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Do adverse perinatal events predict mortality in schizophrenia during midlife?

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ABSTRACT

Background: We examined mortality in schizophrenia spectrum disorder (SSD) and non-schizophrenic psychosis (NSSD) compared to individuals without psychosis, and whether perinatal factors predict mortality.
Methods: Within Northern Finland Birth Cohort 1966 (n = 10 933; 203 with SSD, 178 with NSSD), mortality was followed until end of 2011 by national register. Wantedness of pregnancy, mother's antenatal depression, smoking and age, parity, paternal socio-economic status (SES) and family type at birth were examined as predictors of mortality.
Results: Mortality was higher in SSD (hazard ratio (HR) 3.60; 95% confidence interval (CI) 2.38–5.45) and NSSD (4.05; 2.65–6.17) compared to persons without psychoses after adjustment for gender. HR for natural death was 2.01 (0.82–4.91) in SSD and 4.63 (2.43–8.80) in NSSD after adjustment for gender. Corresponding figures for unnatural deaths were 4.71 (2.94–7.54) and 2.94 (1.56–5.55), respectively. Among non-psychotic persons, mother's depression, smoking and low SES predicted mortality after adjustment for gender and parental psychoses (and SES), whereas among psychosis those whose father was a farmer had lower risk of mortality compared to those with high SES.
Conclusions: Individuals with SSD had a higher risk of unnatural death and individuals with NSSD of natural and unnatural deaths. Perinatal factors seem to be more important predictors of mortality in individuals without psychoses than with psychoses. According to population-based long follow-up data, it is important to pay attention to somatic morbidity behind natural causes of death in psychoses and to prevent suicides in order to prevent excess mortality.

1. Introduction

Excess mortality in psychotic disorders is a major public health concern and therapeutic challenge (Crump et al., 2013b; Saha et al., 2007; Termorshuizen et al., 2013; Walker et al., 2015; Ösby et al., 2000). Individuals with psychotic disorders have over a 2- to 4-fold higher all-cause mortality risk than the general population (Crump et al., 2013b; Høye et al., 2011; Kiviniemi et al., 2010; Lumme et al., 2016; Olfson et al., 2015; Saha et al., 2007; Termorshuizen et al., 2013) and their life expectancy is 10–25 years lower (Crump et al., 2013b; Tiihonen et al., 2009). Furthermore, those differences are continuing into old age (Talaslahti et al., 2015).

The mortality rate is higher for natural and unnatural causes (Crump et al., 2013b; Kiviniemi et al., 2010; Reininghaus et al., 2015; Ösby et al., 2000). Common natural causes of death in schizophrenia are diseases of the circulatory system (Brown et al., 2000; Bushe et al., 2010; Crump et al., 2013b; Kiviniemi et al., 2010; Ösby et al., 2000), neoplasms (Brown et al., 2000; Bushe et al., 2010; Crump et al., 2013b; Ösby et al., 2000), diabetes (Crump et al., 2013b; Schoepf et al., 2014) and respiratory illnesses (Crump et al., 2013b; Kredentser et al., 2014; Termorshuizen et al., 2013; Ösby et al., 2000). About 2-fold ischemic heart disease and 1.5-fold cancer mortality risks have been shown in schizophrenia

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compared to the rest of the population (Crump et al., 2013b). Diseases of the digestive system, especially alcohol-related ones are also common causes of death (Reininghaus et al., 2015). From the unnatural causes of death, the leading cause is suicide (Brown et al., 2000; Reininghaus et al., 2015) with the risk being 12- to 20-fold compared to the general population (Reininghaus et al., 2015; Saha et al., 2007; Ösby et al., 2000). Most of the suicides are committed during the first years after the onset of psychoses (Alaräisänen et al., 2009; Ösby et al., 2000). The risk for accidental/injury deaths is also higher for schizophrenia sufferers than the general population (Crump et al., 2013a; Crump et al., 2013b; Kredentser et al., 2014).

Few studies have examined differences in mortality in schizophrenia and non-schizophrenic psychoses (Castagnini et al., 2013; Healy et al., 2012). Individuals with schizophrenia may die younger than those with other psychotic disorders (Healy et al., 2012), but natural-cause mortality did not differ between schizophrenia and acute and transient psychotic disorders (ATPD) (Castagnini et al., 2013). However, individuals with ATPD were more likely to commit suicide during the first year following the initial episode than individuals with schizophrenia (Castagnini et al., 2013).

Suggested reasons for excess mortality are unhealthy lifestyle (Connolly and Kelly, 2005; Laursen et al., 2012; Ringen et al., 2014; Suvisaari et al., 2013) and use (Joukamaa et al., 2006) or non-use of antipsychotics (Tiihonen et al., 2016; Torniainen et al., 2015). Studies have mainly focused on predictors of mortality prevalent in the later stages of life (Fazel et al., 2014; Joukamaa et al., 2006; Suvisaari et al., 2013; Tiihonen et al., 2016) reporting that self-harm, alcohol/drug use disorders (Fazel et al., 2014), older age at onset of schizophrenia, long duration of illness and inability to work are predictors of mortality (Ran et al., 2007). More information also from earlier stages of life is needed. As far as we know, paternal older age in women (Miller et al., 2010) and lower maternal education have predicted mortality in psychoses (Dickerson et al., 2016). Furthermore, birth complications in men have predicted mortality in psychoses (Fazel et al., 2014). Because deviances in environment in early life are risk factors for schizophrenia (Laurens et al., 2015; Matheson et al., 2011), it is important to study whether they also predict prognosis of psychoses.

The aim of this study was to examine mortality and causes of death in schizophrenia spectrum disorder (SSD) and non-schizophrenic psychoses (NSSD) compared to individuals without psychosis and whether perinatal circumstances predict mortality in all psychoses. We hypothesized that unwanted pregnancy, mother's antenatal depression and smoking, mother's young or old age, low or high parity, low paternal socio-economic status (SES) and single-parent family at birth would increase the risk of mortality.

2. Methods

This study is based on the Northern Finland Birth Cohort 1966 (NFBC1966) concerning 12,058 live-born children in 1966 in the provinces of Oulu and Lapland (Rantakallio, 1969). Individuals, who were alive and living in Finland at the age of 16 years (n = 11,017) were included in this study. Overall, 84 of them denied use of their data, thus leading to the sample of 10,933 individuals. Study design was approved by the Ethical Committee of the Northern Ostrobothnia Hospital District, and Ministry of Social and Health Affairs gave permission to gather the data.

2.1. Psychoses

Psychoses are based on the registers of Statistics Finland (Care Register for Health Care (CRHC), formerly the Finnish Hospital Discharge Register, followed until the end of 2011, the Register of Specialty Outpatient Health Care from 1998 until 2011 and Primary Care Outpatient Register from 2011) and Register of the Finnish Centre for Pensions (FCP) until 2011 and the Registers of the Social Insurance Institution (reimbursed medicine until 2005, pension until 2000 and sick days until the end of 1999).

Individuals were classified as having SSD (ICD-8 (1968–1986): 295, ICD-9 (1987–1995): 295, 2954, 2957, 297 and ICD-10 (1996–2013): F20, F22, F25), other NSSD (psychotic bipolar disorder (ICD-8: 2961–2969, ICD-9: 2962E, 2963E, 2964E, 2967, ICD-10: F30.2, F31.2, F31.5)) psychotic depression (ICD-8: 2960, 2980, ICD-9: 2961E, ICD-10: F32.3, F33.3) brief/reactive psychosis (ICD-8: 2981–2983, 2988, 2989, ICD-9: 2988, ICD-10: F23) and other psychosis (ICD-8: 299, ICD-9: 2989, ICD-10: F28, F29)) and without psychosis. Overall, 203 individuals had SSD (narrow ICD-8 & 9: 2950–2953, 2955, 2956, 2958, 2959, 295, ICD-10: F20 n = 149, spectrum ICD-8 & 9: 2954, 2957, 297, ICD-10: F22, F24, F25 n = 54) and 178 NSSD (psychotic bipolar disease n = 22, psychotic depression n = 62, brief or reactive psychosis n = 29 and undefined other psychosis n = 65). For further analyses, SSD and NSSD were combined as having psychosis.

2.2. Causes of mortality

Information on time and causes of death until 31st December 2011 were obtained from the Cause of Death Register from the Statistics Finland. The register contains data from death certificates (Lahti and Penttilä, 2001). Causes of death were classified according to ICD-8, 9 or 10, depending on the time of the death (Table 2). From the external causes of morbidity and mortality, suicide or intentional self-harm was classified in its own class. Classes from infections to congenital malformations, deformations and chromosomal abnormalities were classified as natural and classes concerning external causes of morbidity/mortality and suicide to unnatural causes of death (Table 2). Classes concerning symptoms, signs and abnormal clinical findings and no basic statistical cause of death were defined as unknown causes of death.

2.3. Predictors of mortality

We selected as predictors of mortality the same variables from perinatal circumstances, which have been studied earlier as predictors of suicides in the NFBC1966 (Alaräisänen et al., 2012). Data on perinatal circumstances were gathered by interviews conducted by nurses with the help of questionnaires during mothers' visits to antenatal clinics at gestation weeks of 24–28 and from the Population Register Centre (PRC).

Wantedness of pregnancy was asked with the question, whether mothers had wanted the pregnancy, would have preferred it later or had not wanted. Responses were dichotomized to wanted/mistimed or unwanted (Myhrman et al., 1996).

Mother's antenatal depressed mood was asked with the question, whether they felt that their mood was normal, depressed or very depressed during pregnancy. Responses were classified to normal and depressed (Alaräisänen et al., 2012).

Mother's smoking during pregnancy was classified as no, if she did not smoke or had stopped before the pregnancy and yes, if she had smoked at least one cigarette daily (Mäki et al., 2010).

Mother's age at birth was received from the PRC and was classified as under 20 years, 20–35 years and over 35 years (Keskinen et al., 2013).

Parity at birth was classified as 1, 2–5 and over 5 (Alaräisänen et al., 2012).

Family type at birth was based on the marital status of the mother during pregnancy (married, divorced, widowed and never married) and was classified as two-parent families (full) or single-parent families (Alaräisänen et al., 2012).

SES at birth was based on the father's occupation and were classified as high (classes I and II), low (classes III and IV) and farmers (class V) (Alaräisänen et al., 2012).

Parental psychosis was deemed as yes if one of the parents had any psychosis (i.e. ICD-8: 295–299; ICD-9: 295, 2961E, 2962E, 2963E, 2964E, 2967 and 297–299; ICD-10: F20 and F22-F29) based on the CRHC (1972–2012), Specialized Outpatient Care Register (1998–2012), Register of Primary Health Care Visits (2011 — 2012), and FCP (disability pensions, 1964–2011).

Duration of illness was calculated by using the date of death and the date of onset of psychosis based on the registry entry.

2.4. Statistical analyses

Analyses were conducted by IBM SPSS Statistics 22 (SPSS., Inc., and IBM company, 1989, 2013). Gender, perinatal circumstances, parental psychosis and causes of death between individuals with SSD, NSSD and without psychoses were examined by using cross-tabulation and χ^2- exact tests. Cox regression analyses were used to examine mortality according to perinatal circumstances, after adjustment for gender, parental psychosis and SES at birth in psychoses and without psychoses. Natural and unnatural death were examined according to duration of illnesses in SSD and NSSD. The results are expressed as hazard ratios (HRs) with 95% confidence intervals (95% CIs). Date of death, date of emigration or end of the follow-up 31st December 2011 was set as an end-point, whichever came sooner in the analyses. Furthermore, interactions between statistically significant predictors and diagnosis groups in psychoses (SSD vs. NSSD) were tested.

3. Results

Individuals with SSD were more often men and unwanted during pregnancy than those without psychoses (Table 1). Mothers of individuals with NSSD were more often smokers during pregnancy than those without psychoses. Overall, persons with psychosis were more often the offspring of mothers with antenatal depression and the offspring of a parent with psychoses (Table 1).

3.1. Mortality and causes of death

Overall, 3.5% of cohort members had died by the age of 45 years: 11.8% with SSD, 12.9% with NSSD and 3.2% without psychoses (Table 2, Fig. 1). Mortality risk was 3.60-fold (95% CI 2.38–5.45) in SSD and 4.05-fold (95% CI 2.65–6.17) in NSSD compared to those without psychosis after adjustment for gender. Overall, mortality risk was 3.80-fold (95% CI 2.80–5.16) in all psychoses compared to those without psychosis after adjustment for gender.

20.8% of deaths were due to natural causes among individuals with SSD, 43.5% among those with NSSD and 38.6% among those without psychoses. Corresponding figures for unnatural causes were 79.2% 43.5% and 59.0%, respectively (Table 2). Individuals with SSD had 2.01-fold (95% CI 0.82–4.91) and NSSD 4.63-fold (95% CI 2.43–8.80) risk for natural death compared to non-psychotic individuals after adjustment for gender. Correspondingly, persons with SSD had 4.71-fold (95% CI 2.94–7.54) and NSSD 2.94-fold (95% CI 1.56–5.55) risk for unnatural death. Overall, the risk of natural (HR 3.23, 95% CI 1.89–5.51) and unnatural death (HR 3.90, 95% CI

Table 1
Gender, perinatal circumstances and parental psychosis in schizophrenia spectrum disorder (SSD), non-schizophrenic psychosis (NSSD), all psychosis and no psychosis at the Northern Finland Birth Cohort 1966 (χ^2- exact test).

	SSD (1) n = 203		NSSD (2) n = 178		All psychoses (3) n = 381		No psychosis (4) n = 10,552		1 vs. 4 p-value	2 vs. 4 p-value	3 vs. 4 p-value
	n	%	n	%	n	%	n	%			
Gender											
Men	118	58.1	96	53.9	214	56.2	5375	50.9	0.047	0.450	0.047
Women	85	41.9	82	46.1	167	43.8	5177	49.1			
Wantedness of pregnancy											
Wanted/mistimed	160	81.6	144	84.2	304	82.8	9080	88.4	0.005	0.117	0.002
Unwanted	36	18.4	27	15.8	63	17.2	1197	11.6			
Mothers' antenatal depressed mood											
Normal	160	81.6	141	81.5	301	81.6	8871	86.2	0.075	0.076	0.012
Depressed	36	18.4	32	18.5	68	18.4	1417	13.8			
Mother's smoking during pregnancy											
No	169	87.1	131	78.0	300	82.9	8628	85.1	0.477	0.012	0.260
Yes	25	12.9	37	22.0	62	17.1	1506	14.9			
Mother's age at birth											
<20 years	16	7.9	17	9.6	33	8.7	994	9.4	0.293	0.992	0.602
20–35 years	145	71.4	132	74.2	277	72.7	7764	73.7			
>35 years	42	20.7	29	16.3	71	18.6	1771	16.8			
Parity at birth											
1	66	32.7	52	29.4	118	31.1	3381	32.1	0.113	0.342	0.060
2–5	103	51.0	98	55.4	201	53.0	5910	56.1			
6 or more	33	16.3	27	15.3	60	15.8	1246	11.8			
Family type at birth											
Full	193	95.1	168	94.4	361	94.8	10,187	96.5	0.331	0.143	0.066
Single	10	4.9	10	5.6	20	5.2	365	3.5			
Paternal socio-economic status at birth											
High (I–II)	18	8.9	8	4.5	26	6.8	763	7.3	0.171	0.366	0.517
Low (III–IV)	155	76.7	134	75.3	289	76.1	7719	73.5			
Farmer (V)	29	14.4	36	20.2	65	17.1	2023	19.3			
Parental psychosis											
No	169	83.3	148	83.1	317	83.2	9878	93.6	<0.001	<0.001	<0.001
Yes	34	16.7	30	16.9	64	16.8	674	6.4			

Table 2
Causes of death (according to ICD-8, 9 and 10 categories) in individuals with schizophrenia spectrum disorder (SSD), non-schizophrenic psychoses (NSSD) and without psychoses (M = men, W = women).

	SSD n = 24 (M/W:18/6)		NSSD n = 23 (M/W:20/3)		All psychoses n = 47 (M/W:38/9)		No psychoses n = 339 (M/W:249/90)	
	n	%	n	%	n	%	n	%
Infections	0	0	0	0	0	0	1	0.3
Neoplasms	0	0	2	8.7	2	4.3	37	10.9
Endocrine, nutritional and metabolic diseased	0	0	2	8.7	2	4.3	5	1.5
Mental, behavioural and neurodevelopmental diseases[a]	1	4.2	0	0	1	2.1	6	1.8
Diseases of the nervous system	0	0	0	0	0	0	14	4.1
Diseases of the circulatory system	4	16.7	4	17.4	8	17.0	35	10.3
Diseases of the respiratory system	0	0	0	0	0	0	8	2.4
Diseases of the digestive system	0	0	2	8.7	2	4.3	16	4.7
Diseases of the musculoskeletal system and connective tissue	0	0	0	0	0	0	2	0.6
Diseases of the genitourinary system	0	0	0	0	0	0	1	0.3
Pregnancy childbirth and the puerperium	0	0	0	0	0	0	2	0.6
Congenital malformations, deformations and chromosomal abnormalities	0	0	0	0	0	0	4	1.2
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified[b]	0	0	3	13.0	3	6.4	0	0
External causes of morbidity/mortality	8	33.3	2	8.7	10	21.3	116	34.2
Suicides	11	45.8	8	34.8	19	40.4	84	24.8
No basic statistical cause of death	0	0	0	0	0	0	8	2.4

[a] Cause of death was alcohol dependence in all 7 cases.
[b] Cause was unspecified cause of mortality in all three individuals.

2.64–5.76) was higher in psychosis than non-psychosis after adjustment for gender. Fig. 2 presents natural and unnatural mortality according to duration of illness in individuals with SSD and NSSD.

3.2. Parental psychoses and perinatal circumstances as predictors of mortality in individuals with psychosis or without psychoses

Parental history of psychoses did not seem to predict mortality in psychoses (HR 1.28, 95% CI 0.62–2.66) contrary to non-psychoses (HR 1.74, 95% CI 1.23–2.47) after adjustment for gender. In individuals with psychoses, those whose father belonged to SES class of farmers (V) had a lower risk of mortality than individuals, whose father belonged to a high SES class (I–II) even after adjustment for gender and parental psychoses (Table 3). There was no interaction between paternal SES and diagnosis of psychoses. In individuals without psychoses, mother's antenatal depression, mothers smoking during pregnancy and SES (III–IV, V) predicted higher mortality even after adjustments (Table 3).

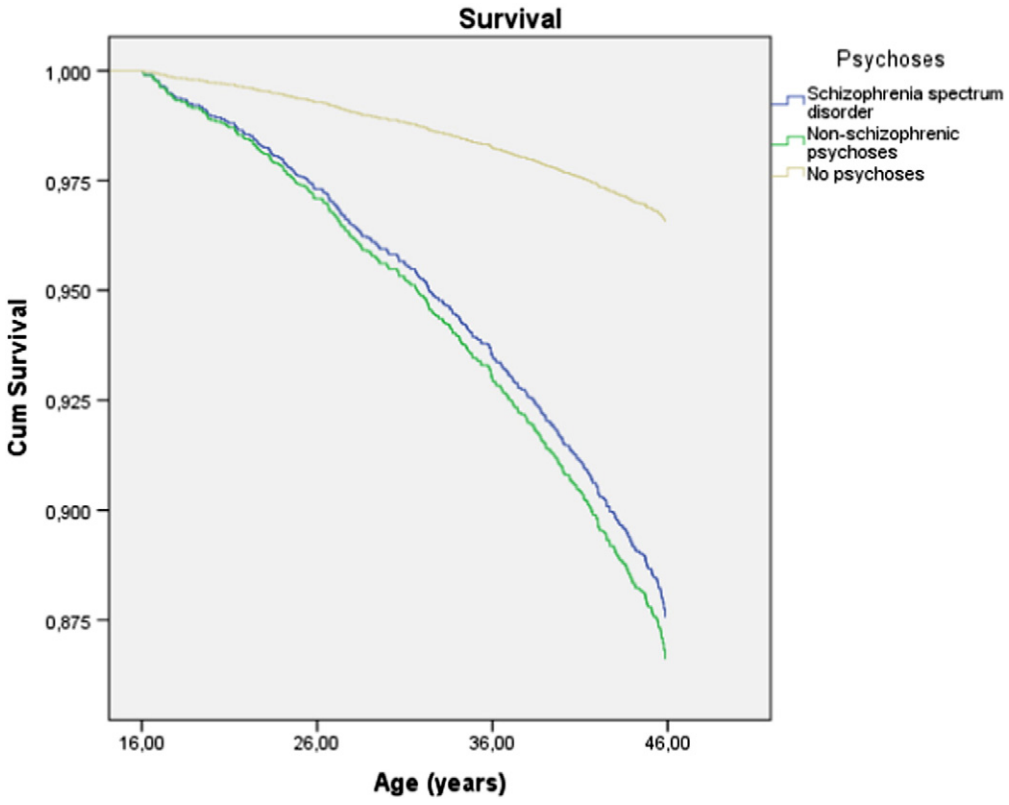

Fig. 1. Survival curve for all-cause mortality in individuals with schizophrenia spectrum disorder (SSD), other non-schizophrenic psychoses (NSSD) and without psychoses by the age of 45 years until the end of 2011.

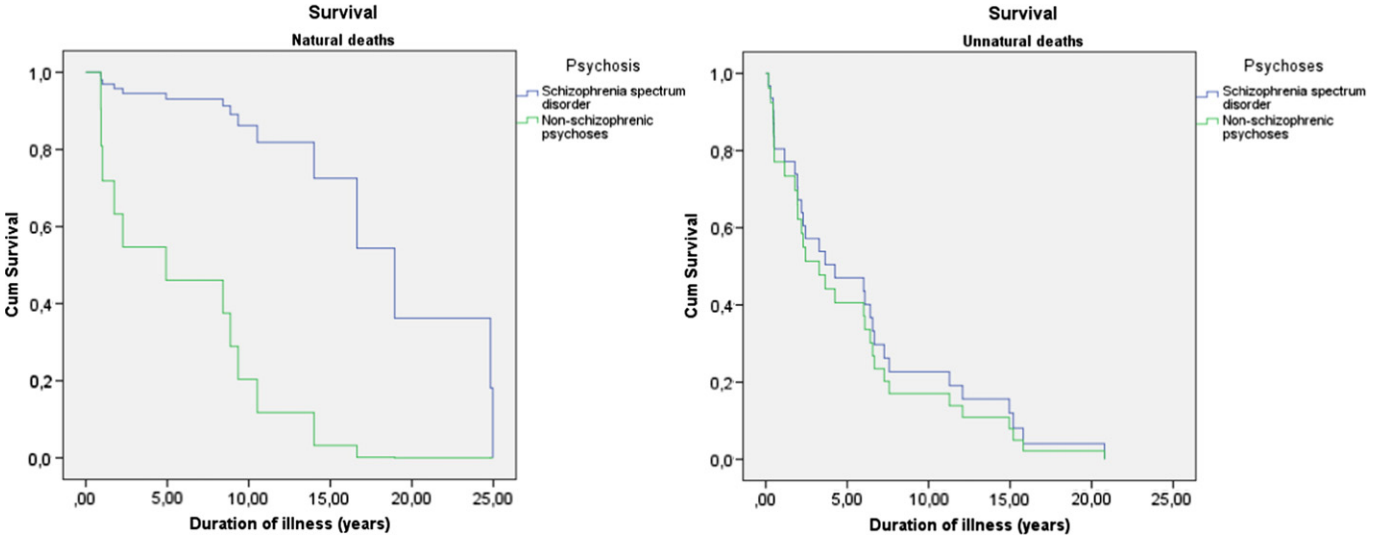

Fig. 2. Natural and unnatural mortality from the onset of psychoses according to schizophrenia spectrum disorder (SSD) and other non-schizophrenic psychoses (NSSD).

Table 3
Perinatal circumstances as predictors of all-cause mortality until 31st December 2011 in individuals with psychoses and without psychoses in the Northern Finland Birth Cohort 1966.

All-cause mortality				
Perinatal circumstances	Psychoses		No psychoses	
	Unadjusted HR (95% CI)	Adjusted HR(95% CI)[a]	Unadjusted HR (95% CI)	Adjusted HR (95% CI)[a]
Wantedness of pregnancy				
Wanted/mistimed	1.00	1.00	1.00	1.00
Unwanted	1.02 (0.48–2.17)	1.27 (0.59–2.76)	1.31 (0.96–1.77)	1.26 (0.93–1.72)
Mothers' antenatal depressed mood				
Conventional	1.00	1.00	1.00	1.00
Depressed	1.07 (0.52–2.21)	1.12 (0.54–2.34)	1.37 (1.03–1.81)	1.33 (1.00–1.77)
Mother's smoking during pregnancy				
No	1.00	1.00	1.00	1.00
Yes	1.84 (0.95–3.56)	1.71 (0.88–3.34)	1.42 (1.07–1.86)	1.34 (1.02–1.77)
Mother's age at birth				
20–35 years	1.00	1.00	1.00	1.00
<20 years	1.19 (0.47–3.03)	1.07 (0.41–2.76)	1.23 (0.88–1.73)	1.17 (0.84–1.65)
>35 years	0.77 (0.34–1.73)	0.80 (0.35–1.82)	0.92 (0.68–1.24)	0.94 (0.69–1.28)
Parity at birth				
2–5	1.00	1.00	1.00	1.00
1	1.33 (0.71–2.51)	1.35 (0.71–2.55)	0.89 (0.70–1.14)	0.86 (0.67–1.10)
6 or more	1.25 (0.56–2.80)	1.59 (0.70–3.62)	1.30 (0.96–1.77)	1.39 (1.02–1.91)
Family type at birth				
Full	1.00	1.00	1.00	1.00
Single-parent	1.23 (0.38–3.96)	1.36 (0.42–4.44)	1.39 (0.84–2.30)	1.36 (0.82–2.24)
Paternal socio-economic status at birth				
High (I–II)	1.00	1.00[b]	1.00	1.00[b]
Low (III–IV)	0.68 (0.27–1.74)	0.68 (0.27–1.73)	2.23 (1.25–3.98)	2.25 (1.26–4.00)
Farmers (V)	0.22 (0.05–0.92)	0.19 (0.05–0.82)	1.82 (0.98–3.38)	1.87 (1.00–3.48)

HR = hazard ratio, CI = confidence interval.
[a] Adjusted for gender, socio-economic status at birth and parental psychoses.
[b] Adjusted for gender and parental psychosis.

4. Discussion

4.1. Main results

Individuals with SSD and NSSD had about a 4-fold mortality risk compared to those without psychoses. Individuals with NSSD had over 4.5-fold risk for natural death compared to non-psychotic individuals and the most common cause was diseases of the circulatory system. The risk of unnatural death was over 4.5-fold in individuals with SSD and almost 3.0-fold with NSSD compared to non-psychotic individuals. Suicide was a cause of death for nearly half of the persons with SSD, for about one third with NSSD and one quarter of those without psychoses. In individuals with psychoses, those whose father belonged to the SES class of farmers had a lower risk of mortality than individuals, whose father belonged to a high SES class. Instead, in individuals without psychoses, mother's antenatal depression and smoking during pregnancy as well as paternal low SES predicted higher mortality.

4.2. Comparison with previous research

Our results concerning excess mortality in psychosis is in line with the earlier studies (Kiviniemi et al., 2010; Kredentser et al., 2014; Reininghaus et al., 2015; Saha et al., 2007). However, our results highlight the greater occurrence of somatic diseases behind natural causes of death in NSSD compared to those without psychoses. It could be that higher natural mortality in NSSD is due to delayed diagnosis or treatment of somatic illness. For example, individuals with schizophrenia expressed physical complaints at more serious stages of the illness (Oud and De Meyboom, 2009) and despite having twice as many healthcare contacts, they were not diagnosed with ischemic heart disease, and they had elevated mortality risk due to this condition (Crump et al., 2013b).

Interestingly, individuals with psychosis, whose father was a farmer had lower mortality than individuals, whose father had a higher SES. This result may be a chance finding or partly due to living environment as individuals with schizophrenia born in rural areas may have in general better outcomes, e.g. a good employment outcome (Munk-Jørgensen and Mortensen, 1992). The result differs from our result concerning non-psychotic individuals showing that individuals with low paternal SES had a higher mortality risk than those with a high SES. This is in line with the results of the systematic review concerning the general population (Galobardes et al., 2008). The low number of individuals with psychoses whose father was a farmer may have an effect on the results and in general farms were small in 1966 in Finland. There

were more perinatal predictors of mortality in individuals without psychoses than with psychoses. It seems that deviances in early life environment may not be predictors of prognosis of psychoses. The course of psychoses during life-course is complex and does not follow the same kind of continuum as in individuals without psychoses.

4.3. Strengths and limitations of the study

The strengths of the study were that NFBC1966 was a population-based cohort study and we were able to focus also on individuals with NSSD, who are studied less often (Castagnini et al., 2013; Healy et al., 2012). Prospective collection of data was unique (Rantakallio, 1969) applying to study perinatal circumstances as predictors of mortality in a long 45-year follow-up. In studies where participants are older, mortality due to diseases is more often detected along with suicides, which are the usual causes of death during the first years after mental illness (Bushe et al., 2010; Räsänen et al., 1998; Ösby et al., 2000).

Limitations include that we were not able to study specific causes of mortality, because of the small number of cases. It may be also so that the longer the follow-up is, the worse the predictive power of early life factors, especially in individuals with psychoses, whose onset of illness was later. Mediating factors near the onset of psychoses maybe more important predictors of mortality (Suvisaari et al., 2013; Fazel et al., 2014; Joukamaa et al., 2006; Ran et al., 2007; Tiihonen et al., 2016), which was not the focus of our study. Due to the small number of deaths in women with psychoses we were not able to conduct gender-specific analyses. In addition, in the analyses there were no adjustments for multiple comparisons.

5. Conclusions

Individuals with psychosis, also in NSSD, had excess mortality compared to individuals without psychosis. As already known, individuals with SSD had a higher risk of unnatural death compared to those without psychoses. A new finding is that individuals with NSSD had over a 4.5-fold risk of natural death than individuals without psychoses. Perinatal circumstances seem to be more important predictors of mortality in individuals without psychoses than with psychoses, describing the complex trajectory of course and severity of illness in psychoses. It is important to pay attention to early diagnosis and adequate follow-up and treatment of somatic morbidity not only in SSD, but also in NSSD. In addition, we should improve access to healthcare and prevent suicides in individuals with psychoses in order to prevent their excess mortality.

Conflicts of interest

None.

Contributors

NR, JM, EJ, MI and JS designed the study. TN and NR undertook the statistical analyses. NR searched and read the literature and wrote the first version of the manuscript. All authors contributed to and approved the final manuscript.

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The funding bodies had no role in the study design, in the collection, analysis and interpretation of data, or writing of the paper.

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