Parental hospital-treated somatic illnesses and psychosis of the offspring -the Northern Finland Birth Cohort 1986 study

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Key words: Parental somatic illness, psychosis, healthcare, offspring, children

Abstract

Aim: The aim of this study was to investigate whether parental somatic illnesses during childhood increase the risk for later psychosis in the offspring. In addition, we examined which parental illnesses in particular are associated with increased risk of psychosis in the offspring. **Method**: The data of the Northern Finland Birth Cohort 1986 (NFBC 1986), included 9,137 children born alive in northern Finland between the 1st of July 1985 and the 30th of June 1986. Information regarding the parents' somatic morbidity was collected through various health care registers up to age 28 of the cohort members. **Results**: Psychosis was diagnosed in 169 (1.8%) of the cohort members between the ages of 16 and 28. Accumulation of parental somatic diseases was related to later psychosis in the offspring. In addition, some specific somatic diagnostic groups of parents were emphasised in relation to psychosis in the offspring. **Conclusions**: Our study findings indicated that parental somatic illness should be taken into account in the prevention of serious mental health problems in their offspring.

Introduction

Psychosis, especially its most extreme form, schizophrenia, is a serious and intense psychiatric disorder, which causes significant burden not only for the patient and his/her family, but also for society. Psychosis is one of the most researched topics in psychiatry, and much ongoing research aims to identify the risk factors behind the illness. There are two significant paths in this research, namely genetic and environmental.[1, 2, 3]

Parental psychosis is regarded as a major risk factor for offspring's psychosis through both genetic and environmental factors. Genetic vulnerability to psychosis has been one of the main focuses in the research.[3] The research on environmental risk factors of psychosis has paid attention to the impact of adverse life events on the development of psychosis, and a clear link between childhood adversity and psychosis has been confirmed.[4] For example, childhood abuse, especially sexual abuse, has been found to be linked with later psychosis of the victim.[3] Parental death and divorce have also been shown to be associated with increased risk of psychosis in offspring.[4,5,6,7]

Parental somatic illnesses occurring during an offspring's childhood are evidently a significant source of adversity, with a negative effect on the later psychological well-being of the offspring. For example, the association of parental illnesses such as cancer, human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS), or neurological illnesses such as multiple sclerosis, with children's current and later psychological adversities, have been studied comprehensively. These illnesses have been found to correlate, for example, with anxiety and depression levels of affected children and adolescents.[8, 9, 10, 11, 12]

Hitherto, only a very few studies have examined an association between parental somatic illness occurring during childhood of the offspring and later psychosis of the offspring. The results of these studies are not consistent. In a large nationwide Danish cohort study, the authors concluded that parental cancer was not associated with schizophrenia of the offspring. In their study, maternal small cell lung cancer was found to be positively related to the onset of schizophrenia in the offspring, but the finding was explained by parental smoking, a well-recognized risk factor for mental health.[13] Similarly, a nationwide Finnish birth cohort study did not find an association between parental cancer and psychosis in the offspring followed up to age 21.[14] However, in a study with a rather small sample of adult patients with non-affective psychosis (34 cases, 52 controls), a statistically significant association was observed between a parental history of type 2 diabetes and offspring psychosis.[15]

We urgently need research-based evidence of the impact of parental somatic illnesses on psychosis in the offspring, controlling for parental mental disorders and other risk factors which are already known to be associated with later psychosis in the offspring. Such evidence is important for many reasons—in particular because the families can be reached in adult healthcare units as part of the parent's treatment for somatic illnesses. This makes preventive actions for the children possible. Therefore, the aim of this study was to determine whether parental somatic illness *per se* was associated with increased risk for later psychosis in the offspring, and if so, which specific parental illnesses were most relevant in this respect.

Methods

Data of the Northern Finland Birth Cohort 1986 (NFBC 1986) study population

The study population utilized for this research was the Northern Finland Birth Cohort 1986 (NFBC 1986). NFBC 1986 is a prospective longitudinal study that initially consisted of 9,432 children born alive in northern Finland, in the provinces of Oulu and Lapland, between the 1st of July, 1985 and the 30th of June, 1986. Total of 91 cohort members have died before the age of 16 years and total of 251 members denied the use of their data. Therefore total of 9137 cohort members was included in the analyses. Follow-up data have been collected on various occasions through postal questionnaires and clinical examinations. The cohort data have also been combined with various hospital records and statistical registers. [16]

Psychosis of cohort members and psychiatric morbidity of parents

Psychoses (ICD-9: 2950-2959, 2961E, 2962E, 2963E, 2964E, 2967, 297, 2988, 2989; ICD-10: F20-F25, F28, F29, F302, F312, F315, F323, F333) of cohort members diagnosed between the ages of 16 and 28 years, and parental psychiatric morbidity (ICD-8/9: 290-319, ICD-10: F-codes) when the offspring was under 18 years of age, were defined to be present if found from the following Finnish national registers: Care Register for Health Care (CRHC) (inpatient treatments 1969- 2013), Finnish outpatient registers (outpatient visits in specialized care 1998-2013, primary care 2011-2013), Social Insurance Institution registers (parents' reimbursable medicines from the offspring's birth until 2005) and Finnish Centre for Pensions (parents' disability pensions from the offsprings' birth until 2013).[17] The Finnish national registers have been shown to be valid tools for scientific research.[18]

Hospital-treated somatic diseases of the parents

All somatic diagnoses (codes A-E, G-Z) of parents of cohort members from the CRHC were categorised according to the main diagnostic categories of the ICD diagnostic system (ICD-10 Version: 2016.[19] This information covers all parental somatic illnesses which were severe enough to require treatment in hospital inpatient care and which had occurred when a cohort member was under 18 years of age.

Statistical analyses

Statistical significance of group differences was assessed in categorical variables with the Pearson Chi-Square test (with exact 2-sided p-values), and in continuous variables with the Student's T-test or Mann-Whitney U-test. The Benjamini-Hochberg procedure was used to control for the false discovery rate [20]. Binary logistic regression analysis (Odds Ratios, OR, with 95% confidence interval, CI) was used to examine the association of parental somatic diseases with psychosis in cohort members after controlling for factors that, on the basis of the existing literature, are known to increase the risk for psychosis: parental psychiatric diagnoses (hospital treatments, see above) [3], gender of cohort members [21], father's age at child's birth, [22] socio-economic status of the family at birth, [23] perinatal complications [24] and information about use of cannabis at age 16.[25] The statistical software used in analyses was IBM SPSS Statistics 22.

Results

Psychosis by the age of 28 years was found in 169 (1.8%) of all cohort members. In cohort members with psychosis, some hospital-treated disease, occurring when the cohort member was below 18 years of age, was found in 147 (84.0%) of their mothers, 109 (62.6%) of their fathers, and 164 (93.7%) of at least one parent. Correspondingly, in cohort members without psychosis, hospital-treated disease was found in 7128 (77.4%) of their mothers, 5370 (58.8%) of their fathers and 8315 (90.2%) of at least one parent.

Table 1 shows the characteristics of cohort members with and without psychosis. Parental psychiatric morbidity (any hospital-treated mental, behavioural or neurodevelopmental disorder), when the cohort member was under 18 years old, was statistically significantly more common in cohort members with psychosis.

Insert table 1 about here

The results of bivariate analyses (Table 2) showed that cohort members with psychosis more commonly had a mother with a hospital treatment due to injury, poisoning and certain other consequences of external causes during the childhood of the cohort member (16.0% vs. 10.2%, p=0.017) as compared to cohort members without psychosis. After adjusting, however, this result did not reach statistical significance.

Regarding the somatic diseases of the fathers, psychosis of cohort members was positively associated with the fathers' hospitalizations due to infectious and parasitic diseases (8.3% vs. 4.1%,

p=0.012), neoplasms (8.3% vs. 3.5%, p=0.003), diseases of the digestive system (20.8% vs. 14.4%, p=0.021), external causes for morbidity (13.7%% vs. 8.6%, p=0.026), and factors influencing health status and contact with health services (7.7% vs. 3.8%, p=0.015). After controlling for covariates the results remained statistically significant in terms of the father's diagnosis of neoplasms (model 1: OR 2.73, 95% CI 1.34-5.57, p=0.006; model 2: OR 2.75, 95% CI 1.35-5.62, p=0.006),~~,~~ and those relating to factors influencing health status and contact with health services (model 1: OR 2.67, 95% CI 1.35-5.26, p=0.005; model 2: OR 2.66, 95% CI 1.35-5.27, p=0.005).

When somatic diseases of parents were analysed in combination, psychosis of offspring were more common if parents had hospital treatment due to certain infectious and parasitic diseases (10.0% vs.7.9%, p=0.017), neoplasms (22.5% vs. 14.0%, p=0.002), diseases of the digestive system (32.0% vs. 24.5%, p=0.030), injury, poisoning and certain other consequences of external causes (32.5% vs. 24.2%, p=0.015) and external causes for morbidity (24.9% vs. 18.4%, p=0.036). Adjusted models with combined data did not reveal any significant associations of parental somatic illnesses to psychosis of offspring.

Insert Table 2 about here

Table 3 presents the sum of different disease categories of parents of cohort members with and without psychosis. Fathers, as well as mothers, of cohort members with psychosis had accumulated more diagnoses of different disease categories compared to cohort members without psychosis.

Insert Table 3 about here

Discussion

The main purpose of this study was to determine whether parental hospital-treated somatic illnesses occurring when the offspring was under 18 years of age increased the risk for later psychosis of the affected offspring by the age of 28. The second aim was to identify those parental somatic illnesses which, in particular, were associated with later psychosis in the offspring. We assumed that parental somatic illness plays a role as a stressor in the affected offspring in the same way as various other adverse childhood life events which are known to be associated not only with psychological wellbeing, but also with development of a most severe mental disorder, psychosis.[3] The findings of our study gave support to our assumption that parental somatic illnesses are associated with the risk of psychosis in offspring in two ways: specific to some parental somatic illnesses and also the

accumulation of different somatic illnesses. Therefore, it can be regarded that parental somatic illnesses occurring during the childhood of offspring are a possible risk factor for later psychosis of the offspring and, thus further research is needed.

Interestingly, hospital-treated somatic illnesses of the fathers were more commonly the case than those of the mothers when the risk of later psychosis in the offspring was considered. To the best of our knowledge, there are no previous studies with which to compare this gender-related finding. One explanation for this finding may relate to low economic status of a family, which is known to be an independent risk factor for a child's psychological development.[23] Although Finland has good social security services providing all citizens equally, it could be possible that onset of parental somatic illness may impact the economic situation of families more than that of maternal illness. Further, there was an economic regression in Finland during the 1990s, which caused widespread unemployment and economic crises [26] when the cohort members were at school age. Thus, parental somatic illnesses requiring inpatient treatment in hospital and co-occurring economic regression may have worsened adversities in the family, with a negative effect on the offspring's mental health.

Another explanation may relate to the father's different way- in comparison to the mother's - of reacting psychologically to severe illness. That is, the mother's way of sharing illness-related feelings could make children more aware what is going in the family, thereby reducing any anxiety of the children. Men suffering from cancer and who are fathers of young children are reported to have elevated levels of anxiety in comparison to men with cancer but having no children.[27] High level of anxiety might block communication in the families. This study did not reveal the impact of the mother's psychological reactions to her spouse's illness, which in another study has been reported to impact adversely on children. [28] Parents' psychological symptoms are known to increase their children's adverse psychological reactions.[28] Our results of combined analyses of parents indicated that maternal hospital-treated somatic illness may also have an important role in children's later psychosis, although this could not be confirmed in our study. This calls for further studies, since specific cancers in mothers were reported in one study to be associated with an increase in offspring psychosis.[13]

Another interesting finding was that some particular types of parental somatic illnesses were emphasized in association with offspring psychosis. Firstly, parental cancer, in the fathers, was shown to be associated with an increased likelihood for offspring psychosis. In several studies,

parental cancer has been reported to have an adverse impact on families and on children's mental health [8, 9, 10, 11, 12] Cancer often comes rapidly into the life of a family, it impacts on everyday life in a very intensive way and, in most severe cases, leads to the parent's death. Therefore, cancer of a parent causes anxiety, distress and existential pain in the family members and might conceivably also be associated with an increased likelihood of severe mental disorder, such as psychosis, in the children. Secondly, being close to a marginally significant level, our finding of association of parental illnesses of the digestive system on offspring psychosis may indicate that illnesses causing a long-term stressful situation without a traumatic sudden onset of illness may increase the risk of later psychosis in the affected offspring. Illnesses of the digestive system are often quite different compared to cancer. Digestive system illnesses are usually chronic, and although they impact on everyday life in many ways, they are not life-threatening in the same way as cancer. Our result is in line with one earlier study finding that Type 2 diabetes of parents is associated with offspring psychosis.[15] Due to explanatory nature of our study further research is needed to confirm our preliminary findings.

Thirdly, a greater proportion of fathers of cohort members with psychosis had used health services without clear illness-related medical diagnoses compared to fathers of offspring without psychosis. These Z -codes "factors influencing health status and contact with health services" diagnoses were set in inpatient hospital units and are thus based on reliable examinations. The diagnoses are merely functional rather than illness diagnoses, which often indicate psychosomatic problems. This may indicate that behind an offspring's psychosis there may be unrecognized parental psychological problems with somatic manifestation, which are common in healthcare. [29-31] It is known that medically unexplained somatic symptoms are strongly associated with common mental disorders, [32] but "at least a third of those with somatisation have no comorbid mental disorder". [33] Our result indicates that it would be important to recognise psychological factors behind unexplained somatic symptoms, not just for the patient himself, but also for the affected children in the family.

Our results showed that an increasing number of different hospital-treated somatic illnesses of parents may also relate to increased likelihood of later psychosis in the offspring. This may indicate that not only specific parental somatic illnesses, but also accumulation of somatic illnesses, may cause an excessive or repetitive psychosocial burden in a family. Frequent and repetitive adverse experiences as stressors in everyday life, and especially decreasing social relations, have been proposed to be one of the intermediating factors behind psychosis. [34, 35] In healthcare, recognising multi-morbidity of illnesses, i.e. the co-existence of multiple chronic illnesses where one is not

necessarily more dominant than the others, is essential not just for the patient, but also for the affected children and family. [36, 37]

On the basis of the findings of this study, an association between parental somatic illness and later psychosis in the offspring appears to be present. This means that families with young children and with parental somatic illness represent an important target group for psychosocial support in adult health care in order to prevent children's later psychosis. When providing support, it is essential to summarise the information relating to children's protective factors in this target group. The information of protective factors must serve as a basis for interventions which are safe, feasible and effective in clinical practice. There is evidence in psychiatry that adverse impact of parental psychiatric illness on children can be prevented [38], and that the psychosocial well-being of children affected by parental cancer can be improved.[39] In three Nordic countries (Finland, Norway and Sweden), there is a legislation which requires that the psychosocial needs of children of parents who use social and healthcare services are taken into account (for Finland see Section 70 "Consideration of a child in services provided for adults", http://www.finlex.fi/en/laki/kaannokset/2010/en20101326.pdf). Our results highlight that it is time to systematically fulfil the requirements of the law.

Strengths and limitations

The strength of this study derives from the use of information from the Finnish National registers, which have been found to be valid tools for research purposes. [18] It was possible to follow the whole birth cohort via the comprehensive national health care registers without attrition. The study population was large enough for reliable statistical analyses. However, the low number of cases in some sub-group analyses may have caused lack of power (Type 2 error) in statistical analyses. On the other hand, due to the several statistical comparisons performed, the possibility of chance findings cannot be excluded (Type 1 error). Our study was explanatory to its nature. The main findings rely on conservative approach for statistical significance testing, although Benjamini-Hochberg method was also applied to control for the false discovery rate. As generally present in multiple comparison corrections, the adjusted p-values, however, may increase the likelihood for false negative findings.[20] When combing the data of mother and father, some somatic illness of parents showing reverse association with offspring may have eliminated some findings. If available, comprehensive information of treatments in outpatient settings would have provided a broader insight for our research and also increased the statistical power of analyses.

Conclusions

Parental somatic diagnoses in the childhood and adolescence of offspring appear to be associated with later psychosis in the offspring, cumulatively in general and in relation to some paternal somatic diagnoses such as neoplasms and those associated with factors influencing the use of health care services. Parents' illness-related factors, e.g. intensity or duration of the illness, together with additional known risk factors such as parental mental health problems and poor economic status of the family, together with parental somatic illnesses, appear to impact the association between parental illness and offspring psychosis. This result indicates that adult healthcare should take into account patients' psychological needs as well as the affected children's needs for maintenance of psychosocial wellbeing. Psychosis is regarded as one of the most severe psychiatric disorders and any associated links with parental somatic diagnoses needs to be fully understood. Beyond that, there is also urgent need for research concerning parental somatic illnesses as risk factor for less severe psychiatric disorders among offspring.

References

1. Karanikas E, Antoniadis D, Garyfallos GD. The role of cortisol in first episode of psychosis: a systematic review. Curr Psychiatry Rep 2014; 16: 503-014-0503-7.
2. Kim JS, Lee SH. Influence of interactions between genes and childhood trauma on refractoriness in psychiatric disorders. Prog Neuropsychopharmacol Biol Psychiatry 2016.
3. Longden E, Read J. Social Adversity in the Etiology of Psychosis: A Review of the Evidence. Am J Psychother 2016; 70: 5-33.
4. Matheson SL, Shepherd AM, Pinchbeck RM, Laurens KR, Carr VJ. Childhood adversity in schizophrenia: a systematic meta-analysis. Psychol Med 2013; 43: 225-238.
5. Rosenberg SD, Lu W, Mueser KT, Jankowski MK, Cournos F. Correlates of adverse childhood events among adults with schizophrenia spectrum disorders. Psychiatr Serv 2007; 58: 245-253.
6. Varese F, Smeets F, Drukker M, et al. Childhood adversities increase the risk of psychosis: a meta-analysis of patient-control, prospective- and cross-sectional cohort studies. Schizophr Bull 2012; 38: 661-671.
7. Isohookana R, Riala K, Hakko H, Rasanen P. Adverse childhood experiences and suicidal behavior of adolescent psychiatric inpatients. Eur Child Adolesc Psychiatry 2013; 22: 13-22.
8. Grabiak BR, Bender CM, Puskar KR. The impact of parental cancer on the adolescent: an analysis of the literature. Psychooncology 2007; 16: 127-137.
9. Osborn T. The psychosocial impact of parental cancer on children and adolescents: a systematic review. Psychooncology 2007; 16: 101-126.

10. Sieh DS, Meijer AM, Oort FJ, Visser-Meily JM, Van der Leij DA. Problem behavior in children of chronically ill parents: a meta-analysis. Clin Child Fam Psychol Rev 2010; 13: 384-397.
11. Krattenmacher T, Kuhne F, Fuhrer D, et al. Coping skills and mental health status in adolescents when a parent has cancer: a multicenter and multi-perspective study. J Psychosom Res 2013; 74: 252-259.
12. Morris JN, Martini A, Preen D. The well-being of children impacted by a parent with cancer: an integrative review. Support Care Cancer 2016; 24: 3235-3251.
13. Benros ME, Laursen TM, Dalton SO, Nordentoft M, Mortensen PB. The risk of schizophrenia and child psychiatric disorders in offspring of mothers with lung cancer and other types of cancer: a Danish nationwide register study. PLoS One 2013; 8: e79031.
14. Niemela M, Paananen R, Hakko H, Merikukka M, Gissler M, Rasanen S. Mental disorder diagnoses of offspring affected by parental cancer before early adulthood: the 1987 Finnish Birth Cohort study. Psychooncology 2016.
15. Fernandez-Egea E, Miller B, Bernardo M, Donner T, Kirkpatrick B. Parental history of type 2 diabetes in patients with nonaffective psychosis. Schizophr Res 2008; 98: 302-306.
16. Jarvelin MR, Hartikainen-Sorri AL, Rantakallio P. Labour induction policy in hospitals of different levels of specialisation. Br J Obstet Gynaecol 1993; 100: 310-315.
17. Filatova S, Marttila R, Koivumaa-Honkanen H, et al. A comparison of the cumulative incidence and early risk factors for psychotic disorder in young adults in the Northern Finland Birth Cohorts 1966 and 1986. Epidemiol Psychiatr Sci 2016: 1-11.
18. Miettunen J, Suvisaari J, Haukka J & Isohanni M (2011) Use of Register Data for Psychiatric Epidemiology in the Nordic Countries: Textbook of Psychiatric Epidemiology.In: Tsuang M, Tohen M & Jones P (eds) Textbook of Psychiatric Epidemiology. , Wiley-Blackwell.
19. http://apps.who.int/classifications/icd10/browse/2016/en cited 06.23.2016
20. Benjamini, Y. Discovering the false discovery rate. Journal of the Royal Statistical Society: Series B Statistical Methodology. 2010. 72 : 405–416.
21. Ochoa S, Usall J, Cobo J, Labad X, Kulkarni J. Gender differences in schizophrenia and first-episode psychosis: a comprehensive literature review. Schizophr Res Treatment 2012; 2012: 916198.
22. Miller B, Messias E, Miettunen J, et al. Meta-analysis of paternal age and schizophrenia risk in male versus female offspring. Schizophr Bull 2011; 37: 1039-1047.
23. Hur JW, Choi SH, Yun JY, Chon MW, Kwon JS. Parental socioeconomic status and prognosis in individuals with ultra-high risk for psychosis: A 2-year follow-up study. Schizophr Res 2015; 168: 56-61.
24. Verdoux H, Geddes JR, Takei N, Lawrie SM, Bovet P, Eagles JM, Heun R, McCreadie RG, McNeil TF, O'Callaghan E, Stöber G, Willinger MU, Wright P, Murray RM. Obstetric complications and age at onset in schizophrenia: an international collaborative meta-analysis of individual patient data. Am J Psychiatry. 1997: 9:1220-7.
25. Miettunen J, Törmänen S, Murray GK, Jones PB, Mäki P, Ebeling H, Moilanen I, Taanila A, Heinimaa M, Joukamaa M, Veijola J. Association of cannabis use with prodromal symptoms of psychosis in adolescence. Br J Psychiatry. 2008:192:470-1.

26. Tapia Granados JA, Rodriguez JM. Health, economic crisis, and austerity: A comparison of Greece, Finland and Iceland. Health Policy 2015; 119: 941-953.
27. Ernst J, Gotze H, Krauel K, et al. Psychological distress in cancer patients with underage children: gender-specific differences. Psychooncology 2013; 22: 823-828.
28. Niemela M, Paananen R, Hakko H, Merikukka M, Gissler M, Rasanen S. The prevalence of children affected by parental cancer and their use of specialized psychiatric services: the 1987 Finnish Birth Cohort study. Int J Cancer 2012; 131: 2117-2125.
29. Prince M, Patel V, Saxena S, et al. No health without mental health. Lancet 2007; 370: 859-877.
30. Escobar JI, Waitzkin H, Silver RC, Gara M, Holman A. Abridged somatization: a study in primary care. Psychosom Med 1998; 60: 466-472.
31. Gureje O, Simon GE, Ustun TB, Goldberg DP. Somatization in cross-cultural perspective: a World Health Organization study in primary care. Am J Psychiatry 1997; 154: 989-995.
32. Henningsen P, Zimmermann T, Sattel H. Medically unexplained physical symptoms, anxiety, and depression: a meta-analytic review. Psychosom Med 2003; 65: 528-533.
33. Barsky AJ, Orav EJ, Bates DW. Somatization increases medical utilization and costs independent of psychiatric and medical comorbidity. Arch Gen Psychiatry 2005; 62: 903-910.
34. Selten JP, Cantor-Graae E. Hypothesis: social defeat is a risk factor for schizophrenia?. Br J Psychiatry Suppl 2007; 51: s9-12.
35. van Nierop M, van Os J, Gunther N, et al. Does social defeat mediate the association between childhood trauma and psychosis? Evidence from the NEMESIS-2 Study. Acta Psychiatr Scand 2014; 129: 467-476.
36. Holden L, Scuffham PA, Hilton MF, Muspratt A, Ng SK, Whiteford HA. Patterns of multimorbidity in working Australians. Popul Health Metr 2011; 9: 15-7954-9-1
37. Sondergaard E, Willadsen TG, Guassora AD, et al. Problems and challenges in relation to the treatment of patients with multimorbidity: General practitioners' views and attitudes. Scand J Prim Health Care 2015; 33: 121-126.
38. Siegenthaler E, Munder T, Egger M. Effect of preventive interventions in mentally ill parents on the mental health of the offspring: systematic review and meta-analysis. J Am Acad Child Adolesc Psychiatry 2012; 51: 8-17.e8.
39. Inhestern L, Haller AC, Wlodarczyk O, Bergelt C. Psychosocial Interventions for Families with Parental Cancer and Barriers and Facilitators to Implementation and Use - A Systematic Review. PLoS One 2016; 11: e0156967.

Table 1. Characteristics of cohort members with and without psychosis

	Any psychosis between 16 and 28 years				
	No (n=8968)		Yes (n=169)		
	N	(%)	N	(%)	*P*
Gender of cohort member					
male	4611	(51.4)	91	(53.8)	0.536
female	4356	(48.6)	78	(46.2)	
Family socioeconomic status					
High	1573	(19.9)	24	(17.4)	0.594
Middle	1905	(24.1)	38	(27.5)	
Low	3930	(49.7)	70	(50.7)	
Farmers	493	(6.2)	6	(4.3)	
Perinatal complications					
no	8394	(93.6)	156	(92.3)	0.524
yes	574	(6.4)	13	(7.7)	
Father's age at child's birth (Mean (sd))	30.7	(6.0)	30.9	(6.4)	0.698
Have tried/used cannabis at age 16					
no	6118	(94.4)	93	(85.3)	<0.001
yes	361	(5.6)	16	(14.7)	
Any parental hospital-treated mental, behavioural or neurodevelopmental disorder when the offspring was below 18 years of age	1400	(15.6)	53	(31.4)	<0.001

Table 2. Parental illnesses occurring at age below 18 years of cohort members in association with psychoses of cohort members between ages 16 and 28.

	Any psychosis of cohort members between ages 16 and 28											
Parental somatic illnesses occurring at age	No		Yes				Model 1[2]			Model 2[3]		
below 18 years of cohort members	N	(%)	N	(%)	p	B-Hp[1]	OR	(95 % CI)	p	OR	(95 % CI)	p
Mother												
Neoplasms	984	(11.0)	26	(15.4)	0.082	0.861	0.93	(0.48-1.81)	0.828	0.92	(0.47-1.79)	0.805
Injury, poisoning and certain other consequences of external causes	916	(10.2)	27	(16.0)	0.017	0.357	1.04	(0.53-2.02)	0.918	1.00	(0.51-1.96)	0.995
Father												
Certain infectious and parasitic diseases	367	(4.1)	14	(8.3)	0.012	0.126	1.83	(0.79-4.24)	0.162	1.88	(0.81-4.38)	0.141
Neoplasms	309	(3.5)	14	(8.3)	0.003	0.063	2.73	(1.34-5.57)	0.006	2.75	(1.35-5.62)	0.006
Diseases of the nervous system	613	(6.9)	18	(10.7)	0.064	0.224	1.61	(0.85-3.34)	0.146	1.58	(0.82-3.01)	0.169
Diseases of the digestive system	1285	(14.4)	35	(20.8)	0.021	0.110	1.63	(0.99-2.68)	0.053	1.61	(0.98-2.65)	0.060
Injury, poisoning and certain other consequences of external causes	1431	(16.1)	36	(21.4)	0.072	0.216	1.59	(0.98-2.59)	0.061	1.62	(0.99-2.63)	0.054
External causes for morbidity	761	(8.6)	23	(13.7)	0.026	0.109	1.46	(0.79-2.71)	0.228	1.49	(0.81-2.77)	0.204
Factors influencing health status and contact with health services	340	(3.8)	13	(7.7)	0.015	0.105	2.67	(1.35-5.26)	0.005	2.66	(1.35-5.27)	0.005
Either parent												
Certain infectious and parasitic diseases	706	(7.9)	22	(13.0)	0.017	0.119	1.62	(0.86-3.08)	0.138	1.63	(0.85-3.44)	0.136
Neoplasms	1253	(14.0)	38	(22.5)	0.002	0.042	1.39	(0.82-2.36)	0.219	1.38	(0.82-2.35)	0.146
Diseases of the digestive system	2195	(24.5)	54	(32.0)	0.030	0.158	1.41	(0.91-2.20)	0.129	1.42	(0.91-2.21)	0.122
Injury, poisoning and certain other consequences of external causes	2174	(24.2)	55	(32.5)	0.015	0.158	1.25	(0.79-1.97)	0.340	1.25	(0.79-1.98)	0.333
External causes for morbidity	1647	(18.4)	42	(24.9)	0.036	0.151	1.08	(0.65-1.81)	0.765	1.07	(0.64-1.79)	0.789

[1] Benjamini-Hochberg corrected p-value

[2]Adjusted for gender of cohort member, parental socioeconomic status, father's age and parent's psychiatric morbidity

[3] Adjusted for gender of cohort member, parental socioeconomic status, father's age, parent's psychiatric morbidity, perinatal complications and information about use of cannabis at age 16

Table 3. Accumulation of different somatic illness categories of parents of cohort members with and without psychosis.

	Any psychosis, 16 to 28 years								
	No				Yes				
	Mean	(SD)	Median	(IQR)	Mean	(SD)	Median	(IQR)	*P* (Mann-Whitney U)
Mother sum	1.89	(1.71)	2.00	(1.00-3.00)	2.07	(1.63)	2.00	(1.00-3.00)	0.081
Father sum	1.22	(1.47)	1.00	(0.00-2.00)	1.65	(1.76)	1.00	(0.00-3.00)	0.004
Parents sum	2.95	(2.09)	3.00	(1.00-4.00)	3.45	(2.16)	3.00	(2.00-5.00)	0.002