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Martta Kerkelä

CHANGES IN THE INCIDENCE OF MENTAL DISORDERS IN FINNISH COHORTS AND THE EFFECTS OF BEING A PARTICIPANT OF THE NORTHERN FINLAND BIRTH COHORTS

UNIVERSITY OF OULU GRADUATE SCHOOL;
UNIVERSITY OF OULU,
FACULTY OF MEDICINE

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Abstract

Prospective birth cohort studies are longitudinal research studies that follow a group of individuals from birth throughout their lifespan, collecting data on various factors over time. The data collection methods may include clinical examinations, questionnaires, tests, interviews, and linkage to existing data, enabling the examination of multiple risk factors and potential interactions between them. The follow-up procedures raise a question about whether intensive follow-up could affect the study population in any way.

This study focuses on the association between participation in longitudinal follow-up studies and the use of psychiatric care services and cardiometabolic disorders in two prospective birth cohort studies, the Northern Finland Birth Cohort 1966 (NFBC1966) and the Northern Finland Birth Cohort 1986 (NFBC1986). The hypothesis is that participation in the NFBC studies may increase the use of psychiatric healthcare services and reduce suicidal behaviour, and that cohort participants may live healthier lives and have fewer cardiometabolic disorders than comparison cohorts. In addition, we explored the changes in the incidences of hospital-treated psychiatric disorders in five large Finnish birth cohorts of individuals born between 1966 and 1997.

The results show somewhat inconsistent effects of participation in the NFBC1966 and NFBC1986 studies. Female participants of NFBC1966 had a significantly younger onset of several cardiometabolic disorders, while female participants of NFBC1986 used less psychiatric care services and male participants of NFBC1986 had a decreased risk for several cardiometabolic disorders. In addition, the incidence of hospital-treated psychiatric disorders increased over the decades in the five birth cohorts in Finland, which is somewhat opposite to the Finnish psychiatric health policy plan.

It is important to note that the cohort participants of NFBC1986 are still relatively young, and an accurate assessment of the differences in the incidence of cardiometabolic disorders can only be made as they age. Furthermore, the NFBC studies may not be fully representative of the general population in terms of psychiatric or cardiometabolic outcomes. These preliminary results suggest potential health-promoting effects of the NFBC studies, but further research is needed to fully understand the effects of longitudinal follow-up studies on health outcomes.

Keywords: cohort studies, psychiatric disorders, cardiometabolic disorders, follow-up study, participation

Kerkelä, Martta, Mielenterveyshäiriöiden ilmaantuvuuden muutokset suomalaisissa kohorteissa ja Pohjois-Suomen syntymäkohorttiin osallistumisen vaikutukset

Oulun yliopiston tutkijakoulu; Oulun yliopisto, Lääketieteellinen tiedekunta

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Tiivistelmä

Prospektiiviset syntymäkohorttitutkimukset ovat pitkittäistutkimuksia, joissa tutkimusväestöä seurataan syntymästä lähtien läpi elämän keräämällä tietoja eri tekijöistä ajan kuluessa. Tietoja voidaan kerätä kliinisillä tutkimuksilla, kyselyillä ja haastatteluilla, mikä mahdollistaa useiden riskitekijöiden ja niiden mahdollisten vuorovaikutusten tutkimisen. Prospektiivisten syntymäkohorttien pitkä seuranta herättää kysymyksen, voiko intensiivinen seuranta vaikuttaa tutkimusväestöön millään tavalla.

Tämä tutkimus keskittyy pitkittäisseurantaan osallistumisen ja psykiatristen terveydenhuoltopalveluiden käytön sekä kardiometabolisten häiriöiden väliseen yhteyteen kahdessa prospektiivisessa syntymäkohorttitutkimuksessa, Pohjois-Suomen syntymäkohortti 1966:ssa (NFBC1966) ja Pohjois-Suomen syntymäkohortti 1986:ssa (NFBC1986). Hypoteesina on, että osallistuminen NFBC-tutkimuksiin saattaa lisätä psykiatristen terveydenhuoltopalveluiden käyttöä ja vähentää itsemurhakäyttäytymistä, sekä se, että kohortin osallistujat saattavat elää terveellisemmin ja kärsiä vähemmän kardiometabolisista häiriöistä kuin vertailukohortit. Lisäksi tutkitaan sairaalassa hoidettujen psykiatristen häiriöiden esiintyvyyden muutoksia viidessä suuressa suomalaisessa syntymäkohortissa, joiden osallistujat ovat syntyneet vuosien 1966 ja 1997 välillä.

Tulokset osoittavat jonkin verran epäjohdonmukaisia vaikutuksia NFBC1966- ja NFBC1986-syntymäkohortteihin osallistumisella. NFBC1966:n naisosallistujilla oli tilastollisesti merkitsevästi nuorempi sairastumisikä kardiometabolisiin sairauksiin, NFBC1986:n naisosallistujat käyttivät vähemmän psykiatrisia hoitopalveluita ja NFBC1986:n miesosallistujilla oli pienentynyt riski sairastua kardiometabolisiin sairauksiin vertailukohorttiin verrattuna. Lisäksi sairaalassa hoidettujen psykiatristen häiriöiden esiintyvyys kasvoi viimeisten vuosikymmenten aikana viidessä syntymäkohortissa Suomessa, mikä on jonkin verran ristiriidassa Suomen psykiatrisen terveyspolitiikan kanssa.

Asiasanat: kohorttitutkimus, psykiatriset häiriöt, kardiometaboliset sairaudet, seurantatutkimus, osallistuminen

To my family

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Oulu, October 2023 Martta Kerkelä

Abbreviations

ADHD	Attention-deficit hyperactivity disorder
ALSPAC	Avon Longitudinal Study of Parents and Children
BT20	Mandela's Children: The 1990 birth to twenty study in South Africa
CAD	Coronary artery disease
CBT	Cognitive behavioural therapy
CI	Confidence interval
CLHNS	Cebu Longitudinal Health and Nutrition Survey
CRHC	Care Register for Health Care
BMI	Body mass index
DNBC	Danish National Birth Cohort
DSM	Diagnostic and Statistical Manual
ELSPAC	European Longitudinal Study of Pregnancy and Childhood
FBC	Finnish Birth Cohort
FBCS 1981	The Finnish 1981 Birth Cohort
HHf2	Healthy Habits for Two
HR	Hazard ratio
HSCL-25	Hopkins Symptom Checklist-25
ICD	International Classification of Diseases
IQR	Interquartile range
IRR	Incidence rate ratio
MAAS	Manchester Asthma and Allergy Study
MBNS	Mental, behavioural or neurodevelopmental disorders
MHFA	Mental Health First Aid
MoBa	Norwegian Mother, Father, and Child Cohort Study
MUSP	Mater – University of Queensland Study of Pregnancy
MRI	Magnetic resonance imaging
NDBC	New Delhi Birth Cohort
NFBC	Northern Finland Birth Cohort
PIN	Personal identification number
PROD	Prodromal symptoms of psychosis
PTSD	Post-traumatic stress disorder
QE	Quantile estimation
Raine	Western Australian Pregnancy Cohort
RR	Risk ratio

RR_{MH}	Mantel-Haenszel risk ratio
SCID	Structured clinical interview
SWAN	Strengths and Weakness of Attention-Deficit/Hyperactivity Disorders Symptoms and Normal Behaviour Scale
UKKI	Uusikaupunki and Kemijärvi study
YSR	Youth Self-Report
WHO	World Health Organization
WTBC	Wuhan Twin Birth Cohort

Original publications

This thesis is based on the following publications, which are referred to throughout the text by their Roman numerals:

I Kerkelä, M., Gyllenberg, D., Gissler, M., Sillanmäki, L., Keski-Säntti, M., Hinkka-Yli-Salomäki, S., Filatova, S., Hurtig, T., Miettunen, J., Sourander, A., & Veijola, J. (2021). Cumulative incidences of hospital-treated psychiatric disorders are increasing in five Finnish birth cohorts. *Acta Psychiatrica Scandinavica*, *143*(2), 119–129. https://doi.org/10.1111/acps.13247

II Kerkelä, M., Gissler, M., & Veijola, J. (2022). Association of participation in the Northern Finland Birth Cohort 1986 with mental disorders and suicidal behaviour. *Epidemiology and Health, 44*, e2022005. https://doi.org/10.4178/epih.e2022005

III Kerkelä, M., Gissler, M., Nordström, T., & Veijola, J. (2023). Association between participation in the Northern Finland Birth Cohort 1966 study and use of psychiatric care services. *PLoS One*, *18*(3), e0282714. https://doi.org/10.1371/journal.pone.0282714

IV Kerkelä, M., Gissler, M., Nordström, T., Ukkola, O., & Veijola, J. (2023). Association between participation in the Northern Finland Birth Cohorts and cardiometabolic disorders. *Annals of Medicine, 55*(1), 1123–1133. https://doi.org/10.1080/07853890.2023.2186478

Contents

1 Introduction

Prospective birth cohort studies are a type of longitudinal research that follows a group of individuals from birth through their life span, gathering data on a range of variables over time. The data collection procedures may include clinical examinations, questionnaires, tests, interviews, and linkage to existing data (Szklo, 1998). Prospective birth cohort studies are highly regarded because of their unique advantages. The longitudinal design allows researchers to collect data at multiple time points and assess causal relationships between exposures and outcomes. Data are collected on a range of factors, which enables the examination of multiple risk factors and potential interactions between them (Euser et al., 2009). The follow-up procedures in longitudinal birth cohort studies raise the question of whether the intensive follow-up could have affected the study population in any way. Even though the idea is not to intervene, in order to obtain a representative sample of the population, the studies conducted during follow-up may affect the target population in various ways.

The Hawthorne Effect is a social psychological phenomenon where individuals modify their behaviour as a result of being observed. This can result in improved performance or compliance with expectations, as individuals want to appear competent or to conform to societal norms. The effect can be explained by the psychological principle of reactivity, where people respond to the presence of an observer by changing their behaviour. The Hawthorne Effect was first identified by researchers at the Hawthorne Works factory in Illinois in the 1920s and 1930s. The researchers sought to improve worker productivity by manipulating factors such as lighting and break length. However, they found that regardless of the changes made, productivity improved. This was because the workers were aware that they were being studied and therefore modified their behaviour in response. (Adair, 1984; Jones, 1992; McCambridge et al., 2014.)

The Finnish population-based Uusikaupunki and Kemijärvi (UKKI) study explored the stability and changes in mental health in the 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 various register information such as healthcare service utilization, mortality rates, medication usage, sick leave, and social welfare service utilization was examined by comparing the participants to a matched control group. The UKKI study participants were found to have used public health services, social welfare services, and psychiatric healthcare 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 (Lehtinen et al., 1993).

We were able to study the association between participation in a longitudinal follow-up study and the use of psychiatric care services and cardiometabolic disorders in two longitudinal studies which started prospectively in the antenatal period: namely the Northern Finland Cohort 1966 (NFBC1966) (University of Oulu, 1966) and the Northern Finland Birth Cohort 1986 (NFBC1986) (University of Oulu, 1986). Since birth, both birth cohorts have undergone several follow-ups such as surveys and clinical examinations. Even though the follow-ups of the NFBC studies were not supposed to be interventions, many of them included questions and screenings on lifestyle, exercise, diet, mental health, and the use of intoxicants. Several follow-ups in the NFBC studies also included clinical examinations, in which weight and height, blood pressure, physical activity, and numerous other clinical measurements were measured. In studies focusing on psychiatric healthcare, our hypothesis was that participation in the NFBC studies would increase the use of psychiatric healthcare services and reduce suicidal behaviour because of participation in the follow-up studies. In a study focusing on cardiometabolic disorders, the hypothesis was that the participants of the NFBC studies might live healthier lives because of the follow-up and therefore have fewer cardiometabolic disorder diagnoses than comparison cohorts. In addition, we explored the changes in the incidences of childhood and early adulthood hospital-treated psychiatric disorders in five large Finnish birth cohorts of individuals born between 1966 and 1997.

2 Review of literature

2.1 Prospective birth cohort studies

In prospective birth cohort studies, a defined population is selected for the longitudinal assessment of exposure-outcome relations. Prospective birth cohort studies are relevant study settings to understand life-course determinants from infancy to older age. The data collection procedures include questionnaires, clinical examinations, interviews, tests, or linkage to existing datasets (Szklo, 1998).

Prospective birth cohort studies can be accurate in the information collected about exposure, endpoints, and confounders, and the study setting makes it possible to examine multiple exposures and outcomes in the same dataset. Prospective birth cohort studies are a time-effective way to study new hypotheses with existing data. (Euser et al., 2009.) The prospective birth cohort setting provides the possibility to collect transgenerational data. This allows for the investigation of intergenerational effects of exposures on health outcomes across multiple generations. In addition, prospective birth cohort studies can provide valuable information on the transmission of genetic and epigenetic factors from parents to offspring, which is important for understanding the inheritance of disease risk. (Lawlor et al., 2009.)

The broad data collection in a prospective birth cohort study allows other variables, confounders, to be taken into account. The confounders might explain the association found between exposure and outcome, but usually in many prospective studies, the confounders are unmeasured, insufficiently accurate, or even unknown (Euser et al., 2009). On the other hand, prospective birth cohorts are expensive and complex to maintain, and recruitment and data collection can be time-consuming (White et al., 1998). It is also difficult to establish a causal effect, while the exposure has not been allocated randomly and the association might be explained by other factors. Another difficulty with follow-ups of prospective birth cohort studies is that it might be hard to anticipate what data researchers will require in the future (Lawlor & Mishra, 2009). The data collected decades ago may not provide an accurate representation of the contemporary context due to significant changes in the environment, behaviours, and clinical practices (Lin et al., 2022). For instance, there have been noticeable alterations in air and water pollution levels, as well as changes in food and housing quality (Brook et al., 2010). Exposure to air pollutants has been linked to various cardiovascular and neurological effects, as well as an increased risk of low birth weight (Manisalidis et al., 2020). These

findings underscore the potential impact of environmental changes on health outcomes and emphasize the importance of considering such factors when interpreting data from longitudinal studies.

The participation rate in epidemiological studies has decreased in recent decades. There are a few main reasons for non-participation: the increasing number of requests to participate in a study; a general decrease in volunteerism in western countries; people are reluctant to participate in studies that do not have a personal salience; and the data collection has become more complicated (include many steps, e.g., surveys, biological samples, informed consent is needed). Non-participation increases the risk of non-participation bias because of systematic differences between participants and non-participants. (Galea & Tracy, 2007.) Participants tend to have better somatic and psychiatric health, lower mortality rates, have higher socioeconomic status, and are less often smokers compared to non-participants. Conversely, non-participants tend to have poorer health, higher mortality rates, lower socioeconomic status, and a higher prevalence of smoking compared to participants. (Drivsholm et al., 2006; Knapstad et al., 2016; Lundberg et al., 2005; May et al., 2012.)

2.1.1 Existing birth cohort studies

The majority of the existing birth cohort studies have been conducted in high-income countries and are located in northern and western Europe (Lawlor et al., 2009; Larsen et al., 2013). Low- and middle-income countries have difficulties with prospective birth cohort studies, while (medical) research funding is minor. In high-economy countries, births typically occur in hospitals, rather than at home, and national databases are more advanced. Particularly in northern Europe, the unique personal identification number (PIN) is used nationwide, enabling the data to be linkable to other datasets. (Batty et al., 2007.)

One of the oldest prospective birth cohort studies, the 1946 National Birth Cohort (MRC National Survey of Health and Development), follows 5,362 persons born in England, Scotland, or Wales. The cohort consists of a socially stratified sample of singleton babies born to married parents during one week in March 1946. The baseline study included an interview with mothers, clinical examinations, and questionnaires for children, with 25 follow-up waves. The data collection is still ongoing. (Wadsworth et al., 2006) One of the largest prospective birth cohorts, the Norwegian Mother, Father, and Child Cohort Study (MoBa) recruited 95,000 pregnant women from 1998 to 2009. The mothers, children (N=114,000), and

fathers (N=75,000) have been followed with multiple questionnaires and clinical examinations. Follow-up waves have been conducted at the age of 6 and 18 months, and 3, 5, 7, 8, 13 and 16 to 17 years. The collected data have been linked to national health registers. (Magnus et al., 2016.)

Besides the population-based prospective birth cohort study settings, it is possible to construct a birth cohort solely from registers. For example, the MATEX cohort is a fully register-based birth cohort comprising all births in Finland from 1987 to 2018 (information on births has been obtained from the Finnish Medical Birth Register). The data have been linked to health registers, population registers, and building registers. It is also possible to establish birth cohorts in special populations. For example, the Wuhan Twin Birth Cohort (WTBC) is based on three twin samples. The first sample consists of 6,920 twin pairs (enrolment period from 2013 to 2016), the second sample 6,949 twin pairs (enrolment period from 2013 to 2020), and the third sample has a target of 1,000 twin pairs and their mothers (from 2016 onwards). The first and second samples include pregnancy information and children's healthcare information until the age of 7, and the third sample participants participate in a periodic health examination from the first trimester of pregnancy to 18 years. Health and lifestyle history (physical characteristics, mental health, and behaviour) is planned to be collected from twins and their mothers. (Zhao et al., 2017.)

As there exists a relatively large number of birth cohorts, we limit the description of birth cohorts to birth cohorts with a similar setting to the birth cohorts of interest, the Northern Finland Birth Cohorts. We include prospective birth cohort studies where mothers were recruited before or during pregnancy, the baseline cohort includes over 1,000 baseline participants (offspring), the offspring have been followed until adulthood and these results have been until the end of 2022. (Table 1).

Table 1. Prospective birth cohort studies, which include mother-child pairs, mothers were recruited before or during pregnancy, all participants have been followed until adulthood and had over 1,000 baseline participants.

Name	Abbreviation	Recruitment year	Country	Number of offspring
The Northern Finland Birth Cohort 1966	NFBC1966	1965–1966	Finland	12,231
The New Delhi Birth Cohort	NDBC	1969–1972	India	8,181
The 1969-73 Vellora Birth Cohort Study in South India		1969–1973	India	10,670
Cebu Longitudinal Health and Nutrition Survey	CLHNS	1983–1984	Philippines	3,080
Mater – University of Queensland Study of Pregnancy	MUSP	1981–1982	Australia	7,223
Healthy Habits for Two	HHf2	1984–1987	Denmark	11,144
The Northern Finland Birth Cohort 1986	NFBC1986	1984–1985	Finland	9,479
Mandela's children: The 1990 birth to twenty study in South Africa	BT20	1989	South Africa	3,273
The Western Australian Pregnancy Cohort	Raine	1989–1991	Australia	2,868
The European Longitudinal Study of Pregnancy and Childhood	ELSPAC	1991–1992	Czech Republic	7,589
The Avon Longitudinal Study of Parents and Children	ALSPAC	1991–1992	England	14,775
The Manchester Asthma and Allergy Study	MAAS	1996–1998	England	1,085
The Danish National Birth Cohort	DNBC	1996–2002	Denmark	100,000
Project VIVA		1999–2002	USA	2,128

Northern Finland Birth Cohorts (NFBC)

The NFBC studies covered people with an expected date of birth in the year 1966 (NFBC1966) and from July 1985 to June 1986 (NFBC1986) in the former provinces of Oulu and Lapland in Finland. In both cohorts, the initial data collection began during the mother's pregnancy and the women were recruited from antenatal clinics. The NFBC1966 included 12,231 and the NFBC1986 9,479 offspring. Multiple follow-up waves have been conducted in both cohorts, at pregnancy, age of 1 (participation rate 88.5%), 14 (90.0%), 31 (71.4%), and 46 years (58.4%) in the NFBC1966 and at pregnancy, 7–8 (88.3%), 15–16 (75.8%) and 33–35 years (34.0%) in the NFBC1986. The data collection consists of multiple questionnaires (including e.g., background information, psychiatric screens) and clinical examinations. (University of Oulu, 1966; University of Oulu, 1986.)

The New Delhi Birth Cohort (NDBC)

The New Delhi Birth Cohort (NDBC) recruited 20,755 married women of reproductive age in South Delhi, India, between 1969 and 1972. Women were assessed every other month to identify pregnancies, and pregnant women visited health visitors every two months. During the enrolment period, there were 8,181 live births. Offspring were followed at birth, at 6-month intervals until they were 21 years old (participation rate from 36.0% to 88.6%), and at age 26–32 years (19.0%) and 32–37 years (14.3%). The follow-ups included questionnaires and interviews (data collection on e.g., income, education, substance use and physical activity) and clinical examinations (e.g., blood pressure, blood glucose concentrations, lipids and body composition). (Bhargava et al., 2004; Richter et al., 2012; Sinha et al., 2022.)

The 1969–73 Vellora Birth Cohort Study in South India

The 1963–73 Vellora Birth Cohort Study in South India recruited 20,626 non-pregnant married women with childbearing potential in the defined areas of Tamil Nadu state in South India. Women were visited once every five weeks to assess their menstrual status and were classified into a non-pregnancy follow-up or an in-pregnancy follow-up. The cohort comprised 10,670 single live-born babies born to these women during the study period (1969–1973). Offspring have been followed

up from birth at childhood (6–8 years), adolescence (10–15 years) and adulthood (26–32 years). Of the original cohort participants, 51.9% participated in both childhood and adolescence follow-up and 20.8% in adulthood follow-up. The data collection in childhood focused on children's growth (physical growth, mental age, and intelligence quotient) and children's clinical aspects. In young adulthood, the data collection included background information, substance use, diet, physical activity, and clinical measurements focusing on cardiovascular risk factors (e.g., fasting plasma glucose, insulin, and lipid concentrations). (Antonisamy et al., 2009.)

Cebu Longitudinal Health and Nutrition Survey (CLHNS)

The CLHNS recruiting process was based on a single-stage cluster-sampling process, in which 33 barangays from the 243 barangays of Metro Cebu, Philippines, were selected. In the selected areas, households were surveyed to locate all pregnant women. To those women, 3,080 offspring were born between May 1983 and April 1984 and were included in the offspring cohort. Follow-ups were conducted during pregnancy, at birth, at 2-month intervals until the children were 2 years old (participation rate 79.9–84.4%) and at age 8 (73.5%), 11 (71.0%), 15 (67.8%), 19 (65.7%), 22 (61.3%) and 24 years (59.0%). All the data were collected during home interviews, and include information on for example, diet, physical activity, background factors and mental health. (Adair et al., 2011; Richter et al., 2012.)

Mater – University of Queensland Study of Pregnancy (MUSP)

The Mater University of Queensland Study of Pregnancy (MUSP) recruited pregnant women after their first clinic visit in 1981, collecting 7,223 mother-offspring pairs into the Australian MUSP cohort. In later phases, data were collected using biological samples, clinical examinations and questionnaires with mothers and offspring at various times. For offspring, the follow-ups have been conducted at birth, age 6 months (participation rate 93%), and age 5 (73.5%), 14 (72.2%), 21 (52.7%) and 30 years (40.0%). Data have been collected on background, substance use, health and behaviour, mental health, and lifestyle. (Najman et al., 2015.)

Healthy Habits for Two (HHf2)

HHf2 started as a health campaign targeting a large group of pregnant women, to analyse subsequent risk behaviours. A total of 11,980 women were recruited from antenatal clinics in late pregnancy in 1984–1987 in Odense municipality, Denmark. Women filled in the questionnaire and were offered brochures about smoking and drinking habits during pregnancy. The cohort consists of 11,144 offspring, who were followed at age 14 years (questionnaire filled in by mothers) and 18 years. The data collection includes information on the offspring's diet, physical activity, mental health, socioeconomic factors, and development. National register data have been linked to the collected data. (Larsen et al., 2013; Olsen et al., 1989.)

Mandela's Children: The 1990 birth to twenty study in South Africa (BT20)

Mandela's Children, previously named Birth to ten (BT10) and Birth to Twenty (BT20), recruited pregnant women from antenatal clinics in the Johannesburg area who were predicted to deliver their babies during the 7-week enrolment period in late 1989. The cohort includes all 3,273 singleton offspring born in the 7-week enrolment period. The offspring have been followed up since birth, and the cohort includes multiple follow-up waves: at age 6 months (participation rate 58.2%), and age 1 (67.6%), 2 (56.1%), 3–4 (56.7%), 5 (48.5%), 7–8 (61.8%), 9–10 (45.8%), 11–12 (54.8%), 13 (52.9%), 14 (63.6%), 15 (64.2%), 16, 17, 18, 19 (57.1%), 22 and 28 (~60%) years. The data collection was conducted with mothers and offspring, and included questionnaires (e.g., maternal stress and health, offspring's cognitive development and psychological assessments) and clinical examinations (Richter et al., 2007, 2012, 2021.)

The Western Australian Pregnancy Cohort (Raine)

The Raine Study recruited 2,968 pregnant women from antenatal clinics in Perth, Australia, between May 1989 and November 1991. Mothers were followed up during pregnancy and delivered 2,868 live-born offspring. The first evaluation was performed at 18 weeks' gestation, followed by follow-ups at 34 weeks, birth, and age 1 (participation rate 85.2%), 2 (69.3%), 3 (79.4%), 5 (78.0%), 8 (74.6%), 10 (71.4%), 14 (65.0%), 17 (60.2%), 20 (51.0%), 22 (43.0%) and 27 years. Data collection includes questionnaires (e.g., background information, children's growth, cardiovascular health and risk factors, physical activity, diet, and mental health)

and clinical assessments (e.g., DNA samples, vitamin levels, fatty acids and inflammatory markers). (Straker et al., 2017.)

ELSPAC

Pregnant women whose expected date of delivery fell between 1 March 1991 and 30 June 1992 living in a selected geographical area in the Czech Republic were recruited for the study. Parents filled in the first questionnaire during pregnancy and at birth. The cohort consists of 7,589 offspring. The follow-up has consisted of questionnaires at age 6 (participation rate 61.8%) and 18 months (48.2%), and age 3 (49.0%), 5 (48.0%), 7 (43.6%), 11 (33.3%), 15 (21.7%), and 19 years (7.4%). Offspring were also invited for medical assessments at ages 8, 11, 13, 15, 18, and 19 years. (Piler et al., 2017.)

The Avon Longitudinal Study of Parents and Children (ALSPAC)

The British birth cohort The Avon Longitudinal Study of Parents and Children (ALSPAC) recruited pregnant women in the area of Avon whose due date fell between April 1991 and December 1992. The baseline sample consisted of 14,062 live-born offspring. Follow-ups of children were conducted in infancy (0–2 years; participation rate 79.1–87.8%), in childhood (2–7 years; participation rate 60.4–74.1%), in late childhood (7–13 years; participation rate 53.3–59.1%), in adolescence (13–16 years; participation rate 38.7–50.7%), during the transition to adulthood (16–18 years; participation rate 36.5%) and in adulthood (18 years and older), having more than 68 data collection points between birth and 18 years of age. The data collection has included self-reported questionnaire measures (e.g., background information, substance use, development, mental health), physiological clinical measurements (e.g., blood pressure, fitness, allergy tests) and cognitive clinical assessments (IQ, motor skills, memory, reading ability). (Boyd et al., 2013.)

The Manchester Asthma and Allergy Study (MAAS)

Between October 1995 and July 1997, 3,618 mothers and 2,172 fathers were recruited in the MAAS cohort from antenatal clinics, with a skin-prick test and structured questionnaire. A total of 1,085 children born between February 1996 and April 1998 are included in the cohort. The offspring have been followed up at age

1, 3, 5, 8, 11, 13–16, and 18 years with health questionnaires and clinical assessments (lung function, skin tests for allergies, and blood samples). (Belgrave et al., 2018; Custovic et al., 2002.)

The Danish National Birth Cohort (DNBC)

In the Danish National Birth Cohort (DNBC) initial data collection information was conducted through telephone interviews with pregnant women in 1996–2002, recruiting circa 100,000 women in early pregnancy. At the follow-ups, the mothers and offspring answered multiple interviews and questionnaires, including questions about background, offspring's growth and health, diet, physical activity, substance use, and mental health. The follow-ups for offspring have been conducted at birth, age 7 (participation rate ~75%), 11, 14, and 18 years (participation rate ~70%) of age. (Olsen et al., 2001.)

Project VIVA

Mothers were recruited from their initial obstetric visits from April 1999 to November 2002 in Massachusetts. The follow-up for mothers was conducted mid-pregnancy and just after birth. A total of 2,128 live-born offspring are included in the cohort. The data collection has comprised in-person visits during infancy (6 months; participation rate 58.4%), early childhood (~3 years; participation rate 67.2%), mid-childhood (~7 years; participation rate 58.0%), early teens (~12–13 years), and mid-teens (~17 years). In-person data collection has included interviews, questionnaires (on background information, children's behaviour, health, and living habits) and clinical measures (e.g., blood pressure, vision tests, cognition tests, and blood collection). Between in-person visits, a questionnaire has been sent annually to mothers and offspring (from age 9 years onwards), the latest conducted in young adulthood (age 19). The questionnaires include questions on background information. living habits (sleep, diet), and mental and physical health. (Oken et al., 2015; Project Viva, 2022.)

2.1.2 Awareness of participation

In all the aforementioned prospective population-based birth cohort studies, multiple research questions have been studied in different fields, mental health has been screened, and cardiometabolic risk factors measured. The varying follow-up

procedures in prospective birth cohort studies raise the question of whether the intensive follow-up could have affected 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.

The Hawthorne Effect describes the awareness of the participants being studied and the possible impact on their behaviour (Jones, 1992). In the Derbyshire Smoking Study, the Hawthorne Effect of repeatedly measured smoking behaviour of about 6,000 adolescents was studied annually by questionnaire from 1974 to 1978 in selected schools. The self-reported smoking habits were compared to adolescents whose smoking habits were measured for the first time in 1978. The findings revealed that the prevalence of smoking was lower in those schools which had been surveyed for five years. (Murray et al., 1988.) McCambridge et al. combined the results of the Hawthorne Effect of the aforementioned study and eighteen other studies (eight randomised controlled trials, five quasi-experimental studies, and six observational evaluations) published before 2012. Of the 19 selected studies, in 14 studies some evidence of possible Hawthorne Effect was found and in five studies no evidence of effect was found. The pooled results indicated that consequences of research participation for behaviours being investigated do exist, but the results are incoherent, and the magnitude and mechanism are still unclear. (McCambridge et al., 2014.) Afterwards, Berkhout et al. pooled the findings of 15 studies published in 2012–2022 on the Hawthorne Effect in primary care, outpatient clinics, or healthy subjects. In the meta-analysis, the Hawthorne Effect was defined as "an aware or unconscious complex behavioural change in a study environment, related to the interaction of four biases affecting the study subjects and investigators: selection bias, commitment and congruence bias, conformity and social desirability bias, and observation and measurement bias". The findings demonstrate that medical research is unavoidably prone to the Hawthorne Effect, which restricts its external validity, beginning with the intentional or unintentional selection of the study population. (Berkhout et al., 2022.)

2.2 Health registers

Like other Nordic countries, Finland has national electronic health registers that were first created primarily for administrative purposes to track how much each Finnish resident uses healthcare over the course of their lifespan (Kurki et al., 2023).

The first nationwide, computerised health register, the Cancer Register, was started in 1952. As the personal identification number (PIN) system was launched in 1964 and the Finnish Personal Central Population Register was created at the same time, the registers have been linkable to each other since then. (Gissler & Haukka, 2004.) With a history of data collecting spanning more than 50 years, these registers cover almost all significant health-related events, such as hospitalisations, visits to primary health care, prescription drug purchases, and causes of death. The population-based health registers offer an epidemiological research tool since they made it feasible to examine relationships that otherwise would not have been possible to address. Many countries have social security numbers or other personal identifiers, but they do not always cover the entire population within a particular geographical or administrative area. For instance, in the United States, a social insurance number only applies to those who are insured. (Allebeck, 2009.)

Finnish registers have been confirmed to have good quality. For instance, a meta-analysis revealed that the completeness and accuracy of the care register for health care (CRHC) varies from satisfactory to very good (Sund, 2012). The validity of dementia and Alzheimer's diagnosis has been studied to have very good accuracy, a schizophrenia diagnosis study showed that when a broad definition of schizophrenia was used, the registers' schizophrenia diagnoses are reliable and diagnosis of bipolar I disorder is highly reliable and stable in the CRHC (Solomon et al., 2014; Mäkikyrö et al., 1998; Kieseppä et al., 2000). Also, coding causes of death for mortality statistics is appropriate, with a sincere quality coding process (Lahti & Penttilä, 2001). The validity of stroke diagnosis was proven to be high in CRHC and causes of death registers, enabling its use as an endpoint in epidemiological research (Leppälä et al., 1999).

2.3 Classification of diseases

The International Classification of Diseases (ICD) was originally published to classify the causes of death, by some scholars tracking the origin of the ICD in the 17th century. The new era in international vital and health statistics began when the ICD 6th version was revealed in 1948. The 6th revision was under the auspices of the World Health Organization (WHO) and included a coding system for mortality and morbidity. The ICD 7th revision was published in 1955, the 8th revision in 1965, the 9th revision in 1975, the 10th revision in 1992, and the newest 11th revision in 2019. (WHO Team: Classifications and Terminologies, n.d.) The broad classification codes have changed with the different ICD versions, and the codes

are not equal across the ICD versions. For example, infantile autism spectrum disorder was regarded as part of schizophrenia in the ICD-8 classification (Ousley & Cermak, 2014). Also, the implementation time of the ICD coding system has varied across countries; for example, Denmark took ICD-10 as the official classification system in 1994, Finland in 1996, and Sweden in 1997. Even though the ICD classification is international, the translated terminology might vary across countries. (Munk-Jørgensen et al., 1999.) Also, there are several modifications by country, e.g., ICD-10-AM in Australia, ICD-10-CM in the United States of America, and ICD-10-TM in Thailand. Different translational issues and modifications of ICD classifications potentially threaten the international comparability of morbidity and mortality data. (Jetté et al., 2010.)

The transition from one version of the ICD to the next can have an impact on research. There might be changes in diagnostic criteria and classification systems between ICD versions and this can affect the prevalence rates of certain disorders, making it difficult to compare results between studies that use different versions of the ICD. For example, in ICD-10 mental, behavioural or neurodevelopmental disorders (MBNS) were grouped into 11 groups, whereas ICD-11 includes 21 MBNS groups. ICD-11 also introduced totally new diagnoses like gaming disorder, prolonged grief disorder, and compulsive sexual behaviour disorder, which were not present in ICD-10 (WHO, 2019). Changes in diagnostic criteria in ICD-11 may affect the prevalences of certain disorders; for example, some studies suggest that the incidence of post-traumatic stress disorder (PTSD) according to ICD-11 criteria is comparatively lower than that of the ICD-10 criteria because ICD-11 recognises only the more severe cases of PTSD (Wisco et al., 2016).

Psychiatric epidemiology studies began properly when ICD-6 was published in 1948. ICD-6 was the first ICD to include mental disorder classifications, and soon after that in 1956, the American Psychiatric Association Committee on Nomenclature published the Diagnostic and Statistical Manual: Mental Disorders (DSM-I), a variant of ICD-6 coding. DMS-I was the first official manual of mental disorders to focus on clinical utility and provided a statistical classification of mental disorders (60 diagnoses). DSM-II was published in 1986 (185 diagnoses), DSM-III in 1980 (265 diagnoses), DSM-IV in 1994 (365 diagnoses), and DSM-5 (541 diagnoses) in 2013. (Buka et al., 2014.) DSM-III was the first psychiatric classification to include definitions and criteria for specific psychiatric diagnoses. ICD-10 was the first ICD classification including such definitions and criteria. In Finland, the ICD-9 classification, used from 1987 to 1995, included the DSM-III-R criterion for psychiatric disorders.

2.4 Psychiatric disorders

In 2019, around 12.5% of the world's population currently suffered from a psychiatric disorder, with anxiety disorders and depression being the most common, placing psychiatric disorders among the top ten leading causes of burden worldwide (Institute of Health Metrics and Evaluation; GBD 2019 Mental Disorders Collaborators, 2022). The incidence of diagnosed psychiatric disorders has increased globally over the past several decades. Many disorders usually diagnosed in childhood and adolescence, neurodevelopmental disorder diagnoses such as attention deficit hyperactivity disorder (ADHD) and autism spectrum disorders, have increased in prevalence in Western countries (Elsabbagh et al., 2012).

Protective factors for mental disorders have also been described. Lifestyle modifications have a beneficial effect on mental health. Physical activity and exercise have been shown to have numerous positive impacts on people with a wide range of mental disorders, as well as the potential to prevent common disorders like depression and anxiety disorders (Schuch & Vancampfort, 2021). Physical activity also improves depressive symptoms and reduces psychiatric symptoms of schizophrenia-spectrum disorders (Stubbs et al., 2018). The epidemiological evidence supports a relationship between nutrition and psychiatric symptoms (Akbaraly et al., 2009; Sánchez-Villegas et al., 2009). However, the link between nutrition, obesity, stress, and stress-related psychiatric disorders is complicated. A diet high in omega-3 polyunsaturated fats and low in saturated fats may reduce the risk of stress-related psychiatric disorders while also having positive impacts on other health outcomes (Bremner et al., 2020).

Psychiatric disorders result from a complex interplay between genetic and environmental factors, with heritability estimates (including both direct genetic effect and gene-environment interaction) ranging through 80% in autism spectrum disorders, 37% in major depression, 81% in schizophrenia, 75% in attention-deficit disorder, and 73% in bipolar disorder. (Sullivan et al., 2012.) Several environmental factors have been linked to psychiatric illness: cannabis use to psychosis and schizophrenia, childhood adversities to mood disorders, anxiety disorders, behaviour disorders, and substance use disorders, and prenatal famine to schizophrenia in later life (Volkow et al., 2016; Kessler et al., 2010; St Clair et al., 2005; Susser et al., 1996).

A sex difference in the morbidity of psychiatric disorders exists; in the Global Burden of Disease and Injury study, females had greater rates of depression, bipolar

disorders, anxiety, and eating disorders, whereas males had higher rates of substance use disorders, autism spectrum disorder, ADHD, and conduct disorder (Rehm & Shield, 2019). Excess mortality has also been linked to psychiatric disorders (Walker et al., 2015). Psychiatric disorders are not only associated with death due to suicide (especially schizophrenia, affective disorder, and substance use disorder) but also death due to a stroke, coronary heart disease, type II diabetes, respiratory disease, and some cancers (Li et al., 2011; Crump et al., 2013; Høyer et al., 2000).

In the ICD-10 coding system, mental and behavioural disorders are classified into ten main categories (WHO, 2016).

Organic, including symptomatic mental disorders (F00–F09)

The category consists of a variety of psychiatric disorders which have been classified together as all sharing a cerebral disease, brain injury, or another insult that causes cerebral dysfunction as a common aetiology (WHO, 2016). The major diagnosis class in the category, dementia, can be caused by a variety of neurological and underlying medical problems. The main causes of dementia include neurodegeneration, vascular disease, and nutritional and metabolic disorders. (Gale et al., 2018.)

Mental and behavioural disorders due to psychoactive substance use (F10–F19)

This category includes a wide range of conditions that vary in severity and clinical presentation but are all linked to the use of one or more psychoactive substance, which may or may not have been prescribed by a doctor. The class includes mental and behavioural disorders due to alcohol use, opioid use, sedatives of hypnotics use, cocaine use, other stimulant use, and cannabis-related disorder. (WHO, 2016.)

Schizophrenia, schizotypal and delusional disorder (F20–F29)

The most severe mental disorders fall into the category of schizophrenia, schizotypal, and delusional disorder. Schizophrenia is a complicated, heterogeneous behavioural and cognitive condition that appears to result from interference with brain development brought on by hereditary, environmental, or combined factors. The core characteristics of schizophrenia are positive symptoms (delusions and hallucinations; so-called psychotic symptoms), negative symptoms (particularly impaired motivation, reduction in spontaneous speech, and social withdrawal), and cognitive impairment. (Owen et al., 2016.) Schizotypal and delusional disorder are the two other relatively prevalent and severe disorders in this category. Other disorders included in the category are schizotypal disorder, acute and transient psychotic disorders, induced delusional disorder, other non-organic psychotic disorders, and unspecified non-organic psychosis (WHO, 2016).

Mood disorders (F30–F39)

Depressive disorders and bipolar disorders are the two broad categories of mood disorders. Depressive disorders are classified into depressive disorders and recurrent depressive disorders (mild, moderate, and severe depressive episodes with and without psychotic episodes). According to the ICD-10 diagnosis criteria, depression is characterised by significant abnormalities in mood, cognition, and neurovegetative functioning, with episodes lasting at least two weeks (WHO, 2016). Bipolar disorders are characterised by biphasic mood episodes that alternate between depression and mania/hypomania; however, they can also be defined by a single mania episode (Datta et al., 2021).

Neurotic, stress-related and somatoform disorders (F40–F48)

The category includes anxiety disorders, obsessive-compulsive disorder; adjustment disorders, acute stress disorder, post-traumatic stress disorder, and dissociative disorders (WHO, 2016). Anxiety disorders are the most common group of mental disorders and are characterised by excessive fear and anxiety or avoidance of perceived threats that are persistent and impairing. Anxiety disorders comprise social anxiety disorder, generalised anxiety disorder, panic disorder, and specific phobias (Penninx et al., 2021). Obsessive-compulsive disorder is

characterised by recurring and unsettling thoughts (obsessions) and repetitive behaviours (compulsions) that the individual feels compelled to perform (Goodman et al., 2014). Post-traumatic stress disorder is a condition that can occur after experiencing a severe traumatic event and includes symptoms of disturbing and intrusive memories and nightmares of the event, anger, hypervigilance, difficulty sleeping, poor concentration, and emotional withdrawal (Yehuda et al., 2015).

Behavioural syndromes associated with eating, sleep or puerperium (F50–F59)

Eating disorders are characterised by abnormal eating or weight-control behaviour (Treasure et al., 2020). In ICD-10, the eating disorders are classified into two separate main syndromes: anorexia nervosa and bulimia. The diagnosis category also includes non-organic sleep disorders, such as non-organic insomnia, and hypersomnia. Sleep disorders are characterised by unsatisfactory quantity and quality of sleep. (WHO, 2016.)

Disorders of adult personality and behaviour (F60–F69)

Personality disorders are characterised as an ongoing pattern of inner experience and behaviour that significantly deviates from the cultural norms of the person and shows up in cognition, affectivity, interpersonal functioning, and/or impulse control (WHO, 2016). Personality disorders may be grouped into three clusters. Cluster A is characterised by appearing odd or eccentric and includes paranoid, schizoid, and schizotypal personality disorders. Cluster B is characterised by appearing dramatic, emotional, or erratic, and includes antisocial, emotionally unstable, histrionic, and narcissistic personality disorders. Cluster C is characterised by appearing anxious and fearful, and it includes avoidant, dependant, and obsessive-compulsive personality disorders. (Angstman & Rasmussen, 2011.)

Intellectual disability (F70–F79)

Intellectual disability is defined by significant deficits in both intellectual performance and adaptive behaviour beginning before the age of 18. Because of developmental delays, the majority of intellectual disability patients are identified in early childhood. The diagnosis criteria for an intellectual disability include an IQ test score of less than 70. Although intellectual disability can be caused by exogenous factors such as maternal alcohol consumption during pregnancy, infections, delivery difficulties, and severe malnutrition, genetics is recognised to play a significant part in its aetiology. (Vissers et al., 2016.)

Disorders of psychological development (F80–F89)

Disorders of psychological development are usually diagnosed during childhood. The category includes developmental disorders in speech and language, scholastic skills, motor function, pervasive developmental disorders, and other or unspecific disorders of psychological development. Disorders in speech and language are the most commonly identified developmental concerns. The management of speech and language disorders, both primary and secondary, is complicated because of multifactorial aetiology, various symptoms, and difficulty in diagnosis. (O'Hare & Bremner, 2016.) Pervasive disorders are disorders distinguished by qualitative anomalies in reciprocal social relationships and communication patterns, as well as by a constrained, stereotypical, and repetitive range of interests and activities, for example, autism spectrum disorder (McPartland & Volkmar, 2012).

Behavioural and emotional disorders with onset usually occurring in childhood and adolescence (F90–F98)

The category includes hyperkinetic disorders, conduct disorders, mixed disorders of conduct and emotions, emotional disorders, disorders of social functioning, and tic disorders with onset specific to childhood and adolescence, and childhood anxiety disorder. Of the hyperkinetic disorders, ADHD is the most common (Thapar & Cooper, 2016). Key diagnostic symptoms of ADHD include inattentive symptoms (e.g., inability to focus, disorganisation and being easily distracted) and hyperactivity or impulsivity symptoms (impatience, impulsiveness, and restlessness) (WHO, 2016). Conduct disorder often first manifests in childhood or

adolescence and is defined by antisocial and aggressive behaviour. It typically co-occurs with ADHD and frequently results in antisocial personality disorder in adulthood. (Fairchild et al., 2019.)

2.4.1 Promotion and prevention

Promotion of mental health

Reviews on mental health promotion strategies, programmes and interventions have emphasised their importance in mental health, with growing evidence of their effectiveness (Jané-Llopis et al., 2005). Mental health promotion interventions are applied to individuals and the whole population and can be delivered in various ways, including communication technology, home-based interventions, school/workplace interventions, and community-based interventions (Pollett, 2007; Sharma et al., 2017). Low-level digital mental health interventions, without face-to-face interaction, are proven to improve depression, anxiety, and psychological well-being among college students, and mental health interventions delivered via smartphone to reduce depressive symptoms in adulthood (Lattie et al., 2019; Firth et al., 2017).

Several successful mental health promotion programs have been implemented at the community level. The Rural Mental Health Project in Ireland aimed to promote positive mental health in disadvantaged rural communities through information and general awareness-raising activities, community education workshops and structured positive mental health promotion programmes. The findings suggested that the project had positive effects on community awareness and attitudes at the wider community level, including increased awareness regarding depression and suicide and improved attitudes to help-seeking (Reynolds et al., 2004). The Mental Health First Aid (MHFA) programme aimed to educate the general public on how to recognise and respond to signs of mental health problems, and to provide them with the skills and knowledge to support individuals who may be experiencing mental health difficulties. The programme was designed to be accessible to a wide range of people, including those with no prior knowledge or experience of mental health. Morgan et al. (2018) evaluated the effectiveness of MHFA in a meta-analysis including 18 trials. The results showed strong evidence that the training improved mental health knowledge, moderate improvements in

beliefs about treatments, and small effects on the accurate identification of a person with a mental health problem. (Morgan et al., 2018.)

Prevention of mental disorders

Bellón et al. (2015) combined the results of 12 systematic reviews and meta-analyses of the effectiveness of psychological and/or educational interventions to prevent the onset of episodes of depression. Studies included two types of interventions to prevent depression: cognitive behavioural intervention (such as cognitive behavioural therapy (CBT) and self-help guidelines) and other interventions (such as interpersonal psychotherapy, counselling, life review therapy, motivational interviewing, telephone social support, brochures, and support groups). The study determined that psychological and educational interventions have a small-to-medium preventive effect on the onset of depression episodes. Although there are still some unanswered questions (such as long-term effectiveness, cost-effectiveness, and intervention superiority), the study concluded that it is possible to prevent depression. (Bellón et al., 2015.) Noh and Kim (2023) combined the results of 19 studies focusing on online interventions for preventing mental health problems among adolescents. The interventions in the studies were categorized as follows: CBT-based (6 studies), family-based (5 studies, including 2 using family-based CBT), cognitive training (3 studies), health behaviour (3 studies), acceptance and commitment therapy (2 studies), mindfulness-based (1 study), and problem-solving (1 study). The results showed that online interventions effectively prevented an increase in depression scores. However, there was limited evidence regarding the prevention of increases in stress and anxiety scores. (Noh & Kim, 2023) Mendelson and Eaton's (2018) systematic review suggested that anxiety and depression can be prevented and indicated prevention for first-episode psychosis is promising. The effect sizes in the research were often small to moderate, but even small effects can have a meaningful impact on the population. (Mendelson & Eaton, 2018.)

Psychological and social interventions are effective in preventing self-injurious thoughts and behaviours, with psychotherapy and pharmacotherapy, but less intense mobile-based and internet-based interventions have also proven to be effective, especially CBT- and Dialectical Behavioural Therapy informed interventions (both Internet and mobile application based). (Arshad et al., 2020; Hawton et al., 2016; Turner et al., 2014.) Notable effects in reducing both suicide attempts and ideation have been observed in three large randomized controlled

trials, demonstrating the effectiveness of school-based programs that emphasize mental health literacy, suicide risk awareness, and skills training. Community and family interventions do not effectively prevent suicide in individuals with serious mental illness, but such interventions can increase treatment adherence and lower hospitalisation rates and suicide risk. Structured follow-up of individuals who have attempted suicide has been shown to reduce the number of repeated attempts and suicides in certain studies, although results have varied. Collaborative care with the involvement of primary health-care services in follow-up has been found to be feasible, acceptable, and effective, leading to positive outcomes in reducing ideation among elderly patients with depression and suicidal tendencies, in comparison to standard care. Family interventions aimed at suicidal adolescents have shown promising results in reducing suicidal ideation. (Zalsman et al., 2016.)

The majority of the meta-analyses utilized Cohen's d as a metric for measuring effect size. The effect size categorization followed Cohen's guidelines: effect sizes from 0.20 to 0.49 were considered small, those from 0.50 to 0.80 were classified as medium, and effect sizes greater than 0.8 were regarded as large. Effect size, which is a measure that helps us understand the practical significance or importance of a result, plays a crucial role in assessing the impact of interventions. (Cohen, 1992.) While a larger effect size generally signifies a more substantial impact resulting from an intervention, it's worth noting that even small effects can hold meaningful implications at a population level. As pointed out by Bellon et al., small to moderate effect sizes in depression prevention are comparable to those observed in primary prevention of cardiovascular diseases (Bellón et al., 2015). This underscores the notion that effect size allows us to appreciate both the magnitude and real-world implications of various outcomes, providing a comprehensive perspective on their significance.

There are also several successful suicide prevention programmes, such as the national suicide prevention program in Finland, 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, preventing marginalisation among young males, and providing an enchanting educational and cultural atmosphere. (Hakanen & Upanne, 1996.) Other successful community-based prevention programmes have been conducted in areas of Japan where the suicide rates were elevated for 65-year-olds and older. The programme offered educational health workshops, screening for depression, and health education in community settings. The results suggest that universal prevention programmes involving community-based depression

screening and health education were associated with a reduced risk of completed suicide among older residents. (Oyama et al., 2008.)

2.5 Cardiometabolic disorders

Cardiometabolic disorders are the leading cause of death globally. The development of cardiometabolic disorders may be preventable through healthy lifestyle choices. Major risk factors for cardiometabolic disorders are tobacco use, unhealthy diet and obesity, physical inactivity, and harmful use of alcohol (Buttar et al., 2005; Drozdz et al., 2021; Winzer et al., 2018). Cardiometabolic disorders can be classified into six classes: diabetes mellitus; coronary artery disease; hyperlipidaemia; overweight, obesity and other hyperalimentation, and hypertension (Protsenko et al., 2022).

Diabetes mellitus

Diabetes mellitus is a heterogeneous set of diseases characterised by hyperglycaemia caused by a relative or absolute shortage in insulin synthesis or activity. The most common subtypes are type 1 and type 2 diabetes mellitus. (Alam et al., 2014). Type 1 and type 2 diabetes develop due to interaction between genetic and environmental factors, but more behavioural factors, such as a sedentary lifestyle and poor diet, have been associated with type 2 diabetes. (Gillespie, 2006; Zimmet et al., 2001.) Type 1 diabetes occurs predominantly in young people (diagnosed at 30 years of age or younger), whereas type 2 diabetes generally manifests after the age of 40 years (Bluestone et al., 2010; Vaiserman & Lushchak, 2019).

Coronary artery disease

Coronary artery disease (CAD) is an inflammatory atherosclerotic disease that can manifest as stable angina, unstable angina, myocardial infarction, or sudden cardiac death (Malakar et al., 2019). CAD results from genetic and environmental factors, with heritability estimated to range between 40% and 60% (McPherson & Tybjaerg-Hansen, 2016). Smoking, type 2 diabetes mellitus, hyperlipidaemia, hypertension, and psychosocial stress have been linked to the development of CAD, according to comprehensive epidemiological studies (Price et al., 1999; Bagheri et al., 2016).

Hyperlipidaemia

Hyperlipidaemia is characterised by an increase in cholesterol levels in the blood. Hyperlipidaemia can raise the risk of cardiovascular events such as myocardial infarction and stroke. Diseases such as biliary obstruction, chronic renal disease, type 2 diabetes mellitus, high blood pressure, and hypothyroidism are secondary causes of increased low-density lipoprotein cholesterol. A high saturated or trans-fat diet, physical inactivity, smoking, and obesity are studied risk factors for hyperlipidaemia. (Karr, 2017.) Genetic susceptibility to familial mixed hyperlipidaemia, the most common dyslipidaemia, is determined by several DNA sequence variations and their interactions (Suviolahti et al., 2006).

Overweight, obesity, and other hyperalimentation

Obesity and overweight are described as abnormal or excessive fat accumulations that may have a negative impact on health (WHO, 2022). Obesity is a complex condition caused by genetic, epigenetic, physiological, behavioural, sociocultural, and environmental variables that culminate in an imbalance between energy intake and expenditure over time (Bray et al., 2016). Several risk factors for weight gain have been identified, such as depression, short sleep duration, childhood abuse, low maternal education, and heavy drinking (Solmi et al., 2018; Traversy & Chaput, 2015). Moreover, obesity has been associated with many other cardiometabolic disorders, such as hypertension, coronary artery disease, and diabetes mellitus (Elagizi et al., 2020).

Hypertension

Essential hypertension is defined as an elevation in blood pressure (blood pressure >140/90 mm Hg) caused by an unexplained cause that raises the risk of cerebral, cardiac, and renal problems (Messerli et al., 2007). Over 1.2 billion people worldwide are affected by hypertension, which has emerged as the most serious and expensive public health issue (Rossier et al., 2017). Hypertension is also known as one of the most significant modifiable risk factors for cardiovascular disease and one of the main causes of morbidity and mortality globally (Brouwers et al., 2021). Hypertension is caused by both environmental and hereditary factors; for example, obesity, physical inactivity, chronic stress, preterm birth and low birth weight, and air and noise pollution have been linked to hypertension (Diaz & Shimbo, 2013;

Fuks et al., 2017; Haikerwal et al., 2020; Jiang et al., 2016; Liu et al., 2017). The recommendations of hypertension guidelines consist of the following elements: weight reduction, a healthy diet, dietary sodium reduction, increasing physical activity, quitting smoking, and moderate alcohol consumption (Williams et al., 2018).

Cerebrovascular disorders

In cerebrovascular disorders, one or more cerebral blood arteries are involved in the disease process and a region of the brain is temporarily or permanently impacted by ischaemia or bleeding. Subarachnoid haemorrhage, aneurysms, stroke, and vascular malformations are all examples of cerebrovascular disorders. (Portegies et al., 2016.) Strokes are the most severe cerebrovascular disease. An ischaemic stroke occurs when a cerebral artery becomes clogged, resulting in brain cell loss and neurological damage, and haemorrhagic stroke if brain vessels rupture (Portegies et al., 2016; Prabhakaran et al., 2015). Many risk factors of stroke have been found in epidemiological studies. Stroke has been linked to genetic variations in high blood pressure, myocardial infarction, and atrial fibrillation (Falcone et al., 2014; Komotar et al., 2009). Other cardiovascular diseases, such as hypertension, diabetes mellitus, and obesity have been linked to stroke (Huang et al., 2014; Sarwar et al., 2010; Strazzullo et al., 2010). Also, several lifestyle factors such as smoking), diet and alcohol consumption have been associated with stroke (Meschia et al., 2014; Mons et al., 2015).

2.5.1 Promotion and prevention

The key aspect of preventing cardiometabolic disorders is managing the risk factors. The systematic review suggests that population reductions in weight are achievable through community-based interventions, including interventions which have incorporated educational, health promotion, social marketing, policy, or legislative reform strategies (Wolfenden et al., 2014). Galaviz et al.'s (2018) meta-analysis summarised findings on lifestyle modification techniques for type 2 diabetes prevention. The study discovered that people who received an intervention (group education, telephone counselling or community-wide education by community members, self-directed education via DVDs, group education by a healthcare professional, education via TV, counselling via interactive voice response call, individual counselling by healthcare professional, education and counselling by

telehealth, or education via the internet) had a 29% lower risk of developing diabetes, reduced 1.5 kg more body weight, and reduced fasting blood glucose by 0.09mmol/L more than those in control groups. (Galaviz et al., 2018.)

Mobile application-based interventions (including self-measured blood pressure, online disease management programmes, telemonitoring self-care support systems, social network self-management education, and several specific mobile applications) for hypertensive patients have been reported to be effective in lowering blood pressure and increasing medication adherence (Xu & Long, 2020). Lawlor et al. (2018) combined the results of 31 studies on the effects of community-based interventions for cardiovascular disease secondary prevention on behavioural risk factors, such as physical activity, diet, alcohol use, blood pressure, and cholesterol. Interventions were delivered via the internet, telephone, home visits, or in general practices or outpatient settings. The majority of interventions were multi-component. The review identified evidence that interventions for secondary cardiovascular disorder prevention have positive effects on physical activity, blood pressure, and total cholesterol. (Lawlor et al., 2018.)

The Stanford Community study is one example of a successful community-based intervention in encouraging healthy lifestyles. The interventions included continual exposure to general education, along with multiple risk factor education campaigns per year, aimed at promoting various health behaviours. The program targeted reductions in plasma cholesterol levels, blood pressure, cigarette use, and weight, as well as promoting increased physical activity. Education was delivered through various channels, including television, radio, newspapers, mass-distributed print media, and direct education methods such as face-to-face sessions, contests, and correspondence courses. Additionally, special programs were developed for Spanish-language media and school-based programs were implemented for specific grades, incorporating nutrition, exercise, and smoking sessions, along with materials for parents. After two years of intervention, a significant drop in the population's health factors (cholesterol level, blood pressure, smoking rate) could be seen (Farquhar et al., 1990). Another well-known population-level health intervention is the North Karelia project, in which the aim was to reduce cardiovascular diseases through interventions including broad health promotion and policies in the 1970s. The project was successful, and over the years the death rates due to cardiovascular diseases have declined by 65% in men and 70% in women (Puska et al., 2009).

3 Aims

The main aims of the thesis were to explore the changes in incidences of hospital-treated psychiatric disorders over decades in Finland and explore the possible effects of the follow-up of the Northern Finland Birth Cohort (NFBC) studies on psychiatric diagnosis, use of psychiatric care services, suicidal behaviour, and cardiometabolic disorders.

The aims of the original publications were as follows:

1. To explore the changes in the incidences of childhood and early adulthood hospital-treated psychiatric disorders in five large Finnish birth cohorts of individuals born between 1966 and 1997.
2. To examine whether participation in the NFBC1986 had any effect on the use of psychiatric care services or suicidal behaviour.
3. To examine whether participation in the NFBC1966 had any effect on the use of psychiatric care services.
4. To examine whether participation in the NFBC studies had any effect on the prevalence of cardiometabolic disorders.

4 Material and methods

4.1 Study cohorts

Five different birth cohorts were used in this study: the Northern Finland Birth Cohort 1966 (NFBC1966) and 1986 (NFBC1986), the Finnish 1981 Birth Cohort (FBCS 1981), and the Finnish Birth Cohort 1987 (FBC 1987) and 1997 (FBC 1997).

4.1.1 NFBC 1966 (Studies I, III-IV)

The NFBC1966 covers people whose expected date of birth was in 1966 in the former two northernmost provinces of Finland, Oulu and Lapland. The cohort includes 12,055 mothers and 12,231 children. Of the NFBC1966 participants, 189 (1.5%) were born in 1965, 11,999 (97.9%) in 1966, and 63 (0.5%) in 1967. The NFBC1966 is a longitudinal and prospective birth cohort with several follow-ups. (University of Oulu, 1966.)

Follow-up studies for the whole cohort

The first follow-up for the NFBC1966 cohort was conducted during and just after pregnancy. The follow-up included a questionnaire (including questions about background, life situation and living habits) during pregnancy (from the 24th to the 28th gestational week) collected by midwives in antenatal clinics. The questionnaire included items such as depressed mood and smoking during pregnancy. Delivery information was also collected. (Järvelin et al., 1993.) The second follow-up was conducted at age 1 year, including a questionnaire concerning children's growth, health, and development from children's welfare clinics, with a 91.2% participation rate (von Wendt et al., 1984). The next follow-up was at age 14 years, with a participation rate of 93.6%. The follow-up was conducted with a postal questionnaire, including questions for NFBC1966 participants about their growth and health, living habits (questions about smoking, alcohol, and other intoxicant use), school performance, and family situation. (Rantakallio, 1983.)

The next follow-up for the whole cohort was conducted at age 31 years. The follow-up consisted of a postal questionnaire with a participation rate of 77.4%, which included questions on life situation, background information, exercise and

physical performance (how often and how much), occupation, living environment, health (e.g., height, weight, history of cardiometabolic disorders, use of medications), diet, use of depression, tranquilliser, and sleep medication, questions on possible psychiatric disorders, and living habits (questions on smoking, alcohol, and other intoxicant use). (Järvelin et al., 2004.) The questionnaire included the Hopkins Symptom Checklist-25 (HSCL-25), which screens depressive and anxiety symptoms (Veijola et al., 2003). The clinical examination included a skin-prick allergy test, physical performance tests (step test, grip strength test, back endurance test), blood pressure and pulse, blood tests, other laboratory tests (cholesterol, glucose, insulin, triglyceride), and spirometry (participation rate 71.3%). In the clinical examination, an additional questionnaire was given to the participants. This included several psychiatric screens, such as the Bipolar II scale, Hypomanic Personality Scale, Physical Anhedonia Scale, Social Anhedonia Scale, Perceptual Aberration Scale and Schizoid Scale, Tridimensional Personality Questionnaire and Temperament and Character Inventory (Miettunen et al., 2004; Miettunen et al., 2010).

The latest follow-up has been conducted at age 46 years, with a 66.5% participation rate in the questionnaire and 56.7% in the clinical examination The questionnaire included questions on background, lifestyle (questions on smoking, alcohol, and other intoxicant use), health (e.g., disorders and medications), economy, work, and mental resources. Depressive and anxiety symptoms were questioned using HSCL-25, the Generalized Anxiety Disorder 7 questionnaire, Beck's Depression Inventory 21, and psychological features using the Fear-Avoidance Beliefs Questionnaire. In the clinical examination data on cardiovascular health (brachial pressure, blood pressure, 15-led rest electrocardiogram, echo and carotid ultrasound), allergies (skin allergy test, spirometry, whole body examination by dermatologist), eyes (eye examination), physical activity and fitness (two weeks' accelerometer measurements, back muscle strength test, step test, hand grip strength test), pain perception and tolerance (pressure pain and thermal perception), musculoskeletal health (spinal, ankle and low back movement tests, knee, ankle, and foot radiography, and lumbar magnetic resonance imaging (MRI)), height, weight, waist and hip circumferences, dental health, cognitive tests, and biological samples were collected. The clinical examination also included the cognitive Paired Associative Learning test. (Kujanpää et al., 2017; Nordström et al., 2021; Taivalantti et al., 2020.)

Sub-studies

The follow-up in the NFBC1966 also contains many sub-samples. In 1997–1998, a psychiatric study of people living in the city of Oulu was conducted. The sample was based on the HSCL-25 screening, which was part of a 31-year follow-up. Based on the screening, 234 screen positives (HSCL-25 scores above the mean) and every tenth screen negative were invited for a Structured Clinical Interview for DSM-III (SCID) (Spitzer et al., 1992). A SCID interview consists of two parts; SCID-I for making major DSM-III-R axis-I diagnoses and SCID-II for diagnosing all DSM-III-R personality disorders. The interview was conducted on 209 screen positives and 112 screen negatives (Veijola et al., 2003).

A sub-study of individuals with psychosis and their controls was conducted in 1999–2001. Out of the 142 invited individuals with psychosis, 91 took part in the sub-study. Comparison subjects were sex-matched randomly selected from NFBC1966 participants who were known not to have had a psychotic episode. A total of 187 controls were invited, and 104 subjects participated in the study. (Tanskanen et al., 2005.) The data were collected through SCID-I interviews, questionnaires (including questions about the use of antipsychotic medication, social background, and substance use), brain MRI scans, and cognitive tests (Haapea et al., 2007). The follow-up for the sub-sample was conducted in 2008–2011, also including new subjects, 107 cases with psychotic disorders, 54 subjects with schizophrenia, and 194 controls. The follow-up included psychiatric interviews, questionnaires, brain MRI scans, and cognitive tests (Jääskeläinen et al., 2015). In studies conducted on individuals with psychosis and their controls, 54 cases with psychotic disorder and 76 controls participated in both sub-studies.

One of the sub-studies focusing on the health and life satisfaction of male cohort participants was conducted on a random sub-sample of males at age 24 years (N=2,500) (Pietilä, 1994). The follow-up consisted of a questionnaire including questions about physical activity, diet, smoking habits, overall health, and relationships. Another sub-study focusing on health was conducted on a random sub-sample of 31-year-old follow-up participants (N=196). The follow-up consisted of exercise and food diaries for 7 days. (Laitinen et al., 2005.)

4.1.2 NFBC1986 (Studies I-II, IV)

The NFBC1986 study covered people with an expected date of birth between 1 July 1985, and 30 June 1986, in the two northernmost former provinces in Finland, Oulu

and Lapland. The cohort comprises 9,362 mothers and 9,479 children. The NFBC 1986 is a longitudinal and prospective birth cohort with several follow-ups. (University of Oulu, 1986.)

Follow-up studies for the whole cohort

In the NFBC1986, the first follow-up was conducted during and just after pregnancy. The follow-up included three questionnaires for the mother. In addition, clinical data from antenatal clinics were collected. The questionnaires included questions about background, smoking and alcohol use, general health, fatigue during pregnancy, and delivery information. (Järvelin et al., 1997.)

In the autumn of the first school year at age 7, the next follow-up was conducted. The follow-up was conducted by questionnaire to parents (participation rate 90%) including information on children's growth, development and health, and social situation (Taanila et al., 2004). In the spring of the children's first school year, the next follow-up was conducted. Two questionnaires were sent to parents, one for themselves and the other for the children's teachers. Parents completed a modified (one of the internalising items was modified) Rutter A2, and teachers filled in a Rutter B2 questionnaire on children's psychomotor development and behaviour (Elander & Rutter, 1996; Rutter, 1967). The participation rate for the parents' Rutter A2 was 90% and for teachers, the participation rate for the Rutter B2 was 92% (Miettunen et al., 2014). The Rutter scales screen children's behavioural and emotional features (Rutter, 1967).

The next follow-up for the whole cohort was conducted at age 15–16 years. The follow-up consisted of a questionnaire (participation rate 77.9%) and clinical examination (participation rate 73.7%). The questionnaire included questions about family, school health (history of heart diseases, weight and height, blood pressure), physical activity (e.g., times and duration of physical exercise), sexual behaviour, substance use (smoking, alcohol, or other intoxicants), diet (eating habits, use of sugar and fat, amount and times of eating bread, dairy products, sweets, etc.), living habits, and hobbies. The questionnaire included several psychiatric screening tools: the 21-item PROD-Screen for prodromal psychotic symptoms, the Youth Self Report (YSR) for evaluating the competencies and problems of 11 to 18-year-old adolescents, the Strengths and Weakness of Attention-Deficit/Hyperactivity Disorders Symptoms and Normal Behaviour Scale (SWAN) to detect ADHD symptoms, and the Toronto Alexithymia Scale to measure alexithymia (Achenbach & Rescorla, 1991; Bagby et al., 1994; Heinimaa et al., 2003; Swanson et al., 2001).

Clinical examinations included weight, height, waist-hip measurements, sitting height, spirometry, blood pressure, pulse rate, blood samples, physical activity (bicycle ergometer) test, prick tests, and questions about puberty, nutrition, smoking, and use of alcohol.

The latest follow-up has been conducted at age 33–35 years, with a questionnaire (participation rate 36.3%), clinical examinations (participation rate 31.4%) and cognitive tests (participation rate 16.2%). The questionnaire included questions about background, life satisfaction, physical activity, diet, substance use, work, and mental resources. In the clinical examination, cardiovascular, dental, and musculoskeletal health was measured, and biological samples taken.

Sub-studies

The NFBC1986 also includes multiple sub-studies. One of the psychiatric sub-samples was based on the SWAN screening at the 16-year follow-up, including 268 likely ADHD cases and 196 controls (Smalley et al., 2007). Participants were interviewed (ages 16–18 years) using the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (Kaufman et al., 1997). The follow-up also included several intelligence and cognitive tests. Parents also completed a questionnaire concerning their attention problems using the ADHD-Rating Scale-IV and background information.

The next psychiatric sub-study (the Oulu Brain and Mind Study I) was conducted in 2007–2010 (participants age 21–24 years) (Veijola et al., 2013). In total 329 of the invited 763 participants of the NFBC1986 participated. The sample was based on participants at risk of developing psychosis (familial risk for psychosis: N=78 and symptomatic risk for psychosis: N=58), and the comparison group included 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). In addition, 34 individuals who had participated as controls in the earlier ADHD study participated in the Oulu Brain and Mind I study. Participants completed a questionnaire including questions on their background information, relationships, quality of life, substance use, and several psychiatric and psychological screening instruments. The clinical examination included blood sampling (DNA from blood) and a urine sample (to detect the use of drugs and medications). Psychiatric nurses also interviewed participants with questions about illness and treatments, evaluated current ADHD symptoms using a semi-structured interview, adapting criteria from ICD-10 and DSM-5, the Structured Interview for Prodromal Syndromes, and the

Structured Clinical Interview for DSM-IV Axis-I Disorders (SCID-I) (First et al., 1997; Lindholm et al., 2019; Miller et al., 1999) . Furthermore, the participants underwent structural MRI, diffusion-tensor imaging, resting-state functional MRI, and functional MRI with three different tasks: the Sternberg verbal working memory task, the Human Causal Learning prediction error task, and a facial recognition task (Corlett et al., 2006; Johnston et al., 2003; Sternberg, 1966). The MRI scans were performed with a 1.5 T scanner and the entire procedure took 60–75 minutes. The participants also received several cognitive tests. Information about the results of the MRI scans was given to the participants.

The next psychiatric sub-study (the Oulu Brain and Mind Study II) was conducted at the age of 25–27 years (Björnholm et al., 2020). The cases in the study were selected based on prenatal exposure to maternal cigarette smoking (N=253), and the controls were matched by maternal education and geographical region (N=218). The participants completed a questionnaire including information about their background factors, lifestyle, and several screening instruments. Structural MRI, diffusion-tensor imaging, magnetisation transfer imaging, and resting-state functional MRIs were conducted. The MRI scanning was performed with a 1.5 T scanner and the entire procedure took 45–60 minutes. The participants were also assessed using several cognitive tests. Blood and urine samples were also taken. The interviews included, among other things, a psychiatric SCID-I screen. The participants received information about the results of the MRI scans, cognitive tests, and possible mental disorders.

In the Oulu Back Study, a questionnaire including questions about low back pain history, background factors, leisure activities, and history of injuries was sent to cohort participants living in Oulu and surrounding municipalities at age 18 years (Auvinen et al., 2009). The following sub-study was conducted when the cohort participants were 19–22 years and 29–32 years with an MRI scan of the lumbar spine (Mäki et al., 2019). A sub-population of the NFBC1986 at age 24 years took part in the ESTER – Preterm Birth, Pregnancy and Offspring Health in Adult Life study. The study included blood sampling, blood pressure, body mass index (BMI), waist, and hip measurements (Sipola-Leppänen et al., 2015). At age 26 years, the gynaecological health of young women was studied, and questions about socio-demographic and other health background factors mainly about reproduction, menstruation, and infertility were sent to a sub-population of the NFBC1986 (West et al., 2014).

4.1.3 Finnish 1981 Birth Cohort, The Finnish Birth Cohorts 1987 and 1997 (Study I)

The FBCS 1981

The Finnish 1981 Birth Cohort (FBCS 1981) is based on a random sample including 10% (N=5,417) of Finnish children born in 1981. The cohort includes 2,722 males and 2,695 females. The sample was drawn in a two-stage procedure in the catchment areas of the five child psychiatric departments of the university hospitals in Finland (Helsinki, Kuopio, Oulu, Tampere, and Turku). Data have been collected from mothers during pregnancy and delivery. The first follow-up for the cohort participants was conducted at age 8, with a 97% participation rate. Teachers and parents filled in a questionnaire on psychiatric symptoms, bullying behaviour, and family structure. The next follow-up was conducted on males at age 18 during military call-up. The participants were assessed for psychiatric symptoms and sense of coherence. (Almqvist et al., 1999; Filatova et al., 2019.)

The Finnish Birth Cohort 1987 and 1997 studies

The Finnish Birth Cohort 1987 (FBC 1987) and 1997 (FBC 1997) are national, register-based follow-up studies which follow cohorts born in the years 1987 and 1997, excluding those who died during the perinatal period. The FBC 1987 comprises 59,476 children and the FBC 1997 58,802 children. The FBC studies are register-based, and all the collected data are obtained from several registers. Participants of the FBC studies have never been contacted. (Gyllenberg et al., 2018; Paananen & Gissler, 2012.)

4.2 Measures

The outcomes of interest in this study were psychiatric disorders, use of psychiatric care services, suicidal behaviour, and cardiometabolic disorders.

4.2.1 Psychiatric disorders (Studies I and II)

Data on psychiatric disorder diagnosis and the use of psychiatric care services were obtained from the CRHC. A broad range of ICD codes for psychiatric disorders

were classified into several classes. The ICD-8 (from 1969 to 1986), ICD-9 (from 1987 to 1995), and ICD-10 (from 1996 onwards) codes were harmonised (Table 2).

Table 2. Psychiatric diagnostic groups with respective codes according to ICD-8, ICD-9, and ICD-10 classifications. (Under CC BY-NC licence from Original publication I © 2020 Authors).

Diagnostic group	ICD-8 1969–1986	ICD-9 1987–1995	ICD-10 1996–2017
Any psychiatric or neurodevelopmental disorder	290–301, 303–305, 3060–3067, 307–309	290–301, 303–316	F00–F53, F60–F63, F68–F69, F80–F99
Organic mental disorders	290, 292–294, 309	290, 293, 294, 310	F00–F09
Mental disorders due to psychoactive substance use	291, 303–304	291, 292, 303–305	F10–F19
Alcohol	291, 303	291, 303, 3050A	F10
Other substances	304	292, 304, 3051–3059	F11–F19
Schizophrenia, schizotypal and delusional disorders	295, 297, 2982–2983, 29899, 299	295, 297, 2988A, 2989X, 3013C	F20–F29
Schizophrenia	295	295	F20, F25
Other non-affective psychosis	297, 2982–2983, 29899, 299	297, 2988A, 2989X, 3012C	F21–F24, F28, F29
Mood disorders	296, 2980, 3004, 79020	296, 3004A	F30–F34
Mania and bipolar	2961–2963, 29688	2962–2964, 2967A	F30, F31
Depression	2960, 2980, 30040–30041, 79020	2961, 2968A, 3004A	F32–F34
Neurotic, stress-related and somatoform disorders	3000–3003, 3005–3009, 305, 30799	3000–3003, 3006–3009, 3078A, 3090A, 3092C–E, 3098A, 3098X, 3099X	F40–F48
Obsessive-compulsive disorder	3003	3003A	F42
Anxiety disorders	3000–3002	3000A–C, 3002B–X	F40.0–F40.2, F40.8–F41.1, F41.3, F41.8, F41.9
Post-traumatic stress disorder		3098X	F43.1
Behavioural syndromes associated with eating, sleep, or puerperium	3064–3065	3071A, 3074A, 3074F–H, 3075A–C, 3075E	F50, F51, F53
Eating disorders	3065	3071A, 3075A–C, 3075E	F50

Diagnostic group	ICD-8 1969–1986	ICD-9 1987–1995	ICD-10 1996–2017
Disorders of adult personality	301	3010A, 3011D, 3012A, 3014A, 3015A–B, 3016A, 3017A, 3018B–X	F60, F61, F62
Paranoid Personality	3010	3010A	F60.0
Schizoid Personality	3012	3012A	F60.1
Dissocial Personality	3017	3017A	F60.2
Emotionally unstable personality	3013	3018D	F60.3
Disorders diagnosed in childhood or adolescence	3060–3063, 3066–3067, 30899	299, 313–315, 3120A, 3123C-D, 3070A–B, 3072A-D, 3073A, 3075D, 3076A–C, 3077A, 3092A-B, 3093A, 3094A	F80–F84, F88–F95, F98
Autism spectrum disorders		299	F84.0, F84.5, F84.8, F84.9
Learning and coordination disorders		315	F80–F83
ADHD		314	F900
Tic disorders	3062	3072A-D	F95
Conduct and oppositional disorders	30899	3120A, 3123C–D, 3138A	F90.1, F91.0–F91.3, F91.8–F92.0, F92.8, F92.9

4.2.2 Suicidal behaviour (Study II)

In the second study, suicidal behaviour was studied with two outcome variables: suicidal behaviour (including suicide attempts and self-harm) and suicides from 2 years 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 suicidal behaviour, including self-harm or suicide attempt. Death by suicide was defined using the relevant statistical underlying cause-of-death diagnoses, obtained from the Cause of Death Registers at Statistics Finland. (Table 3)

Table 3. Suicidal behaviour codes in ICD-9 and ICD-10 classifications. (Under CC BY 4.0 licence from Original publication II © 2022 Authors).

Diagnostic group	ICD-9 1987–1995	ICD-10 1996–2017
Suicidal behaviour	E950A–E959X	X60–X84, Z91.5, Z72.8, Y87.0
Death by suicide	E950-E959B, E959X, E950A–K, E951–E959C, E959X	X60–X84, Y87.0

4.2.3 Use of psychiatric care services (Study III)

In research question 3 we examined the use of psychiatric care services between the 10th and 50th birthdays in the studied cohorts by using several variables. First, we created a variable indicating if the study subject had had any visits to a psychiatric speciality (outpatient or inpatient). The second variable indicated if the study subject had had any psychiatric hospitalisation. The third variable indicated the number of days of psychiatric hospitalisation of those who had had any psychiatric hospitalisation.

4.2.4 Cardiometabolic disorders (Study IV)

In research question 4, the following cardiometabolic disorders were studied in the NFBC1966 and NFBC1986: diabetes mellitus, coronary artery disease; hyperlipidaemia; overweight, obesity and other hyperalimentation; hypertension; cerebrovascular disorder and any aforementioned cardiometabolic disorder. The CRHC was used to identify patients who had a diagnosis (primary diagnosis or secondary diagnosis) of the above-described cardiometabolic disorders (Table 4).

Cardiometabolic-related deaths were defined with the corresponding ICD codes (Table 4) from statistical underlying cause-of-death diagnoses. The cause-of-death codes were obtained from the Cause of Death Register.

Table 4. Cardiometabolic disorder groups with respective codes according to ICD-8, ICD-9, and ICD-10 classifications. (Under CC BY 4.0 licence from Original publication IV © 2023 Authors).

Cardiometabolic disorder	ICD-8 1969–1986	ICD-9 1987–1995	ICD-10 1996–2017
Diabetes mellitus	250	250	E10–E14
Type 1		2500B–2508B	E10
Type 2		2500A–2508A	E11
Coronary artery disease	410–414	410–414	I20–I25
Hyperlipidaemia	272	272	E78
Overweight, obesity and other hyperalimentation	27799	278	E65–E68
Hypertension	400–404	401–405	I10–I15
Cerebrovascular disorders	430–438	430–438	I60–I69
Any cardiometabolic disorder	250, 272, 27799, 400–404, 410–414, 430–438	250, 272, 278, 401–405, 410–414, 430–438	E10–E14, E65–E68, E78, I10–I15, I20–I25, I60–I69

In the NFBC1966, cardiometabolic disorders were followed from the age of 7 to 50 years (from 1972 to 2017), while the information in the CRCH was incomplete before 1972. In the NFBC1986 the follow-up on cardiometabolic disorders covered the age from 0 to 29 years (1986–2016).

4.2.5 Other variables of interest (Study II)

A few covariates of interest, marital status, and education were considered in Study II. Marital status was classified into two classes: married and single. Education indicated the highest achieved level of education at the end of follow-up (secondary education or less and tertiary education). Information on covariates was obtained from Statistics Finland.

4.3 Final study samples

Study I

In the first study, the final dataset included a total of 145,405 subjects, of which 71,209 were males and 65,190 were females. By cohort, the numbers were as follows: 12,231 from the NFBC1966; 5,417 from the FBCS 1981; 9,479 from the NFBC1986; 59,476 from the FBC 1987 and 58,802 from the FBC 1997.

Study II

In the second study, the study sample consisted of the NFBC1986 and its comparison cohort. The comparison cohort was a sub-sample from the FBC 1987, which comprised all people born in the Lapland and Oulu provinces in 1987. From the NFBC1986, we excluded those who did not survive the perinatal period (stillbirths: N=7, 0.5%; those who died within the first 7 days of life: N=36, 0.4%) to make the datasets comparable. After exclusion, 9,396 participants of the NFBC1986 (male: N=4,839, 51.5%; female: N=4,557, 48.5%) and 8,959 participants from the comparison cohort (male: N=4,550, 50.8%; female: N=4,409, 49.2%) were included in the analyses.

Study III

The study cohort comprised all the people born in the provinces of Oulu and Lapland in 1966. In 1966 there were 12,043 births in the provinces of Lapland and Oulu, of which 96.3% are participants of the NFBC1966. The comparison cohort comprises all the people born in the provinces of Lapland and Oulu in the years 1965 and 1967. The cohort includes 24,471 subjects, 12,465 (50.9%) born in 1965 and 12,006 (49.1%) born in 1967. Personal identification numbers and dates of death were obtained from the Digital and Population Data Services Agency. Medical history was obtained from the registers at the Finnish Institute of Health and Welfare (THL). From both datasets, we included in our analysis those who were living in Finland at the beginning of follow-up at age 10 years. In the study cohort, N=53 (0.4%) died before their 10th birthday and N=543 (4.5%) were living abroad at age 10 years. The respective numbers in the comparison cohort are N=86 (0.4%) and N=1046 (4.3%). After exclusions, 11,447 study subjects in the study cohort and 23,339 subjects in the comparison cohort were included in the analysis.

Study IV

The study sample consisted of the NFBC1986 and NFBC1966 and their comparison cohorts. From the NFBC1966 we excluded those who were born in 1965 (N=186) or 1967 (N=63) and stillbirths (N=153) while the comparison cohort comprises live-born children in 1965 and 1967. The final dataset of the NFBC1966 comprised 11,723 subjects, 6,000 males and 5,723 females. The comparison dataset comprised 24,471 participants, 12,511 males and 11,960 females. The study sample for the NFBC1986 and its comparison cohort was the same as used in Study II (NFBC1986 N=9,396; comparison cohort N=8,959).

4.4 Statistical methods

Study I

The cumulative incidences of the first hospitalisation due to psychiatric disorder were analysed in three different periods: childhood and adolescence (under 18 years old), young adulthood (18–28 years) and ages 0–28 years in each cohort separately. Analysis of childhood and young adulthood was treated independently; in young adulthood, the incidence was new hospitalisations due to certain disorders disregarding whether there had been previous psychiatric contact before age 18 years.

In childhood and adolescence analysis in the diagnosis classes other substance use disorder; schizophrenia, mania and bipolar; obsessive-compulsive disorder; post-traumatic stress disorder, and tic disorder, the number of cases were too low to be analysed properly in both sexes, and in anxiety disorders in males and other non-affective psychosis: autism spectrum disorders and ADHD in females. In post-traumatic stress disorder, autism spectrum disorder, learning and coordination disorders and ADHD, there was no ICD-8 code, so the NFBC1966 was not included in the analysis of those diagnosis classes.

Disorders usually diagnosed during childhood were not included in the early adulthood analysis and organic psychiatric disorders were excluded from the analysis. In the diagnosis classes, organic mental disorders, obsessive-compulsive disorders, post-traumatic stress disorder, paranoid personality disorder, schizoid personality disorder, and dissocial personality disorder in both sexes and in eating disorders in males, the number of cases was also too low to be analysed properly.

Pearson's chi-squared test was conducted to assess the equality of proportions. We analysed the difference in proportions using a Poisson regression with an offset variable. The model was created using a number of subjects with the first hospitalisation due to a specific psychiatric disorder as a dependent variable, the cohort year as the independent variable and the logarithmic number of populations as an offset variable, and incidence rate ratios (IRR) with a 95% confidence interval (CI) are reported. The IRR estimates the change in proportions per birth cohort. All analysis was conducted separately in males and females. The risk ratio with a 95% confidence interval for sex was also calculated to compare the sex difference in different cohorts.

Study II

The cumulative incidence rates of psychiatric disorders and suicidal behaviour at ages 2–28 years were calculated for both cohorts (NFBC1986 and the comparison cohort) and the significance of differences was estimated with the Chi-square test. Risk ratios (RRs) with 95% confidence intervals (CIs) were calculated by sex separately in each diagnosis group where the number of cases was large enough. In addition, the Mantel-Haenszel risk ratio (RR_{MH}) was used to calculate the adjusted RRs (adjusted for general characteristics: education, and marital status) in each diagnosis group where the number of cases within each adjustor was large enough. The numbers of suicidal behaviour within each general characteristic were too low to be analysed with RR_{MH}.

Study III

We used several analysis methods to estimate the use of psychiatric care services between the study and the comparison cohort. First, we analysed the difference in visits to a psychiatric speciality and psychiatric hospitalisation between the study and comparison cohort with the Chi-square test. The number of days of psychiatric hospitalisation was analysed with the Mann-Whitney U-test. The age of the first visit to psychiatric speciality and the age of the first psychiatric hospitalisation was analysed using Welch's t-test.

Then, for the first visit to a psychiatric speciality and the first psychiatric hospitalisation, we fitted the Cox proportional hazards regression models to calculate the hazard ratios (HR) with 95% confidence intervals (CI). We also fitted the Kaplan-Meier curves and calculated the equality of survival functions with the

Log-rank-test. Time of emigration and death were used as a censoring point in analyses (information from the Population Register Centre). A number of days of psychiatric hospitalisation was analysed with Zero-Truncated Negative Binomial Regression and incidence rate ratios (IRR) with 95% CIs are reported.

Study IV

The cumulative incidence rates of cardiometabolic disorders in hospital-treated cardiometabolic disorders (including inpatient and specialised outpatient visits) were calculated for the study and comparison cohorts covering the full follow-up (age 7–50 years in the NFBC1966; age 0–29 in the NFBC1986). Different types of diabetes mellitus were examined from 1987 onwards (age 2–29 years in the NFBC1986 and age 22–50 years in the NFBC1966). Because of the small number of cases of hyperlipidaemia and coronary artery disorders in the younger population (follow-up ends at age 29 years), the separate diagnosis classes are not included in the analysis. Risk ratios (RRs) with 95% confidence intervals (CIs) were calculated by sex separately in each diagnosis group. The age of the first onset of cardiometabolic diagnosis (median with IQR) is reported in each diagnosis group. The difference between the medians was estimated using quantile estimation (QE) and Q with p-values is reported (McGrath et al., 2020). The age of the first onset of cardiometabolic disorders was plotted over the full follow-up period in both NFBCs, separated by sex. Cumulative incidences of cardiometabolic-related causes of death were calculated for the NFBC1966 and comparison cohorts at age 0–50 years. The age of death caused by any cardiometabolic disorders (median with IQR) by sex is also reported.

5 Ethical considerations

5.1 Ethical considerations

The Northern Finland Birth Cohorts are kept under review by the ethical committee of the Northern Ostrobothnia Hospital District (Ethical Committee 94/2011 and 108/2017) and permission to gather data was obtained from the Finnish Ministry of Social Affairs and Health. The register-based FBC 1987 and FBC 1997 obtained ethics approval from the Finnish Institute for Health and Welfare (Ethical Committee 28/2009). The FBCS 1981 obtained ethics approval from the Hospital District of Southwest Finland (Ethical Committee 12/2006).

We also collected data from several registrars. By Finnish law, informed consent is not always required when using only register data. Register-based studies can be conducted without subjects' informed consent if the following requirements are met: research cannot otherwise be carried out without identifying the person (The Data Protection Act; Chapter 5, Section 29); appropriate research plan where persons responsible for the research are named as well as everyone who had to have access to the data; data that pertains to a given individual may not be disclosed to outsiders at any stage; and the data file is archived, destroyed, or made unidentifiable after ending the project (The Data Protection Act; Chapter 5, Section 31).

5.2 Personal involvement

The PhD student planned the thesis together with supervisors Professor Juha Veijola and Research Professor Mika Gissler. The PhD student was the primary person responsible for carrying out the data application for the register data. The PhD student was solely in charge of designing and executing the statistical analyses and preparing all tables and figures. The PhD student wrote the first and final versions of all four publications and the summary part of the thesis.

6 Results

6.1 Cumulative incidences of psychiatric disorders in NFBC, FBC and FBCS 1981 (Study I)

The total cumulative incidences of psychiatric disorders at age 0–28 were 6.2% in the NFCB1966, 9.0% in the FBC 1981, 8.5% in the NFBC1986, and 7.4% in the FBC 1987 (difference in proportions analysed with incidence rate ratio IRR: 1.01, 95% CI: 1.01–1.02) among males. The respective numbers among females were 3.4%, 5.4%, 6.7%, and 7.6% (IRR: 1.04, 95% CI: 1.03–1.05). (Figure 1)

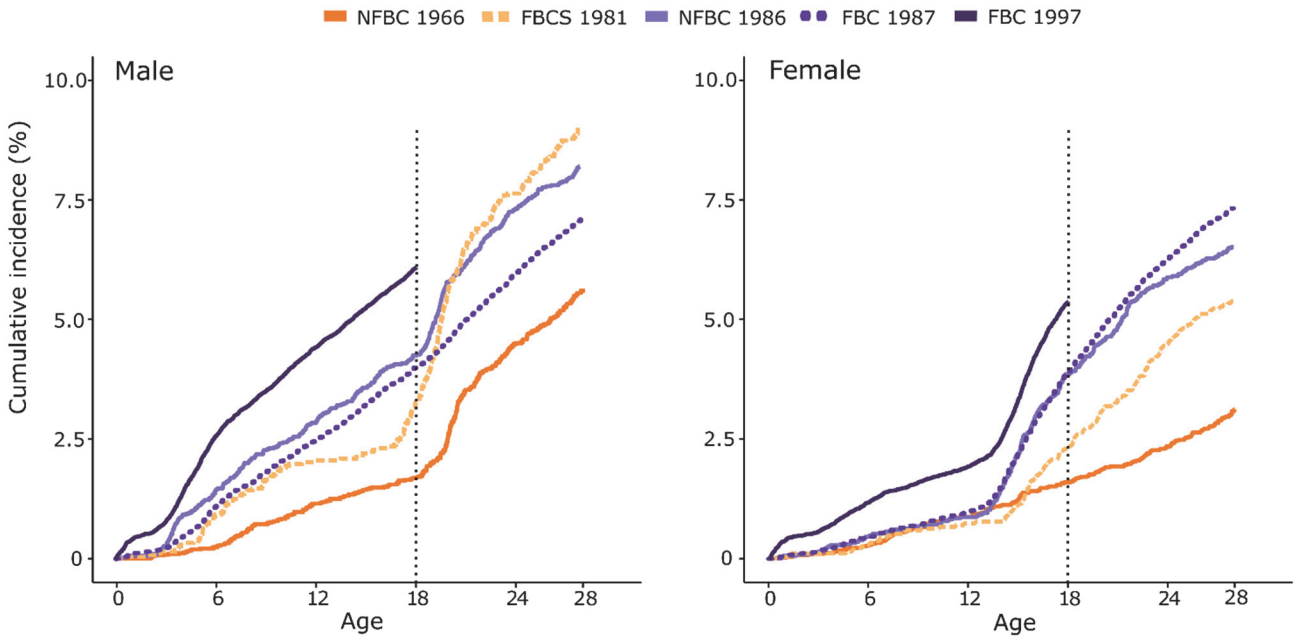

Fig. 1. Cumulative incidences of any psychiatric disorders in studied cohorts by sex (Under CC BY-NC licence from Original publication I © 2020 Authors).

6.1.1 Psychiatric disorders in childhood and adolescence

In childhood and adolescence (age 0–17 years), the cumulative incidences of any psychiatric disorders in males were 1.7% in the NFBC1966, 3.2% in the FBCS 1981, 4.4% in the NFBC1986, 4.2% in the FBC 1987, and 6.3% in the FBC 1997 (IRR: 1.04, 95% CI: 1.04–1.05). Respective numbers among females were 1.6%, 2.3%, 4.1%, 4.0%, and 5.5% (IRR: 1.04, 95% CI: 1.03–1.04) (Figure 1). Cumulative incidences of separate diagnosis classes by sex are reported in Study I, Tables 1–2.

A statistically significant increase in the cumulative incidences from the NFBC1966 to the FBC 1997, in both males and females, was found in several diagnosis classes: mental and behavioural disorders due to psychoactive substance use; mood disorders; depression; neurotic, stress-related, and somatoform disorders; disorders usually diagnosed in childhood or adolescence; learning and coordination disorders; and conduct and oppositional disorders. A significant increase only in males was found in autism spectrum disorders and ADHD, and in females in anxiety disorders, behavioural syndromes associated with eating, sleep, or puerperium, and eating disorders. (Figure 2)

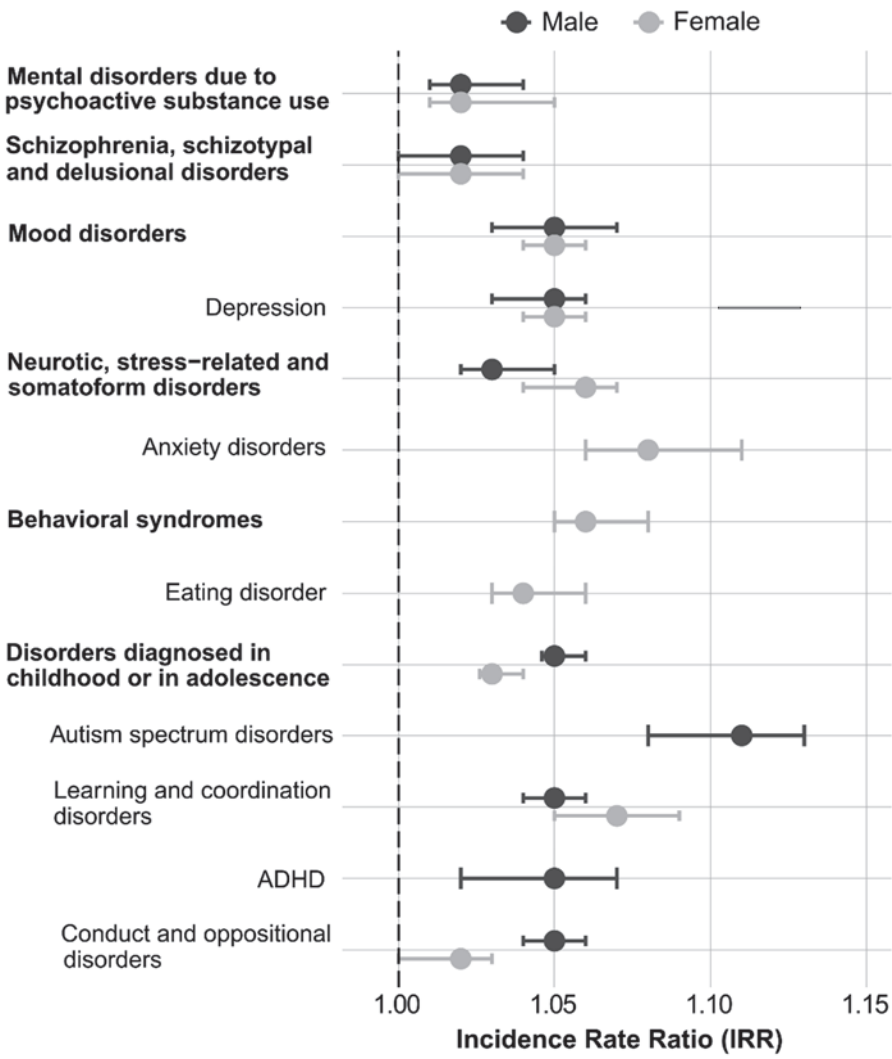

Fig. 2. Incidence Rate Ratios (IRR) with 95% CI from the NFBC1966 to the FBC 1997 analysed with Poisson regression with offset variable by sex in childhood and adolescence (age 0–17 years).

6.1.2 Psychiatric disorders in early adulthood

In early adulthood (age 18–28), the cumulative incidences of any psychiatric disorders in males were 4.4% in the NFBC1966, 6.7% in the FBCS 1981, 4.8% in the NFBC1986, and 3.9% in the FBC 1987 (IRR: 0.99, 95% CI: 0.99–1.00). Respective numbers among females were 1.8%, 3.6%, 3.5% and 4.5% (IRR: 1.04, 95% CI: 1.03–1.05) (Figure 1). Cumulative incidences are reported in Study I, Tables 3–4.

In early adulthood among both sexes, the significant increase in cumulative incidences from the NFBC1966 to the FBC 1987 was seen in several classes: mental disorders due to psychoactive substance use; other substance use disorders; mood disorders; and depression. In males, a significant decrease was found in neurotic, stress-related and somatoform disorders; anxiety disorders; disorders of adult personality and emotionally unstable personality disorders. In females, a significant increase was detected in neurotic, stress-related and somatoform disorders; anxiety disorders; behavioural syndromes associated with eating, sleep, or puerperium; eating disorders; and in emotionally unstable personality disorder.

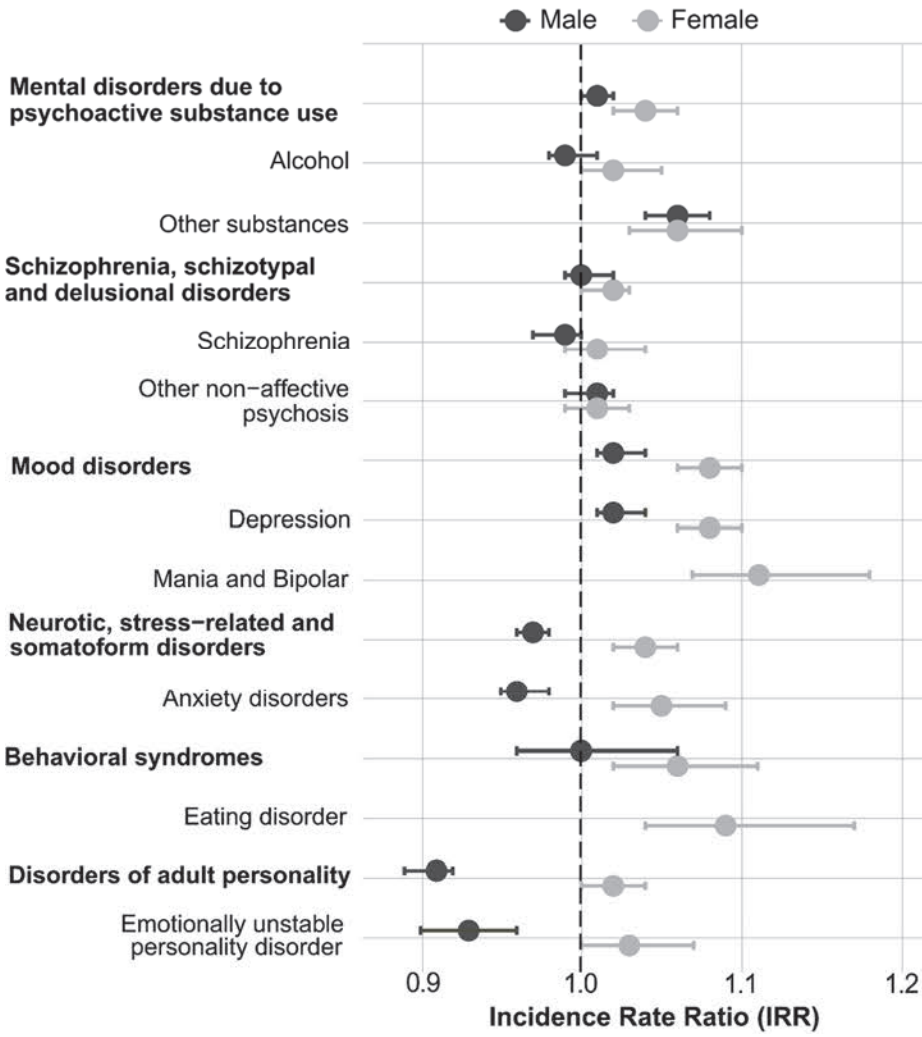

Fig. 3. Incidence Rate Ratios (IRR) with 95% CI. from the NFBC1966 to the FBC 1987 analysed with Poisson regression with offset variable by sex in early adulthood (age 18–28 years).

6.1.3 Sex difference

In the NFBC1966, children and adolescent males had a 1.07-fold (95% CI: 0.81–1.41) risk of being hospitalised for any psychiatric disorder compared to females. The risk was statistically nonsignificant in the FBCS 1981 (RR: 1.34, 95% CI:

0.97–1.85), NFBC1986 (1.09, 0.90–1.32), and FBCS 1987 (1.04, 0.96–1.12), but not for the FBCS 1997 (1.14, 1.07–1.21). Males in the NFBC1966 had an increased risk for hospitalisation for a depressive disorder (1.43, 0.24–8.54) compared to females in the NFBC1966, but the risk was decreased for males in the other cohorts: 0.66 (0.32–1.37) in the FBCS 1981, 0.43 (0.26–0.69) in the NFBC1986, 0.33 (0.27–0.40) in the FBC 1987, and 0.35 (0.31–0.43) in the FBC 1997.

In the NFBC1966, the young adult males had a 2.27-fold (95% CI: 1.83–2.82) risk of being hospitalised for any psychiatric disorders compared to females and the risk decreased from 1.28 (0.92–1.76) in the FBCS 1981, 1.34 (1.10–1.64) in the NFBC1986 to 0.88 (0.81–0.95) in the FBC 1987. Males had a 1.90-fold (1.11–3.24) risk of being hospitalised for a depressive disorder compared to females in the NFBC1966, 0.63 (0.30–1.30) in the FBCS 1981, 0.70 (0.48–1.02) in the NFBC1986, and 0.57 (0.50–0.65) in the FBC 1987. At age 18–28 years, males in NFBC1966 had a 3.97-fold (2.42–6.54) risk of being hospitalised for a disorder of adult personality compared to females, and the risk decreased from 0.64 (0.33–1.23) in the NFBC1986 to 0.30 (0.21–0.43) in the FBC 1987.

6.2 Psychiatric disorders and suicidal behaviour in the NFBC1986 (Study II)

The distributions of background factors are presented in Study II, Table 3. In the comparison of psychiatric disorder diagnosis at age 2–28 years between the NFBC1986 and the comparison cohort, no significant differences were found in males in crude or adjusted analysis (Figure 4; Study II, Table 4). In females, decreased risk in the NFBC1986 compared to the comparison cohort was found in several diagnostic categories: schizophrenia, schizotypal and delusional disorders; other non-affective psychosis; neurotic, stress-related, and somatoform disorders; anxiety disorder; post-traumatic stress disorder; learning and coordination disorders; and any psychiatric or neurodevelopmental disorder (Figure 4; Study II, Table 5). After adjusting the risk ratios for education and marital status, a decreased risk in female participants of the NFBC1986 compared to females in the comparison cohort was found for neurotic, stress-related, and somatoform disorders (RR_{MH}: 0.80, 95% CI: 0.70–0.91); anxiety disorder (RR_{MH}: 0.81, 95% CI: 0.67–0.98); post-traumatic stress disorder (RR_{MH}: 0.61, 95% CI: 0.42–0.90); and learning and coordination disorders (RR_{MH}: 0.52, 95% CI: 0.33–0.82). (Study II, Table 5)

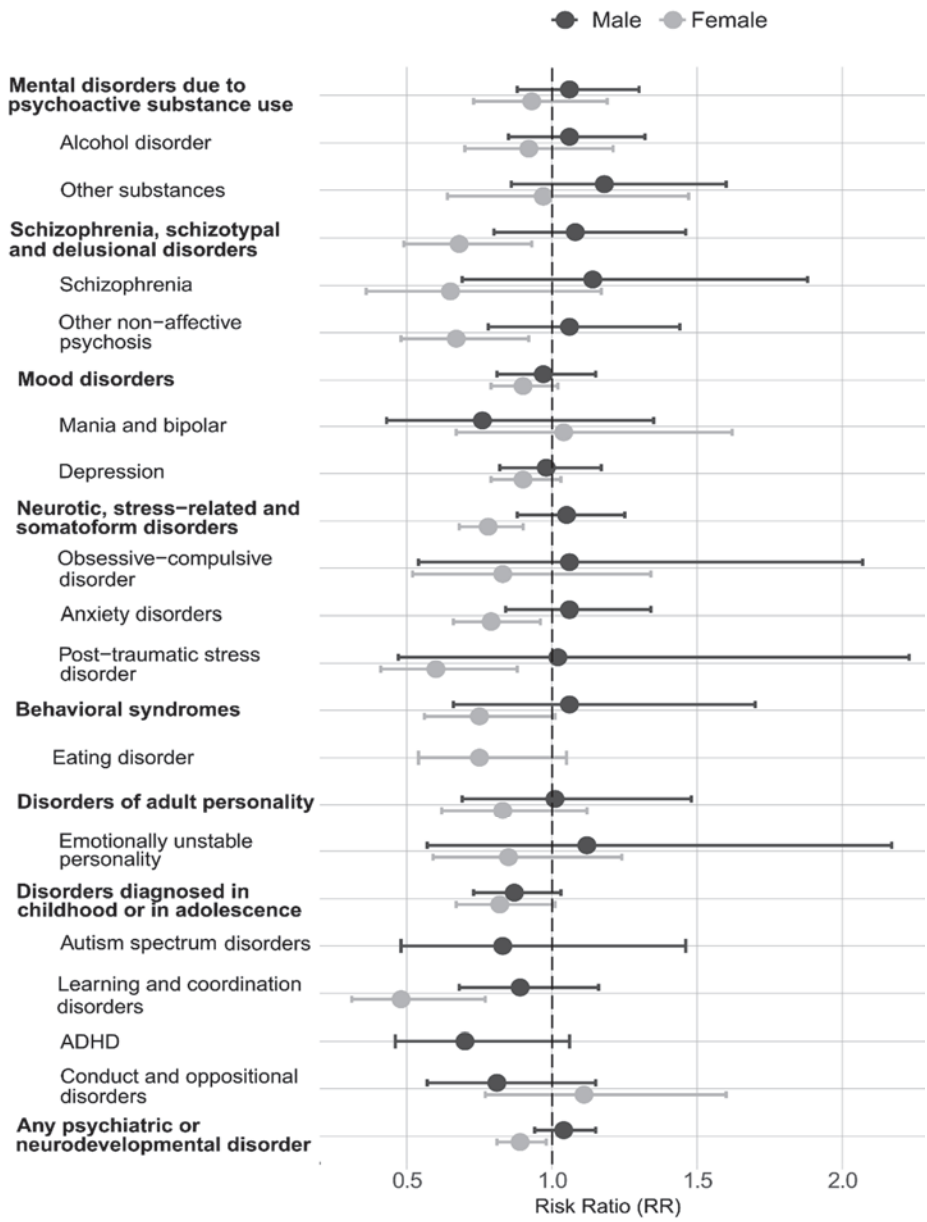

Fig. 4. Risk Ratios with 95% CI of psychiatric diagnosis in NFBC1986 and comparison cohort by sex.

No significant differences were found in suicidal behaviour for males between the NFBC1986 and the comparison cohort. In females, there was a decreased risk for suicidal behaviour in the NFBC1986 cohort (RR: 0.67, 95% CI: 0.49-0.92). The numbers of suicides were too low to be analysed. (Table 5)

Table 5. Cumulative incidence N (%) and comparative risk (RR, Risk Ratio) for suicidal behaviour in participants age 2–28 years by sex. (Under CC BY 4.0 licence from Original publication II © 2022 Authors).

Diagnostic group	NFBC 1986	Comparison cohort	χ^2	p-value	RR (95 % CI)	p-value
Males						
Suicidal behaviour	70 (1.4)	83 (1.8)	1.86	0.173	0.79 (0.58–1.09)	0.148
Suicide	29 (0.6)	22 (0.5)	0.39	0.534	1.24 (0.71–2.15)	0.446
Females						
Suicidal behaviour	65 (1.4)	94 (2.1)	6.01	0.014	0.67 (0.49–0.92)	0.011
Suicide	6 (0.1)	5 (0.1)			-	

6.3 Use of psychiatric care services in the NFBC1966 (Study III)

There was no difference between the study and the comparison cohort in any visit to a psychiatric speciality or any psychiatric hospitalisation between the 10th and 50th birthdays. Among those who had had psychiatric hospitalisation, there were statistically significant results for days in psychiatric hospitalisation: males in the study cohort had a lower median number of days of psychiatric hospitalisation (study cohort median 28 days, comparison cohort median 31 days (U: 1.51×105, $p<0.001$)), whereas females in the study cohort had a higher median number of days of psychiatric hospitalisation than the comparison cohort (study cohort median 39, comparison cohort median 38 days (U: 7.57×104, $p<0.001$)). When analysed further using Zero-Truncated Binomial Regression, the significance diminished (Males: IRR: 0.92, 95% CI: 0.74–1.17, p=0.530; Females: IRR: 0.86, 95% CI: 0.68–1.10, p=0.231). Age at the first visit to a psychiatric speciality or age at first psychiatric hospitalisation did not differ between the study and comparison cohorts. (Study III, Table 3). No difference was found in age at first visit or hospitalisation in a psychiatric speciality (Table 6).

Table 6. Results of comparison between study and comparison cohorts analysed with the Cox Proportional Hazard model (HR). The comparison cohort is the reference group in all models. (Under CC BY 4.0 licence from Original publication III © 2023 Authors).

Use of psychiatric care service	Males		Females	
	HR (95% CI)	p-value	HR (95% CI)	p-value
First visit to a psychiatric speciality	1.05 (0.96–1.15)	0.244	0.98 (0.90–1.07)	0.672
Hospitalisation in a psychiatric speciality	1.09 (0.97–1.22)	0.133	1.03 (0.90–1.17)	0.705

The results of the Kaplan-Meier survival curves are presented in Figures 5 and 6. The survival curves for the first visit to a psychiatric speciality (Figure 5) or first psychiatric hospitalisation (Figure 6) between the study and comparison cohorts did not differ.

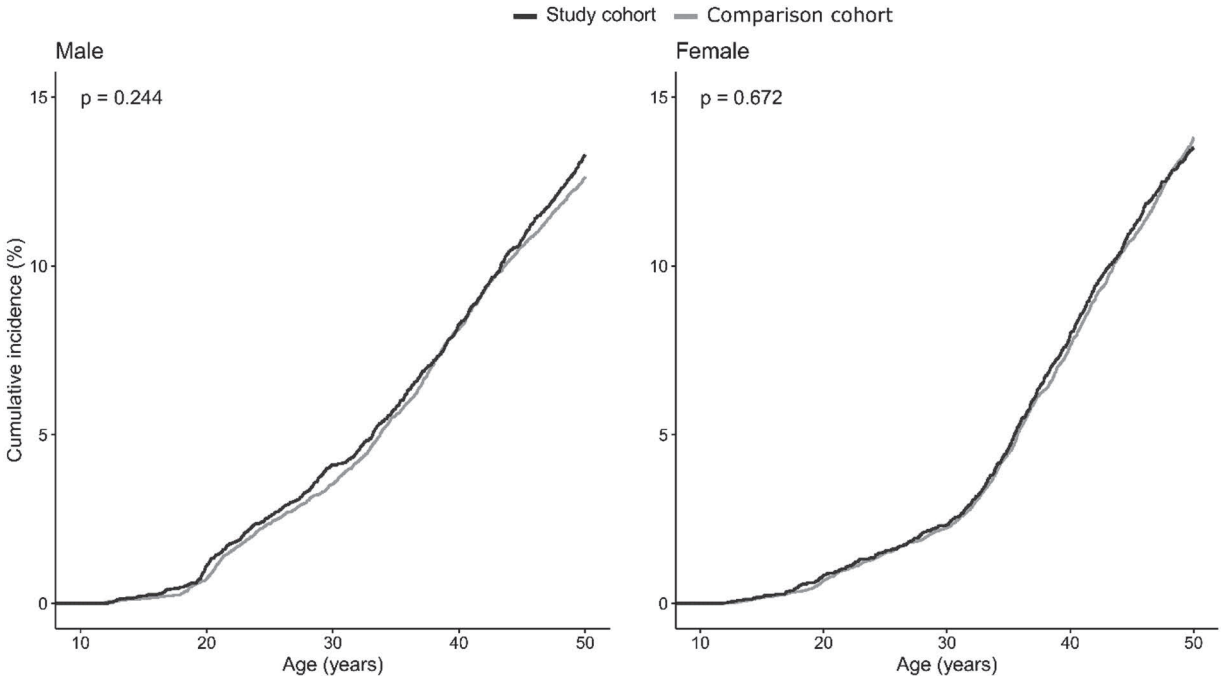

Fig. 5. Kaplan-Meier curve for the first visit to the psychiatric speciality for study and comparison cohorts by sex with p-value from log-rank test. (Under CC BY 4.0 licence from Original publication III © 2023 Authors).

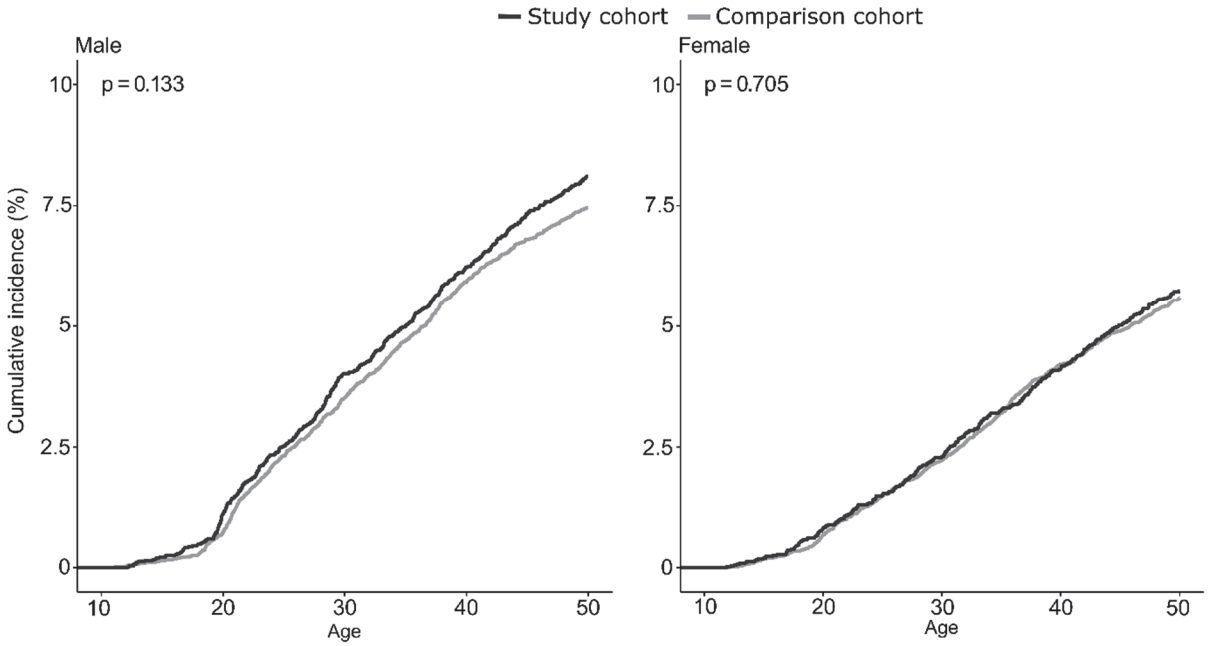

Fig. 6. Kaplan-Meier curve for first psychiatric hospitalisation for study and comparison cohorts by sex with p-value from log-rank test. (Under CC BY 4.0 licence from Original publication III © 2023 Authors).

6.4 Cardiometabolic disorders in NFBC studies (Study IV)

Table 7 reports the risk ratios (RR) with 95% confidence intervals (CI) of cardiometabolic disorders in the NFBC1966 compared to the comparison cohort at age 7–50 years and the NFBC1986 compared to the comparison cohort at age 0–29 years. In the NFBC1966 no significant differences were found. In the NFBC1986 male participants had lower risk for type 2 diabetes (RR: 0.41, 95% CI: 0.20–0.86); overweight, obesity, and other hyperalimentation (RR: 0.45, 95% CI: 0.27–0.75) and any cardiometabolic disorder (RR: 0.75, 95% CI: 0.59–0.95). (Study IV, Tables 2, 4–5, 7)

Table 7. Risk Ratios (RRs) with 95% CI of all hospital-treated cardiometabolic disorders at age 7–50 years in the NFBC1966 compared to its comparison cohort and at age 0–28 years in the NFBC1986 compared to its comparison cohort.

Diagnostic group	age 7–50 years in NFBC1966		age 0–29 years in NFBC1986	
	RR (95 % CI.)	p-value	RR (95 % CI.)	p-value
Males				
Cerebrovascular disorders	0.93 (0.75–1.14)	0.465	1.04 (0.55–1.97)	0.893
Coronary artery disease	0.93 (0.78–1.12)	0.466	-	
Diabetes mellitus	0.98 (0.84–1.16)	0.851	0.71 (0.49–1.03)	0.067
Type 1*	0.95 (0.73–1.24)	0.716	0.82 (0.55–1.21)	0.315
Type 2*	0.96 (0.80–1.15)	0.641	0.41 (0.20–0.86)	0.015
Hyperlipidaemia	0.84 (0.69–1.03)	0.091	-	
Hypertension	0.93 (0.83–1.06)	0.276	0.75 (0.44–1.28)	0.295
Overweight, obesity, and other hyperalimentation	0.89 (0.69–1.14)	0.351	0.45 (0.27–0.75)	0.001
Any cardiometabolic disorder	0.96 (0.88–1.04)	0.282	0.75 (0.59–0.95)	0.015
Females				
Cerebrovascular disorders	1.05 (0.84–1.31)	0.673	1.26 (0.55–2.87)	0.584
Coronary artery disease	0.92 (0.68–1.25)	0.598	-	
Diabetes mellitus	0.84 (0.68–1.04)	0.118	0.89 (0.59–1.34)	0.561
Type 1*	0.97 (0.69–1.35)	0.841	0.80 (0.60–1.49)	0.800
Type 2*	0.81 (0.63–1.04)	0.091	0.76 (0.35–1.67)	0.494
Hyperlipidaemia	0.86 (0.63–1.18)	0.353	-	
Hypertension	1.03 (0.90–1.18)	0.651	0.77 (0.40–1.49)	0.443
Overweight, obesity, and other hyperalimentation	0.94 (0.76–1.16)	0.560	0.81 (0.62–1.06)	0.117
Any cardiometabolic disorder	1.01 (0.92–1.11)	0.844	0.87 (0.71–1.07)	0.180

*At age 22–50 years in NFBC1966 analysis, at age 2–29 years in NFBC1986 analysis

Female participants of the NFBC1966 had a lower age of onset of coronary artery disease (median age of onset 42.5 years vs 45.8 years; Q: 3.85, p=0.049), diabetes mellitus (median age of onset 38.1 years vs 41.7 years; Q: 8.28, p=0.004) and any cardiometabolic disorder (median age of onset 42.1 years vs 43.1 years; Q: 4.16, p=0.041) compared to the comparison cohort (Figure 7). Male participants of the NFBC1986 had a higher age of onset of obesity (median age of onset 21.3 years vs. 15.1 years; Q: 10.76, p=0.001) and any cardiometabolic disorder (median age of onset 17.6 years vs. 17.0 years; Q: 5.29, p=0.022) and female participants of

diabetes mellitus (median age of onset 15.1 years vs.10.1 years; Q: 8.06, p=0.005) than the comparison cohort. (Figure 8, Study IV Tables 3, 6) No other significant difference between the medians of the age of onset of cardiometabolic disorders was found.

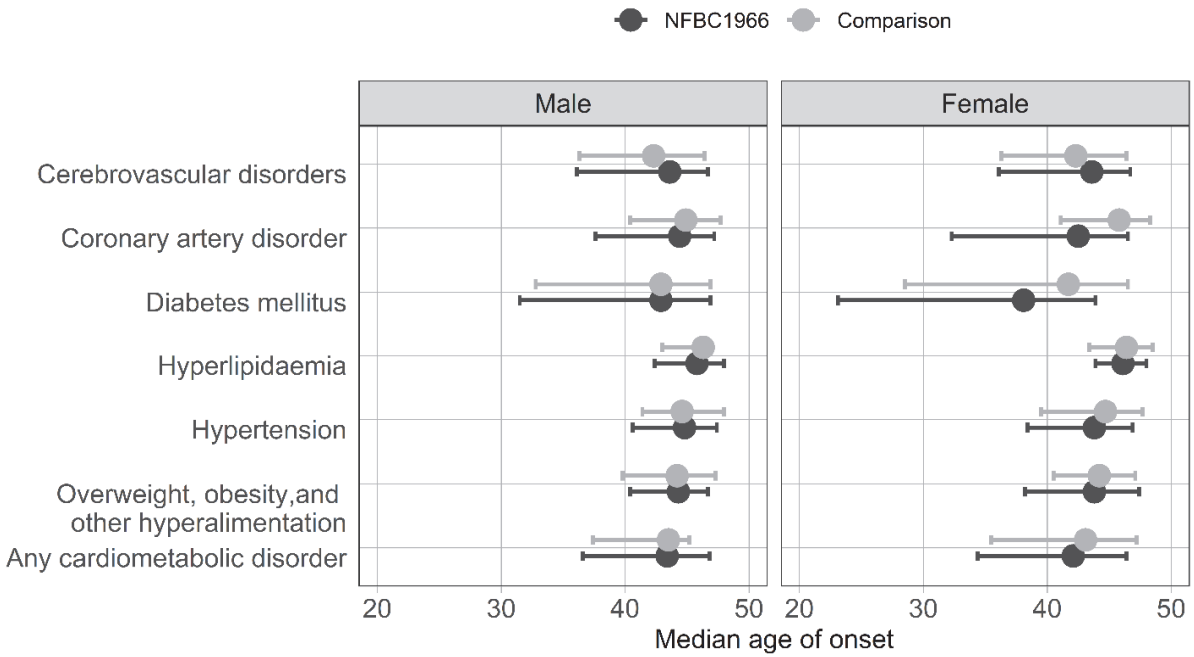

Fig. 7. Age of onset (Median with IQR) of cardiometabolic disorders in NFBC1966 and comparison cohort at age 7–50 in males and females.

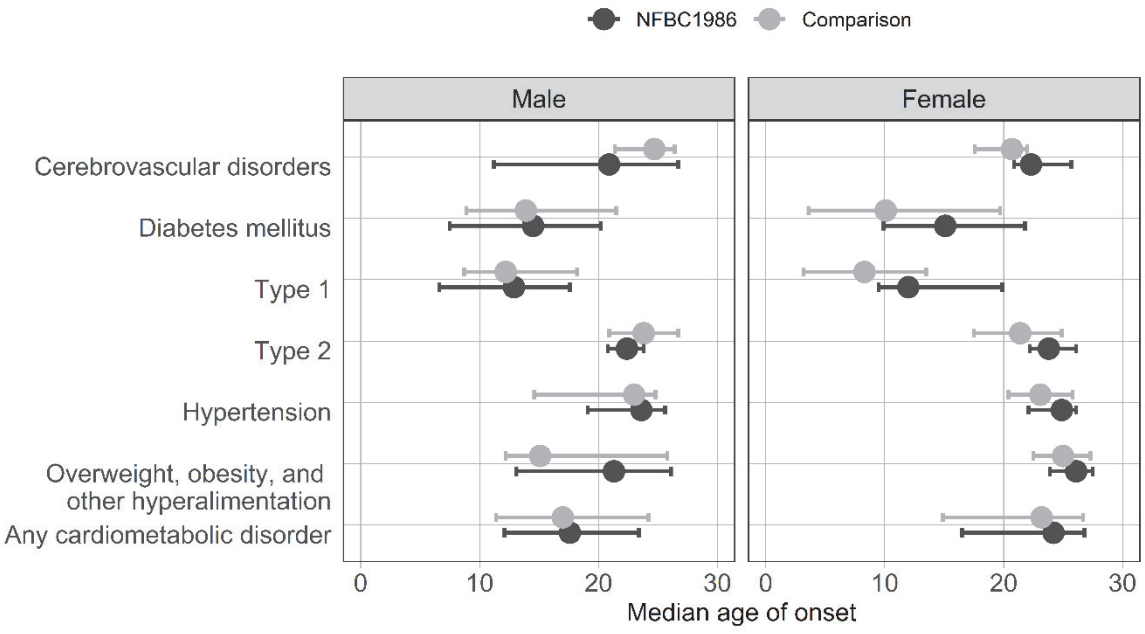

Fig. 8. Age of onset (Median with IQR) of cardiometabolic disorders in NFBC1986 and comparison cohort at age 2–29 in males and females.

Cardiometabolic-related deaths in the NFBC1966 and the comparison cohort by sex are reported in Table 8. No significant difference between the NFBC1966 and the comparison cohort was found (males RR: 1.06, 95% CI: 0.68–1.64, p=0.794; females RR: 1.93, 95% CI: 0.88-4.22, p=0.095). Age of death did not differ between the NFBC1966 and the comparison cohort in males (Q: 0.50, p=0.481) or females (Q: 0.00, p=0.973).

Table 8. Cumulative incidence % (N) of cardiometabolic-related deaths, and age of death caused by any cardiometabolic disorder at age 0–50 years in NFBC1966 with comparison cohort by sex. (Under CC BY 4.0 licence from Original publication IV © 2023 Authors).

Cause of death	Males		Females	
	NFBC1966	Comparison	NFBC1966	Comparison
Cerebrovascular disorders	0.1 (6)	0.1 (10)	0.1 (4)	0.1 (6)
Coronary artery disease	0.3 (18)	0.3 (41)	0.1 (4)	0.0 (4)
Diabetes mellitus	0.1 (4)	0.0 (2)	0.1 (4)	0.0 (2)
Hypertension	0.0 (2)	0.0 (6)	0.0 (0)	0.0 (1)
Any cardiometabolic disorder	0.5 (30)	0.5 (59)	0.2 (12)	0.1 (13)
Age of death (Median (IQR))	42.6 (36.1–46.7)	44.1 (38.2–47.9)	43.0 (41.6–46.2)	42.9 (40.0–44.3)

7 Discussion

7.1 Trends in cumulative incidences of hospital-treated psychiatric disorders

Childhood and adolescence

The cumulative incidences of any psychiatric disorders increased significantly in males and females in childhood and adolescence from the NFBC1966 to the FBC1997. For females aged 12–14 years, there appears to be a peak in the incidence of hospital-treated psychiatric disorders in all cohorts, except the NFBC1966. Previous reports show the median age of onset in childhood and adolescence for an anxiety disorder to be 6 years, and 13 years for mood disorders (McGorry et al., 2011). Mood disorder was the most or second-most common disorder in childhood or adolescence in all studied cohorts, except the NFBC1966, which explains the growth of diagnosis at age 12 to 14. The above disorders were also more common among females. An increase in depression in adolescence has also been reported elsewhere (Mojtabai et al., 2016; Sawyer et al., 2018).

In males, the incidence of disorders diagnosed in childhood or adolescence increased significantly from the NFBC1966 to the FBC1997. A meta-analysis indicated an increase in the incidence of many disorders usually diagnosed in childhood in Western countries, such as neurodevelopmental disorders, including ADHD and autism spectrum disorders (Elsabbagh et al., 2012). The increase of cumulative incidence in hospital-treated disorders usually diagnosed during childhood or adolescence is not necessarily caused by an increased incidence of psychiatric disorders in the population but rather by changes in clinical practices, new treatment possibilities, treatment-seeking behaviour, or changes in diagnostic criteria. For example, an increase in the cumulative incidence of autistic disorder might be explained by a broadening diagnostic criterion (Elsabbagh et al., 2012). The broad classification codes have changed through the different ICD classifications, and the codes are not completely equal across the different ICD versions.

An increase in eating disorders was found to be significant only among females. Eating disorder diagnosis codes have broadened since ICD-8 and the diagnosis codes have become more specific: In the 1970s, anorexia nervosa was the most common eating disorder, whereas nowadays, most eating disorders are diagnosed

as eating disorders not otherwise specified. The rise in the incidence of anorexia nervosa is widely debated. A meta-analysis pointed out that until the 1970s, the incidence increased, and since then it has remained rather stable (Hoek, 2006). Previous studies have indicated a link between anxiety disorder and disordered eating (Kaye et al., 2004; Menatti et al., 2015). The increase in anxiety disorder was significant among females, but not among males. Anxiety disorder rarely requires inpatient treatment, and patients with anxiety disorders are mostly treated in outpatient care (Bandelow & Michaelis, 2015).

Early adulthood

In early adulthood, the most remarkable increase in the cumulative incidence among females was in mood disorders. Among males, the increase was significant but not as major as in females. Females are more likely to develop depression than men during their lifetime, and in Finland, the prevalence of depressive disorder has increased from 2000 to 2011, especially among females (Albert, 2015; Markkula et al., 2015).

Among males, there was a major decrease in hospital-treated personality disorders, whereas, among females, no significant trend was found. A Spanish study pointed out that the trend in personality disorder diagnoses among hospitalised patients is dependent on the disorder. In a ten-year follow-up, there was an increase in emotionally unstable, dependent, anxious-avoidant and narcissistic personality disorders diagnoses, and a decrease in paranoid and histrionic personality disorder diagnoses and non-specific, antisocial, schizoid and obsessive-compulsive personality disorders diagnoses stayed stable (Fontalba Navas et al., 2015).

Sex difference

Hospitalization rates for psychiatric disorders have been increasing among young adult females but not males. Currently, females are hospitalized more frequently for psychiatric disorders compared to males, whereas in the past, the opposite was true. An Irish study report a similar phenomenon: over the course of 50 years, males typically had higher admission rates than females, but in recent times, the gap had significantly closed to almost equal rates in Ireland (Walsh & Daly, 2016). An increase in self-harm among females in adolescence and young adulthood has been

reported and this may be connected to our findings (Griffin et al., 2018; Reuter et al., 2016). It is noteworthy that hospitalisations typically involve severe mental disorders, with self-endangerment often being a criterion for compulsory admission in Finland. The considerable reforms in treatment procedures over the past decades, along with potentially differing attitudes towards mental disorders in the 1970s and 1980s, might contribute to the observed sex differences in the oldest cohort.

Our analysis revealed a decrease in the risk ratio of hospitalization for depressive disorders between males and females in both studied age groups when comparing the cohort born in 1966 to the youngest cohort. In the 1966 cohort, males had a higher likelihood of being hospitalized for a depressive disorder, whereas in the 1987 cohort, the opposite pattern was observed. These findings align with several studies that have reported varying results. Some studies indicate no sex difference in the prevalence of depression among boys and girls during preadolescence, while others suggest a higher prevalence for boys (Avenevoli et al., 2008). However, a comprehensive meta-analysis demonstrates a sex gap in depression diagnosis prevalence, reaching its peak during adolescence, narrowing in subsequent years, and remaining stable into adulthood (Salk et al., 2017).

The presence of sex differences in personality disorders is highly inconsistent, with varying findings reported across different study settings (Schulte Holthausen, 2018). In our study, we observed time-dependent sex differences. Among the cohort born in 1966, males had a 3.5-fold higher risk of being hospitalized due to adult personality disorders compared to females. However, in the cohort born in 1987, females had a 2.9-fold higher risk compared to males. These findings highlight the dynamic nature of sex differences in the risk of hospitalization for personality disorders over time.

7.2 Effects of participation in the NFBC studies

The findings from the studies examining the association of NFBC studies with the use of psychiatric care services and cardiometabolic disorders were inconsistent, as some associations were identified but they were not consistent across all the studies. The validity of the original Hawthorne studies and the existence of the Hawthorne Effect in longitudinal studies has been a subject of debate among researchers. The original studies, which were conducted at the Hawthorne Works factory in the 1920s and 1930s, have been criticised for methodological flaws, such as a lack of control groups, small sample sizes, and a lack of long-term follow-up. (Landsberger, 1958.) There have been some longitudinal studies that have found evidence of a

similar effect, where people change their behaviour simply because they are aware that they are being observed, but the relationship is often found to be complex, with multiple factors influencing the outcome (Berkhout et al., 2022; Jones, 1992; McCambridge et al., 2014).

The contradicting results might be explained by the difference in follow-up waves in the NFBC1966 and NFBC1986. The follow-up for the NFBC1986 cohort was more extensive during childhood and adolescence, with follow-up waves at ages 7, 8, and 15–16 years. In contrast, the NFBC1966 cohort only had one follow-up during childhood and adolescence at age 14, which consisted of a questionnaire. The 15–16-year follow-up study for the NFBC1986 also aimed to identify potential cardiometabolic risks by including wide-ranging questions on health, lifestyle choices, and dietary habits. Psychiatric screening tools such as PROD-Screen, YSR, and SWAN were also used in the follow-up, as well as a clinical examination that involved measuring blood pressure, height, and weight, and a physical fitness test. The follow-up survey for the NFBC1966 cohort at age 14 years included only basic questions related to activity levels, BMI, and substance use. The data collection on cardiometabolic risk factors was limited. Moreover, the first clinical examination in the follow-up for the whole cohort in the NFBC1966 was conducted during the 31-year follow-up study. The younger cohort might have been influenced by information on healthier lifestyle choices in adolescence via follow-ups conducted at 15–16 years old. In the 31-year and 46-year follow-ups of the NFBC1966 eating habits, physical exercise, and overall health were explored widely, but there was no difference in cardiometabolic disorders from age 7–50 years between the NFBC1966 and the comparison cohort.

Participation in the follow-up studies

In the NFBC1966 participation rate in the follow-up studies decreased from 91.2% in the 1-year study, 93.6% in the 14-year study, 77.4% in the 31-year study to 66.5% in the 46-year study. It is already known that participants of the NFBC1966 in the 31-year and 46-year studies are more often female, were less often unemployed, and are from higher social class and subjects with psychiatric disorders participated less actively than those without any psychiatric disorders in the 31-year study (Haapea et al., 2008; Nordström et al., 2021). In NFBC1986, the participation rate was 91.1% in 7-year follow-up, 73.7% in 15–16-year follow-up, and 36.2% in 33–35-year study. In the 15–16-year follow-up study, there was lower participation

among males compared to females, as well as among participants residing in urban areas. Additionally, adolescents with a parental history of psychiatric disorders had lower participation rates compared to those without parental psychiatric disorders. (Miettunen et al., 2014) The selective non-participation bias does exist in the NFBCs. However, as the aim of the study was to examine the effects of participation in the longitudinal follow-up study and the postal follow-up questionnaires have been sent to 83%-97% of original cohort participants, the vast majority of participants of NFBCs have been aware of longitudinal follow-up.

7.2.1 Psychiatric care

Psychiatric disorder diagnoses in the NFBC1986 (Study II)

Participation in the NFBC1986 did not increase the use of mental health services; instead, the opposite occurred in females. The female participants of the NFBC1986 did seek help for mental health problems less often than the comparison cohort and therefore had fewer neurotic, stress-related and somatoform disorders; anxiety disorders; post-traumatic stress disorders; and learning and coordination disorder diagnoses in the healthcare registers. The observed differences may also be influenced by the participation of the NFBC1986, which might have altered the patterns of seeking help for mental health issues and conceivably reduced the occurrence of mild mental health problems.

Several studies have reported higher levels of mental healthcare utilisation among females (Alonso et al., 2004). Sex differences in the use of mental health services have been associated with sex-specific patterns in the pathology of mental disorders: females more frequently experience anxiety and depressive disorders, while males are more likely to suffer from impulsivity and addiction (Young & Pfaff, 2014). Sex differences in the use of mental healthcare have been explained in terms of differences in the need for care, as well as attitudinal differences, psychosocial factors, and associations with several socioeconomic and family-related determinants (Koopmans & Lamers, 2007). The above findings might be relevant to our findings. The follow-up of the NFBC1986 might have affected female participants differently than male participants.

Computer-assisted and internet-based treatments for anxiety disorder and depression have grown over recent decades, and previous findings have substantiated the efficacy of e-interventions for adult and youth anxiety and

depression. Internet-based psychotherapy for anxiety disorder and depression has been proven to be clinically effective, with outcomes equivalent to those of face-to-face psychological therapy. (Christensen et al., 2014; Wagner et al., 2014.) For example, the internet-based myCompass programme (a fully automated, self-help, public health intervention) reduced symptoms for individuals with mild to moderate depression, anxiety, and stress (Proudfoot et al., 2013). 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 an explanation of the findings of the present study: the contact and questionnaires used in the NFBC1986 might have helped some participants with mild anxiety and stress symptoms, as a lower risk for anxiety disorder and post-traumatic stress disorder was found in the NFBC1986 cohort. A limitation of our study was that we had no data on the use of primary healthcare services, and thus on e-interventions.

Learning disorders are usually diagnosed in the early school years, and the DSM-IV describes learning disorders as occurring when an individual's achievement on individually administered standardised tests is substantially below that expected for their age, schooling, and level of intelligence (Guze, 1995). In the NFBC1986, the first follow-ups after the antenatal period were conducted in the children's first school year: in the autumn, parents completed a questionnaire about the children's growth and development, and in the spring, parents and teachers evaluated the children's behaviour with the Rutter scale.

Our second hypothesis was partly supported by the suicidal behaviour findings. Suicidal behaviour was lower in female NFBC1986 participants, but that was not due to a higher incidence of using mental health services. The effect of interventions on suicidal behaviour has been previously reported. The intervention does not need to be intensive to be effective; for example, media sources have an important degree of leverage in influencing the suicide rate by reporting suicides. An awareness programme has also been reported to be successful in preventing suicide (Bachmann, 2018).

Use of psychiatric care services (Study III)

No evidence of an association between longitudinal follow-up and the use of psychiatric care services was found in the population born in 1966 and the comparison cohort in terms of the use of psychiatric care services. There was a significant result on the median number of days of psychiatric hospitalisation, but

when analysed further using Zero-Truncated Binomial Regression, the significance diminished. The results indicate that even a long follow-up with many follow-ups does not necessarily affect participants' life or behaviour, at least in the use of psychiatric care services. Of the 12.7% participants of the study cohort who visited a psychiatric speciality, the mean ages at first visit to a psychiatric speciality were between 35 and 37 years, and of that 6.7% who had psychiatric hospitalisation, the mean ages at first psychiatric hospitalisation were between 31 and 32 years in the study cohort. The follow-ups for the whole cohort including psychiatric screens were conducted at ages 31 and 46, and the sub-studies focused on psychiatric measurements at ages 33 and 42. The associations of participation in an epidemiological follow-up study are rarely studied, and the results need to be replicated. The NFBC1966 may be regarded as representative at the population level in terms of psychiatric outcomes despite the personal follow-up of the birth cohort.

The UKKI study, in which the study participants had used psychiatric healthcare services more often than the control group, was a long follow-up psychiatric study aiming to find people with psychiatric disorders using psychiatric interviews (Lehtinen et al., 1991). Compared to the UKKI study, the NFBC1966 did not focus on psychiatric outcomes but covered all aspects of health-related issues. In the NFBC1966 only a minority of the participants were interviewed using psychiatric methods. In the psychiatric UKKI study, participants were interviewed twice, which might have motivated people to seek treatment for their psychiatric ill health (Bijl et al., 2003; Roberts et al., 2018).

7.2.2 Cardiometabolic disorders

Male participants of the NFBC1986 had a decreased risk of overweight, obesity, and other hyperalimentation, type II diabetes and any cardiometabolic disorder diagnosis at age 0–29 years. In the NFBC1966 study, there was no significant difference in the overall incidence of coronary artery disease, diabetes mellitus, or any cardiometabolic disorder between the study and comparison cohorts. However, the onset of these disorders occurred at a younger age in females within the study cohort. This may indicate that female participants of the NFBC1966 tended to seek medical treatment more frequently, potentially due to the follow-up studies conducted in the NFBC1966. It is also possible that participants of the NFBC1966 are generally more self-aware about their health, leading to earlier detection and treatment of these conditions. Further research is needed to fully understand the

factors that may have contributed to the observed differences in age of onset between the study and comparison cohorts.

Eurostat reports that the prevalence of self-reported overweight and obesity (BMI ≥ 25) was 39.3% among Finnish males of age 18–29 years and 66.0% among Finnish males of age 25–64 years in 2014 (Eurostat, n.d.). Diagnoses related to overweight and obesity cases are seldom given in specialised care: 0.5% in the NFBC1986 and 1.0% in the comparison cohort had a healthcare diagnosis of overweight, obesity, and other hyperalimentation until the age of 29; 1.3% of males in the NFBC1966, and 1.5% of the comparison cohort from age 7–50 years. Nevertheless, obesity is preventable via lifestyle choices. The systematic review suggests that population reductions in weight are achievable through community-based interventions, including interventions that have incorporated educational, health promotion, social marketing, policy, or legislative reform strategies (Wolfenden et al., 2014). The multiple follow-up studies conducted on the NFBC1986 during childhood and adolescence might have encouraged the participants of the NFBC1986 towards healthier lifestyle choices, and therefore the male participants of the NFBC1986 did have less overweight, obesity, and other hyperalimentation diagnoses.

Male participants of the NFBC1986 had a lower risk for type 2 diabetes and female participants had a higher age of onset of diabetes mellitus than the comparison cohort, but that was mostly due to the age at type 1 diabetes mellitus diagnosis. If the follow-up has encouraged the participants to make healthier lifestyle choices, it has likely affected the onset of type 2 diabetes, rather than type 1 diabetes.

7.3 Strengths of the studies

To our knowledge, the effects of participation in a prospective epidemiological study have rarely been studied. The data used in this study were from Finnish registers, which have been found to be high quality. The quality of the CRHC is high (Sund, 2012) and the coding of causes of death for mortality statistics is appropriate, with a sincere quality coding process (Lahti & Penttilä, 2001). It is obligatory for all healthcare providers to report the causes (ICD codes) for utilisation of the healthcare system. The ICD-coded diagnoses were harmonised to present the same disorders. Even though the quality of Finnish registers is good, the harmonisation process was needed to ensure comparable data. All the studies

had large sample sizes with long follow-ups. The response rate in the NFBC studies can be considered high. In many other birth cohort studies, poor response rates in follow-up cohort studies are causing increasing concern. Even though the study cohort of study III did not cover the full NFBC1966, 96.3% of the study cohort were originally participants of the NFBC1966. The NFBC studies and comparison cohorts were born in the same area one to two years apart, so it could be assumed that the socio-demographic background factors did not vary across the cohorts and the possible difference in outcome measures was truly the effect of the follow-up in the NFBC studies.

7.4 Limitations

The Finnish register data also has its limitations. The CRHC did not have complete registration of PIN until 1969, so there is a three-year gap in diagnosis in the NFBC1966. This may affect the cumulative incidence of disorders usually diagnosed in early childhood in particular. Also, before 1994, the CRHC lacked information on specialised outpatient care. Although the NFBCs are relatively large birth cohorts, the numbers of some of the studied psychiatric disorders, cardiometabolic disorders and suicides were too low for analysis in some analyses. Despite being minor, some of the found differences in incidences were statistically significant. The magnitude of the difference varied in some diagnostic groups substantially. Also, only a few of the many questionnaires and clinical examinations were focused on cardiometabolic or psychiatric measurements. In addition, in study III we could not identify those in our study cohort who really participated in the NFBC1966 and took part in follow-up studies. Furthermore, the fact that the NFBC data could not be combined with other datasets due to the data protection act further limited the scope of statistical analysis that could be conducted.

8 Conclusion

8.1 Main findings

The main finding was that the cumulative incidence of hospital-treated psychiatric disorders increased over the decades in the five birth cohorts in Finland, which is somewhat opposite to the Finnish psychiatric health policy plan aiming to treat people with psychiatric disorders mainly in outpatient services. In the oldest cohort, males had a higher incidence than females, whereas in the youngest cohorts, the cumulative incidence of hospital-treated psychiatric disorders was at the same level in males and females.

The results of the effects of participation in the NFBC1966 and NFBC1986 studies were somewhat inconsistent. The follow-up studies may have an impact on health-related behaviour, such as diet and exercise habits, which may in turn affect the prevalence of cardiometabolic disorders and psychiatric outcomes. Female participants of NFBC1966 had a significantly younger onset of several cardiometabolic disorders, male participants of NFBC1986 had a decreased risk for several cardiometabolic disorders, and the female participants of the NFBC1986 did seek help for mental health problems less often than the comparison cohort. Although these preliminary results suggest potential health-promoting effects, it is important to note that the cohort participants of NFBC1986 are still relatively young, and an accurate assessment of the differences in the incidence of cardiometabolic disorders can only be made as they age. The NFBC studies may not be fully representative of the general population in terms of psychiatric or cardiometabolic outcomes.

8.2 Clinical implications

The findings suggest that being aware of participation in longitudinal studies may have positive health implications. The knowledge of being monitored may lead to increased health consciousness, improved self-care behaviours, and heightened motivation to make positive lifestyle changes. Importantly, the findings suggest that the effectiveness of follow-up in promoting healthier lifestyles and reducing cardiometabolic disorders does not necessarily require intensive or frequent interventions. Despite the infrequency of the follow-ups in the NFBC1986, potential health benefits were still observed. This implies that even periodic check-

ins and minimal interventions as part of a longitudinal follow-up approach can yield positive health outcomes. These findings highlight the potential of incorporating longitudinal monitoring and follow-up strategies within healthcare systems to support individuals in living healthier lives and reduce the burden of cardiometabolic diseases.

8.3 Recommendations for future studies

Previous studies have not thoroughly explored the potential effects of participation in epidemiological follow-up studies on various health outcomes. Therefore, it is necessary to replicate the current findings with broader outcomes and in other prospective birth cohort settings. This will help to provide a more comprehensive understanding of the impact of participation in these studies on overall health and well-being. The current studies were primarily focused on examining the relationship between participation in epidemiological follow-up studies and the development of psychiatric outcomes and cardiometabolic disorders. While these outcomes are undoubtedly critical, there is a need for further exploration of other outcomes that may be affected by participation in these studies. For example, even though the psychiatric disorder diagnosis and use of psychiatric care services were studied, the use of psychiatric medications might prove an important area for future research.

In conclusion, while the current studies provide valuable insights into the potential effects of participation in epidemiological follow-up studies, there is still much to learn about the broader impact of the follow-up on different outcomes. Therefore, further investigation is needed to better understand the long-term effects of participation in these studies on overall health and well-being. In addition, future studies should explore whether the effects of participation in epidemiological follow-up studies are primarily preventive or health-promoting and whether these effects vary by demographic or other characteristics of the study population.

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I Kerkelä, M., Gyllenberg, D., Gissler, M., Sillanmäki, L., Keski-Säntti, M., Hinkka-Yli-Salomäki, S., Filatova, S., Hurtig, T., Miettunen, J., Sourander, A., & Veijola, J. (2021). Cumulative incidences of hospital-treated psychiatric disorders are increasing in five Finnish birth cohorts. *Acta Psychiatrica Scandinavica, 143*(2), 119–129. https://doi.org/10.1111/acps.13247

II Kerkelä, M., Gissler, M., & Veijola, J. (2022). Association of participation in the Northern Finland Birth Cohort 1986 with mental disorders and suicidal behaviour. *Epidemiology and Health, 44*, e2022005. https://doi.org/10.4178/epih.e2022005

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1742. Ylimartimo, Aura Tellervo (2023) Complications and outcomes of patients after emergency laparotomy

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