
Child sex									
Males	29,659	2.85	1.00	17,827	1.71	0.98	12,413	1.19	1.01
Female	27,415	2.86	ref	16,698	1.74	ref	11,308	1.18	ref
Low birthweight									
No	52,970	2.81	ref	31,870	1.69	ref	22,167	1.18	ref
Yes	4,104	3.5	1.25	2,655	2.27	1.34	1,554	1.33	1.13
Preterm birth									
No	52,063	2.8	ref	31,225	1.68	ref	21,879	1.18	ref
Yes	5,011	3.61	1.29	3,300	2.38	1.42	1,842	1.33	1.13
Birth order									
1	33,462	2.97	ref	19,742	1.75	ref	14,380	1.28	ref
2	17,927	2.55	0.86	10,924	1.55	0.89	7,360	1.05	0.82
≥3	5,685	3.33	1.31	3,859	2.26	1.46	1,981	1.16	1.10
Complex chronic conditions									
No	52,894	2.83	ref	31,927	1.71	ref	22,045	1.18	ref
Yes	4,180	3.14	1.11	2,598	1.95	1.14	1,676	1.26	1.07
Parent characteristics									
Paternal age at birth (years)									
<25	4,090	4.02	1.60	1,783	1.75	1.07	2,382	2.34	2.52
25-29	12,336	2.82	1.12	7,690	1.75	1.07	4,855	1.11	1.19
30-34	19,304	2.52	ref	12,542	1.64	ref	7,117	0.93	ref
35-39	13,643	2.85	1.13	8,272	1.73	1.05	5,680	1.19	1.28
40-44	5,395	3.38	1.34	3,033	1.9	1.16	2,520	1.58	1.70
≥45	2,305	4.18	1.66	1,204	2.19	1.34	1,167	2.12	2.28
Maternal age at birth (years)									
<20	1,286	3.61	1.37	485	1.36	0.78	817	2.29	2.41
20-24	8,977	3.42	1.30	4,138	1.58	0.91	4,972	1.89	1.99
25-29	18,118	2.7	1.02	11,126	1.66	0.95	7,344	1.09	1.15
30-34	19,215	2.64	ref	12,681	1.74	ref	6,922	0.95	ref
35-39	8,174	3.1	1.17	5,279	2	1.15	3,140	1.19	1.25
≥40	1,304	3.58	1.36	816	2.24	1.29	526	1.44	1.52
Unmarried mother									
No	53,194	2.75	ref	31,941	1.65	ref	22,293	1.15	ref
Yes	3,880	6.06	2.20	2,584	4.04	2.45	1,428	2.23	1.94
Foreign-born mother									
No	51,454	2.85	ref	33,731	1.87	ref	18,842	1.04	ref
Yes	5,620	2.89	1.01	794	0.41	0.22	4,879	2.51	2.41

	Parental SMI			Maternal SMI			Paternal SMI		
	n[&]	%	RR	n[&]	%	RR	n[&]	%	RR
Socio-economic status									
Urbanicity of residence									
1 (highest urbanicity)	11,601	2.87	ref	7,068	1.75	ref	4,785	1.18	ref
2	19,708	3.05	1.06	12,257	1.9	1.09	7,888	1.22	1.03
3	12,373	2.62	0.91	7,462	1.58	0.90	5,143	1.09	0.92
4	8,068	2.81	0.98	4,739	1.65	0.94	3,467	1.21	1.03
5	991	2.99	1.04	506	1.53	0.87	501	1.51	1.28
6	2,064	2.99	1.04	1,167	1.69	0.97	947	1.37	1.16
7	2,269	2.59	0.90	1,326	1.52	0.87	990	1.13	0.96
Family income									
High	8,179	2.04	ref	5,251	1.31	ref	3,052	0.76	ref
Upper-middle	8,904	2.22	1.09	5,833	1.45	1.11	3,242	0.81	1.07
Middle	11,562	2.71	1.33	7,281	1.7	1.30	4,478	1.05	1.38
Lower-middle	12,871	3.18	1.56	7,324	1.81	1.38	5,799	1.43	1.88
Low	15,412	4.27	2.09	8,743	2.42	1.85	7,097	1.97	2.59
Paternal occupation									
Civil servants and teachers	2,945	2.63	1.02	1,885	1.68	1.04	1,115	1	0.99
Laborers, employers and professionals	38,486	2.59	ref	24,089	1.62	ref	15,077	1.01	ref
Union members, farmers and fishermen	3,648	3.34	1.29	1,940	1.78	1.10	1,799	1.65	1.63
The unemployed and low-income households	9,057	4.58	1.77	4,889	2.47	1.52	4,450	2.25	2.23
Dependents	2,201	3.4	1.31	1,199	1.85	1.14	1,060	1.64	1.62
Maternal occupation									
Civil servants and teachers	2,509	2.31	0.94	1,516	1.4	0.93	1,028	0.95	0.95
Employees, employers and professionals	30,863	2.46	ref	18,924	1.51	ref	12,498	1	ref
Union members, farmers and fishermen	2,078	3.01	1.22	1,429	2.07	1.37	702	1.02	1.02
The unemployed and low-income households	7,610	5.62	2.28	5,201	3.84	2.54	2,695	1.99	1.99
Dependents	13,742	3.24	1.32	7,312	1.72	1.14	6,669	1.57	1.57
Parental physical illness									
Paternal Elixhauser index									
0	51,353	2.74	ref	32,034	1.71	ref	20,288	1.08	ref
1	4,204	4.23	1.54	1,874	1.89	1.11	2,478	2.5	2.31
>1	1,517	5.31	1.94	617	2.16	1.26	955	3.35	3.10
Maternal Elixhauser index									
0	53,316	2.79	ref	31,791	1.66	ref	22,583	1.18	ref
1	3,181	4.06	1.46	2,296	2.93	1.77	975	1.25	1.06
>1	577	6.14	2.20	438	4.66	2.81	163	1.73	1.47
Death occurred in the first five years of life									
Paternal death									
No	56,530	2.84	ref	34,336	1.72	ref	23,342	1.17	ref
Yes	544	6.24	2.20	189	2.17	1.26	379	4.34	3.71
Maternal death									
No	56,853	2.85	ref	34,337	1.72	ref	23,667	1.19	ref
Yes	221	8.97	3.15	188	7.63	4.44	54	2.19	1.84
Child's death									
No	56,873	2.85	ref	34,410	1.73	ref	23,627	1.19	ref
Yes	201	3.38	1.19	115	1.94	1.12	94	1.58	1.33
Censored									
No	56,125	2.83	ref	34,045	1.72	ref	23,201	1.17	ref
Yes	949	5.61	1.98	480	2.84	1.65	520	3.08	2.63

Abbreviation: SMI: serious mental illness; RR: unadjusted relative risk; ref: reference group
&number of children with parental SMI onset before birth

S-Table 10 Associations between parent's serious mental illness onset in the first five years of life and covariates among children in the study population

	Parental SMI			Maternal SMI			Paternal SMI		
	n[&]	Rate*	IRR	n[&]	Rate*	IRR	n[&]	Rate*	IRR
Birth year									
2004-2007	18,169	4.95	ref	12,514	3.35	ref	6,581	1.75	ref
2008-2010	10,120	4.33	0.87	6,789	2.85	0.85	3,921	1.63	0.93
2011-2014	5,548	3.92	0.79	3,678	2.56	0.76	2,163	1.50	0.86
Children's characteristics									
Child sex									
Males	17,803	4.59	1.02	12,184	3.09	1.03	6,581	1.66	0.99
Female	16,034	4.52	ref	10,797	2.99	ref	6,084	1.68	ref
Low birthweight									
No	31,310	4.47	ref	21,159	2.97	ref	11,808	1.65	ref
Yes	2,527	6.08	1.36	1,822	4.3	1.45	857	2	1.21
Preterm birth									
No	30,813	4.45	ref	20,766	2.95	ref	11,676	1.65	ref
Yes	3,024	5.99	1.35	2,215	4.31	1.46	989	1.89	1.15
Birth order									
1	18,925	4.45	ref	12,785	2.96	ref	7,120	1.64	ref
2	11,527	4.49	1.01	7,840	3.01	1.02	4,287	1.63	0.99
≥3	3,385	5.58	1.24	2,356	3.81	1.27	1,258	2.01	1.23
Complex chronic conditions									
No	30,944	4.49	ref	20,934	2.98	ref	11,691	1.65	ref
Yes	2,893	5.54	1.23	2,047	3.85	1.29	974	1.81	1.10
Parent characteristics									
Paternal age at birth (years)									
<25	3,168	8.03	1.98	2,085	5.12	1.90	1,287	3.17	2.16
25-29	8,573	4.98	1.23	5,965	3.41	1.26	3,076	1.74	1.18
30-34	11,470	4.05	ref	7,743	2.7	ref	4,261	1.47	ref
35-39	7,010	4.09	1.01	4,745	2.72	1.01	2,639	1.5	1.02
40-44	2,529	4.46	1.10	1,708	2.94	1.09	975	1.68	1.14
≥45	1,087	5.64	1.39	735	3.68	1.36	427	2.15	1.46
Maternal age at birth (years)									
<20	1,412	9.94	2.68	866	5.87	2.39	621	4.26	3.11
20-24	6,954	6.54	1.76	4,823	4.41	1.79	2,557	2.34	1.71
25-29	11,800	4.49	1.21	8,123	3.05	1.24	4,289	1.6	1.17
30-34	9,619	3.71	ref	6,459	2.46		3,635	1.37	ref
35-39	3,478	3.96	1.07	2,334	2.61	1.06	1,331	1.48	1.08
≥40	574	4.84	1.30	376	3.11	1.26	232	1.9	1.39
Unmarried mother									
No	31,516	4.39	ref	21,363	2.93	ref	11,777	1.6	ref
Yes	2,321	9.52	2.17	1,618	6.4	2.18	888	3.45	2.16
Foreign-born mother									
No	30,470	4.58	ref	21,147	3.13	ref	10,956	1.61	ref
Yes	3,367	4.34	0.95	1,834	2.28	0.73	1,709	2.18	1.35

	Parental SMI			Maternal SMI			Paternal SMI		
	n[&]	Rate*	IRR	n[&]	Rate*	IRR	n[&]	Rate*	IRR
Socio-economic status									
Urbanicity of residence									
1 (highest urbanicity)	6,291	4.3	ref	4,243	2.85	ref	2,424	1.62	ref
2	11,346	4.74	1.10	7,723	3.17	1.11	4,247	1.73	1.07
3	7,698	4.39	1.02	5,301	2.98	1.05	2,811	1.57	0.97
4	5,116	4.74	1.10	3,452	3.14	1.10	1,907	1.73	1.07
5	614	4.74	1.10	406	3.06	1.07	245	1.85	1.14
6	1,272	4.76	1.11	885	3.24	1.14	446	1.63	1.01
7	1,500	4.49	1.04	971	2.85	1.00	585	1.71	1.06
Family income									
High	4,525	3	ref	3,031	1.99	ref	1,650	1.07	ref
Upper-middle	5,373	3.57	1.19	3,688	2.42	1.22	1,901	1.24	1.16
Middle	6,903	4.31	1.44	4,796	2.95	1.48	2,455	1.5	1.40
Lower-middle	7,954	5.25	1.75	5,396	3.49	1.75	2,996	1.93	1.80
Low	8,952	7.04	2.35	5,970	4.56	2.29	3,621	2.76	2.58
Paternal occupation									
Civil servants and teachers	1,709	4.04	0.99	1,188	2.77	1.00	603	1.39	0.99
Employees, employers and professionals	22,182	4.07	ref	15,385	2.78	ref	7,838	1.41	ref
Union members, farmers and fishermen	2,289	5.21	1.28	1,491	3.31	1.19	931	2.07	1.47
The unemployed and low-income households	5,381	7.28	1.79	3,508	4.59	1.65	2,282	2.99	2.12
Dependents	1,668	6.39	1.57	994	3.71	1.33	779	2.91	2.06
Maternal occupation									
Civil servants and teachers	1,391	3.38	0.89	891	2.14	0.87	541	1.29	0.90
Employees, employers and professionals	17,053	3.78	ref	11,243	2.46	ref	6,605	1.43	ref
Union members, farmers and fishermen	1,406	5.11	1.35	979	3.5	1.42	494	1.74	1.22
The unemployed and low-income households	4,261	9.26	2.45	3,109	6.53	2.65	1,519	3.14	2.20
Dependents	9,481	5.5	1.46	6,581	3.73	1.52	3,422	1.93	1.35
Parental physical illness									
Paternal Elixhauser index									
0	31,036	4.45	ref	21,390	3.02	ref	11,212	1.57	ref
1	2,052	5.83	1.31	1,196	3.28	1.09	1,016	2.81	1.79
>1	749	7.85	1.76	395	3.87	1.28	437	4.45	2.83
Maternal Elixhauser index									
0	32,075	4.5	ref	21,662	2.99	ref	12,106	1.66	ref
1	1,536	5.89	1.31	1,140	4.3	1.44	495	1.82	1.10
>1	226	7.74	1.72	179	6	2.01	64	2.04	1.23
Death occurred in the first five years of life									
Paternal death									
No	33,357	4.51	ref	22,721	3.02	ref	12,412	1.64	ref
Yes	480	24.44	5.42	260	6.7	2.22	253	12.6	7.68
Maternal death									
No	33,664	4.54	ref	22,841	3.03	ref	12,609	1.66	ref
Yes	173	33	7.27	140	26.68	8.81	56	5.31	3.20

	Parental SMI			Maternal SMI			Paternal SMI		
	n[&]	Rate*	IRR	n[&]	Rate*	IRR	n[&]	Rate*	IRR
Child's death									
No	33,601	4.53	ref	22,806	3.02	ref	12,591	1.66	ref
Yes	236	48.37	10.68	175	35.2	11.66	74	14.75	8.89
Censored									
No	32,962	4.46	ref	22,416	2.99	ref	12,286	1.62	ref
Yes	875	29.82	6.69	565	11.63	3.89	379	10.76	6.64

Abbreviation: SMI: serious mental illness; IRR: unadjusted incidence rate ratio; ref: reference group
&number of children with parental serious mental onset after birth
*Incidence rate: per 1,000 person-years. Censored when the child or any parent died.

S-Table 11 Incidence rates of injury-related healthcare visits among children in the study population, stratified by child age and by exposure to parental serious mental illness

Age (years)	Unexposed periods		Exposed periods		Rate difference (95% CI)	Unadjusted IRR (95% CI)
	Visits*	Rate[#] (95% CI)	Visits*	Rate[#] (95% CI)		
0-1	405,152	218.8 (218.1-219.5)	15,566	264.8 (260.7-269.0)	46.0 (41.8-50.2)	1.21 (1.19-1.23)
1-2	972,907	581.2 (580.0-582.3)	40,497	666.5 (660.1-673.0)	85.4 (78.8-92.0)	1.15 (1.14-1.16)
2-3	826,359	556.8 (555.6-558.0)	38,937	638.5 (632.2-644.9)	81.7 (75.2-88.2)	1.15 (1.14-1.16)
3-4	562,021	433.5 (432.3-434.6)	29,714	496.0 (490.4-501.7)	62.6 (56.8-68.3)	1.14 (1.13-1.16)
4-5	425,239	374.3 (373.1-375.4)	24,162	416.5 (411.3-421.8)	42.2 (36.9-47.6)	1.11 (1.10-1.13)

Abbreviation: CI: Confidence intervals; IRR: incidence rate ratio.
*Visits: including injury-related outpatient/inpatient visits. Visits on the same day were counted once. Child age was determined by the age when an episode occurred.
#Incidence rate: per 1,000 person-years. The follow-up time was censored when the child died

S-Table 12 Incidence rates of injury events among children in the study population, stratified by child age and by exposure to parental serious mental illness for each injury type

Age (years)	Unexposed periods		Exposed periods		Rate difference (95% CI)	Unadjusted IRR (95% CI)
	Events	Rate[#] (95% CI)	Events	Rate[#] (95% CI)		
Fracture skull vault/base						
0-1	1,069	0.58 (0.54-0.61)	45	0.77 (0.57-1.03)	0.19 (-0.04-0.41)	1.33 (0.98-1.79)
1-2	585	0.35 (0.32-0.38)	24	0.40 (0.26-0.59)	0.05 (-0.11-0.21)	1.13 (0.75-1.70)
2-3	304	0.20 (0.18-0.23)	24	0.39 (0.26-0.59)	0.19 (0.03-0.35)	1.92 (1.27-2.91)
3-4	235	0.18 (0.16-0.21)	15	0.25 (0.15-0.42)	0.07 (-0.06-0.2)	1.38 (0.82-2.33)
4-5	193	0.17 (0.15-0.20)	15	0.26 (0.16-0.43)	0.09 (-0.04-0.22)	1.52 (0.90-2.57)
Fracture skull (apart from vault/base)						
0-1	773	0.42 (0.39-0.45)	16	0.27 (0.17-0.44)	-0.15 (-0.28--0.01)	0.65 (0.40-1.07)
1-2	742	0.44 (0.41-0.48)	37	0.61 (0.44-0.84)	0.17 (-0.03-0.36)	1.37 (0.99-1.91)
2-3	587	0.40 (0.36-0.43)	34	0.56 (0.40-0.78)	0.16 (-0.03-0.35)	1.41 (1.00-1.99)
3-4	444	0.34 (0.31-0.38)	31	0.52 (0.36-0.74)	0.18 (-0.01-0.36)	1.51 (1.05-2.17)
4-5	425	0.37 (0.34-0.41)	26	0.45 (0.31-0.66)	0.07 (-0.10-0.25)	1.20 (0.81-1.78)
Intracranial Injury						
0-1	30,109	16.26 (16.08-16.45)	1,429	24.31 (23.08-25.60)	8.05 (6.78-9.32)	1.50 (1.42-1.58)
1-2	31,864	19.03 (18.83-19.24)	1,500	24.69 (23.47-25.97)	5.65 (4.39-6.92)	1.30 (1.23-1.37)
2-3	21,734	14.64 (14.45-14.84)	1,146	18.79 (17.74-19.91)	4.15 (3.04-5.25)	1.28 (1.21-1.36)
3-4	13,705	10.57 (10.39-10.75)	765	12.77 (11.90-13.71)	2.20 (1.28-3.12)	1.21 (1.12-1.30)

Age (years)	Unexposed periods Events	Rate# (95% CI)	Exposed periods Events	Rate# (95% CI)	Rate difference (95% CI)	Unadjusted IRR (95% CI)
4-5	9,256	8.15 (7.98-8.31)	602	10.38 (9.58-11.24)	2.23 (1.39-3.08)	1.27 (1.17-1.38)
Nerve and spinal cord						
0-1	807	0.44 (0.41-0.47)	21	0.36 (0.23-0.55)	-0.08 (-0.23-0.08)	0.82 (0.53-1.26)
1-2	450	0.27 (0.25-0.29)	12	0.20 (0.11-0.35)	-0.07 (-0.19-0.04)	0.73 (0.41-1.30)
2-3	431	0.29 (0.26-0.32)	29	0.48 (0.33-0.68)	0.19 (0.01-0.36)	1.64 (1.12-2.38)
3-4	282	0.22 (0.19-0.24)	11	0.18 (0.10-0.33)	-0.03 (-0.15-0.08)	0.84 (0.46-1.54)
4-5	235	0.21 (0.18-0.24)	15	0.26 (0.16-0.43)	0.05 (-0.08-0.19)	1.25 (0.74-2.11)
Burn						
0-1	13,412	7.24 (7.12-7.37)	531	9.03 (8.30-9.84)	1.79 (1.01-2.57)	1.25 (1.14-1.36)
1-2	45,524	27.19 (26.95-27.44)	1,999	32.90 (31.49-34.38)	5.71 (4.24-7.17)	1.21 (1.16-1.27)
2-3	34,263	23.09 (22.84-23.33)	1,794	29.42 (28.09-30.81)	6.33 (4.95-7.72)	1.27 (1.22-1.34)
3-4	18,414	14.20 (14.00-14.41)	1,056	17.63 (16.60-18.72)	3.43 (2.34-4.51)	1.24 (1.17-1.32)
4-5	11,523	10.14 (9.96-10.33)	690	11.89 (11.04-12.82)	1.75 (0.85-2.66)	1.17 (1.09-1.27)
Fracture- neck and trunk						
0-1	154	0.08 (0.07-0.10)	8	0.14 (0.07-0.27)	0.05 (-0.04-0.15)	1.64 (0.80-3.33)
1-2	155	0.09 (0.08-0.11)	3	0.05 (0.02-0.15)	-0.04 (-0.1-0.01)	0.53 (0.17-1.67)
2-3	153	0.10 (0.09-0.12)	6	0.10 (0.04-0.22)	0 (-0.09-0.08)	0.95 (0.42-2.16)
3-4	114	0.09 (0.07-0.11)	7	0.12 (0.06-0.25)	0.03 (-0.06-0.12)	1.33 (0.62-2.85)
4-5	96	0.08 (0.07-0.10)	9	0.16 (0.08-0.30)	0.07 (-0.03-0.17)	1.84 (0.93-3.64)
Fracture- upper limb						
0-1	5,334	2.88 (2.80-2.96)	168	2.86 (2.46-3.32)	-0.02 (-0.46-0.42)	0.99 (0.85-1.16)
1-2	8,086	4.83 (4.73-4.94)	316	5.20 (4.66-5.81)	0.37 (-0.21-0.95)	1.08 (0.96-1.20)
2-3	8,421	5.67 (5.55-5.80)	354	5.81 (5.23-6.44)	0.13 (-0.49-0.75)	1.02 (0.92-1.14)
3-4	7,503	5.79 (5.66-5.92)	367	6.13 (5.53-6.79)	0.34 (-0.30-0.98)	1.06 (0.95-1.18)
4-5	6,987	6.15 (6.01-6.30)	347	5.98 (5.38-6.65)	-0.17 (-0.81-0.48)	0.97 (0.87-1.08)
Fracture- lower limb						
0-1	932	0.50 (0.47-0.54)	46	0.78 (0.59-1.04)	0.28 (0.05-0.51)	1.55 (1.16-2.09)
1-2	2,327	1.39 (1.33-1.45)	81	1.33 (1.07-1.66)	-0.06 (-0.35-0.24)	0.96 (0.77-1.20)
2-3	2,989	2.01 (1.94-2.09)	148	2.43 (2.07-2.85)	0.41 (0.02-0.81)	1.21 (1.02-1.42)
3-4	2,245	1.73 (1.66-1.80)	120	2.00 (1.68-2.40)	0.27 (-0.09-0.64)	1.16 (0.96-1.39)
4-5	1,959	1.72 (1.65-1.80)	118	2.03 (1.70-2.44)	0.31 (-0.06-0.68)	1.18 (0.98-1.42)
Multiple fractures of limbs						
0-1	49	0.03 (0.02-0.04)	0	0		
1-2	47	0.03 (0.02-0.04)	0	0		
2-3	10	0.007 (0.004-0.013)	0	0		
3-4	3	0.002 (0.001-0.007)	0	0		
4-5	6	0.005 (0.002-0.012)	0	0		
Internal trauma						
0-1	295	0.16 (0.14-0.18)	19	0.32 (0.21-0.51)	0.16 (0.02-0.31)	2.03 (1.28-3.23)
1-2	351	0.21 (0.19-0.23)	20	0.33 (0.21-0.51)	0.12 (-0.03-0.27)	1.57 (1.00-2.46)
2-3	316	0.21 (0.19-0.24)	19	0.31 (0.20-0.49)	0.10 (-0.04-0.24)	1.46 (0.92-2.32)
3-4	290	0.22 (0.20-0.25)	17	0.28 (0.18-0.46)	0.06 (-0.08-0.20)	1.27 (0.78-2.07)
4-5	249	0.22 (0.19-0.25)	16	0.28 (0.17-0.45)	0.06 (-0.08-0.19)	1.26 (0.76-2.09)
Vascular injury						
0-1	424	0.23 (0.21-0.25)	9	0.15 (0.08-0.29)	-0.08 (-0.18-0.03)	0.67 (0.35-1.29)
1-2	528	0.32 (0.29-0.34)	16	0.26 (0.16-0.43)	-0.05 (-0.18-0.08)	0.83 (0.51-1.37)
2-3	312	0.21 (0.19-0.23)	20	0.33 (0.21-0.51)	0.12 (-0.03-0.26)	1.56 (0.99-2.45)
3-4	209	0.16 (0.14-0.18)	19	0.32 (0.20-0.50)	0.16 (0.01-0.30)	1.97 (1.23-3.15)
4-5	148	0.13 (0.11-0.15)	17	0.29 (0.18-0.47)	0.16 (0.02-0.30)	2.25 (1.36-3.72)

Age (years)	Unexposed periods Events	Rate# (95% CI)	Exposed periods Events	Rate# (95% CI)	Rate difference (95% CI)	Unadjusted IRR (95% CI)
Crush injury						
0-1	1,766	0.95 (0.91-1.00)	77	1.31 (1.05-1.64)	0.36 (0.06-0.65)	1.37 (1.09-1.73)
1-2	8,764	5.24 (5.13-5.35)	360	5.93 (5.34-6.57)	0.69 (0.07-1.31)	1.13 (1.02-1.26)
2-3	8,400	5.66 (5.54-5.78)	392	6.43 (5.82-7.10)	0.77 (0.12-1.42)	1.14 (1.03-1.26)
3-4	6,072	4.68 (4.57-4.80)	313	5.23 (4.68-5.84)	0.54 (-0.05-1.13)	1.12 (1.00-1.25)
4-5	4,275	3.76 (3.65-3.88)	242	4.17 (3.68-4.73)	0.41 (-0.13-0.95)	1.11 (0.97-1.26)
Open wounds						
0-1	35,729	19.3 (19.1-19.5)	1,455	24.75 (23.51-26.06)	5.46 (4.17-6.75)	1.28 (1.22-1.35)
1-2	154,020	92.00 (91.55-92.46)	6,595	108.55 (105.96-111.20)	16.54 (13.88-19.2)	1.18 (1.15-1.21)
2-3	145,398	97.97 (97.47-98.48)	6,868	112.63 (109.99-115.32)	14.65 (11.94-17.36)	1.15 (1.12-1.18)
3-4	106,281	81.97 (81.48-82.46)	5,589	93.30 (90.89-95.78)	11.33 (8.83-13.83)	1.14 (1.11-1.17)
4-5	77,511	68.22 (67.74-68.70)	4,433	76.41 (74.2-78.7)	8.19 (5.89-10.49)	1.12 (1.09-1.15)
Superficial injuries and contusion						
0-1	186,262	100.59 (100.14-101.05)	6,978	118.72 (115.96-121.53)	18.12 (15.30-20.95)	1.18 (1.15-1.21)
1-2	296,918	177.36 (176.73-178.00)	11,951	196.70 (193.21-200.26)	19.34 (15.75-22.92)	1.11 (1.09-1.13)
2-3	210,211	141.64 (141.04-142.25)	9,723	159.44 (156.31-162.64)	17.80 (14.57-21.03)	1.13 (1.10-1.15)
3-4	140,933	108.70 (108.13-109.26)	7,407	123.65 (120.86-126.50)	14.95 (12.08-17.83)	1.14 (1.11-1.16)
4-5	109,548	96.42 (95.85-96.99)	6,278	108.22 (105.57-110.93)	11.80 (9.06-14.54)	1.12 (1.09-1.15)
Dislocations, strains, and sprains						
0-1	9,721	5.25 (5.15-5.36)	366	6.23 (5.62-6.90)	0.98 (0.33-1.62)	1.19 (1.07-1.32)
1-2	27,289	16.3 (16.11-16.5)	1,000	16.46 (15.47-17.51)	0.16 (-0.88-1.20)	1.01 (0.95-1.08)
2-3	28,741	19.37 (19.14-19.59)	1,277	20.94 (19.82-22.12)	1.57 (0.40-2.74)	1.08 (1.02-1.14)
3-4	19,370	14.94 (14.73-15.15)	958	15.99 (15.01-17.04)	1.05 (0.02-2.09)	1.07 (1.00-1.14)
4-5	16,804	14.79 (14.57-15.02)	915	15.77 (14.78-16.83)	0.98 (-0.06-2.03)	1.07 (1.00-1.14)
Foreign body						
0-1	13,272	7.17 (7.05-7.29)	473	8.05 (7.35-8.81)	0.88 (0.14-1.61)	1.12 (1.02-1.23)
1-2	26,072	15.57 (15.39-15.76)	1,160	19.09 (18.02-20.22)	3.52 (2.40-4.63)	1.23 (1.16-1.30)
2-3	40,820	27.51 (27.24-27.77)	1,831	30.03 (28.68-31.43)	2.52 (1.12-3.92)	1.09 (1.04-1.14)
3-4	36,911	28.47 (28.18-28.76)	1,837	30.67 (29.30-32.10)	2.20 (0.77-3.63)	1.08 (1.03-1.13)
4-5	29,804	26.23 (25.94-26.53)	1,594	27.48 (26.16-28.86)	1.25 (-0.14-2.63)	1.05 (1.00-1.10)
Poisoning						
0-1	20,257	10.94 (10.79-11.09)	752	12.79 (11.91-13.74)	1.85 (0.93-2.78)	1.17 (1.09-1.26)
1-2	28,692	17.14 (16.94-17.34)	1,268	20.87 (19.75-22.05)	3.73 (2.57-4.90)	1.22 (1.15-1.29)
2-3	15,978	10.77 (10.6-10.93)	823	13.50 (12.60-14.45)	2.73 (1.79-3.67)	1.25 (1.17-1.34)
3-4	8,568	6.61 (6.47-6.75)	511	8.53 (7.82-9.30)	1.92 (1.17-2.67)	1.29 (1.18-1.41)
4-5	5,667	4.99 (4.86-5.12)	321	5.53 (4.96-6.17)	0.55 (-0.07-1.16)	1.11 (0.99-1.24)

Abbreviation: CI: Confidence intervals. IRR: Incidence rate ratio
#Incidence rate: per 1,000 person-years. Censored when the child died. Otherwise, a person was assumed to have continuous enrollment.

S-Table 13 Associations between childhood injury events in the first five years of life and covariates among children in the study population

	Follow-up period		Unexposed periods		Exposed periods	
	Rate#	IRR (95% CI)	Events	Rate#	Events	Rate#
Birth year						
2004-2007	249	ref	909,847	248	41,834	284
2008-2010	265	1.06 (1.06-1.06)	614,968	263	29,634	299
2011-2014	267	1.07 (1.07-1.07)	375,411	265	15,683	318

	Follow-up period		Unexposed periods		Exposed periods	
	Rate[#]	IRR (95% CI)	Events	Rate[#]	Events	Rate[#]
Children's characteristics						
Child sex						
Males	278	1.18 (1.18-1.19)	1,072,319	277	49,097	319
Female	235	ref	827,907	234	38,054	269
Low birthweight						
No	258	ref	1,797,208	257	81,194	295
Yes	250	0.97 (0.96-0.97)	103,018	248	5,957	288
Preterm birth						
No	257	ref	1,770,453	256	79,437	294
Yes	259	1.01 (1.00-1.01)	129,773	257	7,714	299
Birth order						
1	265	ref	1,120,321	264	52,369	299
2	246	0.93 (0.93-0.93)	627,873	245	26,663	287
≥3	253	0.95 (0.95-0.96)	152,032	251	8,119	295
Complex chronic conditions						
No	256	ref	1,755,568	254	79,484	292
Yes	279	1.09 (1.08-1.10)	144,658	277	7,667	322
Parent characteristics						
Paternal age at birth (years)						
<25	284	1.10 (1.09-1.11)	111,422	283	7,239	307
25-29	272	1.05 (1.05-1.06)	465,759	270	20,584	298
30-34	258	ref	726,231	256	29,742	298
35-39	246	0.95 (0.95-0.96)	418,228	244	19,084	286
40-44	239	0.93 (0.92-0.93)	134,101	236	7,383	288
≥45	234	0.91 (0.90-0.92)	44,485	231	3,119	291
Maternal age at birth (years)						
<20	280	1.11 (1.10-1.12)	39,573	279	2,607	303
20-24	270	1.08 (1.07-1.08)	286,209	269	15,700	297
25-29	264	1.05 (1.05-1.05)	689,112	262	29,880	300
30-34	251	ref	648,040	250	27,073	292
35-39	241	0.96 (0.95-0.96)	210,096	239	10,323	286
≥40	232	0.92 (0.91-0.93)	27,196	230	1,568	274
Unmarried mother						
No	257	ref	1,836,620	256	81,041	295
Yes	264	1.02 (1.02-1.03)	63,606	261	6,110	294
Foreign-born mother						
No	261	ref	1,721,710	259	78,736	298
Yes	232	0.89 (0.89-0.89)	178,516	230	8,415	271
Socio-economic status						
Urbanicity of residence						
1 (highest urbanicity)	241	ref	349,733	239	16,171	281
2	251	1.04 (1.04-1.05)	597,689	249	29,224	286
3	258	1.07 (1.07-1.08)	450,855	257	18,827	293
4	270	1.12 (1.12-1.13)	289,694	269	13,243	308
5	294	1.22 (1.21-1.23)	37,833	292	1,796	335
6	281	1.17 (1.16-1.18)	74,645	279	3,630	329
7	301	1.25 (1.24-1.26)	99,774	299	4,260	348

	Follow-up period		Unexposed periods		Exposed periods	
	Rate[#]	IRR (95% CI)	Events	Rate[#]	Events	Rate[#]
Family income						
High	243	ref	365,461	242	11,981	281
Upper-middle	256	1.05 (1.05-1.06)	382,686	254	13,760	291
Middle	267	1.10 (1.09-1.10)	425,733	266	18,663	305
Lower-middle	264	1.08 (1.08-1.09)	396,612	262	20,620	302
Low	257	1.06 (1.05-1.06)	324,574	255	21,803	289
Paternal occupation						
Civil servants and teachers	262	1.02 (1.02-1.03)	110,160	261	4,975	314
Employees, employers and professionals	257	ref	1,392,376	255	57,460	294
Union members, farmers and fishermen	276	1.08 (1.07-1.08)	120,627	274	6,392	314
The unemployed and low-income households	250	0.97 (0.97-0.98)	182,755	247	13,370	287
Dependents	249	0.97 (0.96-0.98)	64,629	247	3,581	277
Maternal occupation						
Civil servants and teachers	251	0.98 (0.97-0.98)	102,688	250	3,872	295
Employees, employers and professionals	258	ref	1,156,787	256	44,934	294
Union members, farmers and fishermen	292	1.14 (1.13-1.14)	79,980	291	3,914	337
The unemployed and low-income households	265	1.03 (1.02-1.04)	120,697	262	10,895	301
Dependents	252	0.98 (0.97-0.98)	431,072	250	23,011	288
Parental physical illness						
Paternal Elixhauser index						
0	256	ref	1,777,425	255	78,360	293
1	277	1.08 (1.07-1.09)	96,596	274	6,499	315
>1	278	1.08 (1.07-1.10)	26,205	275	2,292	319
Maternal Elixhauser index						
0	257	ref	1,819,536	255	81,568	293
1	280	1.09 (1.08-1.10)	72,290	277	4,769	328
>1	291	1.14 (1.11-1.16)	8,400	288	814	331
Death occurred in the first five years of life						
Paternal death						
No	258	ref	1,895,396	256	86,651	295
Yes	251	0.97 (0.95-1.00)	4,830	247	500	299
Maternal death						
No	258	ref	1,898,948	256	86,896	295
Yes	261	1.01 (0.96-1.06)	1,278	249	255	340
Child's death						
No	258	ref	1,898,966	256	87,054	295
Yes	266	1.03 (0.98-1.09)	1,260	257	97	478
Censored						
No	258	ref	1,892,960	256	86,321	295
Yes	254	0.99 (0.97-1.01)	7,266	249	830	321

Abbreviation: CI: Confidence intervals; IRR: unadjusted incidence rate ratio.
Incidence rate: per 1,000 person-years. Censored when the child or any parent died.

S-Table 14 Associations between injury hospitalization in the first five years of life and covariates among children in the study population

	Follow-up period		Unexposed periods		Exposed periods	
	Rate[#]	IRR (95% CI)	Events	Rate[#]	Events	Rate[#]
Birth year						
2004-2007	4.19	ref	15,086	4.1	890	6
2008-2010	3.55	0.85 (0.83-0.87)	8,135	3.5	522	5.3
2011-2014	3.25	0.78 (0.75-0.80)	4,522	3.2	237	4.8
Children's characteristics						
Child sex						
Males	4.28	1.30 (1.27-1.33)	16,285	4.2	973	6.3
Female	3.29	ref	11,458	3.2	676	4.8
Low birthweight						
No	3.75	ref	25,801	3.7	1,500	5.5
Yes	4.79	1.28 (1.22-1.34)	1,942	4.7	149	7.2
Preterm birth						
No	3.74	ref	25,393	3.7	1,461	5.4
Yes	4.79	1.28 (1.23-1.33)	2,350	4.7	188	7.3
Birth order						
1	3.55	ref	14,805	3.5	883	5
2	3.91	1.10 (1.08-1.13)	9,833	3.8	571	6.1
≥3	5.21	1.47 (1.41-1.52)	3,105	5.1	195	7.1
Complex chronic conditions						
No	3.64	ref	24,674	3.6	1,446	5.3
Yes	5.99	1.64 (1.59-1.71)	3,069	5.9	203	8.5
Parent characteristics						
Paternal age at birth (years)						
<25	5.81	1.66 (1.59-1.73)	2,268	5.8	160	6.8
25-29	4.17	1.19 (1.16-1.23)	7,073	4.1	402	5.8
30-34	3.50	ref	9,747	3.4	511	5.1
35-39	3.45	0.99 (0.96-1.02)	5,802	3.4	344	5.2
40-44	3.73	1.06 (1.02-1.11)	2,053	3.6	156	6.1
≥45	4.31	1.23 (1.15-1.32)	800	4.2	76	7.1
Maternal age at birth (years)						
<20	7.07	2.21 (2.07-2.35)	993	7	72	8.4
20-24	5.32	1.66 (1.61-1.72)	5,568	5.2	373	7.1
25-29	3.87	1.21 (1.17-1.24)	9,960	3.8	577	5.8
30-34	3.20	ref	8,170	3.2	432	4.7
35-39	3.08	0.96 (0.92-1.00)	2,645	3	169	4.7
≥40	3.49	1.09 (0.99-1.20)	407	3.4	26	4.5
Unmarried mother						
No	3.73	ref	26,328	3.7	1,474	5.4
Yes	6.01	1.61 (1.53-1.69)	1,415	5.8	175	8.4
Foreign-born mother						
No	3.71	ref	24,205	3.6	1,419	5.4
Yes	4.67	1.26 (1.22-1.30)	3,538	4.6	230	7.4

Socio-economic status						
Urbanicity of residence						
1 (highest urbanicity)	2.99	ref	4,285	2.9	256	4.4
2	3.33	1.11 (1.07-1.15)	7,806	3.3	499	4.9
3	3.73	1.25 (1.20-1.30)	6,437	3.7	339	5.3
4	4.67	1.56 (1.50-1.63)	4,942	4.6	296	6.9
5	5.70	1.91 (1.77-2.06)	726	5.6	42	7.8
6	5.75	1.93 (1.82-2.04)	1,513	5.7	87	7.9
7	6.25	2.09 (1.99-2.20)	4,285	2.9	256	4.4
Family income						
High	2.51	ref	3,779	2.5	124	2.9
Upper-middle	3.17	1.26 (1.21-1.32)	4,726	3.1	197	4.2
Middle	4.07	1.62 (1.56-1.68)	6,397	4	376	6.2
Lower-middle	4.09	1.79 (1.72-1.86)	6,685	4.4	426	6.2
Low	4.88	1.94 (1.87-2.02)	6,057	4.8	522	6.9
Paternal occupation						
Civil servants and teachers	2.84	0.80 (0.76-0.85)	1,190	2.8	56	3.5
Employees, employers and professionals	3.54	ref	19,041	3.5	977	5
Union members, farmers and fishermen	5.52	1.56 (1.49-1.62)	2,379	5.4	159	7.8
The unemployed and low-income households	4.98	1.40 (1.36-1.45)	3,555	4.8	358	7.7
Dependents	4.24	1.20 (1.13-1.27)	1,091	4.2	72	5.6
Maternal occupation						
Civil servants and teachers	2.34	0.68 (0.64-0.73)	953	2.3	40	3
Employees, employers and professionals	3.42	ref	15,230	3.4	745	4.9
Union members, farmers and fishermen	5.20	1.52 (1.44-1.60)	1,399	5.1	94	8.1
The unemployed and low-income households	5.58	1.63 (1.56-1.70)	2,503	5.4	264	7.3
Dependents	4.41	1.29 (1.26-1.32)	7,474	4.3	492	6.2
Parental physical illness						
Paternal Elixhauser index						
0	3.77	ref	25,896	3.7	1,441	5.4
1	4.28	1.13 (1.08-1.19)	1,449	4.1	145	7
>1	4.49	1.19 (1.09-1.30)	398	4.2	63	8.8
Maternal Elixhauser index						
0	3.77	ref	26,442	3.7	1,531	5.5
1	4.48	1.19 (1.12-1.26)	1,133	4.3	99	6.8
>1	5.91	1.57 (1.36-1.81)	168	5.8	19	7.7
Death occurred in the first five years of life						
Paternal death						
No	3.80	ref	27619	3.73	1626	5.53
Yes	6.92	1.82 (1.55-2.14)	124	6.34	23	1.38
Maternal death						
No	3.80	ref	27685	3.73	1634	5.54
Yes	12.41	3.27 (2.60-4.11)	58	11.31	15	20.01

Child's death						
No	3.77	ref	27456	3.70	1631	5.52
Yes	59.77	15.85 (14.16-17.74)	287	58.58	18	88.66
Censored						
No	3.76	ref	27284	3.69	1596	5.45
Yes	16.09	4.28 (3.92-4.67)	459	15.71	53	20.47

Abbreviation: CI: Confidence intervals; IRR: unadjusted incidence rate ratio.
Incidence rate: per 1,000 person-years. Censored when the child or any parent died.

S-Table 15 Number of children and child outcomes excluded in sensitivity analyses

	Number of children excluded (%) *	Number of episodes excluded (%) #	
		Unexposed periods	Exposed periods
Any injury event			
Children with complex chronic conditions	132,991 (6.65%)	150,284 (7.89%)	8,485 (9.65%)
Children with a parent having multiple IDs	105,327 (5.27%)	110,330 (5.79%)	5,611 (6.38%)
Children with a parental death before age 5 years	11,181 (0.56%)	6,090 (0.32%)	751(0.85%)
Overall episodes of common infectious disease			
Children with complex chronic conditions	132,991 (6.65%)	3,117,031 (7.67%)	155,442 (9.34%)
Children with a parent having multiple IDs	105,327 (5.27%)	2,477,673 (6.09%)	109,346 (6.57%)
Children with a parental death before age 5 years	11,181 (0.56%)	125,757 (0.31%)	12,812 (0.77%)

* Denominator: number of children in the study population.
# Denominator: number of episodes in each period.

S-Table 16 Sensitivity analyses of associations between parental serious mental illness and any childhood injury event

	Adjusted incidence rate ratio (95% confidence intervals)		
Child age (years)	**Model 1**	**Model 2**	**Model 3**
Excluding children with complex chronic conditions			
0-1	1.21 (1.18-1.23)	1.20 (1.18-1.22)	1.20 (1.18-1.22)
1-2	1.14 (1.12-1.16)	1.13 (1.12-1.15)	1.13 (1.12-1.15)
2-3	1.14 (1.12-1.16)	1.13 (1.11-1.15)	1.13 (1.11-1.15)
3-4	1.13 (1.11-1.15)	1.13 (1.11-1.14)	1.13 (1.11-1.14)
4-5	1.10 (1.08-1.12)	1.10 (1.08-1.12)	1.10 (1.08-1.12)
Excluding children with a parent having multiple IDs			
0-1	1.20 (1.18-1.22)	1.19 (1.17-1.22)	1.19 (1.17-1.22)
1-2	1.14 (1.12-1.16)	1.13 (1.12-1.15)	1.13 (1.12-1.15)
2-3	1.14 (1.12-1.16)	1.13 (1.12-1.15)	1.13 (1.11-1.15)
3-4	1.13 (1.11-1.15)	1.12 (1.10-1.14)	1.12 (1.10-1.14)
4-5	1.12 (1.10-1.14)	1.11 (1.09-1.13)	1.11 (1.09-1.13)

Child age (years)	Adjusted incidence rate ratio (95% confidence intervals) Model 1	Model 2	Model 3
Excluding children with a parental death before age 5 years			
0-1	1.20 (1.18-1.23)	1.20 (1.18-1.22)	1.20 (1.17-1.22)
1-2	1.14 (1.13-1.16)	1.13 (1.12-1.15)	1.13 (1.12-1.15)
2-3	1.14 (1.13-1.16)	1.13 (1.12-1.15)	1.14 (1.12-1.15)
3-4	1.13 (1.11-1.15)	1.12 (1.10-1.14)	1.12 (1.10-1.14)
4-5	1.11 (1.09-1.13)	1.10 (1.08-1.12)	1.10 (1.08-1.13)

Model 1: adjusted for birth year, child sex, child age, birth order, maternal and paternal ages, foreign-born mother, and urbanicity of residence.
Model 2: adjusted for the above variables and unmarried mother, family income, maternal and paternal occupations, and maternal and paternal Elixhauser indexes.
Model 3: adjusted for the above variables and child's LBW and preterm birth.

S-Table 17 Stratified analysis of association between parental serious mental illness and childhood injury event and injury hospitalization by urbanicity of residence

Urbanicity of residence	Adjusted incidence rate ratio (95% confidence intervals) 1	2	3	4	5	6	7
Any injury	1.16 (1.14-1.19)	1.14 (1.12-1.16)	1.13 (1.11-1.15)	1.13 (1.11-1.16)	1.14 (1.08-1.22)	1.17 (1.11-1.22)	1.15 (1.10-1.20)
Injury hospitalization	1.52 (1.34-1.73)	1.49 (1.36-1.64)	1.44 (1.29-1.61)	1.49 (1.32-1.69)	1.39 (1.01-1.90)	1.37 (1.10-1.71)	1.72 (1.43-2.07)

adjusted for birth year, child sex, birth order, parental ages, foreign-born mother

S-Table 18 Stratified analysis of association between parental serious mental illness and childhood injury event and injury hospitalization by parental occupation

	Adjusted incidence rate ratio (95% confidence intervals) Civil servants and teachers	Employees, employers and professionals	Union members, farmers and fishermen	The unemployed and low-income households	Dependents
Maternal occupation					
Any injury	1.17 (1.13-1.22)	1.14 (1.13-1.15)	1.15 (1.11-1.20)	1.14 (1.12-1.17)	1.14 (1.12-1.16)
Injury hospitalization	1.35 (0.98-1.85)	1.45 (1.35-1.56)	1.63 (1.31-2.03)	1.42 (1.24-1.61)	1.45 (1.32-1.60)
Paternal occupation					
Any injury	1.19 (1.15-1.23)	1.14 (1.13-1.16)	1.14 (1.11-1.18)	1.14 (1.12-1.17)	1.11 (1.06-1.15)
Injury hospitalization	1.24 (0.94-1.63)	1.44 (1.35-1.54)	1.46 (1.23-1.73)	1.64 (1.46-1.83)	1.35 (1.06-1.70)

adjusted for birth year, child sex, birth order, parental ages, foreign-born mother, and urbanicity of residence

S-Table 19 Secondary analyses of associations between parent's serious mental illness and any childhood injury

	Adjusted Incidence rate ratio (95% Confidence intervals)					
Child's age	***0-5***	**0-1**	**1-2**	**2-3**	**3-4**	**4-5**
Which parent(s) had serious mental illness						
Model 1						
Paternal	***1.11 (1.09-1.13)***	1.15 (1.11-1.18)	1.13 (1.10-1.15)	1.10 (1.08-1.13)	1.09 (1.06-1.12)	1.08 (1.05-1.11)
Maternal	***1.17 (1.16-1.18)***	1.25 (1.22-1.28)	1.15 (1.13-1.17)	1.17 (1.14-1.19)	1.15 (1.13-1.18)	1.14 (1.11-1.16)
Both	***1.24 (1.18-1.31)***	1.22 (1.08-1.38)	1.28 (1.18-1.39)	1.25 (1.15-1.36)	1.32 (1.21-1.43)	1.16 (1.05-1.28)
Model 2						
Paternal	***1.12 (1.10-1.13)***	1.15 (1.12-1.19)	1.13 (1.11-1.16)	1.11 (1.08-1.13)	1.10 (1.07-1.13)	1.09 (1.05-1.12)
Maternal	***1.15 (1.14-1.17)***	1.24 (1.21-1.27)	1.14 (1.12-1.16)	1.16 (1.14-1.18)	1.14 (1.12-1.17)	1.13 (1.10-1.15)
Both	***1.25 (1.19-1.31)***	1.22 (1.08-1.38)	1.28 (1.18-1.38)	1.25 (1.15-1.35)	1.31 (1.21-1.43)	1.16 (1.05-1.27)
Model 3						
Paternal	***1.11 (1.09-1.12)***	1.15 (1.11-1.18)	1.12 (1.10-1.15)	1.10 (1.07-1.13)	1.09 (1.06-1.12)	1.08 (1.05-1.11)
Maternal	***1.14 (1.14-1.16)***	1.23 (1.20-1.26)	1.13 (1.11-1.15)	1.15 (1.13-1.17)	1.14 (1.11-1.16)	1.12 (1.09-1.15)
Both	***1.23 (1.17-1.29)***	1.20 (1.06-1.36)	1.26 (1.16-1.36)	1.23 (1.13-1.33)	1.29 (1.18-1.40)	1.13 (1.02-1.25)
Model 4						
Paternal	***1.11 (1.09-1.12)***	1.15 (1.11-1.18)	1.12 (1.10-1.15)	1.10 (1.07-1.13)	1.09 (1.06-1.12)	1.08 (1.05-1.11)
Maternal	***1.15 (1.14-1.16)***	1.23 (1.20-1.26)	1.13 (1.11-1.15)	1.15 (1.13-1.17)	1.14 (1.11-1.16)	1.12 (1.09-1.15)
Both	***1.23 (1.17-1.29)***	1.20 (1.06-1.36)	1.26 (1.16-1.36)	1.23 (1.13-1.33)	1.29 (1.18-1.40)	1.13 (1.02-1.25)
Timing of onset of maternal and paternal disorders						
Paternal						
Model 1						
Before childbirth	***1.11 (1.09-1.13)***	1.14 (1.10-1.17)	1.14 (1.11-1.16)	1.10 (1.07-1.13)	1.09 (1.06-1.13)	1.07 (1.03-1.11)
After childbirth	***1.12 (1.10-1.14)***	1.10 (1.05-1.15)	1.10 (1.07-1.14)	1.14 (1.10-1.18)	1.15 (1.10-1.19)	1.12 (1.08-1.17)
Model 2						
Before childbirth	***1.12 (1.10-1.14)***	1.14 (1.11-1.18)	1.14 (1.12-1.17)	1.11 (1.08-1.13)	1.10 (1.07-1.14)	1.08 (1.04-1.12)
After childbirth	***1.12 (1.10-1.14)***	1.09 (1.05-1.14)	1.10 (1.07-1.13)	1.14 (1.10-1.17)	1.14 (1.10-1.19)	1.12 (1.07-1.17)
Model 3						
Before childbirth	***1.11 (1.09-1.12)***	1.13 (1.10-1.17)	1.13 (1.10-1.15)	1.09 (1.06-1.12)	1.09 (1.06-1.12)	1.07 (1.03-1.11)
After childbirth	***1.11 (1.09-1.13)***	1.08 (1.04-1.13)	1.09 (1.06-1.12)	1.13 (1.09-1.17)	1.14 (1.09-1.18)	1.11 (1.06-1.16)
Model 4						
Before childbirth	***1.11 (1.09-1.12)***	1.13 (1.10-1.17)	1.13 (1.10-1.16)	1.09 (1.06-1.12)	1.09 (1.06-1.12)	1.07 (1.03-1.11)
After childbirth	***1.11 (1.09-1.13)***	1.08 (1.04-1.13)	1.09 (1.06-1.12)	1.13 (1.09-1.17)	1.14 (1.09-1.18)	1.11 (1.06-1.16)
Maternal						
Model 1						
Before childbirth	***1.17 (1.15-1.18)***	1.23 (1.20-1.26)	1.15 (1.13-1.18)	1.16 (1.14-1.18)	1.15 (1.12-1.18)	1.14 (1.11-1.17)
After childbirth	***1.17 (1.15-1.18)***	1.18 (1.15-1.22)	1.15 (1.12-1.18)	1.19 (1.16-1.22)	1.17 (1.13-1.20)	1.14 (1.11-1.18)
Model 2						
Before childbirth	***1.16 (1.14-1.17)***	1.22 (1.19-1.25)	1.15 (1.13-1.17)	1.15 (1.13-1.18)	1.15 (1.12-1.18)	1.13 (1.10-1.17)
After childbirth	***1.15 (1.14-1.17)***	1.17 (1.14-1.21)	1.14 (1.11-1.16)	1.18 (1.15-1.20)	1.15 (1.12-1.19)	1.13 (1.09-1.16)
Model 3						
Before childbirth	***1.15 (1.13-1.16)***	1.21 (1.18-1.24)	1.14 (1.12-1.16)	1.14 (1.12-1.17)	1.14 (1.11-1.17)	1.12 (1.09-1.16)
After childbirth	***1.15 (1.13-1.16)***	1.16 (1.12-1.20)	1.13 (1.11-1.16)	1.17 (1.14-1.20)	1.15 (1.12-1.18)	1.12 (1.08-1.16)
Model 4						
Before childbirth	***1.15 (1.13-1.16)***	1.21 (1.18-1.24)	1.14 (1.12-1.16)	1.14 (1.12-1.17)	1.14 (1.11-1.17)	1.12 (1.09-1.16)
After childbirth	***1.15 (1.13-1.16)***	1.16 (1.12-1.20)	1.13 (1.11-1.16)	1.17 (1.14-1.20)	1.15 (1.12-1.18)	1.12 (1.09-1.16)

	Adjusted Incidence rate ratio (95% Confidence intervals)					
Child's age	***0-5***	**0-1**	**1-2**	**2-3**	**3-4**	**4-5**
Diagnostic category for maternal and paternal disorders						
Paternal						
Model 1						
Schizophrenia	***1.12 (1.10-1.15)***	1.12 (1.06-1.17)	1.13 (1.09-1.17)	1.12 (1.08-1.16)	1.14 (1.10-1.20)	1.10 (1.04-1.15)
Bipolar disorder	***1.14 (1.12-1.17)***	1.16 (1.11-1.22)	1.13 (1.09-1.18)	1.15 (1.11-1.20)	1.12 (1.07-1.18)	1.14 (1.08-1.21)
Major depression	***1.10 (1.08-1.12)***	1.11 (1.07-1.15)	1.12 (1.09-1.15)	1.09 (1.06-1.12)	1.09 (1.05-1.13)	1.06 (1.02-1.11)
Model 2						
Schizophrenia	***1.13 (1.11-1.16)***	1.12 (1.07-1.18)	1.14 (1.10-1.18)	1.13 (1.09-1.18)	1.16 (1.11-1.21)	1.11 (1.05-1.16)
Bipolar disorder	***1.15 (1.12-1.17)***	1.17 (1.11-1.22)	1.14 (1.10-1.18)	1.15 (1.11-1.20)	1.13 (1.08-1.18)	1.15 (1.09-1.21)
Major depression	***1.10 (1.08-1.12)***	1.10 (1.07-1.15)	1.11 (1.09-1.15)	1.09 (1.06-1.12)	1.09 (1.05-1.13)	1.06 (1.02-1.11)
Model 3						
Schizophrenia	***1.12 (1.10-1.15)***	1.11 (1.06-1.17)	1.13 (1.09-1.17)	1.12 (1.08-1.16)	1.14 (1.09-1.19)	1.10 (1.04-1.15)
Bipolar disorder	***1.13 (1.10-1.16)***	1.16 (1.10-1.21)	1.12 (1.08-1.16)	1.14 (1.09-1.18)	1.12 (1.06-1.17)	1.13 (1.07-1.20)
Major depression	***1.09 (1.07-1.10)***	1.10 (1.06-1.14)	1.10 (1.07-1.13)	1.08 (1.05-1.11)	1.08 (1.04-1.12)	1.05 (1.01-1.09)
Model 4						
Schizophrenia	***1.12 (1.10-1.15)***	1.11 (1.06-1.17)	1.13 (1.09-1.17)	1.12 (1.08-1.16)	1.14 (1.09-1.19)	1.10 (1.04-1.15)
Bipolar disorder	***1.13 (1.10-1.16)***	1.16 (1.10-1.21)	1.12 (1.08-1.16)	1.14 (1.09-1.18)	1.12 (1.06-1.17)	1.13 (1.07-1.20)
Major depression	***1.09 (1.07-1.10)***	1.10 (1.06-1.14)	1.10 (1.07-1.13)	1.08 (1.05-1.11)	1.08 (1.04-1.12)	1.05 (1.01-1.09)
Maternal						
Model 1						
Schizophrenia	***1.18 (1.15-1.21)***	1.22 (1.16-1.28)	1.13 (1.09-1.18)	1.21 (1.16-1.26)	1.23 (1.17-1.29)	1.13 (1.07-1.20)
Bipolar disorder	***1.18 (1.16-1.21)***	1.24 (1.19-1.29)	1.17 (1.13-1.20)	1.20 (1.16-1.24)	1.17 (1.13-1.22)	1.14 (1.09-1.19)
Major depression	***1.16 (1.14-1.17)***	1.20 (1.17-1.23)	1.15 (1.13-1.17)	1.16 (1.13-1.18)	1.14 (1.11-1.16)	1.14 (1.11-1.17)
Model 2						
Schizophrenia	***1.17 (1.14-1.20)***	1.21 (1.15-1.27)	1.12 (1.08-1.17)	1.20 (1.15-1.25)	1.22 (1.16-1.28)	1.13 (1.07-1.19)
Bipolar disorder	***1.17 (1.15-1.20)***	1.23 (1.18-1.28)	1.16 (1.12-1.19)	1.19 (1.15-1.23)	1.16 (1.12-1.21)	1.13 (1.08-1.18)
Major depression	***1.15 (1.13-1.16)***	1.19 (1.16-1.22)	1.14 (1.12-1.16)	1.15 (1.12-1.17)	1.13 (1.10-1.16)	1.13 (1.10-1.16)
Model 3						
Schizophrenia	***1.16 (1.13-1.19)***	1.19 (1.13-1.25)	1.11 (1.07-1.15)	1.18 (1.13-1.23)	1.21 (1.15-1.26)	1.11 (1.05-1.18)
Bipolar disorder	***1.16 (1.14-1.18)***	1.21 (1.16-1.26)	1.15 (1.11-1.18)	1.18 (1.14-1.22)	1.15 (1.11-1.20)	1.12 (1.07-1.17)
Major depression	***1.14 (1.13-1.15)***	1.18 (1.15-1.21)	1.14 (1.12-1.16)	1.14 (1.12-1.16)	1.12 (1.10-1.15)	1.12 (1.09-1.16)
Model 4						
Schizophrenia	***1.16 (1.13-1.19)***	1.19 (1.13-1.26)	1.11 (1.07-1.16)	1.18 (1.14-1.23)	1.21 (1.15-1.27)	1.11 (1.05-1.18)
Bipolar disorder	***1.16 (1.14-1.18)***	1.21 (1.16-1.26)	1.15 (1.11-1.18)	1.18 (1.14-1.22)	1.15 (1.11-1.20)	1.12 (1.07-1.17)
Major depression	***1.14 (1.13-1.15)***	1.18 (1.15-1.21)	1.14 (1.12-1.16)	1.14 (1.12-1.16)	1.12 (1.10-1.15)	1.12 (1.09-1.16)

Model 1: adjusted for birth year and child sex. Child age was also adjusted in estimating IRR for ages 0-5.
Model 2: adjusted for birth year, child sex, birth order, maternal and paternal ages, foreign-born mother, and urbanicity of residence.
Model 3: adjusted for the above variables and unmarried mother, family income, maternal and paternal occupations, maternal and paternal Elixhauser indexes, and spouse's mental illness (This variable was not included in the models with the exposure as parent(s) with serious mental illness).
Model 4: adjusted for the above variables and child's LBW and preterm birth.

S-Table 20 Secondary analyses of associations between parent's serious mental illness and childhood injury hospitalization

	Adjusted Incidence rate ratio (95% Confidence intervals)					
Child's age	***0-5***	**0-1**	**1-2**	**2-3**	**3-4**	**4-5**
Which parent(s) had serious mental illness						
Model 1						
Paternal	***1.41 (1.30-1.53)***	1.39 (1.13-1.71)	1.49 (1.28-1.72)	1.35 (1.12-1.61)	1.48 (1.22-1.80)	1.29 (1.03-1.62)
Maternal	***1.56 (1.46-1.66)***	1.74 (1.50-2.02)	1.63 (1.45-1.82)	1.56 (1.36-1.78)	1.58 (1.36-1.84)	1.21 (1.01-1.46)
Both	***1.85 (1.38-2.48)***	2.61 (1.41-4.85)	2.28 (1.34-3.88)	1.48 (0.80-2.75)	1.54 (0.80-2.95)	1.48 (0.59-3.70)
Model 2						
Paternal	***1.34 (1.23-1.46)***	1.32 (1.08-1.63)	1.41 (1.22-1.64)	1.28 (1.07-1.53)	1.41 (1.16-1.71)	1.22 (0.97-1.54)
Maternal	***1.58 (1.48-1.68)***	1.78 (1.53-2.07)	1.65 (1.47-1.85)	1.57 (1.37-1.80)	1.59 (1.37-1.85)	1.21 (1.01-1.46)
Both	***1.85 (1.38-2.48)***	2.67 (1.44-4.95)	2.29 (1.35-3.90)	1.48 (0.80-2.75)	1.53 (0.80-2.92)	1.46 (0.58-3.64)
Model 3						
Paternal	***1.28 (1.18-1.40)***	1.25 (1.01-1.53)	1.36 (1.17-1.57)	1.21 (1.01-1.45)	1.36 (1.12-1.65)	1.19 (0.95-1.50)
Maternal	***1.48 (1.38-1.58)***	1.65 (1.41-1.92)	1.54 (1.37-1.73)	1.49 (1.30-1.71)	1.51 (1.29-1.75)	1.13 (0.94-1.37)
Both	***1.62 (1.20-2.18)***	2.31 (1.25-4.29)	2.02 (1.19-3.44)	1.32 (0.71-2.45)	1.22 (0.61-2.44)	1.33 (0.53-3.31)
Model 4						
Paternal	***1.28 (1.18-1.39)***	1.24 (1.01-1.53)	1.36 (1.17-1.57)	1.20 (1.00-1.44)	1.35 (1.11-1.65)	1.19 (0.95-1.50)
Maternal	***1.47 (1.38-1.57)***	1.64 (1.40-1.91)	1.53 (1.36-1.72)	1.48 (1.29-1.70)	1.50 (1.29-1.74)	1.13 (0.93-1.36)
Both	***1.61 (1.20-2.16)***	2.29 (1.24-4.25)	2.01 (1.18-3.42)	1.31 (0.71-2.44)	1.21 (0.61-2.42)	1.32 (0.53-3.29)
Timing of onset of maternal and paternal disorders						
Paternal						
Model 1						
Before childbirth	***1.39 (1.26-1.52)***	1.36 (1.11-1.68)	1.50 (1.29-1.75)	1.24 (1.01-1.52)	1.59 (1.28-1.98)	1.13 (0.84-1.51)
After childbirth	***1.55 (1.38-1.73)***	1.76 (1.39-2.23)	1.54 (1.26-1.87)	1.56 (1.24-1.96)	1.30 (0.98-1.74)	1.58 (1.15-2.17)
Model 2						
Before childbirth	***1.29 (1.17-1.43)***	1.31 (1.06-1.60)	1.44 (1.23-1.68)	1.18 (0.96-1.46)	1.52 (1.22-1.89)	1.08 (0.80-1.44)
After childbirth	***1.46 (1.30-1.65)***	1.67 (1.32-2.12)	1.46 (1.20-1.78)	1.48 (1.18-1.86)	1.24 (0.93-1.65)	1.50 (1.09-2.06)
Model 3						
Before childbirth	***1.24 (1.13-1.36)***	1.22 (0.99-1.50)	1.35 (1.16-1.58)	1.08 (0.88-1.34)	1.41 (1.13-1.76)	1.03 (0.77-1.38)
After childbirth	***1.41 (1.26-1.58)***	1.59 (1.25-2.02)	1.41 (1.16-1.72)	1.39 (1.10-1.76)	1.20 (0.90-1.60)	1.46 (1.06-2.01)
Model 4						
Before childbirth	***1.24 (1.13-1.36)***	1.22 (0.99-1.50)	1.35 (1.16-1.58)	1.08 (0.88-1.34)	1.41 (1.13-1.75)	1.03 (0.77-1.38)
After childbirth	***1.41 (1.26-1.58)***	1.59 (1.25-2.01)	1.41 (1.15-1.72)	1.39 (1.10-1.75)	1.20 (0.90-1.60)	1.46 (1.06-2.00)
Maternal						
Model 1						
Before childbirth	***1.54 (1.42-1.66)***	1.77 (1.52-2.06)	1.60 (1.40-1.82)	1.55 (1.33-1.82)	1.36 (1.11-1.65)	1.18 (0.91-1.52)
After childbirth	***1.61 (1.49-1.75)***	1.71 (1.43-2.06)	1.65 (1.43-1.90)	1.53 (1.29-1.82)	1.83 (1.52-2.20)	1.27 (0.99-1.62)
Model 2						
Before childbirth	***1.59 (1.47-1.71)***	1.82 (1.56-2.12)	1.64 (1.44-1.87)	1.61 (1.37-1.88)	1.41 (1.15-1.71)	1.22 (0.95-1.58)
After childbirth	***1.55 (1.43-1.68)***	1.64 (1.36-1.97)	1.58 (1.37-1.82)	1.47 (1.23-1.74)	1.76 (1.46-2.11)	1.22 (0.95-1.55)
Model 3						
Before childbirth	***1.47 (1.37-1.59)***	1.67 (1.43-1.95)	1.52 (1.34-1.74)	1.50 (1.28-1.76)	1.34 (1.10-1.63)	1.13 (0.87-1.47)
After childbirth	***1.46 (1.34-1.58)***	1.53 (1.27-1.84)	1.50 (1.30-1.74)	1.39 (1.17-1.66)	1.64 (1.36-1.98)	1.11 (0.87-1.43)
Model 4						
Before childbirth	***1.47 (1.36-1.59)***	1.66 (1.42-1.95)	1.52 (1.33-1.73)	1.49 (1.27-1.75)	1.33 (1.09-1.62)	1.13 (0.87-1.46)
After childbirth	***1.45 (1.33-1.57)***	1.52 (1.26-1.83)	1.50 (1.30-1.73)	1.39 (1.16-1.65)	1.63 (1.35-1.97)	1.11 (0.86-1.43)

Adjusted Incidence rate ratio (95% Confidence intervals)						
Child's age	***0-5***	**0-1**	**1-2**	**2-3**	**3-4**	**4-5**
Diagnostic category for maternal and paternal disorders						
Paternal						
Model 1						
Schizophrenia	***1.63 (1.43-1.86)***	1.60 (1.19-2.17)	1.93 (1.58-2.36)	1.43 (1.08-1.90)	1.58 (1.16-2.16)	1.36 (0.90-2.08)
Bipolar disorder	***1.66 (1.45-1.89)***	1.90 (1.44-2.50)	1.42 (1.10-1.83)	1.59 (1.20-2.11)	1.75 (1.28-2.40)	1.86 (1.30-2.66)
Major depression	***1.23 (1.10-1.38)***	1.25 (0.97-1.59)	1.32 (1.09-1.60)	1.20 (0.94-1.52)	1.26 (0.96-1.66)	0.98 (0.70-1.39)
Model 2						
Schizophrenia	***1.47 (1.29-1.68)***	1.43 (1.06-1.93)	1.72 (1.40-2.10)	1.28 (0.96-1.69)	1.41 (1.03-1.92)	1.21 (0.80-1.85)
Bipolar disorder	***1.60 (1.41-1.83)***	1.83 (1.39-2.42)	1.37 (1.06-1.77)	1.54 (1.16-2.03)	1.69 (1.24-2.31)	1.80 (1.26-2.57)
Major depression	***1.22 (1.09-1.37)***	1.23 (0.96-1.58)	1.31 (1.08-1.59)	1.19 (0.93-1.51)	1.26 (0.95-1.65)	0.98 (0.69-1.39)
Model 3						
Schizophrenia	***1.34 (1.18-1.54)***	1.31 (0.97-1.77)	1.61 (1.32-1.97)	1.15 (0.86-1.54)	1.29 (0.94-1.78)	1.15 (0.76-1.75)
Bipolar disorder	***1.48 (1.30-1.69)***	1.68 (1.27-2.23)	1.29 (1.00-1.66)	1.36 (1.02-1.81)	1.60 (1.17-2.18)	1.71 (1.19-2.44)
Major depression	***1.18 (1.05-1.32)***	1.20 (0.94-1.53)	1.26 (1.04-1.53)	1.15 (0.91-1.47)	1.20 (0.91-1.58)	0.96 (0.68-1.36)
Model 4						
Schizophrenia	***1.34 (1.18-1.53)***	1.31 (0.97-1.77)	1.61 (1.32-1.96)	1.15 (0.86-1.53)	1.29 (0.94-1.77)	1.15 (0.75-1.75)
Bipolar disorder	***1.48 (1.29-1.68)***	1.68 (1.27-2.22)	1.29 (1.00-1.66)	1.36 (1.02-1.81)	1.59 (1.16-2.18)	1.70 (1.19-2.43)
Major depression	***1.18 (1.05-1.32)***	1.19 (0.93-1.53)	1.26 (1.04-1.53)	1.15 (0.91-1.46)	1.20 (0.91-1.58)	0.96 (0.68-1.36)
Maternal						
Model 1						
Schizophrenia	***2.06 (1.82-2.35)***	2.36 (1.82-3.07)	1.90 (1.51-2.40)	2.30 (1.80-2.93)	2.13 (1.60-2.85)	1.52 (1.00-2.33)
Bipolar disorder	***1.70 (1.52-1.90)***	1.70 (1.32-2.19)	1.54 (1.25-1.88)	2.09 (1.69-2.58)	1.91 (1.47-2.48)	1.13 (0.77-1.64)
Major depression	***1.41 (1.31-1.51)***	1.61 (1.38-1.89)	1.58 (1.40-1.79)	1.16 (0.98-1.38)	1.33 (1.10-1.60)	1.18 (0.94-1.47)
Model 2						
Schizophrenia	***1.99 (1.75-2.26)***	2.28 (1.76-2.96)	1.84 (1.45-2.32)	2.22 (1.74-2.83)	2.06 (1.54-2.74)	1.47 (0.96-2.26)
Bipolar disorder	***1.70 (1.52-1.90)***	1.70 (1.32-2.19)	1.54 (1.25-1.88)	2.09 (1.70-2.58)	1.91 (1.48-2.48)	1.13 (0.77-1.65)
Major depression	***1.41 (1.31-1.52)***	1.62 (1.39-1.89)	1.59 (1.40-1.79)	1.17 (0.99-1.39)	1.34 (1.11-1.61)	1.18 (0.95-1.48)
Model 3						
Schizophrenia	***1.83 (1.61-2.08)***	2.08 (1.60-2.70)	1.68 (1.33-2.13)	2.03 (1.59-2.60)	1.88 (1.40-2.51)	1.38 (0.90-2.11)
Bipolar disorder	***1.57 (1.40-1.76)***	1.52 (1.17-1.98)	1.44 (1.17-1.76)	1.93 (1.56-2.39)	1.81 (1.40-2.35)	1.03 (0.70-1.52)
Major depression	***1.33 (1.24-1.44)***	1.52 (1.30-1.78)	1.50 (1.33-1.70)	1.12 (0.94-1.33)	1.26 (1.05-1.52)	1.09 (0.86-1.37)
Model 4						
Schizophrenia	***1.81 (1.59-2.06)***	2.06 (1.58-2.68)	1.67 (1.32-2.11)	2.01 (1.58-2.57)	1.86 (1.39-2.49)	1.37 (0.89-2.09)
Bipolar disorder	***1.56 (1.40-1.75)***	1.52 (1.17-1.97)	1.43 (1.16-1.75)	1.92 (1.55-2.38)	1.80 (1.39-2.33)	1.03 (0.70-1.51)
Major depression	***1.33 (1.23-1.43)***	1.51 (1.29-1.77)	1.50 (1.32-1.70)	1.11 (0.94-1.32)	1.26 (1.04-1.52)	1.09 (0.86-1.37)

Model 1: adjusted for birth year and child sex. Child age was also adjusted in estimating IRR for ages 0-5.
Model 2: adjusted for the above variables and birth order, maternal and paternal ages, foreign-born mother, and urbanicity of residence.
Model 3: adjusted for the above variables and unmarried mother, family income, maternal and paternal occupations, maternal and paternal Elixhauser indexes and spouse's mental illness (This variable was not included in the models with the exposure as parent(s) with serious mental illness).
Model 4: adjusted for the above variables and child's LBW and preterm birth.

S-Table 21 Incidence rates of healthcare visits for common infectious disease among children in the study population stratified by child age and by exposure to parental serious mental illness

Age	Unexposed periods		Exposed periods		Rate difference	Unadjusted IRR
(years)	Visits*	Rate# (95% CI)	Visits*	Rate# (95% CI)	(95% CI)	(95% CI)
0-1	21,908,503	11.8 (11.8-11.8)	724,412	12.3 (12.3-12.4)	0.49 (0.46-0.52)	1.04 (1.04-1.04)
1-2	27,464,805	16.4 (16.4-16.4)	997,045	16.4 (16.4-16.4)	0.00 (-0.03-0.04)	1.00 (1.00-1.00)
2-3	22,775,835	15.4 (15.3-15.4)	959,889	15.7 (15.7-15.8)	0.39 (0.36-0.43)	1.03 (1.02-1.03)
3-4	20,281,136	15.6 (15.6-15.7)	954,655	15.9 (15.9-16.0)	0.29 (0.26-0.33)	1.02 (1.02-1.02)
4-5	18,820,796	16.6 (16.6-16.6)	960,806	16.6 (16.5-16.6)	0.00 (-0.04-0.03)	1.00 (1.00-1.00)

Abbreviation: CI: Confidence intervals; IRR: incidence rate ratio.
*Visits: including outpatient/inpatient visits. Visits on the same day were counted once. Child age was determined by the age when an episode occurred.
#Incidence rate: per person-years. The follow-up time was censored when the child died.

S-Table 22 Incidence rates of diarrhea and of respiratory infection among children in the study population stratified by child age and by exposure to parental serious mental illness

Age	Unexposed periods		Exposed periods		Rate difference	Unadjusted IRR
(years)	Events	Rate# (95% CI*)	Events	Rate# (95% CI*)	(95% CI*)	(95% CI*)
Diarrhea						
0-1	1,780,884	0.96 (0.96-0.96)	64,479	1.1 (1.09-1.11)	0.14 (0.13-0.14)	1.14 (1.13-1.15)
1-2	1,997,088	1.10 (1.09-1.11)	77,031	1.19 (1.19-1.19)	0.07 (0.07-0.08)	1.06 (1.06-1.07)
2-3	1,299,974	1.19 (1.19-1.19)	57,371	1.27 (1.26-1.28)	0.06 (0.06-0.07)	1.07 (1.07-1.08)
3-4	988,214	1.27 (1.26-1.28)	48,197	0.88 (0.87-0.88)	0.04 (0.04-0.05)	1.06 (1.05-1.07)
4-5	869,401	0.88 (0.87-0.88)	45,629	0.94 (0.93-0.95)	0.02 (0.01-0.03)	1.03 (1.02-1.04)
Respiratory infections						
0-1	7,768,882	4.20 (4.19-4.20)	252,893	4.30 (4.29-4.32)	0.11 (0.09-0.12)	1.03 (1.02-1.03)
1-2	9,366,162	4.30 (4.29-4.32)	337,608	5.59 (5.59-5.60)	-0.04 (-0.06--0.02)	0.99 (0.99-1.00)
2-3	8,142,937	5.59 (5.59-5.60)	335,712	5.56 (5.54-5.58)	0.02 (-0.00-0.04)	1.00 (1.00-1.01)
3-4	7,319,470	5.56 (5.54-5.58)	340,480	5.49 (5.48-5.49)	0.04 (0.02-0.06)	1.01 (1.00-1.01)
4-5	6,807,887	5.49 (5.48-5.49)	347,420	5.51 (5.49-5.52)	-0.003 (-0.02- 0.02)	1.00 (1.00-1.00)

Abbreviation: CI: Confidence intervals. IRR: Incidence rate ratio
#per person-years. The follow-up time was censored when the child died

S-Table 23 Associations between episodes of common infectious disease in the first five years of life and covariates among children in the study population

	Follow-up period		Unexposed periods		Exposed periods	
	Rate#	IRR (95% CI)	Events	Rate#	Events	Rate#
Birth year						
2004-2007	5.60	ref	20,543,503	5.60	832,297	5.65
2008-2010	5.54	0.99 (0.99-0.99)	12,942,269	5.54	562,092	5.68
2011-2014	4.99	0.89 (0.89-0.89)	7,055,966	4.98	254,805	5.16

	Follow-up period		Unexposed periods		Exposed periods	
	Rate[#]	IRR (95% CI)	Events	Rate[#]	Events	Rate[#]
Children's characteristics						
Child sex						
Males	5.58	1.04 (1.04-1.04)	21,600,530	5.57	876,488	5.69
Female	5.35	ref	18,941,208	5.34	772,706	5.45
Low birthweight						
No	5.47	ref	38,296,779	5.47	1,535,087	5.58
Yes	5.41	0.99 (0.99-0.99)	2,244,959	5.40	114,107	5.52
Preterm birth						
No	5.46	ref	37,756,405	5.46	1,503,395	5.57
Yes	5.53	1.01 (1.01-1.01)	2,785,333	5.52	145,799	5.65
Birth order						
1	5.29	ref	22,463,912	5.29	955,203	5.45
2	5.74	1.08 (1.08-1.09)	14,727,935	5.74	539,616	5.81
≥3	5.53	1.04 (1.04-1.05)	3,349,891	5.53	154,375	5.60
Complex chronic conditions						
No	5.45	ref	37,545,933	5.44	1,509,155	5.55
Yes	5.74	1.05 (1.05-1.06)	2,995,805	5.74	140,039	5.87
Parent characteristics						
Paternal age at birth (years)						
<25	5.58	1.01 (1.01-1.01)	2,200,819	5.58	131,054	5.55
25-29	5.68	1.03 (1.03-1.03)	9,772,848	5.68	398,143	5.76
30-34	5.52	ref	15,621,309	5.52	564,768	5.66
35-39	5.35	0.97 (0.97-0.97)	9,150,232	5.34	365,947	5.48
40-44	5.09	0.92 (0.92-0.92)	2,882,482	5.08	135,826	5.29
≥45	4.76	0.86 (0.86-0.86)	914,048	4.74	53,446	4.99
Maternal age at birth (years)						
<20	5.29	0.98 (0.97-0.98)	750,820	5.29	46,011	5.34
20-24	5.58	1.03 (1.03-1.03)	5,934,718	5.58	299,285	5.66
25-29	5.60	1.03 (1.03-1.03)	14,695,894	5.60	568,747	5.71
30-34	5.42	ref	14,055,396	5.42	513,893	5.55
35-39	5.17	0.95 (0.95-0.95)	4,533,959	5.16	192,683	5.33
≥40	4.83	0.89 (0.89-0.89)	570,951	4.82	28,575	4.99
Unmarried mother						
No	5.48	ref	39,322,998	5.48	1,540,906	5.61
Yes	5.02	0.92 (0.91-0.92)	1,218,740	5.00	108,288	5.21
Foreign-born mother						
No	5.52	ref	36,674,582	5.52	1,487,573	5.62
Yes	5.00	0.90 (0.90-0.91)	3,867,156	4.99	161,621	5.20
Socio-economic status						
Urbanicity of residence						
1 (highest urbanicity)	5.26	ref	7,684,094	5.25	313,451	5.45
2	5.37	1.02 (1.02-1.02)	12,854,196	5.37	559,703	5.49
3	5.55	1.06 (1.06-1.06)	9,731,242	5.55	363,958	5.66
4	5.60	1.07 (1.06-1.07)	6,035,690	5.60	244,248	5.67
5	5.64	1.07 (1.07-1.07)	728,964	5.63	30,968	5.77
6	5.71	1.09 (1.08-1.09)	1,525,098	5.71	63,020	5.71
7	5.94	1.13 (1.13-1.13)	1,982,290	5.94	73,846	6.03

	Follow-up period		Unexposed periods		Exposed periods	
	Rate[#]	IRR (95% CI)	Events	Rate[#]	Events	Rate[#]
Family income						
High	5.39	ref	8,125,617	5.38	237,325	5.56
Upper-middle	5.57	1.03 (1.03-1.04)	8,374,678	5.57	268,203	5.68
Middle	5.64	1.05 (1.05-1.05)	9,024,549	5.63	352,576	5.77
Lower-middle	5.54	1.03 (1.03-1.03)	8,385,359	5.54	385,268	5.65
Low	5.15	0.96 (0.95-0.96)	6,534,359	5.14	400,456	5.32
Paternal occupation						
Civil servants and teachers	5.40	0.98 (0.98-0.98)	2,277,939	5.39	89,448	5.64
Employees, employers and professionals	5.51	ref	30,011,110	5.51	1,101,997	5.64
Union members, farmers and fishermen	5.78	1.05 (1.05-1.05)	2,540,831	5.78	118,380	5.82
The unemployed and low-income households	5.07	0.92 (0.92-0.92)	3,741,802	5.06	245,199	5.26
Dependents	5.35	0.97 (0.97-0.97)	1,395,350	5.34	70,308	5.44
Maternal occupation						
Civil servants and teachers	5.36	0.96 (0.96-0.96)	2,199,005	5.35	73,380	5.59
Employees, employers and professionals	5.58	ref	25,171,763	5.58	873,772	5.71
Union members, farmers and fishermen	5.85	1.05 (1.05-1.05)	1,608,962	5.85	68,430	5.89
The unemployed and low-income households	5.04	0.90 (0.90-0.90)	2,308,206	5.02	189,986	5.25
Dependents	5.27	0.94 (0.94-0.94)	9,072,817	5.26	434,284	5.44
Parental physical illness						
Paternal Elixhauser index						
0	5.46	ref	38,048,667	5.46	1,491,884	5.57
1	5.59	1.02 (1.02-1.02)	1,965,316	5.58	116,672	5.65
>1	5.54	1.01 (1.01-1.02)	527,755	5.53	40,638	5.65
Maternal Elixhauser index						
0	5.46	ref	38,927,981	5.46	1,552,455	5.57
1	5.57	1.02 (1.02-1.02)	1,449,790	5.56	82,577	5.68
>1	5.63	1.03 (1.03-1.04)	163,967	5.62	14,162	5.76
Death occurred in the first five years of life						
Paternal death						
No	5.47	ref	40,441,777	5.46	1,640,404	5.58
Yes	5.12	0.94 (0.93-0.94)	99,961	5.11	8,790	5.26
Maternal death						
No	5.47	ref	40,515,590	5.46	1,645,130	5.58
Yes	5.14	0.94 (0.93-0.95)	26,148	5.10	4,064	5.42
Child's death						
No	5.47	ref	40,519,769	5.46	1,648,193	5.58
Yes	4.50	0.82 (0.81-0.83)	21,969	4.48	1,001	4.93
Censored						
No	5.47	ref	40,395,423	5.46	1,635,519	5.58
Yes	5.03	0.92 (0.92-0.92)	146,315	5.01	13,675	5.28

Abbreviation: CI: Confidence intervals; IRR: unadjusted incidence rate ratio.
Incidence rate: per person-year. Censored when the child or any parent died.

S-Table 24 Associations between antibiotics-treated common infectious disease in the first five years of life and covariates among children in the study population

	Follow-up period		Unexposed periods		Exposed periods	
	Rate[#]	IRR (95% CI)	Events	Rate[#]	Events	Rate[#]
Birth year						
2004-2007	1.03	ref	3,781,858	1.03	158,925	1.08
2008-2010	0.97	0.94 (0.94-0.94)	2,261,153	0.97	101,877	1.03
2011-2014	0.75	0.73 (0.73-0.73)	1,061,178	0.75	39,830	0.81
Children's characteristics						
Child sex						
Males	1.01	1.10 (1.10-1.11)	3,886,496	1.00	163,979	1.07
Female	0.91	ref	3,217,693	0.91	136,653	0.96
Low birthweight						
No	0.96	ref	6,699,478	0.96	279,471	1.02
Yes	0.98	1.02 (1.02-1.02)	404,711	0.97	21,161	1.02
Preterm birth						
No	0.95	ref	6,588,828	0.95	272,484	1.01
Yes	1.02	1.07 (1.07-1.08)	515,361	1.02	28,148	1.09
Birth order						
1	0.91	ref	3,848,355	0.91	171,329	0.98
2	1.03	1.14 (1.14-1.14)	2,647,776	1.03	100,405	1.08
≥3	1.01	1.11 (1.10-1.11)	608,058	1.00	28,898	1.05
Complex chronic conditions						
No	0.94	ref	6,489,823	0.94	270,652	1.00
Yes	1.18	1.25 (1.25-1.25)	614,366	1.18	29,980	1.26
Parent characteristics						
Paternal age at birth (years)						
<25	0.99	1.03 (1.02-1.03)	391,295	0.99	23,322	0.99
25-29	1.00	1.04 (1.04-1.04)	1,725,739	1.00	72,689	1.05
30-34	0.97	ref	2,725,950	0.96	103,212	1.04
35-39	0.93	0.97 (0.97-0.97)	1,596,283	0.93	66,294	0.99
40-44	0.89	0.92 (0.92-0.92)	502,138	0.89	24,973	0.97
≥45	0.85	0.88 (0.88-0.88)	162,784	0.84	10,141	0.95
Maternal age at birth (years)						
<20	0.94	1.00 (0.99-1.00)	133,205	0.94	8,062	0.94
20-24	1.00	1.06 (1.06-1.07)	1,060,404	1.00	55,150	1.04
25-29	0.99	1.06 (1.06-1.06)	2,605,206	0.99	104,615	1.05
30-34	0.94	ref	2,429,803	0.94	92,749	1.00
35-39	0.89	0.95 (0.94-0.95)	777,273	0.89	34,945	0.97
≥40	0.83	0.89 (0.88-0.89)	98,298	0.83	5,111	0.89
Unmarried mother						
No	0.96	ref	6,887,169	0.96	280,617	1.02
Yes	0.90	0.93 (0.93-0.94)	217,020	0.89	20,015	0.96
Foreign-born mother						
No	0.97	ref	6,423,059	0.97	270,677	1.02
Yes	0.88	0.91 (0.91-0.91)	681,130	0.88	29,955	0.96

	Follow-up period		Unexposed periods		Exposed periods	
	Rate[#]	IRR (95% CI)	Events	Rate[#]	Events	Rate[#]
Socio-economic status						
Urbanicity of residence						
1 (highest urbanicity)	0.90	ref	1,312,477	0.90	55,972	0.97
2	0.93	1.04 (1.03-1.04)	2,226,369	0.93	101,358	0.99
3	0.96	1.07 (1.07-1.07)	1,682,039	0.96	65,062	1.01
4	0.99	1.10 (1.09-1.10)	1,060,171	0.98	44,522	1.03
5	1.06	1.18 (1.17-1.18)	136,774	1.06	6,134	1.14
6	1.11	1.23 (1.23-1.24)	296,372	1.11	12,656	1.15
7	1.17	1.30 (1.30-1.30)	389,956	1.17	14,928	1.22
Family income						
High	0.94	ref	1,409,468	0.93	42,416	0.99
Upper-middle	0.97	1.04 (1.04-1.04)	1,459,015	0.97	49,248	1.04
Middle	1.00	1.07 (1.07-1.07)	1,595,938	1.00	65,552	1.07
Lower-middle	0.98	1.05 (1.05-1.05)	1,479,276	0.98	71,288	1.04
Low	0.90	0.96 (0.96-0.97)	1,141,726	0.90	71,053	0.94
Paternal occupation						
Civil servants and teachers	0.96	1.00 (1.00-1.00)	403,205	0.95	16,845	1.06
Employees, employers and professionals	0.96	ref	5,213,552	0.96	199,759	1.02
Union members, farmers and fishermen	1.08	1.12 (1.12-1.13)	472,858	1.08	22,813	1.12
The unemployed and low-income households	0.90	0.93 (0.93-0.94)	660,121	0.89	43,933	0.94
Dependents	0.95	0.99 (0.98-0.99)	246,352	0.94	12,672	0.98
Maternal occupation						
Civil servants and teachers	0.92	0.94 (0.94-0.95)	376,636	0.92	13,133	1.00
Employees, employers and professionals	0.97	ref	4,381,816	0.97	158,638	1.04
Union members, farmers and fishermen	1.11	1.14 (1.14-1.15)	306,071	1.11	12,991	1.12
The unemployed and low-income households	0.89	0.91 (0.91-0.91)	405,398	0.88	34,649	0.96
Dependents	0.93	0.96 (0.95-0.96)	1,600,257	0.93	79,364	0.99
Parental physical illness						
Paternal Elixhauser index						
0	0.96	ref	6,648,669	0.95	270,411	1.01
1	1.02	1.07 (1.06-1.07)	358,254	1.02	22,077	1.07
>1	1.03	1.07 (1.07-1.08)	97,266	1.02	8,144	1.13
Maternal Elixhauser index						
0	0.96	ref	6,810,170	0.95	282,068	1.01
1	1.01	1.06 (1.06-1.06)	263,150	1.01	15,756	1.08
>1	1.06	1.11 (1.10-1.12)	30,869	1.06	2,808	1.14
Death occurred in the first five years of life						
Paternal death						
No	0.96	ref	7,085,408	0.96	298,955	1.02
Yes	0.96	1.00 (0.99-1.02)	18,781	0.96	1,677	1.00
Maternal death						
No	0.96	ref	7,099,310	0.96	299,813	1.02
Yes	0.97	1.01 (0.98-1.04)	4,879	0.95	819	1.09

	Follow-up period		Unexposed periods		Exposed periods	
	Rate[#]	IRR (95% CI)	Events	Rate[#]	Events	Rate[#]
Child's death						
No	0.96	ref	7,097,721	0.96	300,372	1.02
Yes	1.32	1.37 (1.34-1.41)	6,468	1.32	260	1.28
Censored						
No	0.96	ref	7,074,440	0.96	297,915	1.02
Yes	1.02	1.06 (1.05-1.08)	29,749	1.02	2,717	1.05

Abbreviation: CI: Confidence intervals; IRR: unadjusted incidence rate ratio.
Incidence rate: per person-years. Censored when the child or any parent died.

S-Table 25 Associations between episodes of common infectious disease with hospitalization in the first five years of life and covariates in the study population

	Follow-up period		Unexposed periods		Exposed periods	
	Rate[#]	IRR (95% CI)	Events	Rate[#]	Events	Rate[#]
Birth year						
2004-2007	135	Ref	490,083	134	24,536	167
2008-2010	127	0.94 (0.94-0.95)	294,132	126	16,181	163
2011-2014	131	0.97 (0.96-0.97)	182,882	129	8,490	172
Children's characteristics						
Child sex						
Males	143	1.19 (1.19-1.20)	547,872	141	27,655	180
Female	120	Ref	419,225	118	21,552	152
Low birthweight						
No	129	Ref	894,852	128	44,680	162
Yes	176	1.36 (1.35-1.37)	72,245	174	4,527	219
Preterm birth						
No	128	Ref	877,479	127	43,214	160
Yes	180	1.41 (1.40-1.42)	89,618	178	5,993	232
Birth order						
1	128	Ref	536,877	126	28,003	160
2	135	1.05 (1.05-1.06)	342,148	133	15,883	171
≥3	147	1.15 (1.15-1.16)	88,072	145	5,321	193
Complex chronic conditions						
No	123	Ref	840,274	122	41,905	154
Yes	246	2.00 (1.98-2.01)	126,823	243	7,302	306
Parent characteristics						
Paternal age at birth (years)						
<25	172	1.36 (1.35-1.37)	67,658	172	4,194	178
25-29	148	1.17 (1.16-1.18)	252,893	147	12,577	182
30-34	127	Ref	354,965	125	16,384	164
35-39	118	0.93 (0.93-0.94)	200,193	117	10,206	153
40-44	119	0.94 (0.94-0.95)	66,760	118	4,028	157
≥45	130	1.03 (1.01-1.04)	24,628	128	1,818	170

	Follow-up period		Unexposed periods		Exposed periods	
	Rate[#]	IRR (95% CI)	Events	Rate[#]	Events	Rate[#]
Maternal age at birth (years)						
<20	182	1.56 (1.54-1.58)	25,790	182	1,659	193
20-24	166	1.42 (1.41-1.43)	175,243	165	10,022	190
25-29	139	1.19 (1.18-1.19)	360,310	137	17,558	176
30-34	117	Ref	300,057	116	13,828	149
35-39	108	0.92 (0.92-0.93)	93,386	106	5,292	147
≥40	106	0.91 (0.89-0.92)	12,311	104	848	148
Unmarried mother						
No	131	ref	930,601	130	45,528	166
Yes	152	1.16 (1.15-1.17)	36,496	150	3,679	177
Foreign-born mother						
No	130	Ref	855,556	129	43,520	165
Yes	145	1.12 (1.11-1.12)	111,541	144	5,687	183
Socio-economic status						
Urbanicity of residence						
1 (highest urbanicity)	104	Ref	150,597	103	7,748	135
2	120	1.15 (1.14-1.16)	283,557	118	15,907	156
3	128	1.23 (1.23-1.24)	223,189	127	10,322	160
4	161	1.55 (1.54-1.56)	172,296	160	8,794	204
5	168	1.61 (1.59-1.63)	21,528	166	1,053	196
6	179	1.72 (1.70-1.73)	47,376	177	2,352	213
7	207	1.99 (1.97-2.00)	68,552	205	3,031	247
Family income						
High	103	Ref	154,428	102	5,306	124
Upper-middle	121	1.18 (1.17-1.19)	181,337	121	6,940	147
Middle	141	1.37 (1.36-1.37)	223,109	139	10,772	176
Lower-middle	147	1.43 (1.42-1.44)	219,638	145	12,681	186
Low	148	1.43 (1.43-1.44)	185,547	146	13,293	176
Paternal occupation						
Civil servants and teachers	112	0.87 (0.86-0.88)	46,700	110	2,362	149
Employees, employers and professionals	128	Ref	692,386	127	31,712	162
Union members, farmers and fishermen	169	1.31 (1.31-1.32)	73,493	167	4,077	200
The unemployed and low-income households	143	1.11 (1.11-1.12)	104,004	141	8,229	176
Dependents	131	1.02 (1.01-1.03)	33,867	130	1,948	151
Maternal occupation						
Civil servants and teachers	95	0.75 (0.75-0.76)	38,945	95	1,575	120
Employees, employers and professionals	127	Ref	567,292	126	24,217	158
Union members, farmers and fishermen	174	1.37 (1.36-1.38)	47,399	172	2,417	208
The unemployed and low-income households	154	1.21 (1.20-1.22)	69,423	151	6,799	188
Dependents	140	1.11 (1.10-1.11)	239,042	139	13,848	173

	Follow-up period		Unexposed periods		Exposed periods	
	Rate[#]	IRR (95% CI)	Events	Rate[#]	Events	Rate[#]
Parental physical illness						
Paternal Elixhauser index						
0	130	Ref	899,047	129	43,758	163
1	151	1.16 (1.15-1.17)	52,482	149	3,954	192
>1	166	1.28 (1.26-1.30)	15,568	163	1,495	208
Maternal Elixhauser index						
0	130	Ref	917,607	129	45,349	163
1	170	1.31 (1.29-1.32)	43,514	167	3,207	221
>1	209	1.61 (1.57-1.65)	5,976	205	651	265
Death occurred in the first five years of life						
Paternal death						
No	132	Ref	963,819	130	48,896	166
Yes	169	1.28 (1.24-1.33)	3,278	168	311	186
Maternal death						
No	132	Ref	966,205	130	49,049	166
Yes	179	1.36 (1.28-1.44)	892	174	158	211
Child's death						
No	131	Ref	963,256	130	49,048	166
Yes	784	5.97 (5.79-6.16)	3,841	784	159	783
Censored						
No	131	Ref	959,157	130	48,584	166
Yes	269	2.05 (2.01-2.10)	7,940	272	623	241

Abbreviation: CI: Confidence intervals; IRR: unadjusted incidence rate ratio.
Incidence rate: per 1,000 person-years. Censored when the child or any parent died.

S-Table 26 Sensitivity analyses of associations between parental serious mental illness and childhood common infectious disease

	Adjusted incidence rate ratio (95% confidence intervals)		
	Model 1	Model 2	Model 3
Excluding children with complex chronic conditions	1.01 (1.00-1.01)	1.02 (1.01-1.02)	1.02 (1.01-1.02)
Exclude children with a parent having multiple IDs	1.01 (1.01-1.01)	1.02 (1.01-1.02)	1.02 (1.01-1.02)
Excluding children with a parental death before age 5 years	1.01 (1.01-1.01)	1.02 (1.01-1.02)	1.02 (1.01-1.02)

Model 1: adjusted for birth year, child sex, child age, birth order, maternal and paternal ages, foreign-born mother, and urbanicity of residence.
Model 2: adjusted for the above variables and unmarried mother, family income, maternal and paternal occupations, and maternal and paternal Elixhauser indexes.
Model 3: adjusted for the above variables and child's LBW and preterm birth.

S-Table 27 Secondary analyses of associations between parent's serious mental illness and child common infectious disease

	Adjusted Incidence rate ratio (95% Confidence intervals)		
	Model 1	**Model 2**	**Model 3**
Which parent(s) had serious mental illness			
Paternal	1.00 (1.00-1.01)	1.01 (1.00-1.01)	1.01 (1.00-1.01)
Maternal	1.02 (1.01-1.02)	1.02 (1.02-1.02)	1.02 (1.02-1.02)
Both	1.02 (1.01-1.04)	1.03 (1.02-1.05)	1.03 (1.02-1.05)
Timing of onset of maternal and paternal disorders			
Paternal			
Before childbirth	1.00 (1.00-1.01)	1.00 (1.00-1.01)	1.00 (1.00-1.01)
After childbirth	1.01 (1.01-1.02)	1.02 (1.01-1.02)	1.02 (1.01-1.02)
Maternal			
Before childbirth	1.01 (1.01-1.02)	1.02 (1.02-1.02)	1.02 (1.02-1.02)
After childbirths	1.02 (1.02-1.03)	1.03 (1.02-1.03)	1.03 (1.02-1.03)
Diagnostic category for maternal and paternal disorders			
Paternal			
Schizophrenia	1.01 (1.00-1.02)	1.01 (1.00-1.02)	1.01 (1.00-1.02)
Bipolar disorder	1.02 (1.01-1.02)	1.02 (1.01-1.03)	1.02 (1.01-1.03)
Major depression	1.00 (1.00-1.01)	1.00 (1.00-1.01)	1.00 (1.00-1.01)
Maternal			
Schizophrenia	0.98 (0.97-0.99)	0.99 (0.98-1.00)	0.99 (0.98-1.00)
Bipolar disorder	1.02 (1.02-1.03)	1.03 (1.03-1.04)	1.03 (1.03-1.04)
Major depression	1.02 (1.02-1.03)	1.03 (1.02-1.03)	1.03 (1.02-1.03)

Model 1: adjusted for birth year, child sex, child age, birth order, unmarried mother, maternal and paternal age, foreign-born mother, and urbanicity of residence.
Model 2: adjusted for the above variables and family income, maternal and paternal occupations, maternal and paternal Elixhauser indexes, and spouse's mental illness (This variable was not included in the models with the exposure as parent(s) with serious mental illness).
Model 3: adjusted for the above variables and child's LBW and preterm birth.

S-Table 28 Secondary analyses of associations between parent's serious mental illness and child common infectious disease with hospitalization

	Adjusted Incidence rate ratio (95% Confidence intervals)			
	Model 1	**Model 2**	**Model 3**	**Model 4**
Which parent(s) had serious mental illness				
Paternal	1.21 (1.18-1.24)	1.17 (1.14-1.21)	1.14 (1.12-1.17)	1.14 (1.11-1.17)
Maternal	1.38 (1.35-1.41)	1.39 (1.36-1.42)	1.35 (1.32-1.38)	1.34 (1.31-1.37)
Both	1.49 (1.36-1.64)	1.51 (1.37-1.65)	1.41 (1.29-1.55)	1.40 (1.27-1.55)
Timing of onset of maternal and paternal disorders				
Paternal				
Before childbirth	1.21 (1.18-1.24)	1.18 (1.15-1.21)	1.13 (1.10-1.17)	1.13 (1.10-1.16)
After childbirth	1.28 (1.23-1.32)	1.23 (1.19-1.28)	1.20 (1.16-1.24)	1.19 (1.15-1.24)
Maternal				
Before childbirth	1.40 (1.36-1.43)	1.43 (1.40-1.46)	1.38 (1.35-1.41)	1.37 (1.34-1.40)
After childbirth	1.40 (1.37-1.44)	1.36 (1.33-1.40)	1.34 (1.30-1.37)	1.33 (1.29-1.36)

	Adjusted Incidence rate ratio (95% Confidence intervals)			
	Model 1	**Model 2**	**Model 3**	**Model 4**
Diagnostic category for maternal and paternal disorders				
Paternal				
Schizophrenia	1.33 (1.28-1.39)	1.24 (1.19-1.29)	1.19 (1.14-1.24)	1.18 (1.13-1.23)
Bipolar disorder	1.26 (1.20-1.32)	1.24 (1.18-1.29)	1.17 (1.12-1.23)	1.17 (1.12-1.22)
Major depression	1.16 (1.13-1.20)	1.16 (1.12-1.20)	1.13 (1.09-1.17)	1.13 (1.09-1.17)
Maternal				
Schizophrenia	1.44 (1.38-1.52)	1.42 (1.35-1.49)	1.36 (1.30-1.42)	1.34 (1.28-1.40)
Bipolar disorder	1.45 (1.39-1.50)	1.45 (1.40-1.50)	1.40 (1.35-1.45)	1.39 (1.34-1.44)
Major depression	1.37 (1.34-1.40)	1.38 (1.35-1.41)	1.34 (1.32-1.37)	1.34 (1.31-1.37)

Model 1: adjusted for birth year, child sex and child age.
Model 2: adjusted for the above variables and birth order, maternal and paternal age, foreign-born mother, and urbanicity of residence.
Model 3: adjusted for the above variables and unmarried mother, family income, maternal and paternal occupations, maternal and paternal Elixhauser indexes and spouse's mental illness (This variable was not included in the models with the exposure as parent(s) with serious mental illness).
Model 4: adjusted for the above variables and child's LBW and preterm birth.

S-Table 29 Associations between appendicitis in the first five years of life and covariates among children in the study population

	Follow-up period		**Unexposed periods**		**Exposed periods**	
	Rate[#]	**IRR (95% CI)**	**Events**	**Rate[#]**	**Events**	**Rate[#]**
Birth year						
2004-2007	0.65	ref	2,284	0.62	103	0.70
2008-2010	0.42	0.67 (0.62-0.72)	967	0.41	55	0.56
2011-2014	0.31	0.49 (0.44-0.54)	443	0.31	10	0.20
Children's characteristics						
Child sex						
Males	0.55	1.23 (1.15-1.31)	2,117	0.55	95	0.62
Female	0.45	ref	1,577	0.45	73	0.52
Low birthweight						
No	0.49	ref	3,440	0.49	153	0.56
Yes	0.62	1.26 (1.12-1.43)	254	0.61	15	0.73
Preterm birth						
No	0.49	ref	3,377	0.49	146	0.54
Yes	0.64	1.32 (1.18-1.48)	317	0.63	22	0.85
Birth order						
1	0.50	ref	2,117	0.50	98	0.56
2	0.49	0.97 (0.90-1.04)	1,251	0.49	43	0.46
≥3	0.56	1.12 (1.00-1.25)	326	0.54	27	0.98
Complex chronic conditions						
No	0.47	ref	3,225	0.47	144	0.53
Yes	0.90	1.92 (1.75-2.11)	469	0.90	24	1.01

Parent characteristics						
Paternal age at birth (years)						
<25	0.63	1.29 (1.13-1.47)	253	0.64	12	0.51
25-29	0.59	1.19 (1.10-1.29)	1,003	0.58	44	0.64
30-34	0.49	ref	1,389	0.49	52	0.52
35-39	0.45	0.91 (0.83-0.99)	751	0.44	44	0.66
40-44	0.41	0.83 (0.73-0.96)	231	0.41	12	0.47
≥45	0.35	0.71 (0.56-0.90)	67	0.35	4	0.37
Maternal age at birth (years)						
<20	0.52	1.12 (0.89-1.40)	74	0.52	4	0.47
20-24	0.58	1.25 (1.14-1.38)	614	0.58	34	0.64
25-29	0.55	1.18 (1.10-1.28)	1,432	0.55	64	0.64
30-34	0.46	ref	1,197	0.46	49	0.53
≥35	0.38	0.82 (0.73-0.92)	377	0.38	17	0.41
Unmarried mother						
No	0.50	ref	3,561	0.50	156	0.57
Yes	0.55	1.10 (0.93-1.30)	133	0.55	12	0.58
Foreign-born mother						
No	0.51	ref	3,357	0.51	144	0.55
Yes	0.45	0.88 (0.79-0.98)	337	0.43	24	0.77
Socio-economic status						
Urbanicity of residence						
1 (highest urbanicity)	0.29	ref	432	0.30	10	0.17
2	0.49	1.7 (1.52-1.89)	1,177	0.49	53	0.52
3	0.56	1.94 (1.74-2.17)	972	0.56	52	0.81
4	0.73	2.50 (2.22-2.80)	781	0.73	32	0.74
5	0.44	1.51 (1.15-1.98)	59	0.46	0	0.00
6	0.52	1.79 (1.49-2.16)	133	0.50	12	1.09
7	0.43	1.48 (1.23-1.78)	140	0.42	9	0.74
Family income						
High	0.40	ref	597	0.40	16	0.38
Upper-middle	0.50	1.27 (1.14-1.41)	752	0.50	27	0.57
Middle	0.52	1.33 (1.20-1.47)	829	0.52	42	0.69
Lower-middle	0.59	1.49 (1.35-1.65)	892	0.59	39	0.57
Low	0.49	1.25 (1.12-1.39)	620	0.49	44	0.58
Paternal occupation						
Civil servants and teachers	0.44	0.87 (0.75-1.01)	185	0.44	7	0.44
Employees, employers and professionals	0.50	ref	2,736	0.50	103	0.53
Union members, farmers and fishermen	0.57	1.14 (1.00-1.29)	247	0.56	16	0.79
The unemployed and low-income households	0.47	0.93 (0.84-1.04)	340	0.46	29	0.62
Dependents	0.57	1.13 (0.96-1.33)	145	0.56	11	0.85

Maternal occupation						
Civil servants and teachers	0.42	0.84 (0.72-0.98)	175	0.43	4	0.31
Employees, employers and professionals	0.50	ref	2,239	0.50	94	0.62
Union members, farmers and fishermen	0.71	1.42 (1.23-1.63)	191	0.69	12	1.04
The unemployed and low-income households	0.52	1.04 (0.91-1.18)	237	0.52	20	0.55
Dependents	0.49	0.97 (0.90-1.05)	838	0.49	37	0.46
Parental physical illness						
Paternal Elixhauser index						
0	0.50	ref	3,463	0.50	147	0.55
1	0.53	1.07 (0.92-1.23)	182	0.52	16	0.78
>1	0.53	1.06 (0.81-1.38)	49	0.51	5	0.70
Maternal Elixhauser index						
0	0.50	ref	3,541	0.50	160	0.58
≥1	0.53	1.05 (0.90-1.23)	153	0.53	8	0.47
Death occurred in the first five years of life						
Paternal death						
No	0.50	ref	3,676	0.50	168	0.57
Yes	0.85	1.70 (1.07-2.7)	18	0.92	0	0.00
Maternal death						
No	0.50	ref	3,688	0.50	0	0.56
Yes	1.36	2.72 (1.36-5.45)	6	1.17	2	2.67
Child's death						
No	0.50	ref	3,670	0.50	0	0.57
Yes	4.91	9.86 (6.66-14.62)	24	4.91	1	4.93
Censored						
No	0.50	ref	3,647	0.49	165	0.56
Yes	1.57	3.17 (2.40-4.19)	47	1.61	3	1.16

Abbreviation: CI: Confidence intervals; IRR: unadjusted incidence rate ratio.
Incidence rate: per 1,000 person-years. Censored when the child or any parent died.

S-Table 30 Sensitivity analyses of associations between parental serious mental illness and child appendicitis in the first five years of life

	Adjusted incidence rate ratio (95% confidence intervals)		
	Model 1	**Model 2**	**Model 3**
Excluding children with complex chronic conditions	1.08 (0.91-1.28)	1.07 (0.90-1.27)	1.08 (0.92-1.27)
Exclude children with a parent having multiple IDs	1.06 (0.90-1.25)	1.05 (0.89-1.24)	1.05 (0.89-1.24)
Excluding children with a parental death before age 5 years	1.11 (0.94-1.29)	1.09 (0.93-1.28)	1.09 (0.93-1.28)

Model 1: adjusted for birth year, child sex, child age, birth order, unmarried mother, maternal and paternal ages, foreign-born mother, and urbanicity of residence.
Model 2: adjusted for the above variables and family income, maternal and paternal occupations, and maternal and paternal Elixhauser indexes
Model 3: adjusted for the above variables and child's LBW and preterm birth.

VITA

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