Association between participation to the Northern Finland Birth Cohort 1986 and mental disorders and suicidal behaviour

~~Intervention effect of participation in the Northern Finland Birth Cohort 1986 study—Special reference to mental disorders and suicidal behaviour~~

~~Intervention effect~~Effects of participation in the NFBC 1986

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ABSTRACT

Objectives: In the prospective follow-up studies participants are normally contacted during the follow-up. Even though the idea is not to intervene, the studies conducted during follow-up may affect the target population. Our hypotheses were that the participation to prospective Northern Finland Birth Cohort 1986 study (NFBC 1986) increases the use of mental health services and reduces the suicidal behaviour due to participation in follow-up study. due to intervention effect.

Methods: The study cohort NFBC 1986 covers the people born with expected date of birth between July 1985 and June 1986 in northern Finland (N=9,396). The participants of the NFBC 1986 have been followed since antenatal time with follow-ups including clinical examinations. The comparison cohort comprises of people born in the same area in 1987 (N=8,959), who have not been contacted. Register data of psychiatric treatment, suicidal ~~at~~ attempts and suicides were available ~~for both cohorts.~~ Crude risk ratios (RR) and adjusted (with marital status and education) Mantel-Haenszel Risk Ratios (RR_{MH}) were reported.

Results: ~~In males, no significant differences between NFBC 1986 and comparison cohort in the cumulative incidences of mental disorders or in suicidal behaviour were detected. In females, decreased risk in the NFBC 1986 was found for any psychiatric disorder (RR: 0.89 (95% CI: 0.81-0.98), p=0.014) and in suicidal attempts (RR: 0.67 (95% CI: 0.49-0.92), p=0.011).~~ No significant differences between NFBC 1986 and comparison cohorts in any mental disorder were detected. In crude risk ratio analysis of female, the decreased risk for the suicide attempts was found (RR: 0.67 (95% CI: 0.49-0.92), p=0.011).

Conclusions: Results did not support our first hypothesis of increased use of mental health services in the NFBC 1986. On the other hand, our second hypothesis gained some support as female participants of the NFBC 1986 had decreased risk for suicidal ~~at~~ attempts, although it was not due to higher number of participants receiving psychiatric treatment.

Keywords: Psychiatry, Suicide, ~~Intervention effect~~ Follow-up study

1. INTRODUCTION

~~In the prospective follow-up studies study participants are contacted for personal data collection using questionnaires, interviews, and clinical examinations. Even though the idea is not to intervene in order to get a representative sample of the population, the studies conducted during follow-up may affect the target population in various ways.~~

Prospective longitudinal follow-up studies are popular study designs, in which longitudinal exposure-outcome assessments are studied. Data collection procedure include clinical examinations, questionnaires, tests, interviews, or linkage to existing data [1]. British birth cohort The Avon Longitudinal Study of Parents and Children (ALSPAC) originally consisted of pregnant women in the greater Bristol area between April 1991 and December 1992 (N=14,500). The mothers, fathers, children and grandchildren have been followed since with questionnaires and clinical examinations. [2] In Danish National Birth Cohort (DNBC) initial data collection information was collected with telephone interviews with the women during pregnancy (1996-2002), recruiting 100,000 women in early pregnancy. Afterwards the mother's and children's' have answered to multiple interviews and questionnaires. [3] There are also many newer longitudinal follow-up birth cohorts, for example the Korean Ewha Birth and Growth Study recruited 891 pregnant women in the year 2001 in Seoul. The mothers filled multiple follow-up questionnaires and the children have had check-up examinations during childhood and adolescence.[4] In the Canadian largest general population-based longitudinal The Canadian Healthy Infant Longitudinal Development (CHILD) study originally 3624 pregnant women, most partners and 3542 eligible offspring were recruited in 2008-2012. The mothers, partners and children's' have since been followed up with questionnaires, clinical examinations and blood samples. [5] In all above-mentioned birth cohorts multiple research questions have been studied in different fields of research. The follow-ups in the longitudinal birth cohort studies raises a question, could intensive follow-ups have affected to the study population in any way. Even though the idea is not to intervene in order to get a representative sample of the population, the studies conducted during follow-up may affect the target population in various ways.

~~Several studies indicate the unmet need for psychiatric treatment in population and various proportions of the psychiatric conditions or disorders have not been treated at all.~~A large Finnish population based UKKI study explored the stability and changes of mental health in adult Finnish population during 1970-1987. The study sample was followed for 16 years using questionnaires, interviews and health care registers. The association between participation in the UKKI-study and mental health care use was examined by comparing the participants to a matched control group. The

~~UKKI study participants had used the mental health care services more often than the control group during the follow-up. This result may be regarded, at least partly, as an effect of the follow-up in the UKKI-study. The possible intervention effect of the study was examined by comparing the participants to a matched control group. The UKKI study participants had used the mental health care services more often than the control group during the follow-up. This result may be regarded, at least partly, as an intervention effect of the study itself [6][3].~~

There is evidence that psychological [7][4] and social interventions [8][5] can be effective in preventing self-injurious thoughts and behaviours, but also less intense mobile- and internet-based interventions have proven to be effective [9][6]. There are also multiple successful suicide prevention programs. The National suicide prevention program in Finland was one of the successful projects, with a reduction of 9% in the incidence of suicide achieved over the entire duration of the project. Its actions included taking care of high-risk people, prevention of marginalization among young men and enhancing educational and cultural atmosphere [10][7].

~~We were able to study the association between suicidal behaviour, use of mental health services and original participation in a longitudinal study which started prospectively at antenatal time, namely the Northern Finland Cohort 1986 (NFBC 1986). We were able to study the intervention effect to use of mental health services in a longitudinal study which started prospectively at antenatal time, namely the Northern Finland Cohort 1986 (NFBC 1986).~~ The purpose of this study was to examine, if the membership of the NFBC 1986 has any effect on use of mental health services or suicidal behaviour. Our hypotheses were that the participation to NFBC 1986 would increase the use of mental health services and reduces the suicidal behaviour due to ~~intervention effect, participation to follow-up study.~~

2. MATERIALS AND METHODS

2.1 Cohorts

The study cohort NFBC 1986 covers the people born with expected date of birth between July 1st, 1985 and June 30th, 1986 in the two northernmost former provinces in Finland, Oulu and Lapland. The cohort comprises of 9,362 mothers and 9,479 children. The NFBC 1986 is a longitudinal and prospective birth cohort with several follow-ups [11][8]. In the current study, only register data of the members of NFBC 1986 were used, and not the data gathered in the follow-up studies of the NFBC 1986.

The comparison cohort comprises of all the people born in the provinces Lapland and Oulu in 1987. The comparison cohort is a subsample from the Finnish Birth Cohort 1987 (FBC 1987). FBC 1987 study follows all children survived perinatal period (were alive at 7 days from delivery) born in Finland in the year 1987. The FBC 1987 is register-based study and all the collected data were obtained from several registrars [12][9]. The members have never been contacted during the follow-up. The information of the place of birth was obtained from Medical Birth Register, currently maintained by Finnish Institute for Health and Welfare (THL).

2.2 Follow-ups in the NFBC 1986

The first NFBC 1986 follow-ups were conducted during or just after the mother's pregnancy. The follow-up included three questionnaires to mother. Additionally, clinical data from antenatal clinics was collected. The questionnaires included questions of background, smoking and alcohol use, general health, fatigue during pregnancy, and information of delivery. [11][8] (Table 1)

In the autumn of the children's first school year at age 7, the next follow-up was conducted. The follow-up was conducted by questionnaire to the parents (participation rate 90%) and it included information on children's growth, development and health, and social situation [13][10]. In the spring of the children's first school year, the next follow-up was conducted. Two questionnaires were sent to parents, one questionnaire to themselves and another for the children's teachers. Parents assessed a modified (one of the internalizing items was modified) Rutter A2 [14][11] and teachers filled in Rutter B2 [15][12] questionnaire of children's psychomotor development and behaviour. Participation rate for parents Rutter A2 was 90%, and for teachers Rutter B2 was 92%. [16][13] The Rutter scales screen the behavioural and emotional features of the child [15][12]. (Table 1)

The latest follow-up for whole cohort has been conducted at the age of 16 years. The follow-up consisted of a questionnaire (participation rate 77.9%) and clinical examination (participation rate 73.7%). The questionnaire included questions of family, school, physical health, physical activity, sexual behaviour, smoking, alcohol and use of other substances, nutrition, living habits and hobbies. The questionnaire included several psychiatric screens: 21-item PROD-screen for prodromal psychotic symptoms [17][14], The Youth Self Report (YSR) for evaluating the competencies and problems of 11-18-year-old adolescents [18][15], the Strengths and Weakness of Attention-Deficit/Hyperactivity Disorders Symptoms and Normal Behaviour Scale (SWAN) to detect ADHD symptoms [19][16] and Toronto Alexithymia Scale (TAS-20) to measure of alexithymia [20][17].

The clinical examination included, for example, weight, height, and waist-hip measurements, sitting height, spirometry, blood pressure, pulse rate, blood samples, physical activity tests and prick tests. (Table 1) In the 16-year follow-up, consent to use the collected data was asked from the adolescent and the parents.

The follow-up of the NFBC 1986 contains multiple subsamples. One of the psychiatric subsamples was based on the SWAN-screening in the 16-year follow-up, including 268 likely ADHD cases and 196 controls [21][18]. Participants were interviewed (ages 16-18 years) by Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version K-SADS-PL [22][19]. Follow-up also included several intelligence and cognitive tests (more detailed information on the supplementary text). Parents filled also a questionnaire concerning their own attention problems using the ADHD-Rating Scale-IV and background information. (Table 2)

The next psychiatric sub-sample (Oulu Brain and Mind Study I) was conducted in 2007-2010 (participants 21-24 years old) [23][20]. In total 329 of the invited 763 members of the NFBC 1986 participated. The sample was based on cases with risk of developing psychosis (familial risk for psychosis (N=78) and symptomatic risk for psychosis (N=58)) with comparison group including subjects who had been treated for a psychotic episode (N=27), those with ADHD (N=52) and a random sample of the cohort (N=80). Additionally, 34 individuals who had been participated as controls in the earlier ADHD study participated the Oulu Brain and Mind I study. Participants filled a questionnaire including questions of background information, relationships, quality of life, substance use and several psychiatric and psychological screening instruments (more detailed information on supplementary text). Clinical examination included blood sampling (DNA from blood) and urine sample (to detect use of drugs and medications). Psychiatric nurses also interviewed participants with questions of illness and treatments, Structured Interview for Prodromal Syndromes SIPS [24][24], ADHD questionnaire and The Structured Clinical Interview for DSM-IV axis I Disorders SCID I [25][22]. Structural magnetic resonance imaging MRI, diffusion-tensor imaging DTI, resting state functional MRI, Functional MRI with three different tasks: Sternberg verbal working memory task [26][23], Human Causal Learning prediction error task [27][24] and facial recognition task [28][25] were conducted to the participants. The MRI scanning was performed with 1.5T scanner and the whole procedure took 60-75 minutes. Participants also conducted several cognitive tests, of which more detailed information on is found on supplementary text. Information about the results of the MRI scan was given to the participants. (Table 2)

The next psychiatric sub study (Oulu Brain and Mind study II) was conducted at age the of 25-27 years [29][26]. The cases in the study were selected based on parental exposure to maternal cigarette smoking (N=253) and their controls were matched by maternal education and geographical region (N=218). Participants filled questionnaire including information of background factors, lifestyle, and several screening instruments (Supplement text). Structural magnetic resonance imaging MRI, diffusion tensor imaging, magnetisation transfer imaging, and resting state functional MRI, were conducted to the participants. The MRI scanning was performed with 1.5T scanner and the whole procedure took 45-60 minutes. Participants assessed also several cognitive tests (Supplement text). Blood and urine samplings were also taken. Interviews included Structured Interview for Prodromal Syndromes SIPS and Structured clinical interviews for DSM-IV axis I disorders (SCID). Information about the results of the MRI scan, cognitive-test and possible mental disorders were given to the participants. (Table 2)

NFBC 1986 includes also other sub studies. First sub study was conducted to live-born preterm children with birth weight <1750g and their controls at age of 8 years. Sub study included a neurological examination and psychological assessments [30][27]. In the Oulu Back Study, questionnaire including questions low back pain history, background factors, leisure activities and history of injuries was sent to the cohort members living in the Oulu and surroundings municipalities at age of 18-years [31][28]. The following sub-study was conducted when the cohort members were 19-22 years and 29-32 years with MRI-scan of the lumbar spine [32][29]. Subpopulation of the NFBC at age of 24-years took part to an Ester – Preterm Birth, Pregnancy and Offspring Health in Adult Life study. The study included a blood samplings, blood pressure, BMI, waist, and hip measurements [33][30]. At the age of 26 years, the gynaecological health of young women was studied, and a questions on socio-demographic and other health background factors mainly about reproduction, menstruation, and infertility was sent to a subpopulation of NFBC 1986 [34][31]. (Supplement table 1)

2.3 Final datasets of NFBC 1986 and the comparison birth cohort

From NFBC 1986 we excluded those who did not survive perinatal period (stillbirths (N=47, 0.5%) and those who died within first seven days of life (N=36, 0.4%)) in order to make the datasets comparable. After exclusions, 9396 members of NFBC 1986 (N=4839 (51.5%) males and N=4557 (48.5%) females) from the NFBC 1986 and 8959 members from the comparison group (N=4550 (50.8%) males and N=4409 (49.2%) females) were included in ~~the~~ all analysis.

2.4 Mental disorders

The focus of this study was mental disorder diagnoses from age of 2 years to 28 years. Data covers years from 1987 to 2014 in NFBC 1986 dataset and from 1989 to 2015 in the comparison dataset. The data of mental disorder diagnosis were obtained from the Care Register for Health Care (CRHC), maintained by THL. In the present study, we analysed psychiatric disorders in a broad range of ICD-diagnosed (International Statistical Classification of Diseases and Related Health Problems) psychiatric disorders classified into several classes (Supplement Table 2). We used ICD-9 (from the year 1987-1995) and ICD-10 (1996-2015) classifications. The CRHC is one of the oldest individual level hospital discharge registers and it has nationwide hospital discharge information on inpatient visits starting from year 1967. From 1998 onwards, the register also includes the information on specialized outpatient care. We used specialized outpatient care diagnoses from age of 13 to 28 years (in NFBC from 1998 and in [the](#) comparison cohort from 2000). By law, all hospitals are obligated to report all inpatient care. The outpatient care data cover public hospitals only. Several studies indicate that the register quality of CRHC is high [\[35\]](#)~~[32]~~.

2.5 Suicidal behaviour

Suicidal behaviour was studied with two outcome variables: suicide attempts (including self-harm) and suicides from 2 to 28 years of age. The CRHC was used to identify patients who had a diagnosis (primary diagnosis, secondary diagnosis, or external cause diagnosis) of ~~suicide~~[suicidal](#) attempts: self-harm or ~~suicide~~[suicidal](#) attempt (Supplement table 1). Death by suicide was defined by using the relevant statistical underlying causes of death diagnoses, obtained from the Cause of Death Registers at Statistics Finland (Supplement table 1).

2.6 General characteristics

We used marital status and education as confounding factors. Information of marital status at age of 28 years was obtained from Central Population Register and was classified into two classes: married and single. Education indicated the highest achieved education at age of 28 years (secondary education or less and tertiary education). The information of the education was obtained from Statistics Finland.

2.6.7 Statistical analysis

The prevalence's of the general characteristics are reported, and difference was estimated with chi-square test (χ^2). Cumulative incidences of mental disorders and suicidal behaviour at age of 2 to 28 years were calculated for both cohorts (NFBC 1986 and comparison cohort) and the difference was estimated with chi-square test (χ^2). The ~~relative risks~~ Risk Ratios (RR) with 95% confidence intervals

(CI) were calculated by sex separately in each diagnosis groups where number of cases was large enough. Additionally, Mantel-Haenszel Risk Ratio (RR_{MH}) was used to calculate the adjusted risk ratios (adjusted with general characteristics: education and marital status) in each diagnosis groups where number of cases within each adjustor was large enough. The numbers of suicide attempts within each general characteristic were too low to be analysed with RR_{MH} . Analysis were performed using R version 1.4.1106.

3. RESULTS

Table 3 summarizes the general characteristics of the NFBC 1986 and comparison cohort by sex. More female participants of the NFBC 1986 were married compared to female participants of comparison cohort (χ^2 : 5.49 (p=0.019)).

In males no significant differences in mental disorders were found between NFBC 1986 and the comparison cohort (Table 34). In females, a decreased risk in NFBC 1986 was found in several diagnosis classes: Any psychiatric or neurodevelopmental disorder (RR: 0.89 (0.81-0.98), p=0.014); Schizophrenia, schizotypal and delusional disorders (RR: 0.67 (0.48-0.92), p=0.016); Other non-affective psychosis (RR: 0.67 (0.48-0.92), p=0.014); Neurotic, stress-related and somatoform disorders (RR: 0.78 (0.68-0.90) p<.001); Anxiety disorder (RR: 0.79 (0.66-0.96), p=0.015); Post-Traumatic stress disorder (RR:0.60 (0.41-0.88), p=0.008) and in Learning and coordination disorders (RR: 0.48 (0.31-0.77), p=0.002) (Table 5). After adjusting the risk ratios with education and marital status, the decreased risk was found in Neurotic, stress-related and somatoform disorders (RR_{MH} : 0.80 (0.70-0.91), p=0.001); Anxiety disorder (RR_{MH} : 0.81 (0.67-0.98), p=0.029); Post-Traumatic stress disorder (RR_{MH} : 0.61 (0.42-0.90), p=0.011) and in Learning and coordination disorders (RR_{MH} : 0.52 (0.33-0.82), p=0.004) (Table 5).

No significant differences were found in suicidal behaviour for males between NFBC 1986 and the comparison cohort. In females there was a decreased risk for suicide attempt in the NFBC 1986 (RR: 0.67 (0.49-0.92, p=0.011). The numbers of suicides were too low to be analysed: six in NFBC 1986 (0.1%) and five in the FBC 1987 (0.1%). (Table 56)

4. DISCUSSION

The results did not support our first hypothesis, of increased use of mental health services in the NFBC 1986. On the other hand, our second hypothesis gained some support as female participants of

the NFBC 1986 had a decreased risk for suicidal attempts - but it was not due to a higher number of participants receiving psychiatric treatment.

The ~~participation follow-up studies or interventions~~ in the NFBC 1986 did not increase the use of mental health services, rather the opposite occurred in females. The female members of NFBC 1986 did seek help for mental health problems less than the comparison cohort and therefore had less psychiatric diagnoses in healthcare registers. Previous Finnish psychiatric UKKI study found ~~an possible intervention association effect of between participation in a follow-up study and use of ing mental~~ health care services, when study participants had used more psychiatric care services than comparison group. The difference found in UKKI study was possibly due to psychiatric interviews conducted to study participants [6][3]. On the other hand, in a previous study ~~intervention effect of participation in the Northern Finland Birth Cohort 1966 (NFBC 1966) was not associated with for the use of mental health services was found neither in males nor in females [36][33]~~. However, the ~~interventions follow-ups in that birth cohort~~ the NFBC 1966 were less intensive in childhood and adolescence than in the NFBC 1986.

Several studies report higher levels of mental health care utilization among women [37][34]. Gender differences in the use of mental health services have been associated with gender-specific patterns in the pathology of mental disorders; women suffer more anxiety and depressive disorder, men more impulsive and addictive problems [38][35]. The gender difference in the use of mental health care has been explained in the difference in the need for care, but also with an attitudinal differences, psychosocial factors and associations with a number of socioeconomic and family-related determinants [39][36]. Above findings might be associated to our findings. The follow-up of the NFBC 1986 might affect to female differently than males.

Computer-assisted and internet-based treatments (e-interventions) for anxiety disorder and depression have grown over the past decades and previous findings substantiate the efficacy of e-interventions for adult and youth anxiety and depression [40][37]. Internet based psychotherapy for anxiety disorder and depression have been proven to be clinically effective, with outcomes equivalent to face-to-face psychological therapies [40,41][37,38]. For example, internet based myCompass program (a fully-automated, self-help, public health intervention) reduces symptoms for individuals with mild-to-moderate depression, anxiety and stress [42][39]. The effective treatment for anxiety disorder does not need to be long-term and intensive. Very light interventions have been found to be effective. This might be one explanation of the finding of the present study: the contact and questionnaires used in the NFBC 1986 might have helped some participants with mild anxiety and stress symptoms, as decreased risk for anxiety disorder and post-traumatic stress disorder was found

in the NFBC 1986. A limitation of our study was that we had no data on the use of primary health care services, and thus on e-interventions.

Learning disorders are usually diagnosed in early school years and the DSM-IV describes the learning disorders as follows: when the individual's achievement on individually administered standardized tests is substantially below that expected for age, schooling, and level of intelligence [43][40]. In the NFBC 1986 first follow-ups after antenatal time were conducted in the children's first school year: in the autumn parents filled questionnaire of children's growth and development, and in spring parents and teachers evaluated the children's behaviour with Rutter scale.

It is rather difficult to explain results of schizophrenia and other non-affective psychosis. In the NFBC 1986 the incidence of these disorders was significantly lower than in the FBC 1987. It is very unlikely that any light intervention would affect the incidence of severe psychiatric illnesses. Nevertheless, the finding in non-affective psychosis was not, in line with our hypothesis.

Our second hypothesis was partly supported by the suicidal behaviour findings. Suicidal behaviour was in lower in female NFBC 1986 members, but that was not due to higher incidence in using mental health services. The effect of interventions to suicidal behaviour has been previously reported. The intervention does not need to be intensive to be effective, for example, media disposes of an important leverage to influence suicide rates by reporting of suicides. Also, an awareness programs has been reported to be successful in preventing suicides [44][41].

4.1 Strengths

To our knowledge the ~~possible intervention-effects~~ of participation in prospective epidemiological study is rarely studied. The data used in this study were from the Finnish registers, which have been found to be high quality. The quality of CRHC is high [35][32] and the coding of causes of death for mortality statistics is appropriate with a sincere quality coding process [45][42]. ~~The study population and comparison cohort were born in the same area one to two year apart, so it could assume that the sociodemographic background factors did not vary across the cohorts.~~ The response rate in the NFBC 1986 can be considered high, since poor response rates in follow-up cohort studies is causing increasing concern [46][43].

4.2 Limitations

Even though the follow-up in the NFBC includes many questionnaires and a clinical examination, only a few of the themes were focused on psychiatric measurements. Although the NFBC is a relatively large cohort, the numbers of suicides was too low for analyses. Also, the prevalence's were

relatively low in some diagnostic group in both NFBC 1986 and comparison cohort, which could have led to false positive.

4.3 Conclusion

The participation in NFBC 1986 cohort study did not increase the use of mental health services, rather the opposite occurred in females. The Northern Finland Birth Cohort 1986 may not be completely representative on the population level in terms of psychiatric outcomes. The effects of participation in epidemiological follow-up studies have been under-examined earlier, and the results need to be replicated. The follow-up studies conducted to the participants might be considered as interventions. The possible intervention effect of participation in epidemiological follow-up studies has been under-examined earlier, and the results need to be replicated.

STATEMENTS

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Conflicts of Interest

None

Ethical statement

The Northern Finland Birth Cohort 1986 is kept under review by the ethical committee of the Northern Ostrobothnia Hospital District. Register-based 1987 Finnish Birth Cohort obtained ethics approval of the Finnish Institute for Health and Welfare (Ethical committee §28/2009).

Authors Contributions

Conceptualization: MK JV MG. Data curation: MK. Formal analysis: MK. Methodology: MK MG JV. Project administration: JV. Writing – original draft: MK. Writing – review & editing: MK, MG, JV.

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Table 1. Follow-ups of the Northern Finland Birth Cohort 1986 (NFBC 1986).

Age (main reference)	Target Population N	Questionnaire data (Participation rate)	Psychiatric items in the Questionnaires	Clinical Examination (Participation rate)
Antenatal time [8]	All births in the area N=9575	Questionnaire of family's background information for mothers N=9479 (99%)	Maternal fatigue, alcohol use and smoking during pregnancy. Paternal alcohol use and smoking	N/A
7 year [10]	N=9357	Questions of children's growth, development and health, school and family type and social situation from parents N=8416 (90%)	N/A	N/A
8 year [10]	N=9357	N=8525 (91.7%) assessed by teachers, N=8370 (90.0%) assessed by parents	Teachers assessed the children's behaviour with the Rutter B2 scale. Parents filled the modified Rutter A2 scale and questions of children's psychomotor development and behaviour	N/A
15-16 years	N=9340	Family, friends, school, health, behaviour, nutrition, physical activity, living habits and hobbies from adolescent (N= 7182, 71.9%), Of adolescent's health, development and behaviour from parents (N=6866, 75.5%)	PROD-screen for prodromal psychotic symptoms, The Youth Self Report (YSR), The Strengths and Weaknesses of Attention-Deficit/Hyperactivity Disorder Symptoms and Normal Behaviour Scale (SWAN), Toronto Alexithymia Scale (TAS-20) . Smoking and use of alcohol and other substances	Weight, height, waist-hip measurements, spirometry, blood pressure, pulse rate, blood samples., physical activity, prick tests, and questions of puberty, nutrition, use of intoxicants N=6795 (73.5%)

Table 2 Psychiatric sub-studies of the NFBC 1986

Age (main reference)	Target Population N	Questionnaire data (Participation rate)	Psychiatric items in the Questionnaires	Clinical Examination (Participation rate)
ADHD				
16-years [18]	A subsample based on SWAN-screen, cases N=487 and controls N=315	Cases N=268 (55.0%), Controls N=196 (62.2%)		Psychiatric evaluation using the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL), , cognitive tests: WAIS-R Vocabulary and Block Design, The Stop-Signal, Attentional Network Task ANT , The Conners Continuous Performance Test II CPT, WAIS-III Processing Speed Index, the Wechsler Memory Scale,, The Verbal Fluency Test and the Fingertip Tapping Test from the NEPSY, the Trail marking test. Blood sample
Oulu Brain and Mind				
21-24-years [20]	Cases for risk of developing psychosis N=389 and their controls; psychotic episode N=78, ADHD N=103, random sample of the cohort N=193	Background information, relationships, quality of life, substance use, Handedness, Coping. Cases N=136 (35.0%) controls: psychotic episode N=27 (34.6%), ADHD N=52 (50.5%), random sample of the cohort N=80 (41.5%)	Life Orientation Test (LOT), The Relationship Questionnaire (RQ), Sense of Coherence Scale (SOC-13), PROD-screen, Schizotypal Personality (SPQ-B), Adult Self Report (ASR), Parental Bonding Instrument (PBI), Life Event Checklist (LEC), Trauma and Distress Scale (TADS), Magical Ideation Scale (MIS) and Perceptual Aberration Scale (PER).	Cognitive tests: Vocabulary, Matrix Reasoning and Digit Span (WAIS III), California Verbal Learning Test - Research Edition (CVLT), Logical Memory (WMS-R), Verbal fluency, Grooved Pegboard and Cambridge Neuropsychological Test Automated Battery (CANTAB) tests of Paired Associates Learning (PAL), Spatial Working Memory (SWM), Stockings of Cambridge (SOC), Rapid Visual Information Processing (RVP) and Information Sampling Test. Blood and urine sampling. Structural MRI, diffusion-tensor imaging (DTI), resting state functional MRI, Functional MRI (fMRI). Structured Interview for Prodromal Syndromes (SIPS), ADHD interview and The Structured Clinical Interview for DSM-IV axis I Disorders (SCID I).
25-27 years [26]	Cases based on exposure to maternal cigarette smoking (N=698) and their controls (N=698)	Background and lifestyle information, sleep questions, smoking, substance use and gambling, handedness, physical activity, diet, health, LOT. Cases N=218, 31%; Controls N=253, 36%	TADS, LOT, ASR, PROD-screen, Personality Inventory NEO-PI, Temperament and Character Inventory TCI	Interview including SCID-I, family history of psychiatric disorders, psychiatric treatment history, Brief Nicotine Dependence Interview (SAGA). Cognitive tests: Weichel's Adult Intelligence Scale (WAIS-3), PAL, Semantic Fluency, the Grooved Pegboard test, the Stroop test, modified Stop Signal Test (MSST) from CANTAB.

MRI of the brain (T2, DTI, MTR, R-fMRI). Blood and
urine sample

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Table 3 General characteristics N(%) of the NFBC 1986 and comparison cohort by sex.

		Males		Females		
		NFBC 1986	Comparison cohort	NFBC 1986	Comparison cohort	
		N=4839	N=4550	N=4557	N=4409	χ^2 (p-value)
Education						0.14 (0.710)
	Secondary education or less	3470 (71.7)	2706 (71.3)	2483 (55.5)	2490 (56.5)	3.51 (0.061)
	Tertiary education	1369 (28.3)	1304 (28.7)	2074 (45.5)	1919 (43.5)	
Marital status						0.00 (1.000)
	Single	3858 (79.7)	3628 (79.7)	3121 (68.5)	3121 (70.8)	5.49 (0.019)
	Married	981 (20.3)	922 (20.3)	1436 (31.5)	1288 (29.2)	

Table 4 Cumulative incidences % (N), Pearson's chi-square statistics (χ^2), crude Risk Ratio (RR) and Mantel-Haenszel Risk Ratio (RR_{MH}) with 95% CI of psychiatric disorders in males age of 2 to 28 years

Diagnostic group	NFBC 1986	Comparison cohort	χ^2	p-value	RR (95% CI.)	p-value	RR _{MH} (95% CI.) ^a	p-value
Any psychiatric or neurodevelopmental disorder	14.3 (691)	13.7 (625)	0.54	0.461	1.04 (0.94-1.15)	0.443	1.04 (0.94-1.14)	0.489
Organic mental disorders	0.3 (14)	0.1 (3)				N/A		
Mental disorders due to psychoactive substance use	4.3 (206)	4 (181)	0.33	0.563	1.06 (0.88-1.3)	0.529	N/A	
Alcohol	3.4 (164)	3.2 (145)	0.24	0.623	1.06 (0.85-1.32)	0.583	N/A	
Other substances	1.9 (90)	1.6 (72)	0.91	0.341	1.18 (0.86-1.6)	0.302	N/A	
Schizophrenia, schizotypal and delusional disorders	1.9 (91)	1.7 (79)	0.27	0.655	1.08 (0.8-1.46)	0.600	1.08 (0.80-1.45)	0.624
Schizophrenia	0.7 (34)	0.6 (28)	0.16	0.693	1.14 (0.69-1.88)	0.602	N/A	
Other non-affective psychosis	1.8 (86)	1.7 (76)	0.1	0.75	1.06 (0.78-1.44)	0.691	1.06 (0.78-1.44)	0.717
Mood disorders	5.1 (248)	5.3 (241)	0.11	0.743	0.97 (0.81-1.15)	0.708	0.96 (0.81-1.15)	0.673
Mania and bipolar	0.4 (21)	0.6 (26)	0.63	0.426	0.76 (0.43-1.35)	0.346	N/A	
Depression	4.8 (234)	4.9 (225)	0.04	0.843	0.98 (0.82-1.17)	0.806	0.97 (0.82-1.16)	0.771
Neurotic, stress-related and somatoform disorders	5.1 (249)	4.9 (223)	0.24	0.621	1.05 (0.88-1.25)	0.588	1.04 (0.87-1.24)	0.652
Obsessive-compulsive disorder	0.4 (18)	0.4 (16)	0.00	1.00	1.06 (0.54-2.07)	0.870	N/A	
Anxiety disorders	2.9 (141)	2.7 (125)	0.18	0.672	1.06 (0.84-1.34)	0.627	1.06 (0.83-1.34)	0.655
Post-traumatic stress disorder	0.3 (13)	0.3 (12)	0.00	1.00	1.02 (0.47-2.23)	0.963	N/A	
Behavioural syndromes associated with eating, sleep or puerperium	0.8 (37)	0.7 (32)	0.01	0.912	1.06 (0.66-1.7)	0.816	1.08 (0.68-1.74)	0.734
Eating disorders	0.1 (6)	0.1 (4)				N/A		
Disorders of adult personality	1.1 (55)	1.1 (51)	0.00	1.00	1.01 (0.69-1.48)	0.943	N/A	
Emotionally unstable personality	0.4 (19)	0.4 (16)	0.02	0.876	1.12 (0.57-2.17)	0.745	N/A	
Disorders diagnosed in childhood or in adolescence	5 (246)	5.8 (266)	2.5	0.114	0.87 (0.73-1.03)	0.104	0.87 (0.73-1.02)	0.092
Autism spectrum disorders	0.5 (23)	0.6 (26)	0.25	0.615	0.83 (0.48-1.46)	0.518	N/A	
Learning and coordination disorders	2.3 (110)	2.5 (115)	0.64	0.422	0.89 (0.68-1.16)	0.384	0.89 (0.69-1.16)	0.397
ADHD	0.8 (38)	1.1 (51)	2.47	0.116	0.70 (0.46-1.06)	0.094	N/A	

Conduct and oppositional disorders	1.2 (58)	1.5 (67)	1.14	0.286	0.81 (0.57-1.15)	0.247	N/A
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^aAdjusted with marital status and education

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Table 5 Cumulative incidences % (N), Pearson's chi-square statistics (χ^2), crude Risk Ratio (RR) and Mantel-Haenszel Risk Ratio (RR_{MH}) with 95% CI psychiatric disorders in Females age of 2 to 28 year.

Diagnostic group	NFBC 1986	Comparison cohort	χ^2	p-value	RR (95% CI.)	p-value	RR _{MH} (95% CI.) ^a	p-value
Any psychiatric or neurodevelopmental disorder	16.1 (734)	18.0 (796)	5.87	0.015*	0.89 (0.81-0.98)	0.014*	0.91 (0.83-1.00)	0.056
Organic mental disorders	0.2 (7)	0.1 (3)				N/A		
Mental disorders due to psychoactive substance use	2.7 (124)	2.9 (129)	0.27	0.602	0.93 (0.73-1.19)	0.558	0.96 (0.76-1.23)	0.753
Alcohol	2.1 (96)	2.3 (101)	0.27	0.601	0.92 (0.7-1.21)	0.552	0.95 (0.72-1.25)	0.705
Other substances	1.0 (44)	1.0 (44)	0	0.961	0.97 (0.64-1.47)	0.876	N/A	
Schizophrenia, schizotypal and delusional disorders	1.4 (63)	2.0 (90)	5.41	0.02*	0.68 (0.49-0.93)	0.016*	N/A	
Schizophrenia	0.4 (18)	0.6 (27)	1.71	0.191	0.65 (0.36-1.17)	0.145	N/A	
Other non-affective psychosis	1.3 (60)	2.0 (87)	5.59	0.018*	0.67 (0.48-0.92)	0.014*	N/A	
Mood disorders	9.1 (416)	10.2 (450)	2.62	0.105	0.9 (0.79-1.02)	0.098	0.92 (0.81-1.04)	0.175
Mania and bipolar	0.9 (41)	0.9 (38)	0.01	0.937	1.04 (0.67-1.62)	0.848	N/A	
Depression	8.7 (398)	9.7 (428)	2.2	0.138	0.9 (0.79-1.03)	0.128	0.92 (0.81-1.05)	0.214
Neurotic, stress-related and somatoform disorders	7.5 (344)	9.6 (425)	12.22	<.001***	0.78 (0.68-0.90)	<.001***	0.80 (0.70-0.91)	0.001**
Obsessive-compulsive disorder	0.7 (31)	0.8 (36)	0.39	0.531	0.83 (0.52-1.34)	0.454	0.86 (0.53-1.38)	0.520
Anxiety disorders	4.2 (191)	5.3 (233)	5.7	0.017*	0.79 (0.66-0.96)	0.015*	0.81 (0.67-0.98)	0.029*
Post-traumatic stress disorder	0.9 (42)	1.5 (68)	6.62	0.010*	0.60 (0.41-0.88)	0.008**	0.61 (0.42-0.90)	0.011*
Behavioural syndromes associated with eating, sleep or puerperium	1.7 (79)	2.3 (101)	3.29	0.070	0.75 (0.56-1.01)	0.059	0.77 (0.58-1.03)	0.078
Eating disorders	1.3 (61)	1.7 (77)	2.47	0.116	0.75 (0.54-1.05)	0.097	0.78 (0.56-1.09)	0.141
Disorders of adult personality	1.7 (79)	2.1 (92)	1.31	0.252	0.83 (0.62-1.12)	0.222	0.86 (0.64-1.16)	0.330
Emotionally unstable personality	1.1 (52)	1.3 (59)	0.56	0.454	0.85 (0.59-1.24)	0.399	N/A	
Disorders diagnosed in childhood or in adolescence	3.5 (161)	4.3 (189)	3.2	0.074	0.82 (0.67-1.01)	0.065	0.85 (0.69-1.04)	0.122
Autism spectrum disorders	0.2 (9)	0.2 (7)				N/A		
Learning and coordination disorders	0.6 (28)	1.2 (54)	9.31	0.002**	0.48 (0.31-0.77)	0.002**	0.52 (0.33-0.82)	0.004**

	ADHD	0.2 (9)	0.3 (14)				N/A	
	Conduct and oppositional disorders	1.4 (62)	1.2 (54)	0.23	0.635	1.11 (0.77-1.6)	0.57	N/A

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

^aAdjusted with marital status and education

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Table 6 Cumulative incidences % (N), Pearson's chi-square statistics (χ^2) and Relative Risk (RR) with 95% CI of suicidal behaviour in age of 2 to 28 years.

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