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OCCUPATIONAL AND OTHER OUTCOMES IN SCHIZOPHRENIA AND OTHER PSYCHOSES

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OCCUPATIONAL AND OTHER OUTCOMES IN SCHIZOPHRENIA AND OTHER PSYCHOSES

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Abstract

Schizophrenia and other psychoses are psychiatric disorders that are often associated with relatively poor outcomes. Occupational and other outcomes in psychotic disorders are typically the worst of all psychiatric disorders. However, data on these outcomes in long-term follow-up periods are scarce.

The study aimed to investigate long-term occupational and other outcomes in schizophrenia and other psychoses by utilising national register data and questionnaire data from different ages. Outcomes were studied longitudinally at three different stages of illness including onset, over the course of working life, and after years of disability pension. The study was based on the general population-based Northern Finland Birth Cohorts 1966 and 1986.

Persons with psychosis onset at 18–22 years of age had poorer long-term outcomes in terms of marital status, having children, and having substance use disorders compared to psychosis onset before 18 years. People with psychosis onset before the age of 18 years had mainly similar socioeconomic and clinical outcomes compared to non-psychotic psychiatric disorders with onset before 18 years. However, persons with early-onset psychosis were more often on disability pension compared to other early-onset psychiatric disorders. Most individuals with schizophrenia and other psychoses presented with unfavourable employee trajectories reflecting an elevated risk of unemployment and part-time work until midlife. Although schizophrenia is associated with long-term work disability, it is possible to return to the labour market after being on a disability pension. In other psychoses, returning to the labour market is more common than in schizophrenia. In schizophrenia, being married, later onset age of psychosis, shorter length of the latest disability pension and better school performance, and in other psychoses, having children and shorter length of the latest disability pension predicted returning to the labour market.

The study showed that people with psychosis onset before 18 years of age had relatively good outcomes. Occupational outcomes of psychoses were relatively poor although some persons can attain better outcomes, reflecting the occupational capacity of persons with psychoses. To fulfil that potential, development of interventions and studies considering individuals' perspectives on functioning with larger samples are needed.

Keywords: cohort studies, disability pension, early-onset psychosis, employment, follow-up studies, labour market, outcome, prognosis, psychotic disorders, recovery, schizophrenia, trajectory, work

Majuri, Tuomas, Ammatillinen ja muu ennuste skitsofreniassa ja muissa psykooseissa.
Oulun yliopiston tutkijakoulu; Oulun yliopisto, Lääketieteellinen tiedekunta; Medical Research Center Oulu; Oulun yliopistollinen sairaala
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Tiivistelmä

Skitsofrenia ja muut psykoosit ovat mielenterveyden häiriöitä, joiden ennuste on melko heikko. Ammatillinen ja muu ennuste on psykooseissa tavallisesti huonoin kaikista psykiatrisista häiriöistä. Tietoa ennusteesta pitkien seurantajaksojen ajalta on kuitenkin vain vähän.

Tutkimuksen tavoitteena oli selvittää pitkäaikaista ammatillista ja muuta ennustetta skitsofreniassa ja muissa psykooseissa käyttäen eri ikävuosilta kerättyjä rekisteri- ja kyselytietoja. Ennustetta tutkittiin pitkittäisesti sairauden puhkeamisvaiheessa, sairaudenkulun aikana sekä vuosien työkyvyttömyyseläkkeellä olon jälkeen. Tutkimus perustui Pohjois-Suomen vuoden 1966 ja 1986 väestöpohjaisiin syntymäkohortteihin.

Henkilöillä, jotka sairastuivat psykoosiin 18–22-vuotiaina oli huonompi pitkäaikaisennuste siviilisäädyn, lasten saamisen ja päihdehäiriöiden suhteen verrattuna ennen 18:aa ikävuotta sairastuneisiin. Henkilöillä, jotka sairastuivat psykoosiin ennen 18:aa ikävuotta, oli pääosin samanlainen sosioekonominen ja kliininen ennuste verrattuna muihin mielenterveyden häiriöihin sairastumiseen ennen 18:aa ikävuotta. Varhain puhkeavaan psykoosiin sairastuneet olivat kuitenkin muihin varhain puhkeaviin mielenterveyden häiriöihin verrattuna useammin työkyvyttömyyseläkkeellä. Suurin osa skitsofreniaa ja muita psykooseja sairastavista henkilöistä oli epävakaalla työurapolulla, jossa työttömyys ja osa-aikaiset työt ovat yleisiä aina keski-ikään asti. Vaikkakin skitsofrenia on yhteydessä pitkäaikaiseen työkyvyttömyyteen, työkyvyttömyyseläkkeeltä työmarkkinoille palaaminen on mahdollista. Muissa psykooseissa työmarkkinoille palaaminen on yleisempää kuin skitsofreniassa. Skitsofreniaa sairastavilla naimisissa olo, myöhempi sairauden puhkeamisikä, viimeisimmän työkyvyttömyyseläkkeen lyhyempi kesto ja parempi koulumenestys olivat yhteydessä työmarkkinoille palaamiseen. Muissa psykooseissa lasten saaminen ja viimeisimmän työkyvyttömyyseläkkeen lyhyempi kesto olivat yhteydessä työmarkkinoille palaamiseen.

Alle 18-vuotiaana psykoosiin sairastuneilla oli kohtalaisen hyvä ennuste. Ammatillinen ennuste skitsofreniassa ja muissa psykooseissa näyttäytyi melko heikkona, mutta osalla sairastuneista työkyvyn ennuste on parempi, ja jopa työmarkkinoille paluu on mahdollista. Työkyvyn hyödyntämiseksi tarvitaan interventioiden kehittämistä ja suurempia tutkimuksia, jotka huomioivat myös sairastuneiden yksilölliset näkemykset toimintakyvystä.

Asiasanat: ammatillinen ennuste, ennuste, kehityskaari, kohorttitutkimukset, psykoottiset häiriöt, seurantatutkimukset, skitsofrenia, toipuminen, työ, työkyvyttömyyseläke, työmarkkinat, työssäolo, varhain puhjennut psykoosi

To my family

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31.01.2023 Tuomas Majuri

Abbreviations

aBIC	adjusted Bayesian information criteria
AOP	adult-onset psychosis
avePP	average latent class posterior probability
CI	confidence interval
CRHC	the Care Register for Health Care
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th edition
e.g.	exempli gratia
EOP	early-onset psychosis
FEAP	first-episode affective psychosis
FEP	first-episode psychosis
FES	first-episode schizophrenia
FCP	the Finnish Centre for Pensions
GAF	the Global Assessment of Functioning
HC	healthy controls, i.e., individuals without psychotic disorder
ICD	International Statistical Classification of Diseases and Related Health Problems
i.e.	id est
IPS	Individual Placement and Support
IQR	interquartile range
ISCED	the International Standard Classification of Education
LHC	life history calendar
LMR-LRT	Lo-Mendell-Rubin likelihood ratio test
Md	Median
NFBC	Northern Finland Birth Cohort
NFBC1966	Northern Finland Birth Cohort 1966
NFBC1986	Northern Finland Birth Cohort 1986
NP	non-psychotic psychiatric disorder
NP13-18y	non-psychotic psychiatric disorder at the age of 13–18 years
NP<18y	non-psychotic psychiatric disorder before the age of 18 years
NP18-22y	non-psychotic psychiatric disorder at the age of 18–22 years
OP	other psychosis
OR	odds ratio
p	p-value, significance probability
P	psychosis

P13-18y	psychosis diagnosis at the age of 13–18 years
P<18y	psychosis diagnosis before the age of 18 years
P18-22y	psychosis diagnosis at the age of 18–22 years
PANSS	the Positive and Negative Syndrome Scale
RTW	return to work
SD	standard deviation
SES	socioeconomic status
SII	the Social Insurance Institution of Finland
SOFAS	the Social and Occupational Functioning Assessment Scale
SZ	schizophrenia

List of original publications

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

I Majuri, T., Haapea, M., Nordström, T., Säynäjäkangas, V., Moilanen, K., Tolonen, J., Ala-Mursula, L., Miettunen, J., & Jääskeläinen, E. (2022). Effect of onset age on the long-term outcome of early-onset psychoses and other mental disorders: a register based Northern Finland Birth Cohort 1986 study. *Manuscript.*

II Majuri, T., Alakokkare, A-E., Haapea, M., Nordström, T., Miettunen, J., Jääskeläinen, E. & Ala-Mursula, L. (2022). Employment trajectories until midlife in schizophrenia and other psychoses – the Northern Finland Birth Cohort 1966. *Social Psychiatry and Psychiatric Epidemiology. In press.* https://doi.org/10.1007/s00127-022-02327-6

III Majuri, T., Haapea, M., Huovinen, H., Nordström, T., Ala-Mursula, L., Penttilä, M., Martimo, K-P., Miettunen, J., & Jääskeläinen, E. (2021). Return to the labour market in schizophrenia and other psychoses – a register-based Northern Finland Birth Cohort 1966 study. *Social Psychiatry and Psychiatric Epidemiology, 56*(9), 1645–1655. https://doi.org/10.1007/s00127-020-02009-1

Some previously unpublished data are also presented in this thesis.

Contents

1 Introduction

Psychosis is a functionally disruptive symptom of many psychiatric, neurodevelopmental, and other disorders (Arciniegas, 2015). It is composed of hallucinations, delusions, disorganised thinking (speech), grossly disorganised or abnormal motor behaviour (including catatonia), and negative symptoms such as avolition and diminished emotional expression (World Health Organization, 2011). Psychosis causes a loss of contact with reality (Calabrese & Al Khalili, 2022). Schizophrenia and other psychotic disorders have mainly similar clinical presentation (World Health Organization, 2011). These disorders are challenging medical conditions that affect many aspects of life and can be highly distressing to individuals and their close relatives (Calabrese & Al Khalili, 2022).

There are still huge gaps in the scientific knowledge that prevent us from understanding better the recovery and other outcomes of psychotic disorders (Saha et al., 2005). Compared with measuring things such as prevalence and incidence, measuring occupational, clinical and other outcomes of schizophrenia tends to be more complicated (McGrath, 2008).

Society and scientific research have been paying increasing attention to work ability in recent years. Progression in treatment methods due to large amounts of medical knowledge and a booming trend of performance-orientedness have led to increasing occupational demands from individuals' perspective. As life expectancy and retirement ages have become higher, occupation has gained an increasingly important role in people's lives.

Psychotic disorders are often associated with relatively poor outcomes (Huxley et al., 2021; Jääskeläinen et al., 2013). Occupational outcomes of psychoses are typically measured, including domains related to work history, disability pension (Käkelä et al., 2014; Verdoux et al., 2010) or education (Pothier et al., 2019). Neither recovery outcomes of schizophrenia (Huxley et al., 2021; Jääskeläinen et al., 2013; Majuri, 2018) nor general employment rates in psychoses (Ajnakina et al., 2021; Huxley et al., 2021) have improved during the last decades, emphasising the importance of studying the occupational outcomes of psychotic disorders and their predictors.

The occupational outcomes of psychotic disorders are the worst among all psychiatric disorders (Joensuu et al., 2019; Virtanen M et al., 2011). Only 10–40% of individuals with psychotic disorders are employed (Ajnakina et al., 2021; Huxley et al., 2021; Marwaha & Johnson, 2004). In schizophrenia, the poor occupational outcomes are also reflected in unemployment rates between 89–95%

(Hakulinen et al., 2019a; Karpov et al., 2017, Perälä et al., 2008) and disability pension rates between 80–89% (Karpov et al., 2017, Perälä et al., 2008) across different studies. Studies comparing occupational outcomes of schizophrenia and other psychoses are rare. Compared to individuals with schizophrenia, persons with other non-affective psychoses are somewhat less often unemployed (76–84%) (Hakulinen et al., 2019a; Perälä et al., 2008) and receive less often disability pensions (69%) (Perälä et al., 2008).

Efforts to identify different factors associated with greater likelihood of employment are important to encourage employment in individuals with schizophrenia (Ang et al., 2020). Several predictors for occupational outcomes in schizophrenia have been found (Tsang et al., 2010). However, the association with some factors and outcomes, such as younger onset age of psychosis and worse employment outcomes in schizophrenia, is not clear (Tsang et al., 2010; Immonen et al., 2017).

Younger age at illness onset in psychoses is typically linked with poorer outcomes (Clemmensen et al., 2012; Immonen et al., 2017), but associations between earlier onset age and outcomes within early-onset psychoses are inconsistent (Diaz-Caneja et al., 2015). Studies on the effect of age of illness onset on very long-term outcomes in early-onset psychosis and as compared to other psychiatric disorders are missing. Many studies have analysed the effects of onset age on later outcomes as a continuous variable whereas studies adopting categorical classification of onset age are rare. Studying the effect of age of illness onset on later outcomes within the early-onset schizophrenia has been suggested (Vernal et al., 2020). By observing the effect of onset age within early-onset psychosis and as compared to other mental disorders, it would be possible to clarify differences in outcomes between different forms of the disorders.

Studies on employment and other occupational outcomes in psychotic disorders tend to cover only part of working life or to be cross-sectional as opposed to longitudinal. Studies on longer-term patterns of occupational functioning in schizophrenia are limited, none of them focusing specifically on employment (Chan et al., 2020). Very few studies have explored population-level patterning and career development during the work life course and until middle age in relation to psychotic disorders. Further studies with a longer follow-up should be conducted to learn how individuals with psychosis adapt to working life and develop their careers (Carmona et al., 2017).

While we know that occupational functioning among people with psychotic disorders is low and disability pensions are common, it has not been studied

whether recovery is possible to the extent of allowing individuals to return to the labour market from disability pension. Additionally, the potential predictors for return to the labour market are not well-known. This information, however, would be useful for patients, clinicians, and society as a whole.

The current study is based on the Northern Finland Birth Cohorts (NFBC) 1966 (n = 12,058) and 1986 (n = 9,432), which are unselected, general population-based samples. The original data have been supplemented by data collected with postal questionnaires at different ages, national register data and various hospital records.

The comprehensive objective of this thesis was to study the long-term occupational and other outcomes of schizophrenia and other psychoses. Another objective was to find out factors that predict these outcomes in psychoses by utilising data from several national registers and questionnaires at different ages. Outcomes were studied at three different stages of illness including onset, over the course of working life, and after years of disability pension.

2 Schizophrenia and other psychoses

2.1 History

Prior to 1800, persons behaving abnormally were usually homeless or were put in asylums or prisons (Tueth, 1995). However, disorders resembling the disorder we currently recognise as schizophrenia began to appear suddenly in the psychiatric literature of the early 19th century (Heinrichs, 2003), when European psychiatrists described disorders of unknown causes, often affecting the young, and typically progressing to chronic deterioration (Jablensky, 2010). The 19th century witnessed progression in the understanding of these mental disorders. Emil Kraepelin (1856–1926) was the first person to present an original formulation of the nosology of psychoses and integrate these varying clinical pictures into a single entity under the term "dementia praecox" (Jablensky, 2010). This was followed by Eugen Bleuler (1857–1939) modifying Kraepelin's original concept by adding to its scope clinical illnesses which did not lead into chronic deterioration and emphasising these disorders as a broader group of diseases (Jablensky, 2010). Bleuler replaced the concept of dementia praecox with the term schizophrenia, acknowledged the clinical subgroups of the disorder, and also developed the "broader concept" of schizophrenia by listing other psychoses such as atypical depressive states and reactive psychoses belonging to the group of schizophrenias (Jablensky, 2010).

After the beginning of primitive and sometimes abusive inpatient treatment of individuals with psychoses in the 19th century, the early 20th century treatments of psychoses with insulin coma, Metrazol shock, electro-convulsive therapy and frontal leukotomy led to various outcomes (Tueth, 1995). Neuroleptic medication in the 1950s, deinstitutionalisation in the 1960s, and more effective antipsychotic and managed care in the 1990s have gradually led to the current understanding of treatment in psychoses (Tueth, 1995).

Despite the progress in treatments methods, neither the recovery outcomes of schizophrenia (Huxley et al., 2021; Jääskeläinen et al., 2013; Majuri, 2018) nor general employment rates in psychoses (Ajnakina et al., 2021; Huxley et al., 2021) have improved during the last decades, emphasising the importance of studying effective treatments and outcomes of psychotic disorders also in the future.

2.2 Definition and diagnosis

Psychosis is the defining feature of schizophrenia and other psychotic disorders leading to a loss of contact with reality (Calabrese & Al Khalili, 2022). Schizophrenia and other psychoses are psychotic disorders whose exact definition varies between the diagnostic systems used (Jansson & Parnas, 2007). Based on the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10), psychotic disorders mostly belong to the category *"Schizophrenia, schizotypal, delusional, and other non-mood psychotic disorder"* (i.e., category F20-F29) (World Health Organization, 2011). Please see Table 1 for a comprehensive list of psychotic disorders in the ICD-10. Based on the ICD-10, schizophrenia and other psychoses can be divided into subcategories, e.g., F20.0 paranoid schizophrenia or F20.2 catatonic schizophrenia (World Health Organization, 2011). ICD-10 is the diagnostic classification used in clinical health care in Finland.

Table 1. Psychotic disorders in the ICD-10.

Diagnosis code	Psychotic disorder
F00-F09[1,2]	Psychoses due to organic, including symptomatic, mental disorders
F10-F19[1,2]	Psychoses due to psychoactive substance use
F20	Schizophrenia
F21[2]	Schizotypal disorder
F22	Persistent delusional disorders
F23	Acute and transient psychotic disorders
F24	Induced delusional disorder
F25	Schizoaffective disorders
F28	Other nonorganic psychotic disorders
F29	Unspecified nonorganic psychosis
F30.2	Mania with psychotic symptoms
F31.2	Bipolar affective disorder, current episode manic with psychotic symptoms
F31.5	Bipolar affective disorder, current episode severe depression with psychotic symptoms
F32.3	Severe depressive episode with psychotic symptoms
F33.3	Recurrent depressive disorder, current episode severe with psychotic symptoms

[1]Heterogeneous diagnostic categories, only certain diagnoses referred to as psychotic disorder, [2]Not included in psychoses in this study

Another diagnostic classification that is widely used is the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) (American Psychiatric

Association, 2013). In DSM-5, schizophrenia and other psychoses mostly belong to the category *"Schizophrenia spectrum and other psychotic disorders"* (American Psychiatric Association, 2013). The diagnostic criteria for psychoses in DSM-5 differ somewhat from the criteria used in the ICD-10 (American Psychiatric Association, 2013). The main difference in psychosis diagnosis between these two diagnostic classifications is that in ICD-10, duration of psychotic symptoms must have been at least one month whereas in DSM-5, symptoms of the disorder must have persisted for at least six months (American Psychiatric Association, 2013; World Health Organization, 2011). Other differences between ICD-10 and DSM-5 also exist (Valle, 2020). DSM-5 includes functionality criteria used for schizophrenia diagnosis (functioning at work, interpersonal or self-care level is well below the premorbid level) and specifiers characterising the disorder according to its severity, course, and form of presentation (Valle, 2020). DSM-5 excludes the subcategories of schizophrenia and does not emphasise the first-rank symptoms (i.e., certain positive symptoms that seem more likely to be associated with schizophrenia than other psychotic disorders) (Valle, 2020).

ICD-11 (World Health Organization, 2018) published in 2018 includes changes to the diagnostic criteria of schizophrenia compared to ICD-10. The changes have been made to make the ICD-11 criteria more similar to those of DSM-5 and in order to improve the clinical utility of the disorder (Valle, 2020). Schizophrenia and other psychotic disorders are mainly under the chapter "Schizophrenia and other primary psychiatric disorders" in ICD-11 (World Health Organization, 2018). Compared to ICD-10, ICD-11 does not emphasise first-rank symptoms, excludes the subcategories of schizophrenia, and includes both symptom and course specifiers (Valle, 2020). ICD-11 is planned to be implemented in Finland in the future. In psychosis research, the outcomes in different samples can vary because of the different diagnostic criteria and systems used for inclusion (Jansson & Parnas, 2007).

There are also other terms used in the psychosis literature. The term "narrow schizophrenia" includes only F20 diagnosis of schizophrenia based on the ICD-10 (World Health Organization, 2011). The term "schizophrenia spectrum disorder" includes schizoaffective disorder, delusional disorders, and schizophreniform disorder (i.e., disorder closely related to schizophrenia with the exception that the symptoms must last at least one month but not more than six months based on DSM-5). The term "broad schizophrenia" includes both narrow schizophrenia and schizophrenia spectrum disorder diagnoses.

Psychoses can be divided into “affective” and “non-affective” psychosis categories. The term affective psychosis is used for symptoms of psychosis that are present with severe mood disorders (Ramain et al., 2022). The affective psychosis category typically includes bipolar disorder with psychotic features and major depression with psychotic features. Schizoaffective disorder is also included in the affective psychosis category in some studies (Ramain et al., 2022). Non-affective psychoses include schizophrenia and the rest of other psychotic disorders.

Psychoses can also be classified based on the nature (organic vs. non-organic) of the disorder. Psychosis can exist due to an organic cause, including symptomatic mental disorders (certain diagnoses in the F00-F09 category in the ICD-10) or due to psychoactive substance use (e.g., F1x.5 disorders in the ICD-10) such as alcohol, drugs, or medication (World Health Organization, 2011). However, in this thesis organic psychoses were not included in the psychosis category due to the different nature of these disorders. The term non-organic psychosis is used for the rest of the psychoses, i.e., psychoses existing due to other than organic cause.

Psychoses can be divided based on the onset age of the disorder. Late-onset psychosis is defined as onset age after 40 years and very-late onset psychosis as onset age after the age of 60 years (Howard et al., 2000; Suen et al., 2019). The definition for very-early onset psychosis is typically at or before 12 years of age (Lin et al., 2016). The definition for the term early-onset psychosis (EOP), sometimes also referred to as adolescent-onset psychosis, varies more across studies. The most common definition for the term is psychosis with the age of illness onset before age 18 (Clemmensen et al., 2012; Diaz-Caneja et al., 2015; Kendhari et al., 2016; Lachman, 2014; Lin et al., 2016), but onset ages before 21 (Clemmensen et al., 2012) or even before 25 years (Hakulinen et al., 2019b) are also used in some studies.

Schizophrenia and other psychoses in this study

Psychotic disorders can also be classified as schizophrenia and other psychoses. There is variation in the diagnostics between schizophrenia and other psychotic disorders between different studies (Jansson & Parnas, 2007). The diagnostic classification of schizophrenia and other psychoses diagnoses used in the thesis is presented in detail later in the Methods section. The different diagnoses for schizophrenia and other psychosis used in this study are described more precisely below:

Certain disorders are referred to as schizophrenia in the thesis. Schizophrenia (F20) is characterised by the general psychotic symptoms listed later and these symptoms lasting at least for one month (World Health Organization, 2011). Please see Table 2 for the diagnostic criteria for schizophrenia (F20) based on ICD-10. Persistent delusional disorders (F22) include disorders with long-standing delusions as the only or the most noticeable clinical characteristic and which cannot be classified as schizophrenic, organic or affective. Induced delusional disorder (F24) is a genuine psychotic disorder in which a delusional disorder is shared by two or more persons with emotional links and the delusions usually disappear when persons are separated. In schizoaffective disorders (F25), both schizophrenic and affective symptoms are prominent, but the episode of illness does not justify a diagnosis of schizophrenia or depressive or manic episodes.

Table 2. Diagnostic criteria for schizophrenia (F20) based on ICD-10.

Criterion	Description
Duration of the symptoms:	≥ 1 month
At least one of the following (a-d) symptoms:	
	a) Thought echo, thought insertion or withdrawal, or thought broadcasting
	b) Hallucinatory voices commenting or voices conversing or voices coming from some part of the body
	c) Delusions of control, influence, or passivity, clearly referred to body or limb movements or specific thoughts, actions, or sensations; delusional perception
	d) Persistent bizarre delusions
Or at least two of the following (a-d) symptoms:	
	a) Persistent hallucinations in any modality when accompanied by delusions
	b) Neologisms, thought disorder, incoherence, or irrelevant speech
	c) Catatonic behaviour
	d) Negative symptoms
Exclusion criteria (a-b):	
	a) The presence of extensive depressive or manic symptoms before the characteristic schizophrenia (a-d) symptoms
	b) Alcohol/drug intoxication, dependence, or withdrawal state; organic, including symptomatic, mental disorders

The other psychosis category includes many different disorders (World Health Organization, 2011). Acute and transient psychotic disorders (F23) are a heterogeneous group of disorders characterised by the acute onset of psychotic symptoms. Other non-organic psychotic disorders (F28) are hallucinatory or delusional disorders that do not justify a diagnosis of other disorders in the group. Diagnosis code "F29" is named as unspecified non-organic psychosis. Mania with psychotic symptoms (F30.2) is mania in which typical psychotic symptoms are also present. In bipolar affective disorder, current episode manic with psychotic symptoms (F31.2), the individual is manic with psychotic symptoms and has had at least one other affective episode in the past. In bipolar affective disorder, current episode severe depression with psychotic symptoms (F31.5), the person is depressed with psychotic symptoms and has had at least one authenticated manic, hypomanic, or mixed affective episode in the past. Severe depressive episode with psychotic symptoms (F32.3), is an episode of depression with the presence of psychotic symptoms. Recurrent depressive disorder, current episode severe with psychotic symptoms (F33.3), is characterised by episodes of depression, the current episode being severe with psychotic symptoms, and with no previous episodes of mania.

The other psychosis group may include patients who have not yet received a diagnosis of schizophrenia (Ahti et al., 2022). This may be due to a need for an unspecified diagnostic category such as F29 in ICD-10. Unspecified category can be used to capture the different psychotic syndromes not meeting the specified criteria for the diagnoses of schizophrenia or other psychotic disorders due to lack of evidence (Widing et al., 2020). Schizotypal disorder (F21) is included in the psychoses category in ICD-10, but not in DSM-5. However, in this study it is not included in the psychoses categories.

2.3 Epidemiology

According to a meta-analysis of studies in England, the pooled incidence of all psychoses is approximately 32 per 100,000 person-years, 23 for non-affective psychoses, 12 for affective psychoses, and 15 for schizophrenia (Kirkbride et al., 2012). Another earlier review including data from 33 countries found a median incidence rate of 15.2 per 100,000 person-years in schizophrenia (McGrath et al., 2004b). The incidence rate of early-onset (diagnosis before age of 18 years) schizophrenia is around 0.2% based on a population-based cohort study (Jerrell & McIntyre, 2016). In Finland, the rate for first-admitted schizophrenia patients was

37.8 per 100,000 people aged 15–64 years and 22.1 per 100,000 of the total population in 2003 (Salokangas et al., 2011). In terms of early-onset psychotic disorders, the Finnish Birth Cohort study found that 1.5% of males and 0.8% of females had been in psychiatric hospital treatment due to any psychosis between ages 13 and 24 (Gyllenberg et al., 2010). Corresponding rates for admission due to non-affective psychoses were 1.3% for males and 0.5% for females, 0.6% and 0.2% due to schizophrenia, and 0.8% and 0.2% for psychotic disorder not otherwise specified (Gyllenberg et al., 2010).

The median lifetime prevalence of psychosis is approximately 7.5 per 1,000 persons, 8.2 for non-affective psychosis, 6.4 for schizophrenia, and 8.8 for schizophrenia and related disorders (Moreno-Küstner et al., 2018). In Finland, the lifetime prevalence is 3.5% for any psychotic disorders, 2.3% for non-affective psychoses, 0.6% for affective psychoses, and 1.0% for schizophrenia (Perälä et al., 2007). There is also geographic variation in the lifetime prevalence of psychotic disorders in Finland, schizophrenia and other non-affective psychoses being more common among those born in the East and the North (Perälä et al., 2008).

The incidence and prevalence of psychotic disorders varies a lot by gender, age, ethnicity, country, and many other factors (Kirkbride et al., 2012, Moreno-Küstner et al., 2018). The incidence of schizophrenia is higher in men compared to women, the ratio being 1.4:1 (McGrath et al., 2004b), whereas there are no differences in prevalence between the genders (Perälä et al., 2007, Saha et al., 2005). The mortality in schizophrenia is higher for men than women (Joukamaa et al., 2001). Some studies have found earlier onset of schizophrenia for men than women, but these findings are inconsistent, depending on the diagnostic systems used (Eranti et al., 2013).

Schizophrenia is a disorder of all ages (Häfner, 2019); however, late onset and early onset forms of the disorder are somewhat rare. The peak age at the illness onset of schizophrenia-spectrum and primary psychotic disorders is 21 years and the median age at onset is 25 years (Solmi et al., 2022). In men, schizophrenia incidence increases steeply at 15 to 25 years of age whereas in women, incidence reaches peaks at 15–30 and later at menopause, 44–49 years of age (Häfner, 2019). Similar variation in age-specific incidence rates of psychosis between men and women has also been found in other schizophrenia spectrum disorders (Sutterland et al., 2013).

2.4 Aetiology and risk factors

2.4.1 Pathogenesis

Earlier, there was a lack of exact knowledge regarding the pathogenesis of schizophrenia and other psychosis (Pearlson, 2000), but nowadays, understanding on the different factors and their relationship to the abnormal patterns of neurodevelopment leading to psychosis has improved (Millan et al., 2016). The aetiology of psychosis is multifactorial (Stilo & Murray, 2019). Novel disease models show that the risk for schizophrenia and other psychosis appears to be influenced by a complex process combining genetic risk with interacting environmental hits and vulnerability factors occurring at key periods of neurodevelopmental activity (Davis et al., 2016).

Several theories on the aetiology of schizophrenia and psychoses have been suggested over the years (Hanson & Gottesman, 2005). One of the leading theories – the vulnerability model – proposed that each person has a degree of vulnerability for psychosis that will in suitable circumstances express itself as an episode of schizophrenic illness (Zubin & Spring, 1977). Another model – the two-hit hypothesis – suggested that the clinical phenotype of schizophrenia requires two hits to generate the disease, the first as an early priming in a genetically predisposed individual and the second one as an environmental insult (Maynard et al., 2001).

While multiple theories have been suggested regarding the origin of schizophrenia, by far the most evidence points to the current models on neurodevelopment (Fatemi & Folsom, 2009). The modern theory on the pathogenesis – the neurodevelopmental model of psychosis – was first introduced more than 30 years ago and is based mainly on the earlier theories on vulnerability, two-hit hypothesis, and other theories (Davies et al., 2020). This theory suggests that genetic disposition together with prenatal and perinatal insults programmes the developing brain towards later psychosis (Millan et al., 2016). Based on this theory, the initial insult occurring already *in utero* induces dysplasia in neural networks and cascades of aberrant neurodevelopmental processes, leading to a trajectory of vulnerability to later insults in adolescence (Keshavan, 1999). Later refinements for the neurodevelopmental model of psychosis have been suggested. The Developmental Risk Factor Model emphasises the importance of dysregulated striatal dopamine as a step linking the well-known risk factors to psychotic symptoms (Murray et al., 2017). Another refinement of the theory, the extended

neural diathesis-stress model, emphasises the broader neurobiological context of stress psychobiology in psychosis progression (Pruessner et al., 2017).

The neurodevelopmental process of abnormal brain development in schizophrenia starts already in the foetal period (Meyer et al., 2009). This process leads to structural and functional abnormalities in the brain (Meyer et al., 2009). Illness progression in schizophrenia leads to intracranial volume reduction (Haijma et al., 2013). Other regional structural brain differences and abnormalities in schizophrenia include bilaterally reduced volume of medial temporal lobe structures (Wright et al., 2000), thinner cortex (van Erp et al., 2018), whole brain and total white and grey matter reduction as well as an increase in lateral ventricular volume at the illness onset (De Peri et al., 2012).

Certain brain regions are involved in neural circuitry disturbances in schizophrenia (Lewis & Sweet, 2009). Functional changes in the brain in schizophrenia include abnormalities such as altered activity with deficits in the anterior cingulate cortex, dorsolateral prefrontal cortex, and thalamus (Minzenberg et al., 2009). In psychoses, functional neuroimaging has showed abnormal neural activity during various cognitive tasks including those assessing decision making, memory and emotion processing (Karlsgodt et al., 2010). Individuals with psychosis also demonstrate ventral stria hypoactivation during reward anticipation (Radua et al., 2015). In neurotransmitter level, a key feature behind psychotic symptoms is dysregulation in the dopaminergic system (Kesby et al., 2018). The increased subcortical release of dopamine augments dopamine D2 receptor activation and leads to increased presynaptic dopamine function in certain areas (Brisch et al., 2014). Dopamine dysregulations exist especially in the mesolimbic and prefrontal (Brisch et al., 2014) areas and in the nigrostriatal pathway (McCutcheon et al., 2019). Other important functional abnormalities in the brain in schizophrenia include decreased glutamate levels and reduced GABAergic neurotransmission (Marsman et al., 2014) as well as disturbances in the endocannabinoid system (Desfossés et al., 2010).

2.4.2 Risk and protective factors

Various risk and protective factors and markers for the development of schizophrenia have been recognised (Murray et al., 2017). Meta analyses on the risk factors for psychoses (Davies et al., 2020), schizophrenia (Matheson et al., 2011) and schizophrenia spectrum disorders (Belbasis et al., 2018) have been conducted. Based on a recent meta-analysis, several risk and protective factors for

non-organic psychotic disorders including affective and non-affective psychoses appear during the prenatal and perinatal phases (Davies et al., 2020).

Copy number variants of some genes are associated with a higher risk of schizophrenia (Marshall et al., 2017). The most important predictive risk factor for later schizophrenia is a diagnosis of schizophrenia or related disorder in a first-degree relative (Lichtenstein et al., 2009). However, almost any other psychiatric disorder in a first-degree relative increases the risk of later schizophrenia (Mortensen et al., 2010).

Many prenatal and perinatal factors associate with a later onset of psychosis, the risk factors including, e.g., low birthweight and parental psychopathology (Davies et al., 2020). Based on a meta-review on the risk factors for schizophrenia spectrum disorders, the risk factors with the highest quality evidence include advanced paternal age, cannabis use, and obstetric complications (Matheson et al., 2011). Meta-analyses have found central nervous infection during childhood (Khandaker et al., 2012) and urbanicity (Vassos et al., 2012) to be risk factors for non-affective psychoses and adverse life events (Beards et al., 2013; Matheson et al., 2013; Varese et al., 2012) to be risk factors for any psychosis. Deficits in motor function or cognitive function in adolescence are a risk marker for developing schizophrenia (Dickson et al., 2012). Parental communication deviance has been found increasing risk for later schizophrenia in offspring based on a meta-analysis (de Sousa et al., 2014). Other risk factors or markers for psychosis reported in literature include childhood trauma (Green et al., 2014), various infectious agents (Arias et al., 2012; Gutiérrez-Fernández et al., 2015), tobacco smoking (Scott et al., 2018), social defeat (Li et al., 2012), malnutrition (McGrath et al., 2011), vitamin D insufficiency (McGrath et al., 2010), lower premorbid levels of intelligence quotient (Schulz et al., 2014) and immigrant background (Cantor-Graae et al., 2003; Tortelli et al., 2015).

Data on risk factors for other psychoses do not exist as broadly as data on risk factors for schizophrenia (Laurens et al., 2015), one explanation for this being the common inclusion of other psychoses in studies of schizophrenia, psychosis (Keskinen, 2015) or studies of other psychiatric disorders such as depression. For example, a recent meta-analysis (Davies et al., 2020) included other psychoses but conducted the meta-analysis only for psychoses in general and not separately for different psychotic disorders due to the limited number of studies separating these disorders. However, many of the risk factors are non-specific for schizophrenia and overlap with other psychotic disorders as well (McLaughlin et al., 2010).

Only one meta-analysis (Jääskeläinen et al., 2018) has been conducted on the risk factors of psychotic depression. No meta-analyses have been conducted on the risk factors focusing only on other psychoses, and current knowledge on these is thus based mainly on the results of single studies or broader studies including other psychoses within studies of psychosis, schizophrenia, depression or bipolar disorder. Family history of psychosis and bipolar disorder have been found to increase the risk of psychotic depression (Jääskeläinen et al., 2018). In the NFBC 1966, low school sports grade in adolescence and psychiatric illness in the family have been found as risk factors for psychotic depression (Nietola et al., 2020). Based on an umbrella review, the risk factors with the most convincing evidence for depression are physical abuse during childhood, widowhood, sexual dysfunction, job strain, obesity and having 4–5 metabolic risk factors (Köhler et al., 2018), and the risk factors of psychotic depression may also be somewhat similar to these.

Urban residence has been found to associate with psychotic bipolar disorder (Kaymaz et al., 2006). Based on a meta-analysis, some studies have found evidence on the association between maternal influenza infection and bipolar disorder with psychosis, but this finding is not replicated between all studies (Rowland & Marwaha, 2018). Childhood adversity increases the risk of affective psychosis (Matheson et al., 2013). Other risk factors for affective psychoses include some obstetric complications (Bain et al., 2000), uterine atony (Hultman et al., 1999) and late winter birth (Hultman et al., 1999). Multiparity has been found to be a risk factor of reactive psychosis (Hultman et al., 1999). A recent meta-analysis classifying affective psychosis as bipolar disorder (without or with psychotic features) or psychotic depression found high paternal age, early or late gestational age, substance misuse, childhood adversity and background from an ethnic minority to be risk factors for affective psychosis (Rodriguez et al., 2021).

Data on protective factors of psychotic disorders are limited compared to data on risk factors (Keskinen, 2015). Contrary to the risk factors, protective factors for psychosis include factors such as vitamin D supplementation (McGrath et al., 2004a) and healthy family environment (Schlosser et al., 2012).

2.5 Clinical presentation

The term “psychosis” lacks a homogeneous definition, but denotes a clinical construct composed of several symptoms (Gaebel & Zielasek, 2015). Schizophrenia and other psychotic disorders are characterised by abnormalities in

one or more of the following domains: hallucinations, delusions, disorganised thinking (speech), grossly disorganised or abnormal motor behaviour (including catatonia), and negative symptoms such as avolition and diminished emotional expression (American Psychiatric Association, 2013). Abnormalities in the first four of these domains form the so-called positive symptoms of psychosis (World Health Organization, 2011). The clinical presentation of these disorders is close to each other; however, there are small differences between different diagnoses (World Health Organization, 2011). Psychotic disorders affect many aspects of life and that can be highly distressing for patients and their close relatives (Calabrese & Al Khalili, 2022).

The period of symptoms and subclinical signs that precedes the onset of psychosis is called the prodromal phase of psychosis (Larson et al., 2010). The prodromal phase can last from weeks to several years (Rosen et al., 2006) and is characterised by deterioration in the heterogeneous subjective and behavioural symptoms that precede the clinical psychotic symptoms (Larson et al., 2010). Persons in the prodromal phase are often young adults who experience slight disturbances in cognition, perception, different fields of functioning, level of energy and stress tolerance (Olsen & Rosenbaum, 2006).

First-episode psychosis typically occurs in late adolescence or early adulthood (De la Serna et al., 2021). It typically leads to hospitalisation, but after that the course of psychosis is heterogeneous and fluctuating, with varying levels of need for inpatient and outpatient treatment (Ajnakina et al., 2020). The early course of psychosis is often characterised by recurrent relapses (Alvarez-Jimenez et al., 2012).

Besides positive and negative symptoms, ICD-11 emphasises also other important domains of symptoms in schizophrenia, considering depressive symptoms, manic symptoms, cognitive impairments, and psychomotor symptoms in its symptom specifiers when diagnosing and characterising schizophrenia (Valle, 2020). Schizophrenia is associated with a high number of psychiatric (Buckley et al., 2009) and somatic comorbidities, and in particular cardiovascular diseases are common (Dieset et al., 2016). Other psychoses have a somewhat more favourable clinical picture than schizophrenia including less cognitive impairment (Zanelli et al., 2019), better work and social functioning (Harrow et al., 1997), greater number of individuals with complete remission (Harrow et al., 1997) and less psychotic symptoms (Harrow et al., 1997).

2.6 Treatment and rehabilitation

The clinical management of schizophrenia and other psychotic disorders is a comprehensive entity that is mainly composed of medication and psychosocial treatment (Galletly et al., 2016). Other useful treatments include, for example, electroconvulsive therapy (Ali et al., 2019; Tharyan et al., 2005), transcranial magnetic stimulation (He et al., 2017) and treatment of comorbidities such as depressive and anxiety symptoms and substance abuse (Buckley et al., 2009).

Antipsychotic medication is the cornerstone of treatment in these disorders (Huhn et al., 2019; Leucht et al., 2017). Antipsychotic medication is effective in the reduction of positive symptoms but its impact on the negative symptoms is limited (Krause et al., 2018). Antipsychotic medication derives its effect on the positive symptoms of psychosis by blocking dopamine receptors (Howes et al., 2009). Antipsychotic medication can be divided into first-generation antipsychotics (e.g., haloperidol) and second-generation antipsychotics (e.g., risperidone, olanzapine, clozapine) (Zhang et al., 2013). Nowadays, second-generation antipsychotics are recommended in preference to first-generation antipsychotics due to their extrapyramidal side effect profile, better tolerability (Kahn et al., 2008), reduced discontinuation of medication (Martin et al., 2006) and improved relapse prevention (Kishimoto et al., 2013). Antipsychotic treatments are used for both acute and maintenance therapy for schizophrenia (Galletly et al., 2016). Antipsychotic medication is typically used as a monotherapy, but also combination treatment of different antipsychotics can be considered because of suboptimal other treatment methods (Galling et al., 2017; Tiihonen et al., 2019). Long-term antipsychotic use is associated with decreased mortality among individuals with schizophrenia, especially among those treated with clozapine (Taipale et al., 2020). Clozapine is typically considered the most effective antipsychotic to reduce overall symptoms in schizophrenia and related disorders (Huhn et al., 2019). Clozapine and long-acting injectable antipsychotics are the most effective medications to prevent relapses in schizophrenia (Tiihonen et al., 2017).

The effectiveness of antipsychotic therapy is limited, leaving many individuals symptomatic despite ongoing antipsychotic medication (Correll et al., 2017). Besides pharmacological treatment, psychosocial interventions are essential components of effective treatment (Norman et al., 2017). Psychosocial treatment combined with other treatments as personalised and tailored rehabilitation offers the best support for recovery (Hiekkala-Tiusanen et al., 2019). Psychosocial

treatment consists of a wide range of social and therapeutic interventions that have been proven effective (Hiekkala-Tiusanen et al., 2019). In psychosocial treatment, standard care of psychosis is supplemented by additional social and psychological interventions, such as cognitive-behavioural therapy, psychoeducation, supportive therapy, family therapy and other therapies (Jones et al., 2018). Cognitive remediation and cognitive therapy reduce the impact of cognitive impairment and are thus important psychosocial interventions in the treatment and rehabilitation of psychosis (Morin & Franck, 2017). Psychological treatments are important in reducing negative symptoms due to the limited efficacy antipsychotic medication has on them (Lutgens et al., 2017).

Rehabilitation in schizophrenia consists of psychosocial treatment methods and vocational rehabilitation. Vocational rehabilitation has many beneficial effects for well-being and mental health (Noordt et al., 2014), and supporting the ability to work can improve different domains of outcomes in psychosis (Tandberg et al., 2012) and furthermore, provide a normative context that helps individuals develop a sense of control over their lives (Carmona et al., 2017). Vocational rehabilitation can include supported employment, individual placement and support (IPS), sheltered work, job rehabilitation and psychosocial rehabilitation work programmes (Twamley et al., 2003). The utilisation of different methods of vocational rehabilitation varies between countries and districts, making comparison of these methods difficult. Many studies have analysed the effects of specific intervention programmes on the occupational outcomes of psychoses (Caroma et al., 2017). Only few meta-analyses have collected evidence on the effects of different vocational rehabilitation and other vocational interventions in schizophrenia and other psychotic disorders (Carmona et al., 2017; Twamley et al., 2003). These meta-analyses (Carmona et al., 2017; Twamley et al., 2003) and general meta-analyses on mental disorders (de Winter et al., 2022) have linked different vocational interventions with improvement in employment outcomes among individuals with schizophrenia spectrum disorders.

3 Outcomes in schizophrenia and other psychoses

3.1 Definition

The definition for the term "outcome" can be described as the quality and effectiveness of health care as measured by the attainment of a specified result (Jefford et al., 2003). The outcome in schizophrenia and other psychoses is typically relatively poor (Huxley et al., 2021; Jääskeläinen et al., 2013). Outcome in psychoses has heterogeneous definitions (McGrath, 2008). Standard outcome criteria for psychoses have varied over the years because of the wide heterogeneity of its long-term course and the varying effects of different treatment methods (Andreasen et al., 2005). Dimensional symptom measures (e.g., positive or negative symptoms) and other measures of disability (e.g., employment) tend to fluctuate over time showing divergent trajectories whereas categorical outcome measures (e.g., recovery) are not readily operationalised for chronic disorders like schizophrenia (McGrath, 2008). A wide variety of direct and indirect outcome measures are used, the most frequent including hospitalisations, clinical symptoms, mortality, occupational/social/cognitive functioning, burden of care, effect of medication and quality of life (Isaac et al., 2007). Different measures of outcomes can vary from poor (e.g., hospitalised during the last two years; on a disability pension or sick leave) to good (e.g., improvement of functioning; lack of symptoms) (Lipkovich et al., 2009).

However, it is fascinating that psychosis research has focused so much on the onset of these disorders while we still struggle to understand the offset and outcomes (Saha et al., 2005). Compared with measuring things such as prevalence and incidence, measuring clinical, occupational, and social outcomes of schizophrenia tends to be harder (McGrath, 2008). Knowledge on these outcomes of schizophrenia and other psychoses brings useful information for patients and their families on the course of the disease as well as helps us to evaluate the burden of care and the quality of treatment methods (Jääskeläinen et al., 2010).

3.2 Employment and occupational outcomes

Occupational functioning is an important measure of functional capacity among individuals with schizophrenia (Bowie et al., 2008). Occupational outcomes in the

field of psychosis literature are outcomes that are typically measured, including domains related to work history, disability pension (Käkelä et al., 2014; Verdoux et al., 2010) or education (Pothier et al., 2019). Occupational outcomes are closely related to socioeconomic status (SES) or socioeconomic outcomes that are usually measured by work status, education, and income (Adler et al., 1994). Health and employment have a two-way causal relationship: better health influences the chances of being employed, and working affects the health status (Barnay, 2016). Schizophrenia and other psychoses are known to affect individuals already at a young age, presenting as functional deterioration in multidimensional fields (Wang et al., 2020) often leading to poor long-term attachment to working life (Pirkola et al., 2020) and high risk of being outside the labour market (Hakulinen et al., 2019b). People with schizophrenia experience various challenges and barriers that prevent them from being able to adapt to the labour market and from finding employment (Carmona et al., 2019; Marwaha & Johnson, 2004; Soeker et al., 2019).

A few reviews on the employment levels among individuals with schizophrenia or psychosis (Ajnakina et al., 2021; Cohen et al., 2008; Huxley et al., 2021; Marwaha & Johnson, 2004) have been conducted (Table 3). A recent meta-analysis with an average follow-up duration of eight years reported an employment rate of 33% in people with first-episode psychoses (FEP) and 30% in those with first-episode schizophrenia (FES) (Ajnakina et al., 2021). Another recent review found somewhat similar results, reporting employment rates of 39% in Europe, 36% in North America, and 45% in rest of the world among those with broadly defined schizophrenia (Huxley et al., 2021). Marwaha & Johnson (2004) found employment rates between 10–20% in Europe in schizophrenia, while the rates outside Europe were less clear. In line with the more recent reviews, Marwaha & Johnson (2004) reported employment rates in first-episode psychosis to be somewhat higher than in schizophrenia, although no meta-analysis was performed.

That schizophrenia has a better outcome including higher levels of employment in developing countries has become an axiom in international psychiatry (Cohen et al., 2008). Varying results have been presented, Huxley et al. (2021) showing significantly better employment levels in low- and middle-income countries than in high-income countries, but Ajnakina et al. (2021) showing longitudinal studies from Europe and high-income nations with higher rates of employment in FEP compared to non-European and middle-income countries. However, an earlier review has questioned this axiom on better outcomes in developing countries, suggesting a far more complex picture and emphasising the variation in employment levels since different definitions of employment are used

across different countries and studies (Cohen et al., 2008). A higher level of employment among first episode than multiple-episode psychosis patients has been reported (Huxley et al., 2021; Marwaha & Johnson, 2004).

Some studies have explored occupational outcomes of psychoses in Finland. In Finland, the challenges of gaining employment in schizophrenia are reflected in unemployment rates between 89–95% (Hakulinen et al., 2019a; Karpov et al., 2017, Perälä et al., 2008) and disability pension rates between 80–89% (Karpov et al., 2017, Perälä et al., 2008) across different studies. Half of the schizophrenia patients in Finland are granted a disability pension within five years of illness onset (Kiviniemi et al., 2011). In the Northern Finland Birth Cohort 1966 (NFBC1966), almost 60% of persons with schizophrenia received disability pension during the first 10 years after illness onset (Miettunen et al., 2007). An older study analysing occupational outcomes of psychoses in Finland found the employment rate to be 7% in schizophrenia, 20% in other non-affective psychoses, 47% in affective psychoses, and 21% in any psychotic disorder (Perälä et al., 2008). The more recent Finnish SUPER study reported full-time employment levels of 3% in schizophrenia, 5% in schizoaffective disorder, and 10% in both psychotic depression and other psychosis (Ahti et al., 2022). Despite the extremely low full-time employment levels, the same study found rates of individuals working or studying to be 8%, 15%, 19% and 25% for the corresponding diagnostic groups (Ahti et al., 2022). In the NFBC1966, 11% of individuals with schizophrenia spectrum disorder have been reported to be employed when defining employment as being employed for at least 25% of working days (Rautio et al., 2016).

The employment rates of schizophrenia spectrum disorders decrease both before and after the diagnosis (Christensen et al., 2022; Holm et al., 2021) and tend to descend significantly with longer follow-ups (Ajnakina et al., 2021). The working periods of individuals with schizophrenia are typically of short duration and in low-qualified jobs (Verdoux et al., 2010) leading to remarkable losses of income compared to general population (Falk et al., 2016). The societal costs of schizophrenia including hospital admissions, community care services, other treatments costs, social security, and lost productivity due to being outside the labour force are significant (Evensen et al., 2016).

Regarding education, a recent meta-analysis (Dickson et al., 2020) showed that individuals with schizophrenia are significantly less likely to enter higher education and attain significantly lower general academic achievement scores compared to those without schizophrenia. The Psychoses in Finland study found that 20% of individuals with schizophrenia or other non-affective psychosis, 41% of those with

affective psychosis, and 23% of those with any psychotic disorder have high level of education (Perälä et al., 2008). The SUPER study found that 62% of individuals with schizophrenia, 78% with schizoaffective disorder, 73% with psychotic depression, and 70% with other psychosis have intermediate or higher level of education (Ahti et al., 2022).

Studies separating other psychoses from schizophrenia or comparing occupational outcomes in these disorders are rare and mainly focused on Finland. Compared to persons with schizophrenia, persons with other non-affective psychoses are somewhat less often unemployed (76–84%) (Hakulinen et al., 2019a; Perälä et al., 2008) and receive less often disability pensions (69%) (Perälä et al., 2008). Both full- and part-time levels of employment are somewhat higher among individuals with other psychosis than in schizophrenia (Ahti et al., 2022). A study in the NFBC1966 found that individuals with psychotic depression are less often on disability pension and more actively involved in work than individuals with schizophrenia (Nietola et al., 2018). Individuals with other psychotic disorders have more often higher level of education compared to those with schizophrenia (Perälä et al., 2008, Ahti et al., 2022).

Employment in schizophrenia is associated with positive changes in non-occupational domains such as leisure activities (Charzyńska et al., 2015). Promising results have also been found on the effect of employment in the improvement of social functioning, quality of life and other indicators of recovery (Charzyńska et al., 2015). Supporting the ability to work improves functional, clinical, and social outcomes of psychosis (Tandberg et al., 2012).

Table 3. Reviews and meta-analyses on the employment among individuals with psychosis or schizophrenia.

Study	Article type	Location	Diagnoses included; diagnostic system	Main findings
Marwaha & Johnson, 2004	Review	World; mainly Europe	Schizophrenia and FEP; neither diagnostic system nor diagnosis codes reported	European studies reported employment rates between 10–20% in schizophrenia, while the rates outside Europe were less clear. There was a higher level of employment among FEP patients.
Cohen et al., 2008	Review	Low- and middle-income countries	Schizophrenia; neither diagnostic system nor diagnosis codes reported	Variation in employment levels since different definitions of employment across different countries and studies.
Ajnakina et al., 2021	Systematic review and meta-analysis	World	FEP disorders totally and by subcategories: FEP, FES and FEAP; varying standardised diagnostic systems accepted	A total of 32.5% of people with a diagnosis of FEP disorders were employed with employment percentages of 25.9% in FEP, 29.9% in FES and 58.4% in FEAP.
Huxley et al., 2021	Systematic review	World	Broadly defined schizophrenia, both first-episode and multiple episodes of psychosis included; diagnostic systems not reported	Employment rate of 39% in Europe, 36% in North America and 45% in rest of the world; no statistically significant relationship between different regions; significantly better employment levels in low- and middle-income countries than in high-income countries.

Abbreviation: FEP, first-episode psychosis; FES, first-episode schizophrenia; FEAP, first-episode affective psychosis

3.3 Other outcomes

3.3.1 Mortality

Schizophrenia is associated with an average of 14.5 years of potential life lost compared to general population, the average life expectancy being 59.9 years for men and 67.6 years for women (Hjorthøj et al., 2017). In Finland, the life expectancy of persons with schizophrenia (70.1 years) is 7.4 years lower compared to general population (77.5 years) (Tanskanen et al., 2018). Schizophrenia is associated with significantly higher all-cause mortality compared to general population (Correll et al., 2022), the all-cause standardised mortality-ratio being 2.7 for people with schizophrenia in Finland (Tanskanen et al., 2018). Excess mortality due to diseases and medical conditions in persons with schizophrenia spectrum disorder is 3-fold and excess mortality due to suicides is 13-to 23-fold compared to the general population (Nordentoft et al., 2013). The life expectancy of persons with schizophrenia is improving at the same rate as in the general population while there is still a clear disparity in mortality compared to persons without the disorder (Tanskanen et al., 2018). The risk of suicide is elevated among individuals with schizophrenia (Hor & Taylor, 2010). However, suicide rates among individuals with schizophrenia have declined significantly in Finland during the last decades (Tanskanen et al., 2018).

3.3.2 Functioning

Functional outcomes of psychoses include abilities such as performance on neurocognitive tests, living independently in the community, abilities to work or study, interpersonal relations and self-care (Sumiyoshi & Sumiyoshi, 2015). Social and occupational functioning are subtypes of functioning used often to describe individuals' functional capacity (Immonen et al., 2017). Rating scales such as the Global Assessment of Functioning (GAF) and the Social and Occupational Functioning Assessment Scale (SOFAS) are commonly used to evaluate the level of functioning in persons with schizophrenia (Samara et al., 2014). The concept of functional recovery includes multiple aspects of patients' lives, making it difficult to settle on a definition and to develop reliable assessment criteria (Lahera et al., 2018). Based on a Canadian study, the one-year functional recovery in FEP was

51% when the functional recovery was defined by SOFAS score > 60 (Menezes et al., 2009). The recent Finnish SUPER study found that among psychotic disorders, schizophrenia was associated with the worst level of psychosocial functioning in terms of being employed or studying, independent living and having children (Ahti et al., 2022). Among other psychotic disorders, people with other psychosis have better level of psychosocial functioning compared to schizophrenia and they show less differences from schizophrenia than individuals with schizoaffective disorder and psychotic depression (Ahti et al., 2022).

3.3.3 Clinical outcomes

Clinical outcomes of psychoses are typically measured by hospitalisations, discharges, and other episodes of treatment (Killaspy et al., 2016), relapses and medication (Faerden et al., 2008), or rating scales such as the Positive and Negative Syndrome Scale (PANSS) or other tools measuring typical symptoms (Leucht et al., 2005). These clinical domains of outcomes are often acknowledged in studies on remission (Andreasen et al., 2005) and recovery (Jääskeläinen et al., 2013). A recent meta-analysis found that 55% of individuals with first-episode psychoses cases were hospitalised at least once during the average follow-up length of seven years, with the pooled average length of stay being 117 days (Ajnakina et al., 2020). Individuals with schizophrenia have typically more hospitalisations compared to other psychotic disorders, the median number of hospitalisations being 5 for persons with schizophrenia, 3 for psychotic depression, 5 for schizoaffective disorder, and 2 for other psychoses (Ahti et al., 2022).

One-fifth to one-third of all individuals with schizophrenia present with a treatment-resistant form of the disorder (Conley & Kelly, 2001). The definition for the term treatment-resistant schizophrenia varies (Seppälä et al., 2021). One way of defining the term is based on the history of non-response to various numbers of adequate trials of antipsychotic treatment (Seppälä et al., 2021).

3.3.4 Remission and recovery

Definitions for the term remission vary, most of the psychiatric studies applying the concept of a less symptomatic state than previously assumed (Zwart et al., 2019). The widely accepted remission criteria in schizophrenia are defined by two factors: 1) maximum mild severity of core symptoms in schizophrenia, and 2) the duration criterion of at least six consecutive months (Andreasen et al., 2005). Based on these

criteria, remission varies widely in different samples, with remission rates between 17–88% (Emsley et al., 2011). Another review applying these criteria found a remission rate of 58% for people with first-episode psychosis (Lally et al., 2017). However, these remission criteria have later been criticised by being primarily a symptomatic measure (Eberhard et al., 2009) and excluding other measures of outcome such as occupational and functional domains as well as quality of life (Emsley et al., 2011). Compared to schizophrenia, a higher number of individuals with other psychoses achieve complete remission (Harrow et al., 1997).

The term "recovery" in schizophrenia is also problematic because of the many different definitions used in the literature (Faerden et al., 2008). Based on a widely cited meta-analysis, approximately 1 in 7 individuals with schizophrenia meets the recovery criteria including clinical (e.g., no episodes of treatment in 2 years; remission for a minimum of 24 months), social or functional (e.g., having GAF > 60; being employed) dimensions and persistence of good outcome for a minimum of 2 years (Jääskeläinen et al., 2013). Another review applying these criteria found the rate of recovery to be 38% for persons with FEP (Lally et al., 2017). According to a Danish study combining different domains of outcome, 18% of persons with FEP reach recovery (when defined as no psychotic or negative symptoms, living independently, GAF score > 59, and working or studying) (Bertelsen et al., 2009). Recovery rates in schizophrenia and other psychoses have not improved over the years (Jääskeläinen et al., 2013; Lally et al., 2017). Recovery and remission rates in first-episode psychosis are distinctly better than these outcomes in multi-episode psychosis (Huxley et al., 2021; Lally et al., 2017).

Clinical-based definitions for recovery in schizophrenia have been increasingly criticised as not suitable for a persistent disorder such as schizophrenia (Yu et al., 2020) whereas consumer-oriented perspectives acknowledging the concept of personal recovery have been drawing growing attention (Bellack, 2006). The use of personal recovery in the outcome and treatment monitoring of individuals with schizophrenia spectrum disorders has been suggested (Van Eck et al., 2018). Personal recovery is a subjective and multidimensional concept and research using it as an outcome has been rapidly increasing (Leendertse et al., 2021). Personal recovery can be assessed by self-assessment of individuals' quality of life (Dong et al., 2019). Several measures and rating scales have been developed to assess the personal recovery process (Leendertse et al., 2021).

3.4 Outcomes in early-onset psychoses

Most young adults complete their educational degrees and enter working life in early adulthood (Hakulinen et al., 2019b), highlighting the significance of this period for later careers. Psychiatric disorders often begin already in adolescence (McGorry et al., 2011), and when they emerge during this period they can have severe effects on outcomes in later lives. Adolescent mental health disorders are risk factors for future mental distress and psychopathology (Nishida et al., 2016). Early-onset psychosis has an impact on many aspects of life course including transitions to adult roles regarding the act of becoming independent, family formation and entering working life after education (Arango et al., 2022).

Some studies have analysed the occupational outcomes of early-onset psychoses, often associating EOP with unfavourable outcomes. Both schizophrenia and other non-affective psychosis diagnoses between ages 15 to 25 are linked with a high risk of being unemployed and a remarkable loss of income (Hakulinen et al., 2019a). Early-onset schizophrenia (when defined as schizophrenia diagnosis between ages 15 and 25) is associated with a high risk of being outside the labour market, living alone and having no secondary or higher education completed (Hakulinen et al., 2019b). A recent Finnish study found that among mental disorders diagnosed at 10–20 years of age, psychoses were associated with the highest risk of being excluded from education, employment or training later at the age of 20–28 years (Ringbom et al., 2022). The employment rates in early-onset schizophrenia and other early-onset psychoses are typically the lowest among all early-onset mental disorders (Hakulinen et al., 2019a). In terms of education, early-onset schizophrenia has one of the worst prognoses among all mental disorders whereas educational levels in other early-onset psychoses are somewhat better (Hakulinen et al., 2019a).

In terms of clinical outcomes, 69% of individuals with EOP are rehospitalised after 25 years of age (Hakulinen et al., 2019b). A Danish register study found that compared to adult-onset schizophrenia, individuals with early-onset schizophrenia have more inpatient days in the first years after diagnosis whereas the long-term outcome in terms of duration and annual rates of inpatient treatment does not differ thereafter (Vernal et al., 2020). All in all, 21–34% of individuals with early-onset psychosis, with varying definitions for psychosis used, are not in psychiatric care after an average follow-up time of 3–12 years in different studies (Amminger et al., 2011; Boeing et al., 2007; Lay et al., 1997; Lay et al., 2000). Based on a Scottish study, 21% of people with early-onset psychosis were not in contact with mental

health services after a mean follow-up of three years (Boeing et al., 2007). An Australian study reported that 34% individuals with an early onset psychotic disorder were not receiving psychiatric treatment after seven years of follow-up (Amminger et al., 2011). Another study group found that in early-onset schizophrenia, 13–15% of people are in inpatient treatment, 58–59% are in outpatient treatment, and 26–28% are without psychiatric care after 7–12 years of follow-up (Lay et al., 1997; Lay et al., 2000).

3.5 Predictors of outcomes

Identifying potential prognostic indicators in schizophrenia and other psychoses is essential from the perspective of patients, families, and clinicians (Whitty et al., 2008). Predictors of outcomes in schizophrenia have been studied for years (Strauss & Carpenter, 1972) and several predictors of long-term outcomes have been found (Emsley et al., 2008). However, the heterogeneous definitions of predictors and different outcome measures in psychoses makes comparison and combination difficult (Menezes et al., 2006).

Many studies have analysed the predictors of outcome in schizophrenia from a general perspective or have included multiple domains of outcomes. A systematic review of longitudinal outcome studies of FEP including different outcome measures found combination of psychosocial therapy and pharmacotherapy, a developing country of origin and lack of epidemiologic representativeness of the sample to be predictors of better outcomes and the use of typical neuroleptic medication to be associated with worse outcomes (Menezes et al., 2006). A study on predictors of 10-year multi-dimensional outcomes of FEP found baseline negative symptoms, poor pre-morbid functioning and longer duration of untreated psychosis to be associated with poor outcomes (White et al., 2009). Predictors of poor outcomes in psychosis also include schizophrenia diagnosis, higher age, and a higher level of various present state symptoms in PANSS subdomains of negative, positive, disorganisation symptoms and emotional distress (de Nijs et al., 2021). Other predictors of poor outcomes in psychosis include single status, male sex, and poor insight (Gómez-de-Regil et al., 2010). In NFBC1966, father's high social class, lower school performance, lack of friends in childhood and earlier illness onset have been found to predict poor outcomes in schizophrenia (Lauronen et al., 2007).

Different predictors for occupational outcomes of psychoses and schizophrenia have been analysed. Efforts to identify factors associated with greater likelihood of employment are important in order to encourage employment in individuals with

schizophrenia (Ang et al., 2020). Affective psychosis diagnosis has been associated with better employment rates compared to first-episode schizophrenia and first-episode psychosis (Ajnakina et al., 2021). An extensive review found higher cognitive functioning, history of successful employment, younger age a lower level of negative symptoms, a higher level of education, social support and skills, and use of rehabilitation services to be predictors of good vocational outcomes in schizophrenia (Tsang et al., 2010). A recent meta-analysis found that living at home at the time of the first contact with mental health services due to psychosis was associated with a lower proportion of employment in the future (Ajnakina et al., 2021). Influencing individuals' lives already before employment, privileged backgrounds are typically associated with favourable patterns in later careers (Ek et al., 2021). However, a recent study highlighted only a small influence of socioeconomic status for the later occupational outcomes in schizophrenia (Hakulinen et al., 2019b). In NFBC1966, being married or cohabiting has been found to predict better occupational status (Miettunen et al., 2007) and strong educational performance has been found to be a predictor of the non-receipt of disability pension (Lauronen et al., 2007).

A systematic review of predictors of outcome in early-onset psychoses found that the most replicated predictors of worse functional, clinical, and cognitive outcomes were premorbid difficulties and symptom severity at baseline and longer duration of untreated psychosis (Diaz-Caneja et al., 2015). Another review found female sex to be linked with better long-term functional and occupational outcomes in early-onset schizophrenia (Clemmensen et al., 2012). Some studies have found non-schizophrenia diagnosis to be associated with better occupational or educational functioning (Diaz-Caneja et al., 2015) and with better long-term functional and occupational outcomes (Clemmensen et al., 2012) in early-onset psychoses, but these associations are inconsistent.

Compared to men, women generally have better outcomes in psychotic disorders (Grossman et al., 2016; Seeman, 2019). Meta-analyses and systematic reviews focusing on the effect of gender on duration of untreated psychosis (Cascio et al., 2012), response to antipsychotic drugs (Leucht et al., 2022) and cognitive functioning in psychoses (Leger & Neill, 2016) have been conducted. However, no meta-analyses focusing on gender differences in occupational outcomes of psychoses exist. In terms of occupational outcomes, varying results on the effect of gender have been presented. Some studies have reported better occupational outcomes for women (Thorup et al., 2014) whereas some studies have reported better employment rates for men (Novick et al., 2016). Overall, there is no

consensus in gender differences in employment levels among individuals with psychoses (Seeman, 2019).

3.5.1 Age of illness onset

Age of illness onset is one of the most studied predictors of outcomes in psychosis research. Age at illness onset plays a crucial role, being a predictor of long-term outcomes in psychoses, with earlier age of onset usually associating with poorer outcomes and later onset age associating with many good outcomes (Clemmensen et al., 2012; Diaz-Caneja et al., 2015; Immonen et al., 2017; Miettunen et al., 2019). A meta-analysis found younger onset age to be associated with more negative symptoms, more relapses, poorer social or occupational capacity and poorer global outcome (Immonen et al., 2017). Meta-analyses have also found association between younger onset age and more hospitalisations (Ajnakina et al., 2020; Immonen et al., 2017). Younger onset age has been associated with higher suicide risk and treatment resistance in some studies (Suvisaari et al., 2018). The relationship between younger onset age of psychosis and worse employment outcomes in schizophrenia is not clear (Immonen et al., 2017; Tsang et al., 2010), though some studies have reported a significant association between them. In early-onset psychoses, younger age of illness onset has in some studies been associated with poorer occupational, social, and educational functioning and worse quality of psychiatric care (Diaz-Caneja et al., 2015).

3.6 Research gap

Occupational and other outcomes in psychotic disorders are typically the worst among all psychiatric disorders. However, longitudinal data on these outcomes and their predictors over follow-up periods spanning decades is scarce.

Younger age at illness onset in schizophrenia is typically linked with poorer outcomes (Clemmensen et al., 2012; Immonen et al., 2017). However, associations between earlier onset age and later outcomes in EOP are inconsistent (Diaz-Caneja et al., 2015). Some recent studies have suggested more optimistic views of outcomes in early-onset psychoses than previously thought (Vernal et al., 2020; Xu et al., 2020). Much is still unclear regarding the detailed investigation of socioeconomic outcomes such as disability pensions, family status, and education in early-onset schizophrenia (Vernal et al., 2020).

Studies on the effect of age of illness onset on very long-term outcomes in EOP and as compared to other mental health disorders are missing. Many studies have analysed the effects of onset age on later outcomes as a continuous variable whereas studies adapting categorical classification of onset age are rare. The associations between younger onset age and later outcomes among the subgroup of people with early-onset psychoses are unclear (Vernal et al., 2020). By observing the effect of onset age within early-onset psychosis and as compared to other mental disorders it would be possible to clarify differences in socioeconomic and clinical outcomes between different forms of the disorders.

Studies on employment and occupational outcomes in psychotic disorders tend to cover only part of working life or to be cross-sectional, not longitudinal. Studies on longer-term patterns of occupational functioning in schizophrenia are limited, with none focusing specifically on employment (Chan et al., 2020). Very few studies have explored population-level patterning and career development during the working life course and until middle age in relation to psychotic disorders. Further studies with a longer follow-up should be conducted to learn how people with schizophrenia adapt to working life and develop their careers (Carmona et al., 2017).

Only one previous study (Chan et al., 2020) has analysed the longitudinal employment patterns of people with psychoses. The study, which utilised 10-year employment trajectories of individuals with first-episode schizophrenia in Hong Kong, found a long-term benefit of early intervention services on the employment rate of individuals with schizophrenia-spectrum disorders (Chan et al., 2020). They found a significantly greater proportion of individuals in the good employment cluster among those who had received an early intervention service (68%) than among those who had received only standard care (52%) (Chan et al., 2020). However, the study was not observational, utilised a relatively broad definition of employment, and did not take gender differences into account. More studies are needed to estimate the risks among individuals with schizophrenia and other psychoses of experiencing unfavourable employment trajectories characterised by poorer labour market attachment.

Gender differences in the work-family life courses of general population samples have been reported, career breaks and part-time working being more usual among women (McMunn et al., 2015). Women also tend to cut their working hours more often than men when having offspring (Connolly & Gregory, 2008). Due to gender inequalities leading to unequal impact on men's and women's occupational trajectories, gendered de-standardization of these trajectories has received support

(Widmer & Ritschard, 2009). Because men and women work in different occupations with varying employment opportunities and because gender may be associated with psychoses' outcomes (Seeman, 2019), it would be important to study employment trajectories of psychotic disorders stratified by gender.

Despite numerous studies reporting rates of (un)employment and disability pension in psychotic disorders, it has not been studied whether is it possible to return to the labour market from a disability pension. In the general return to work (RTW) literature, a return to existing part- or full-time employment contract during a follow-up time of a few to several weeks has typically been studied (Desiron et al., 2011). However, the lack of comprehensiveness and consistency of measuring return to work is one of the factors compromising advancement in the field of RTW research (Wasiak et al., 2007). Longitudinal studies on RTW in schizophrenia and other psychoses are scarce and originate from Finland (Joensuu et al., 2019; Virtanen M et al., 2011). These studies (Joensuu et al., 2019; Virtanen M et al., 2011) have showed lower employment rates after long-term work disability in psychoses compared to other psychiatric disorders (Table 4).

Joensuu et al. (2019) found that 40% of people with psychotic disorder were employed at any time, and 13% at the end of the 5.6 years of follow-up after a new onset of a fixed-term disability pension. Virtanen M et al. (2011) studied RTW after a long-term sick leave (≥ 90 days) or the receipt of a disability pension. They found that 46% of people with schizophrenia, schizotypal, and delusional disorders returned to work after a disability episode and 41% of them within a year. Higher SES predicted return to work in schizophrenia and related disorders (Virtanen M et al., 2011).

While we know that occupational functioning among people with psychotic disorders is low and disability pensions are common, we know little about the persons on disability pension who are able return to the labour market and its potential predictors. This information, however, would be useful for patients, clinicians, and society.

Table 4. Studies on returning to work after long-term work disability including individuals with psychosis.

Study	Purpose	Sample size; diagnoses; state of illness	Diagnostic system, follow-up time; time of data collection	Definition for work disability or disability pension	Definition for return to work	Main results	Predictors for return to work
Joensuu et al., 2019	To study employment status and its predictors after long-term psychiatric work disability	n=400 with F20-F29 psychotic disorder; various stages of illness	ICD-10, a mean follow-up of 5.6 years; 2005–2013	Only new-onset fixed-term disability pensions included in the study.	Employment outcomes (employed any time and at the end of the follow-up after a fixed-term disability pension) obtained from the records of earnings from the FCP.	40% of people with psychotic disorder were employed at any time during follow-up and 13% were employed at the end of the follow-up.	Predictors for employment after psychotic disorder were not separately studied.
Virtanen M et al., 2011	To examine the associations between SEP and psychiatric work disability	n=283 with F20-F29 psychotic disorder; various stages of illness	ICD-10, a mean follow-up of 6.3 years; 1997–2005	Work disability defined as the first long-term sickness absence (≥ 90 days) or any type of disability pension.	Return to work defined as the date when disability compensation ended using the register kept by the FCP.	46% of people with psychotic disorder returned to work after a disability episode and 41% of them within a year.	Higher SEP predicted return to work in psychotic disorders.

Abbreviation: SEP, socioeconomic position; ICD, International Statistical Classification of Diseases and Related Health Problems; FCP, the Finnish Centre for Pensions

4 Aims of the study

Utilising the Northern Finland Birth Cohorts 1966 and 1986, the overall aim of this thesis was to study occupational and other outcomes of schizophrenia and other psychoses. Another aim was to find out factors that predict outcomes in psychoses by utilising data from several national registers and questionnaires at different ages. The purpose was to study these outcomes longitudinally in terms of three different stages of illness including onset (original study I), over the course of working life (original study II), and after years of disability pension (original study III). The more detailed aims of the original studies were:

I To clarify the effect of illness onset age on later socioeconomic and clinical prognosis in early-onset psychosis with onset before 18 or 23 years of age as compared to other psychiatric illnesses. The follow-up lasted until the age of 33 years.

II To investigate whether the patterning of gender-specific employment trajectories differed between individuals with schizophrenia, other psychoses, and no psychosis between ages 16 and 45.

III To study the proportion and characteristics of persons with schizophrenia and other psychoses who return to the labour market after receiving a disability pension. The follow-up lasted until the age of 50 years.

5 Materials and methods

The study was based on the Northern Finland Birth Cohorts, which are unselected, general population-based samples. The Northern Finland Birth Cohort Studies include two birth cohorts of women and offspring collected at 20-year intervals. The NFBC is a longitudinal end epidemiological research programme aiming to promote health and well-being of the population. The cohort data have been collected prospectively from gestation up to this date. The original data have been supplemented by data collected with postal questionnaires at different ages and national register data. The original studies I and III of this thesis were fully register-based, whereas original study II also included questionnaire data. More details about the NFBC Studies are available on the cohort website (www.oulu.fi/nfbc) (The Northern Finland Birth Cohort, 2021).

5.1 Northern Finland Birth Cohort 1986 (I)

5.1.1 Sample (I)

The original study I was based on the Northern Finland Birth Cohort 1986 (NFBC1986). The NFBC1986 is based on 9,432 live-born children with an expected date of birth between 1 July 1985 and 30 June 1986 in the provinces of Lapland and Oulu (University of Oulu, 1986). The NFBC1986 was originally founded to study mortality and morbidity during childhood with the special purpose of preventing physical and mental handicap (Järvelin et al., 1997). More details about the psychiatric research in this birth cohort are available in the systematic review of the NFBC1986 (Miettunen et al., 2019).

5.2 Northern Finland Birth Cohort 1966 (II, III)

5.2.1 Sample (II, III)

The original studies II and III were based on the Northern Finland Birth Cohort 1966 (NFBC1966) which includes data from 12,058 live-born children with an expected date of birth in 1966 in the provinces of Oulu and Lapland (University of Oulu, 1966). Cohort members have been monitored since each mother's mid-pregnancy (Nordström et al., 2022). The cohort was originally founded to study

risk factors for low birth weight, pre-term birth and perinatal deaths (Rantakallio, 1988). More details about the schizophrenia studies in this birth cohort are available in the systematic review of the NFBC1966 (Jääskeläinen et al., 2015).

5.2.2 Questionnaire data (II)

The original study II included questionnaire data from the 14-, 31-, and 46-year follow-up studies of the NFBC1966. Only little information from the 14- (father's socioeconomic status used as variable) and 31-year (complementary data on the self-reported lifetime-psychosis diagnosis) surveys was used, whereas more data from the 46-year follow-up was used. More details about the 14- and 31-year follow-up studies are available in the recently published NFBC1966 cohort profile article (Nordström et al., 2022).

The 46-year follow-up survey was conducted in 2012, targeting 10,331 cohort members alive and living in Finland with known addresses (86% of the original sample). The questionnaires could be answered either online or on paper. Altogether 6,613 persons (64% of the target population) responded to the questionnaire on work, economy, and resources, including annual employment roles between ages 16 and 45, and allowed their data to be used in the research at the time of the original study II. For more information on the 46-year follow-up study of the NFBC1966, please see Nordström et al. (2022).

5.3 Detection of individuals with psychosis (I, II, III)

Data from various national registers (in original studies II, III) and also from the follow-up questionnaires of the NFBC1966 (in original study II) were used to detect individuals with a history of psychosis and individuals in the comparison groups (Table 5). In the original study I, data on psychiatric diagnoses of NFBC1986 members was available until the end of 2019, but the focus was on diagnoses before the age of 23 years. In the original study II, information on psychiatric diagnoses of NFBC1966 members was collected until the 46-year follow-up in 2012. In the original study III, data until the end of 2016 (50-year follow-up) were used in the detection phase.

In all original studies, the Care Register for Health Care (CRHC) was utilised to find diagnoses of all psychiatric and general hospitalisations and visits to specialised outpatient care (Finnish Institute for Health and Welfare, 2021). Data on psychiatric and general hospitalisations were available from 1994 in original

study I and from 1974 onwards in original studies II and III. Information on visits to specialised outpatient care was available from 1998 onwards in all original studies. The Register of Primary Health Care Visits (2011–) was utilised to find outpatient diagnoses in primary care (Finnish Institute for Health and Welfare, 2021).

The data on lifetime psychiatric diagnoses were complemented by register data from the Social Insurance Institution of Finland (SII, 2021). These data included diagnoses for receiving sickness allowances, diagnoses for received special drug reimbursement, and diagnoses for receiving disability pensions. Data on diagnoses for receiving sickness allowances were available for 1974–1999 for the NFBC1966 (II, III). Information on diagnoses for received special drug reimbursement were available for 2001–2005 for the NFBC1986 (I) and for 1974–2005 for the NFBC1966 (II, III). Data on diagnoses for receiving disability pensions were available for 1981–1998 for the NFBC1966 (II, III). The data were also complemented with data on diagnoses for receiving disability pensions from the Finnish Centre for Pensions (FCP, 2021). These data were available since 1994 for the NFBC1986 (I) and since 1974 for the NFBC1966 (II, III). More details on the registers used for detection of diagnoses are available in the article of cumulative incidences of psychotic disorders in the NFBC1986 and NFBC1966 (Filatova et al., 2017).

In the original study II, the register information was complemented by self-reported lifetime-psychosis diagnosis, obtained by asking the participants in the 31- and 46-year follow-up survey of the NFBC1966 whether they had ever been diagnosed by a physician as having psychosis. This yielded an additional 18 cases, presumably with mild psychoses, as no hospitalisations were recorded in the national register data. These individuals were assumed to have psychoses other than schizophrenia.

Table 5. Sources used to detect study samples in different original studies.

Data collection source	Inclusion in original studies
Register data	
Finnish Institute for Health and Welfare	
Care Register for Health Care: diagnoses of hospital inpatient registers	I, II, III
Care Register for Health Care: diagnoses of visits to specialised outpatient care	I, II, III
Register of primary health care visits: outpatient diagnoses in primary care	I, II, III
Social Insurance Institution of Finland	
diagnoses on receiving sickness allowances	II, III
diagnoses for receiving special drug reimbursement	I, II, III
diagnoses for receiving disability pensions	II, III
Finnish Centre for Pensions	
diagnoses for receiving disability pensions	I, II, III
Questionnaire data	
self-reported lifetime psychosis diagnosis of the NFBC1966 31- and 46-year follow-up surveys	II

Abbreviation: NFBC, Northern Finland Birth Cohort

5.3.1 Diagnostic classification

International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) together with its previous versions (ICD-8 and ICD-9) were the diagnostic classification systems used in this study. The diagnostic categories for psychiatric disorders according to the ICD and used in the original studies are presented in Table 6. In original studies II and III, schizophrenia (SZ) and other psychoses (OP) were studied separately. In original study I, schizophrenia and other psychoses categories were combined as psychosis (P) category. Schizotypal disorder and psychoses due to organic causes or psychoactive substance use were excluded from the psychosis category of the study.

Table 6. Diagnostic categories used in the study (Modified from study III © Springer Nature).

Diagnostic category	ICD-8 (1968–86)	ICD-9 (1987–95)	ICD-10 (1996–)
Psychosis (P)			
Schizophrenia (SZ)	2950–2959, 297	2950–2959, 297	F20, F22, F24, F25
Other psychosis (OP)	2960–2969, 2980–2983, 2988, 2989, 299	2961E, 2962E, 2963E, 2964E, 2967, 2988, 2989	F23, F28, F29, F30.2, F31.2, F31.5, F32.3, F33.3
Non-psychotic psychiatric disorder (NP)	295–308, 310–315[1], 7092, (excluding those with diagnosis of P described above)	295–309, 311–316, 317–319[1] (excluding those with diagnosis of P described above)	F10.1, F10.2, F11.1, F11.2, F12.1, F12.2, F13.1, F13.2, F14.1, F14.2, F15.1, F15.2, F16.1, F16.2, F17.1, F17.2, F18.1, F18.2, F19.1, F19.2, and F20–F69, F70–F79[1], F80–F99 (excluding those with diagnosis of P described above)

[1]Only included in original study III

A hierarchical system was used when setting the main life-time diagnosis for each subject and to deal with individuals with numerous diagnoses or movement between diagnostic categories over the follow-up. In this system, the life-time diagnosis was the disorder that had the highest position in the hierarchy based on severity. The hierarchical order of diagnoses, from the most severe to the least severe disorder, was the following: schizophrenia, other psychosis, and other study groups (i.e., non-psychotic (and non-organic) psychiatric disorders (NP) in original studies I and III, and no psychosis in original study II). In original study I, SZ and OP categories were combined as psychosis (P) category and ranked hierarchically more severe than the non-psychotic disorder diagnosis. In original study I, the hierarchical system was used also within the psychosis category when analysing the occurrence of specific psychosis diagnoses. The hierarchical order within the psychosis category, from the most severe to the least severe disorder, was as follows: schizophrenia, schizophrenia spectrum disorder, affective psychosis, and non-affective psychosis.

Based on the hierarchy, individuals diagnosed with SZ might also have had a diagnosis of some other psychotic disorder before or after schizophrenia, but their life-time diagnosis was interpreted as SZ. Individuals without psychotic disorders

should not have had a diagnosis of psychosis in any of the registers or follow-up questionnaires used because such a diagnosis would have transferred them to the respective psychosis diagnostic group. This hierarchy has been used in previous studies of NFBC1966 (Nietola et al., 2018).

Classification of the study groups (original study I)

In original study I, early-onset psychosis (EOP) was defined as a psychosis diagnosis before the age of 23 years. This definition was based on the earlier literature (Clemmensen et al., 2012; Hakulinen et al., 2019b) together with the upper age limit of adolescent psychiatry services in Finland. For comparison purposes, the same age limit was utilised for non-psychotic psychiatric disorders. To explore the effect of the age of illness onset on later outcomes in EOP, both diagnostic categories were divided into two classes including those with illness onset age before 18 years and those with illness onset between 18–22 years.

The NFBC1986 cohort members diagnosed with psychosis (schizophrenia or other psychosis) or any non-psychotic psychiatric disorder before the age of 23 were searched from the registers. People with a diagnosis of organic psychosis (e.g., ICD-10 codes F00-F09) or mental disability (e.g., ICD-10 codes F70-F79) were excluded from the sample. Persons who had deceased by the end of 2019 were excluded (information on the date of death from the Population Register) (Digital and Population Data Services Agency, 2021). After the exclusions, 102 subjects with psychosis and 872 with a non-psychotic psychiatric disorder (NP) were identified, and these individuals formed the sample of the original study I (n = 974).

In the NFBC1986, 41 individuals had a psychosis diagnosis before the age of 18 years (P<18y) and 61 individuals at the age of 18–22 years (P18-22y). 495 individuals had non-psychotic psychiatric disorders diagnosed before the age of 18 years (NP<18y) and 377 individuals at the age of 18–22 years (NP18-22y).

Classification of the study groups (original study II)

The focus of the original study II was on NFBC1966 cohort members with SZ or OP. For comparison purposes, the remaining cohort members (i.e., healthy controls (HC), meaning individuals with no psychotic disorder in the national registers or questionnaires), were used as controls.

Based on the hierarchical diagnoses and the available employment trajectory information (described in detail later), 62 subjects with SZ, 87 subjects with OP,

and 6,464 subjects with HC were identified, comprising the final sample (n = 6,613) of the original study II.

Classification of the study groups (original study III)

In the original study III, NFBC1966 cohort members with a diagnosis of any mental disorder until 2016 were searched from the registers. Persons with psychiatric disorder were included, excluding those with a diagnosis of organic disorder (e.g., ICD-10 codes F00-F09). In this study, the focus was on individuals with schizophrenia and other psychoses. For comparison purposes, data concerning those with non-psychotic psychiatric disorder was extracted.

Based on the hierarchy, 229 (1.9% of the original NFBC1966 sample) subjects with SZ, 205 (1.7%) with OP, and 1,877 (15.6%) with NP were detected from the registers, and these subjects formed the sample of the original study III.

5.4 Measures of outcome

Data on measures of outcome in the study were retrieved from different national registers (original studies I, II, III) and also from the follow-up questionnaires of NFBC1966 (original study II) (Table 7). The data used, as detailed below, are based on the information at the end of the follow-up of each study unless otherwise marked.

Table 7. Outcome measures and data sources used in different studies.

Outcome measure (data collection source)	Inclusion in original studies
Disability pension data (Social Insurance Institution of Finland)	III
Disability pension data (Finnish Centre for Pensions)	I, III
Educational level, socioeconomic status (Statistics Finland)	I
Marital status, information on children (Digital and Population Data Services Agency)	I
Substance use disorders, psychiatric hospitalisations (Finnish Institute for Health and Welfare)	I
Employment trajectory data (46-year follow-up survey of NFBC1966)	II

Abbreviation: NFBC, Northern Finland Birth Cohort

5.4.1 Original study I

In original study I, subjects of the sample were followed until 31.12.2019 i.e., the age of 33 years. Socioeconomic and clinical outcomes were measured.

Socioeconomic outcomes

The register of Statistics Finland (until 2019) was used to gather data on the highest attained educational level (Statistics Finland, 2020). The different educational level categories used in the study were based on the International Standard Classification of Education (ISCED, 2011). Basic or below basic level category included early childhood education, primary education, and lower secondary education. Secondary level category included upper secondary education and post-secondary non-tertiary education. Tertiary level category included short-cycle tertiary education, Bachelor or equivalent level, Master or equivalent level, and doctoral or equivalent level.

The register of the Digital and Population Data Services Agency (until June 2016) was used to collect information on having children (yes vs no) and marital status (married or registered partnership vs single, divorced, separated, or widowed) (Digital and Population Data Services Agency, 2021).

The register of Statistics Finland (until 2018) was used to gain information on the socioeconomic status at the age of 32 years (Statistics Finland, 2021). SES included the following categories: farmers, entrepreneurs, upper white collar, lower white collar, manual workers, students, pensioners, and others, mostly unemployed. SES was presented by dividing the variable into the following three categories: 1) white collar i.e., lower to upper white collar, 2) pensioners, and 3) others, i.e., farmers, entrepreneurs, manual workers, students, and others.

Information on disability pension was gathered from the registers of Statistics Finland (SES) until 2018 and the Finnish Centre for Pensions (FCP, 2021) until 2019. Disability pensions (fixed-term or permanent) were examined as occurring at the end of the follow-up and at any time point during the follow-up.

Clinical outcomes

The information on the number of psychiatric hospital episodes and days (until 2019) was gained from the CRHC since the beginning of the cohort in 1986. The numbers of psychiatric hospital episodes and days due to psychosis and due to any

psychiatric disorder were analysed. The cumulative number of psychiatric hospital days was counted only for individuals with at least one psychiatric hospital episode.

The information on substance use disorders (i.e., mental and behavioural disorders due to the use of alcohol, cannabinoids, or any other substances) until 2019 were gathered using the CRHC and outpatient registers.

5.4.2 Original study II

Employment trajectory data was created to measure the outcomes in the original study II. To enable latent class analysis of longitudinal employment trajectories, information from a working-life-focused life history calendar (LHC) from the 46-year follow-up survey of NFBC1966 was utilised (Ek et al., 2021). For each year from 1982 to 2011 (ages 16 to 45), the survey participants marked whether they had occupied one or more of the following employment-related roles: 1) student, 2) full-time employed, 3) part-time employed, 4) self-employed, 5) unemployed, 6) on parental leave, or 7) on sabbatical leave or otherwise not working. The LHC survey responses have previously been proven reliable by comparing them with national register employment data (Ek et al., 2021). The sample size of the latent class analysis conducted in the original study II differed from the earlier employment trajectory analysis of the NFBC1966 (Ek et al., 2021). The difference between studies was due to the updated LHC survey data included and participants' most recent consents to use their personal data utilised in the present study.

5.4.3 Original study III

In the Finnish disability pension system, the Social Insurance Institution of Finland pays compensation in the form of a sickness allowance for sick leave lasting up to one year (Finnish Centre for Pensions, 2020). When the ability to work is reduced (due to injury, illness, or handicap) for a longer period, entitlement to a fixed-term (i.e., temporary) or permanent disability pension is considered. A fixed-term disability pension is paid for a fixed period, and it can be granted to individuals who have lost their ability to work temporarily but whose illness, injury or handicap is expected to improve through rehabilitation and treatment. A permanent disability pension is granted directly if return to work (RTW) seems unlikely, or after the fixed-term disability pension when treatment and rehabilitation have not led to sufficient results in terms of ability to work. Multiple periods of fixed-term disability pensions are possible if an individual's return to work remains likely. In

the Finnish earnings-based work pension system, both types of disability pensions can also be granted as part-time benefits (i.e., partial permanent or partial fixed-term disability pension). When the person reaches statutory retirement age, the disability pension will turn into an old-age pension.

In the original study III, registers of the SII and the FCP were used to collect data on disability pensions until the end of the year 2016. Disability pension status was first assessed based on data of the earnings-related pension system from the register of FCP for the years 2005–2016. Rates, reasons (i.e., if the reason for the discontinuation was death) and dates for the start and discontinuation of the disability pension were analysed. Then, data from the FCP were combined to register data from the SII, with data available for whole NFBC1966 until the end of the year 2000. For part of the sample, also register data of the SII for the period 2000–2016 were available.

The register of the FCP includes disability pension information of individuals who have had salaried work contracts/work periods. The register of the SII includes data on disability pensions of individuals who have not been working or who have not earned a salary to the extent of accumulating sufficient pension in their life, including individuals who have received a disability pension at a relatively young age. Information on sickness allowance was based on the register of the SII which includes all sickness allowance periods that exceed a waiting period that normally consists of 10 working days (The Social Insurance Institution of Finland, 2014).

The objective of the original study III was to clarify how many individuals could return to the labour market after receiving fixed-term or permanent disability pensions. Subjects of the sample were followed until the end of the follow-up (31st Dec 2016), or until death or moving abroad (information from the Population Register) (Digital and Population Data Services Agency, 2021). Consecutive disability pension periods were combined into one, and in the case of multiple periods at different times, only the latest one was considered when studying the discontinuation of the disability pension. Authors TM and EJ of the original study III clarified the dates and reasons for the discontinuation, and in the case of unclear information, a solution was found by consensus with authors MH, LAM, and JM. The focus of the study was on psychiatric reasons for disability pension and therefore, the proportions of disability pensions due to somatic reasons were only presented but excluded from further analyses.

An individual was considered as having returned to the labour market if disability pension was coded as terminated, no new disability pension was granted, and the person was alive at the time of discontinuation. Because the register data

was available until the end of the follow-up (31st Dec 2016) disability pension was defined as having ended if it was terminated at least four months before that date.

5.5 Characteristics of sample and predictors of outcome

Numerous variables were used to describe the characteristics of the sample and to analyse the predictors of outcomes in each study. This data included information retrieved from various national registers (original studies I, II, III) and from the follow-up questionnaires of NFBC1966 (original study II). The following variables (from the following sources) were used.

Gender (in original studies I, II, III) was retrieved from national population register. Information from the 14-year NFBC1966 follow-up was used to describe the socioeconomic situation of respondents' childhood family (II). This was based on fathers' socioeconomic status, which was classified as either white collar or not. Information on the study subjects' average school grades (II, III) when leaving basic education at the age of 16 years was gathered from the 1982 register of the Finnish national application system for upper secondary education. In Finland, school grades vary between 4 and 10 (Keskinen et al., 2018), as regulated by the National Board of Education (Isohanni et al., 1999). Data from the follow-up questionnaire of the NFBC1966 by the age of 46 (II) and from the register of Statistics Finland (until 2015) (III) were used to gather information on the highest attained educational level (Statistics Finland, 2020). The educational level categories were based on the ISCED (International Standard Classification of Education, 2011) and categorised similarly as when measuring the socioeconomic outcomes in the original study I.

Survey responses on marital status at age 46 were used and dichotomised as: 1) single, divorced, separated, or widowed and 2) married, registered partnership or cohabiting (II). In original study III, data on marital status (categorised as married or not married) at the initiation of the latest disability pension period and having children (yes or no) by the end of the follow-up were gathered from the register of the Digital and Population Data Services Agency (until June 2016) (Digital and Population Data Services Agency, 2021). Because marital status 'cohabiting' is not registered, it could not be distinguished from the data. Socioeconomic status (II) in 2012 at the age of 46 years was collected from the register of Statistics Finland (Statistics Finland, 2021). SES included the same categories as when measuring the socioeconomic outcomes in the original study I, but these categories were not divided into subcategories in the original study II.

Illness onset, meaning the age at the first occurrence of psychosis (I, II, III) for P, SZ, and OP groups and non-psychotic psychiatric disorder (I, III) for NP, was defined by using the SII registers of reimbursable medicines, the register of the FCP, the CRHC, and Finnish outpatient registers. History of different psychotic and non-psychotic psychiatric disorder diagnoses (I) was gathered using register information from the same national registers. The occurrence of specific psychosis diagnoses (schizophrenia, schizophrenia spectrum disorder, affective psychosis, and other non-affective psychosis) was based on the hierarchical system. The occurrence of specific non-psychotic psychiatric disorder diagnoses was studied. These diagnoses included depression, bipolar disorder, anxiety disorder, alcohol use disorders, cannabis use disorders, and any other substance use disorders.

Data on substance use disorders (III) (until 2015) were obtained from the CRHC and outpatient registers and data on the proportion of time spent in psychiatric hospitalisation after illness onset (III) (until 2015) from the CRHC from the beginning of the cohort in 1966. The proportion of time spent in psychiatric hospitalisation after illness onset was calculated for the period between individual's first psychotic episode and the initiation of the latest disability pension period (Haapea et al., 2007). Information on age at the initiation (III) and length of the latest disability pension periods (III) (in years) until the end of 2016 were gleaned using the registers of the SII and the FCP.

5.6 Missing data and excluded subjects

Since data were acquired from multiple registers and through questionnaires, there were varying amounts of missing data in the study.

In the original study I, data on socioeconomic status were missing from 2–5% of persons in different diagnostic groups. Information on disability pension at the end of the follow-up was missing from 2–5% and information on disability pension at some point during the follow-up from 0–3% of people.

In the original study II, when analysing the sample's characteristics, data on educational level were missing from 3–12% of people in different diagnostic categories; data on father's SES from 13–21%; data on marital status from 0–5%; data on socioeconomic status from 0–3%; data on average school grades from 0–2%, and data on illness onset age from 0–26%. Regarding the employment trajectories, data on father's SES were missing from 13–33% of people; data on average school grades from 0–5%, and data on illness onset age from 0–36%. The

proportions of missing data in attrition and weighted analyses are not presented as part of the thesis but can be found in the original publication II.

In the original study III, data on the age at illness onset was missing from 0–3% and information on comorbid substance use disorder from 0–5% of individuals in different diagnostic groups. In the study groups, one individual with SZ, 5 with OP, and 9 with NP had deceased and did not receive a disability pension, and these individuals were thus excluded from the sample. All individuals who had moved abroad (2 with SZ, 2 with OP, and 24 with NP) were excluded since there was no information available on their pension status.

5.7 Statistical analyses

The appropriate statistical methods were utilised in the study based on the respective variables used. The results are presented as p-values and odds ratios (ORs) with 95% confidence intervals (CIs). P-values < 0.05 indicated statistical significance and all statistical tests were two-tailed. The statistical analyses were conducted using IBM SPSS Statistics, versions 25–28. Latent class analysis in the original study II was conducted using Mplus, version 8.

5.7.1 Original study I

The total rates of psychosis and non-psychotic psychiatric disorder diagnoses from the NFBC1986 sample before age 18 years and between ages 18–22 were calculated and presented by gender.

The background variables were presented for the four (P<18y, P18-22y, NP<18y, and NP18-22y) study groups. The background characteristics were presented by using cross-tabulation (categorical variables) with the chi-square test (or Fisher's exact test when appropriate) or median (Md) with interquartile range (IQR) (continuous variables).

Cross-tabulation and the chi-square test (or Fisher's exact test when appropriate) or Md with IQR and Mann-Whitney Test were utilised to evaluate outcomes between the four study groups.

In the sensitivity analyses, all analyses were reconducted by excluding persons with psychosis or non-psychotic disorder diagnosis < 13 years old from the P<18y and NP<18y groups and comparing the same variables between the new groups (psychosis at the age of 13–18 years (P13-18y), P18-22y, non-psychotic psychiatric disorder at the age of 13-18 years (NP13-18y), and NP18-22y) by using cross-

tabulation and the chi-square test (or Fisher's exact test when appropriate) or median with IQR and Mann-Whitney Test.

5.7.2 Original study II

Latent class analysis to identify employment trajectories

Latent class analysis was performed to identify employment trajectories for combined role statuses at ages 16–45. Seven annual employment-related roles from the life history calendar were used to identify these trajectories. Because gendered trajectories were expected based on the earlier literature (McMunn et al., 2015), the analyses were conducted separately by gender. In the latent class analysis, the probability of occupying a specific status varies between zero and one. The full information maximum likelihood method was used as estimation method, and the link between latent categorical and observed dichotomous variables was logit.

To determine the number of latent classes, varying statistical methods were applied. These methods included the adjusted Bayesian information criteria (aBIC), Lo–Mendell–Rubin likelihood ratio test (LMR-LRT) (Nylund et al., 2007), average latent class posterior probabilities (AvePP) and entropy values that evaluated the discrimination among the latent classes. The AvePPs were calculated for the persons with the highest posterior probability of being assigned to certain latent classes (Nagin, 2005). A value over 0.90 of the average diagonal value in the classes in which persons showed the highest posterior probability described a clear class solution. Entropy values were calculated using the average latent class probabilities, with values varying between zero and one. A high entropy value indicated a high discriminant solution. Finally, to define the number of latent classes, the generalisability of the solution and the clarity of the classes were evaluated by considering the classes' descriptive characteristics in addition to the statistical criteria.

Characteristics of sample and trajectories

The background variables in the different diagnostic categories (SZ, OP, HC) were presented separately by gender using cross-tabulation (categorical variables) and medians with IQR (continuous variables). Characteristics of women and men in the

resulting employment trajectories (see below) were evaluated using cross-tabulation (categorical variables) and median with IQR (continuous variables).

Histories of psychoses and employment trajectories

The numbers of persons with SZ or OP in different employment trajectories were compared to the corresponding numbers of HC.

Both women and men with histories of psychosis were expected to cluster into the least favourable employment trajectories (later termed as floundering trajectories). For that reason, the distribution of pre-employment factors and illness onset ages in relation to belonging to a floundering employee trajectory versus other trajectories were compared. The differences in such characteristics were presented using cross-tabulation (categorical variables) and medians with IQR (continuous variables).

Finally, logistic regression was used to assess the risk of experiencing the least favourable (floundering) employment trajectory in relation to a diagnosis of SZ or OP by using HC as a reference category. Logistic regression was first conducted unadjusted. Then, it was adjusted separately for father's SES at 14 years, average school grades at 16 years, educational level, marital status, and SES at 46 years, and finally, by fully adjusting for all these variables together.

Attrition and weighted analyses

To take into consideration the evident selected participation in relation to a history of psychosis in the 46-year follow-up survey and the formation of employment trajectories, the participants' work situations, educational levels and onset age of psychosis were compared to those of non-participants using the register data. To observe the effect of attrition on the results based on this comparison, all analyses were reconducted by using inverse probability weighting as a sensitivity analysis. The probability of belonging to the study group was analysed by logistic regression using the same variables used in the attrition analysis, i.e., work situation, educational level, and age at the illness onset (for psychoses only), as weights. The details of the attrition and weighted analyses are not presented as part of the thesis but can be found in the original publication II.

5.7.3 Original study III

The background variables in different diagnostic categories (SZ, OP, NP) were presented for individuals who had a disability pension for a psychiatric reason and individuals who did not have it by using cross-tabulation (categorical variables), median with IQR, and mean with standard deviation (SD) (both for continuous variables).

Cross-tabulation and the chi-square test were used to study the characteristics of the disability pension separately in different diagnostic groups.

Logistic regression was used to investigate the association of selected variables with returning to the labour market (instead of having disability pension still running).

6 Ethical consideration and personal involvement

6.1 Ethical considerations

The Ethics Committee of Northern Ostrobothnia Hospital District has accepted the study design of the Northern Finland Birth Cohorts and keeps them under review. All procedures involving human subjects/patients were approved by the relevant Ethics Committee and the relevant keepers of the registers. The study protocol (EETTMK 94/2011) concerning NFBC 1966 was approved on 12th Dec, 2011 and the one (EETTMK 108/2017) for NFBC 1986 on 15th Jan, 2018. Data protection has been scrutinised by the Privacy Protection Agency and in accordance with the principles of the Ministry of Health and Social Affairs. All procedures contributing to this study comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

For solely register-based parts of the study (I, III), individual consents are not required according to Finnish legislation, but permissions have been received from relevant keepers of registers. Informed consent to the use of questionnaire data (II) has been obtained from all cohort members, and during baseline and follow-up studies, written informed consents has been given by each participant. All the cohort members have been assigned an ID number and their identities will not be revealed. Study participants have the right to deny the usage of information concerning themselves at any time.

6.2 Personal involvement

I came into the research group in 2018 to write a licentiate thesis in medicine. I started working with my doctoral thesis and was accepted to the University of Oulu Graduate School in early 2019. I have conducted the thesis at the University of Oulu.

I designed the study together with my supervisors, Adjunct Professor Erika Jääskeläinen, Professor Jouko Miettunen, and Marianne Haapea, PhD, and also with Professor Leena Ala-Mursula (in studies II and III) from the very beginning. I did not participate in the data collection for the NFBC1966 or the NFBC1986 study due to the longitudinal and register-based design of the follow-up studies.

However, I created new data by editing the register data of the FCP together with Adjunct Professor Erika Jääskeläinen in the original study III.

I have written the thesis by myself, and my contribution has been central in all three original publications included in this thesis. I conducted the literature search with supervision from Adjunct Professor Erika Jääskeläinen, Professor Jouko Miettunen in the original studies I, II and III and also from Professor Leena Ala-Mursula in the original studies II and III. The statistical analyses of the study were conducted with the help of statisticians Marianne Haapea, PhD, Tanja Nordström, PhD, Anni-Emilia Alakokkare, MSc, Hanna Huovinen, MSc, and Veera Säynäjäkangas, BSc. However, I have also conducted analyses fully by myself in original studies I and II. I have been working as the first and corresponding author of all these original publications. I have interpreted the study results, written the first and final drafts of the manuscripts and coordinated submission, revision, and resubmissions for the original publications. I have critically revised the manuscripts for the original publications together with my co-authors.

7 Results

7.1 Effect of onset age on the long-term outcome of early-onset psychoses (I)

7.1.1 Characteristics of the sample

In the NFBC1986 sample, 0.1% of men and 0.3% of women had psychosis onset before the age of 18 years (Table 8). Corresponding numbers for psychosis diagnosis between 18–22 years of age were 0.4% for men and 0.2% for women. The total numbers of psychosis onset before age of 23 years were 0.5% for men and 0.6% for women.

Among NFBC1986 members, 2.6% of both men and women had NP onset before the age of 18 years. Corresponding numbers for NP diagnosis between 18–22 years were 1.8% for men and 2.2% for women. The total numbers for NP diagnoses before the age of 23 years were 4.5% for men and 4.8% for women. The number of men (24%) was smaller among P<18y than in other groups (45–62%) (Table 8).

Among individuals with P<18y, 27% had schizophrenia or schizophrenia spectrum disorder, 27% had affective psychosis, and 46% had other non-affective psychosis. Among those with P18-22y, 15% had schizophrenia or schizophrenia spectrum disorder, 26% had affective psychosis, and 59% had other non-affective psychosis (Table 8). Most of the individuals in NP groups had anxiety disorder (prevalence 18–50%) or depression (28–45%).

The median age at psychosis onset was 16 years for those with P<18y and 21 years for P18-22y. The median age at illness onset was 14 in the NP<18y group and 20 years in the NP18-22y group.

By the end of the follow-up, only a few psychosis diagnoses had converted into more severe psychosis diagnoses in the hierarchy. Conversion of the psychosis diagnoses is presented in detail in the manuscript of original publication I.

Table 8. Characteristics of the sample.

Variable	Psychosis <18 years (n=41)	Psychosis 18–22 years (n=61)	Non-psychotic psychiatric disorder <18 years (n=495)	Non-psychotic psychiatric disorder 18–22 years (n=377)
Gender, n (%)				
Man	10 (24.4)	38 (62.3)	249 (50.3)	171 (45.4)
Woman	31 (75.6)	23 (37.7)	246 (49.7)	206 (54.6)
Hierarchical psychosis diagnosis, n (%)[1]				
Schizophrenia	7 (17.1)	8 (13.1)		
Schizophrenia spectrum disorder	4 (9.8)	1 (1.6)		
Affective psychosis	11 (26.8)	16 (26.2)		
Other non-affective psychosis	19 (46.3)	36 (59.0)		
Non-psychotic psychiatric disorder diagnosis, n (%)[1]				
Depression	18 (43.9)	24 (39.3)	137 (27.7)	171 (45.3)
Bipolar disorder	4 (9.8)	4 (6.6)	3 (0.6)	11 (2.9)
Anxiety disorder	11 (26.8)	20 (32.8)	89 (18.0)	188 (49.9)
Alcohol use disorder	3 (7.3)	13 (21.3)	42 (8.5)	48 (12.7)
Cannabis use disorder	0 (0.0)	1 (1.6)	2 (0.4)	6 (1.6)
Other substance use disorder	1 (2.4)	7 (11.5)	8 (1.6)	22 (5.8)
Age of illness onset, psychosis, Md (IQR)	15.9 (14.7–17.0)	20.6 (19.6–21.4)		
Age of illness onset, non-psychotic psychiatric disorder, Md (IQR)	15.1 (13.7–16.0)	19.8 (18.1–21.0)	14.2 (9.0–16.0)	20.3 (19.3–21.6)
Psychosis diagnosis at the end of the follow-up, n (%)				
Schizophrenia	9 (22.0)	19 (31.1)	6 (24.0)	6 (21.4)
Schizophrenia spectrum disorder	5 (12.2)	3 (4.9)	4 (16.0)	4 (14.3)
Affective psychosis	11 (26.8)	13 (21.3)	2 (8.0)	9 (32.1)
Other non-affective psychosis	16 (39.0)	26 (42.6)	13 (52.0)	9 (32.1)

P-values for gender (P<18y vs. P18-22y; P<18y vs. NP<18y; P18-22y vs. NP18-22y; NP<18y vs. NP18-22y): <0.001; 0.001; 0.014; 0.148, for hierarchical psychosis diagnosis (P<18y vs. P18-22y): 0.238[2], for psychosis diagnosis at the end of the follow-up (P<18y vs. P18-22y; P<18y vs. NP<18y; P18-22y vs. NP18-22y; NP<18y vs. NP18-22y): 0.448[2]; 0.312[2]; 0.249[2]; 0.167[2]

[1]During the time leading to belonging to the respective study group, [2]P-value presented by Fisher's exact test

Abbreviation: P<18y, psychosis with onset before 18 years of age; P18-22y, psychosis with onset between 18–22 years of age; NP<18y, non-psychotic psychiatric disorder with onset before 18 years of age; NP18-22y, non-psychotic psychiatric disorder with onset between 18–22 years of age; Md, Median; IQR, interquartile range

7.1.2 Socioeconomic outcomes

Secondary education was the most common educational level in all study groups (51–58%) (Table 9). Tertiary education level was attained by 13% of persons with P18-22y and by 23–28% of people in other groups. The difference in educational level between P18-22y and NP18-22y groups was statistically significant (Table 9).

Marital status was married or registered partnership for 5% of individuals in the P18-22y group and 26–34% for those in other groups ($p < 0.001$). Individuals with P18-22y had significantly less often children (21%) compared to those in other groups (41–48%).

The individuals in all groups were most commonly (43–60%) farmers, manual workers, entrepreneurs, students, or others. Among those with psychoses, 37–46% had been on a disability pension at some point whereas the corresponding numbers for those with NP were 12–14% ($p < 0.001$). At the end of the follow-up, the rates of disability pensions were 28–34% for psychosis groups and 7–8% for NP groups ($p < 0.001$). Onset age did not influence the proportion of disability pensions within either psychoses or non-psychotic psychiatric disorders.

Table 9. Socioeconomic outcomes during the follow-up.

Variable	Psychosis <18 years (n=41)	Psychosis 18–22 years (n=61)	Non-psychotic psychiatric disorder <18 years (n=495)	Non-psychotic psychiatric disorder 18–22 years (n=377)	P<18y vs. P18-22y, p-value	P<18y vs. NP<18y, p-value	P18-22y vs. NP18-22y, p-value	NP<18y vs. NP18-22y, p-value
Educational level, n (%)[1]					0.338	0.658	0.008	0.209
Basic or below basic	10 (24.4)	18 (29.5)	95 (19.2)	60 (15.9)				
Secondary	21 (51.2)	35 (57.4)	286 (57.8)	213 (56.5)				
Tertiary	10 (24.4)	8 (13.1)	114 (23.0)	104 (27.6)				
Marital status, n (%)[2]					<0.001	0.223	<0.001	0.479
Married/registered partnership	14 (34.1)	3 (4.9)	126 (25.5)	104 (27.6)				
Single/divorced/separated/widowed	27 (65.9)	58 (95.1)	369 (74.5)	273 (72.4)				
Having children, n (%)[2]					0.029	0.570	<0.001	0.568
No	24 (58.5)	48 (78.7)	267 (53.9)	196 (52.0)				
Yes	17 (41.5)	13 (21.3)	228 (46.1)	181 (48.0)				
Socioeconomic status, n (%)[3]					0.309	<0.001	<0.001	0.194
White collar	12 (30.0)	10 (16.9)	156 (32.7)	138 (38.3)				
Farmer/entrepreneur/manual worker/student/other	17 (42.5)	30 (50.8)	285 (59.7)	201 (55.8)				
Pensioner	11 (27.5)	19 (32.2)	36 (7.5)	21 (5.8)				
Disability pension at some point, n (%)	15 (36.6)	27 (45.8)	55 (11.5)	53 (14.4)	0.360	<0.001	<0.001	0.197
Disability pension at the end of the follow-up, n (%)	11 (27.5)	20 (33.9)	40 (8.4)	26 (7.2)	0.501	<0.001[4]	<0.001	0.536

[1]At 2019, [2]At June 2016, [3]At 2018, [4]P-value presented by Fisher's exact test

Abbreviation: P<18y, psychosis with onset before 18 years of age; P18-22y, psychosis with onset between 18–22 years of age; NP<18y, non-psychotic psychiatric disorder with onset before 18 years of age; NP18-22y, non-psychotic psychiatric disorder with onset between 18–22 years of age

7.1.3 Clinical outcomes

In the P<18y group, 22% and in the P18-22y group, 41% of individuals had no psychiatric hospital episodes due to psychosis by the age of 33 years (Table 10). In the P<18y group, 34% and in the P18-22y group, 30% had three or more hospital episodes due to psychosis. The difference in hospitalisations due to psychosis was not statistically significant. Few persons in the NP groups had psychiatric hospital episodes due to psychosis later in the follow-up.

Individuals in the NP<18y group had more psychiatric hospitalisations compared to those with NP18-22y ($p < 0.001$). In the NP<18y group, 37% had no psychiatric hospital episodes due to any psychiatric disorder while 23% had three or more hospital episodes. In the NP18-22y group, 53% had no psychiatric hospital episodes due to any psychiatric disorder while 13% had three or more hospital episodes. Most persons in the psychosis groups also had psychiatric hospital episodes due to non-psychotic reasons.

Among individuals with one or more hospital episodes due to any psychiatric reason, the P<18y group had statistically significantly more hospital days compared to the P18-22y group, as did NP<18y compared to NP18-22y.

The number of alcohol use disorders was significantly higher (31%) among persons with P18-22y compared to persons in other groups (12–18%). The numbers of disorders due to the use of cannabinoids were 1–5% in all groups. The numbers of disorders due to the use of any other substances were 8–16% in all groups. Individuals with NP<18y had statistically significantly less use of other substances than those with NP18-22y.

Table 10. Clinical outcomes during the follow-up.

Variable	Psychosis <18 years (n=41)	Psychosis 18–22 years (n=61)	Non-psychotic psychiatric disorder <18 years (n=495)	Non-psychotic psychiatric disorder 18–22 years (n=377)	P<18y vs. P18-22y, p-value	P<18y vs. NP<18y, p-value	P18-22y vs. NP18-22y, p-value	NP<18y vs. NP18-22y, p-value
Number of psychiatric hospital episodes, psychosis, n (%)[1]					0.188	<0.001	<0.001	0.059
0	9 (22.0)	25 (41.0)	482 (97.4)	356 (94.4)				
1	13 (31.7)	11 (18.0)	3 (0.6)	10 (2.7)				
2	5 (12.2)	7 (11.5)	3 (0.6)	5 (1.3)				
3 or more	14 (34.1)	18 (29.5)	7 (1.4)	6 (1.6)				
Hospital days, psychosis, Md (IQR)[2]	161.5 (35–294)	100.5 (34–184.5)	131 (72–306)	29 (10–107)	0.246	0.888	0.094	0.172
Number of psychiatric hospital episodes, any psychiatric, n (%)[1]					0.588[3]	<0.001	<0.001	<0.001
0	4 (9.8)	11 (18.0)	183 (37.0)	199 (52.8)				
1	7 (17.1)	11 (18.0)	150 (30.3)	100 (26.5)				
2	2 (4.9)	5 (8.2)	49 (9.9)	29 (7.7)				
3 or more	28 (68.3)	34 (55.7)	113 (22.8)	49 (13.0)				
Hospital days, any psychiatric, Md (IQR)[2]	224 (98–411)	90 (22–196)	24 (5–56.5)	8 (3–32)	0.002	<0.001	<0.001	<0.001
Substance use disorders during the follow-up, n (%)								

Variable	Psychosis <18 years (n=41)	Psychosis 18–22 years (n=61)	Non-psychotic psychiatric disorder <18 years (n=495)	Non-psychotic psychiatric disorder 18–22 years (n=377)	P<18y vs. P18-22y, p-value	P<18y vs. NP<18y, p-value	P18-22y vs. NP18-22y, p-value	NP<18y vs. NP18-22y, p-value
Any substance use disorder, n (%)	7 (17.1)	23 (37.7)	103 (20.8)	89 (23.6)	0.025	0.569	0.019	0.323
Alcohol use disorder, n (%)	5 (12.2)	19 (31.1)	87 (17.6)	65 (17.2)	0.027	0.380	0.010	0.897
Cannabis use disorder, n (%)	2 (4.9)	3 (4.9)	7 (1.4)	12 (3.2)	1.000[3]	0.146[3]	0.450[3]	0.076
Other substance use disorder, n (%)	5 (12.2)	10 (16.4)	40 (8.1)	46 (12.2)	0.557	0.374[3]	0.363	0.043

[1]Until 2019, [2]Number of psychiatric hospital days counted only for those with one or more hospital episodes until 2019, [3]P-value presented by Fisher's exact test

Abbreviation: P<18y, psychosis with onset before 18 years of age; P18-22y, psychosis with onset between 18–22 years of age; NP<18y, non-psychotic psychiatric disorder with onset before 18 years of age; NP18-22y, non-psychotic psychiatric disorder with onset between 18–22 years of age; Md, Median; IQR, interquartile range

7.1.4 Sensitivity analysis

In the sensitivity analyses, individuals with childhood psychosis or non-psychotic psychiatric disorder (i.e., diagnosis before age 13 years) were excluded. After the exclusions, the new sample sizes were n = 37 for P13-18y and n = 294 for NP13-18y, and n = 769 for the total sample.

The results of the sensitivity analyses were mostly similar to the results of the main analyses. The differences in the number of disorders due to the use of any other substances between the NP groups and in psychiatric hospital episodes due to any psychiatric disorder between the NP groups lost statistical significance in the sensitivity analyses. The results of the sensitivity analyses are not presented as part of the thesis but can be found in the manuscript of the original publication I.

7.2 Employment trajectories in schizophrenia and other psychoses (II)

7.2.1 Identification of employment trajectories

When identifying employment trajectories, the LMR-LRT suggested a three-class model for both genders. The log-likelihood and aBIC continued to decrease for both men and women from a one-class solution to a six-class solution. Entropy remained high (over 0.95) for a five-class solution, as did the AvePPs. Fit indices for the selection of the number of latent classes in yearly employment statuses are not presented as part of thesis but are presented in detail in original study II. Summing up the statistical measures and both genders' characteristics in the five trajectories (presented in detail in original study II) together with the solution in the previous study (Ek et al., 2021), a five-class solution was considered to best fit the data for both men and women. This solution offered meaningful profiles for the identified employment trajectories with small differences by gender.

The annual (from 1982 to 2011, approximately ages 16 to 45) probabilities of each employment-related role status in each employment trajectory were calculated along with the total estimated proportion of membership for each trajectory (latent class; Figures 1 and 2). The employment trajectories were termed similarly to the previous study in the NFBC1966 (Ek et al., 2021), as follows: 1) traditional full-

time employees, 2) highly educated employees, 3) self-employed, 4) delayed full-time employees, and 5) floundering employees.

Certain characteristics for each employment trajectory were found with minor differences between genders. Men's and women's traditional full-time employee trajectories were characterised by elevated probabilities of short education before moving forward to full-time employment. The trajectories of highly educated employees were characterised by approximately ten years of education before progressing to full-time employment. Persons in self-employed trajectories had high probabilities of having spent a few years in post-compulsory education and then some years in full-time employment before moving on to self-employment in early adulthood. Persons in delayed full-time employees' trajectories were likely to have spent time in part-time work, unemployment, or parental leave during their early years in working life before entering full-time employment in their late 30s. For persons in floundering employees' trajectories, part-time work and unemployment were usual throughout the 30-year follow-up; in turn, full-time employment remained rare. In terms of education, in the floundering employees' trajectories, the men were less educated compared to the women.

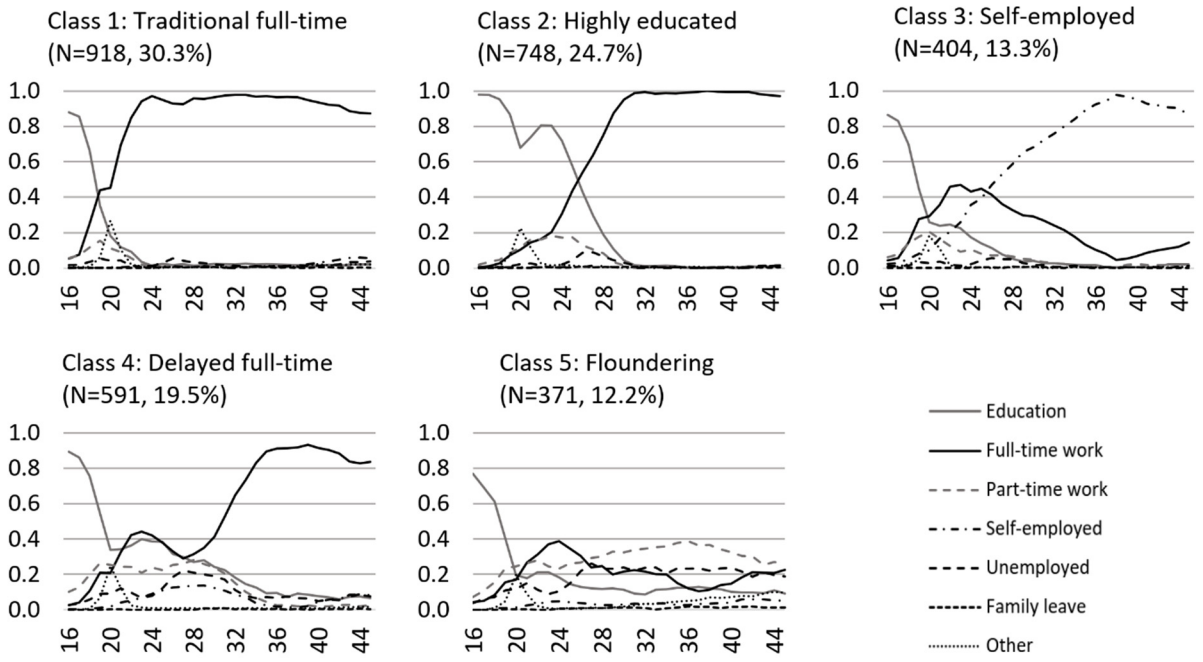

Fig. 1. Five employment trajectories (probabilities of each employment role from 1982 to 2011, ages 16 to 45) found for men (Modified from study II © Authors [CC BY 4.0 license]).

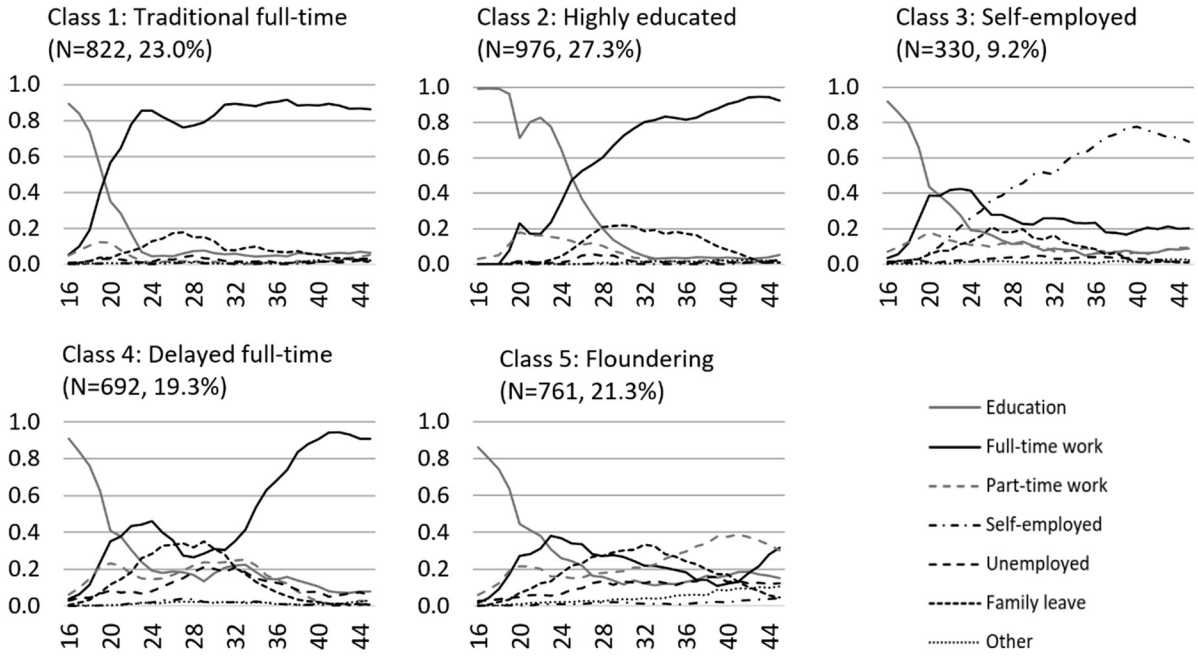

Fig. 2. Five employment trajectories (probabilities of each employment role from 1982 to 2011, ages 16 to 45) found for women (Modified from study II © Authors [CC BY 4.0 license]).

7.2.2 Characteristics of the sample

The proportion of men was similar (46–48%) in the analysed groups (SZ, OP, HC). The persons with SZ (50% of men, 79% of women) and OP (33% of men and women) were often on disability pension. Secondary education was the most common educational level among individuals in the SZ group (75% of men, 87% of women), the OP group (57% of men, 67% of women) and the HC group (68% of men, 64% of women) (Table 11). In the SZ group, 14% of men and 10% of women, in the OP group, 24% of men and 26% of women, and in the HC group, 23% of men and 32% of women had attained tertiary education level. The median age of the first occurrence of psychosis onset was 29 years for men and 31 years for women with SZ, and 38 years for both men and women with OP (Table 11).

Table 11. Characteristics of the sample (Original study II) (n = 6,613): n = 6,464 with no psychosis, n = 87 with other psychosis, n = 62 with schizophrenia (Reprinted [modified] from study II © Authors [CC BY 4.0 license]).

Variable	Men			Women		
	No psychosis (n=2,961)	Other psychosis (n=42)	Schizophrenia (n=29)	No psychosis (n=3,503)	Other psychosis (n=45)	Schizophrenia (n=33)
Father's SES at age 14, n (%)						
White collar	821 (33.0)	9 (27.3)	9 (37.5)	895 (30.0)	11 (28.2)	9 (33.3)
Other	1,664 (67.0)	24 (72.7)	15 (62.5)	2,089 (70.0)	28 (71.8)	18 (66.7)
Educational level by age 46, n (%)						
Basic or below basic	251 (8.9)	7 (18.9)	3 (10.7)	153 (4.6)	3 (7.0)	1 (3.2)
Secondary	1,911 (67.8)	21 (56.8)	21 (75.0)	2,105 (63.5)	29 (67.4)	27 (87.1)
Tertiary	655 (23.3)	9 (24.3)	4 (14.3)	1,057 (31.9)	11 (25.6)	3 (9.7)
Marital status at age 46, n (%)						
Married/registered partnership/cohabiting	2,283 (79.1)	17 (42.5)	8 (27.6)	2,688 (77.9)	23 (51.1)	11 (34.4)
Single/divorced/separated/widowed	602 (20.9)	23 (57.5)	21 (72.4)	762 (22.1)	22 (48.9)	21 (65.6)
Socioeconomic status at age 46, n (%)						
Farmer	92 (3.1)	2 (4.8)	1 (3.6)	51 (1.5)	1 (2.2)	0 (0.0)
Entrepreneur	322 (10.9)	1 (2.4)	0 (0.0)	213 (6.1)	1 (2.2)	0 (0.0)
Upper white collar	679 (23.0)	4 (9.5)	1 (3.6)	801 (22.9)	3 (6.7)	1 (3.0)
Lower white collar	608 (20.6)	4 (9.5)	2 (7.1)	1,668 (47.7)	10 (22.2)	1 (3.0)
Manual worker	840 (28.4)	4 (9.5)	4 (14.3)	383 (11.0)	2 (4.4)	2 (6.1)
Student	37 (1.3)	0 (0.0)	2 (7.1)	65 (1.9)	1 (2.2)	0 (0.0)
Pensioner	61 (2.1)	14 (33.3)	14 (50.0)	69 (2.0)	15 (33.3)	26 (78.8)
Other	267 (9.0)	10 (23.8)	4 (14.3)	201 (5.8)	9 (20.0)	0 (0.0)
Unknown	47 (1.6)	3 (7.1)	0 (0.0)	43 (1.2)	3 (6.7)	3 (9.1)
Average school grades at age 16, Md (IQR)	7.3 (6.7–8.1)	7.0 (6.4–7.8)	7.4 (6.7–7.9)	8.1 (7.4–8.6)	7.9 (7.3–8.4)	7.7 (6.9–8.3)

Variable	Men			Women		
	No psychosis (n=2,961)	Other psychosis (n=42)	Schizophrenia (n=29)	No psychosis (n=3,503)	Other psychosis (n=45)	Schizophrenia (n=33)
Age at onset of psychosis, Md (IQR)		38.2 (31.1–42.0)	29.0 (24.0–38.4)		37.6 (33.3–42.9)	31.4 (25.7–34.2)

Abbreviation: SES, socioeconomic status; Md, median; IQR, interquartile range

7.2.3 Employment trajectories in relation to psychoses

Most often, the persons with SZ (79% of men, 73% of women) or OP (52% of men, 51% of women) had floundering trajectories (Table 12). Among individuals in the HC group, only 11% of men and 20% of women presented with floundering trajectories. Among those in the HC group, men were most often (31%) in a traditional employee trajectory, whereas women were most likely to have a highly educated trajectory (28%). Please see Figure 3 for gendered percentages of individuals with SZ, OP and HC in floundering versus other employment trajectories.

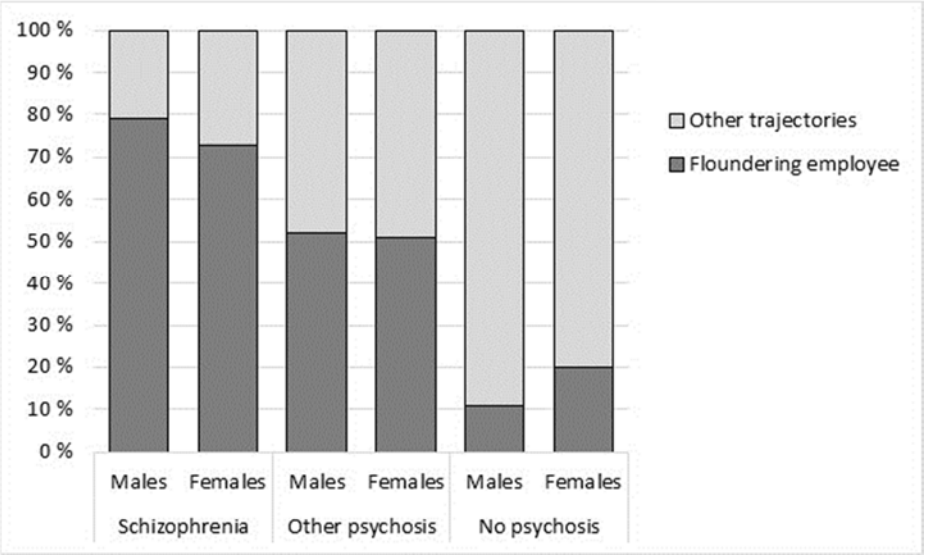

Fig. 3. Gendered percentages of individuals in floundering and other employment trajectories between ages 16 to 45.

Table 12. Distribution of employment trajectories between ages 16 to 45 in relation to a registered history of psychosis until age 46 (Reprinted [modified] from study II © Authors [CC BY 4.0 license]).

Variable	Men						Women					
	No psychosis (n=2,961)		Other psychosis (n=42)		Schizophrenia (n=29)		No psychosis (n=3,503)		Other psychosis (n=45)		Schizophrenia (n=33)	
	n	%	n	%	n	%	n	%	n	%	n	%
Employment trajectories												
Traditional employees	911	30.8	4	9.5	3	10.3	813	23.2	4	8.9	5	15.2
Highly educated employees	744	25.1	3	7.1	1	3.4	969	27.7	5	11.1	2	6.1
Self-employed	400	13.5	3	7.1	1	3.4	323	9.2	5	11.1	2	6.1
Delayed full-time employees	580	19.6	10	28.3	1	3.4	684	19.5	8	17.8	0	0.0
Floundering employees	326	11.0	22	52.4	23	79.3	714	20.4	23	51.1	24	72.7

Compared with the HC category, a schizophrenia diagnosis was associated with an elevated risk of having a floundering employee category (OR 32.88 for men, and 9.91 for women). OP diagnoses were also associated with a high risk of having a floundering employee trajectory (OR 7.41 for men and 3.88 for women). After fully adjusting for father's SES at 14 years, average school grades at 16 years, marital status, educational level and SES at 46 years, the risk of belonging to the floundering employee trajectory remained high in the SZ (OR 21.69 for men and 6.48 for women) and OP (OR 3.87 for men and 3.35 for women) groups. All odds ratios remained statistically significant also when adjusted separately for the same variables (Table 13).

The pre-employment characteristics and illness onset age of men and women in floundering versus other employment trajectories are presented in Tables 14 and 15. In the SZ group, the median ages of psychosis onset were 27 years for men and 30 years for women in the floundering trajectories and 41 for men and 32 for women in other trajectories. Among individuals in the OP group, the corresponding onset ages were 35 for men and women in the floundering trajectories and 40 for men and 41 for women in the other trajectories.

Table 13. Odds ratios of belonging to the floundering employee trajectory vs any other trajectories between ages 16 to 45 in relation to a history of psychosis by age 46 (Reprinted [modified] from study II © Authors [CC BY 4.0 license]).

Variable	Men			Women		
	OR (95% CI)			OR (95% CI)		
	No psychosis	Other psychosis	Schizophrenia	No psychosis	Other psychosis	Schizophrenia
Unadjusted	1	7.41 (3.96–13.85)	32.88 (13.28–81.39)	1	3.88 (2.11–7.14)	9.91 (4.56–21.50)
Adjusted						
Father's SES at 14y	1	6.33 (3.11–12.88)	36.63 (13.38–100.25)	1	4.16 (2.17–7.98)	13.81 (5.55–34.37)
Average school grades at 16y	1	7.48 (3.93–14.24)	38.59 (15.30–97.30)	1	4.05 (2.17–7.53)	9.64 (4.43–21.00)
Educational level	1	6.19 (3.09–12.42)	33.20 (13.18–83.60)	1	3.81 (2.03–7.15)	8.79 (4.00–19.34)
Marital status	1	4.67 (2.38–9.16)	21.36 (8.37–54.48)	1	3.67 (1.99–6.78)	8.63 (3.93–18.91)
SES at 46y	1	5.98 (3.05–11.70)	25.44 (10.02–64.63)	1	3.00 (1.57–5.76)	5.13 (2.30–11.45)
Fully adjusted[1]	1	3.87 (1.70–8.82)	21.69 (7.43–63.34)	1	3.35 (1.63–6.90)	6.48 (2.50–16.80)

[1]Adjusted for father's SES at 14y, average school grades at 16y, educational level, marital status, SES at 46y

Abbreviation: SES, socioeconomic status; OR, odds ratio, CI, confidence interval

Table 14. Pre-employment characteristics and illness onset age among men in floundering versus all other employment trajectories (Reprinted [modified] from study II © Authors [CC BY 4.0 license]).

Variable	No psychosis (n=2,961)		Other psychosis (n=42)		Schizophrenia (n=29)	
	Floundering (n=326)	Other (n=2,635)	Floundering (n=22)	Other (n=20)	Floundering (n=23)	Other (n=6)
Father's SES (14 y), n (%)						
White collar	57 (21.0)	764 (34.5)	3 (18.8)	6 (35.3)	8 (42.1)	1 (20.0)
Other	214 (79.0)	1,450 (65.5)	13 (81.3)	11 (64.7)	11 (57.9)	4 (80.0)
Average school grades at age 16, Md (IQR)	6.9 (6.4–7.6)	7.4 (6.8–8.1)	6.8 (6.4–7.2)	7.4 (6.7–8.5)	7.4 (6.6–7.8)	7.4 (7.0–8.0)
Age at onset of psychosis, Md (IQR)			34.6 (31.1–42.0)	39.5 (31.5–42.0)	27.3 (22.8–32.6)	41.4 (38.1–46.2)

Abbreviation: SES, socioeconomic status; Md, median; IQR, interquartile range

Table 15. Pre-employment characteristics and illness onset age among women in floundering versus all other employment trajectories (Reprinted [modified] from study II © Authors [CC BY 4.0 license]).

Variable	No psychosis (n=3,503)		Other psychosis (n=45)		Schizophrenia (n=33)	
	Floundering (n=714)	Other (n=2,789)	Floundering (n=23)	Other (n=22)	Floundering (n=24)	Other (n=9)
Father's SES (14 y), n (%)						
White collar	177 (29.6)	718 (30.1)	6 (30.0)	5 (26.3)	7 (33.3)	2 (33.3)
Other	421 (70.4)	1,668 (69.9)	14 (70.0)	14 (73.7)	14 (66.7)	4 (66.7)
Average school grades at age 16, Md (IQR)	7.8 (7.2–8.5)	8.1 (7.4–8.7)	8.0 (7.7–8.3)	7.7 (7.2–8.4)	8.1 (7.4–8.4)	7.3 (6.7–7.5)
Age at onset of psychosis, Md (IQR)			35.4 (33.1–39.8)	40.7 (37.6–43.4)	30.4 (25.7–34.0)	31.6 (26.5–37.9)

Abbreviation: SES, socioeconomic status; Md, median; IQR, interquartile range

7.2.4 Attrition and weighted analyses

Based on the registered data of the entire NFBC1966, 111/173 (64%) persons with SZ, 87/174 (50%) with OP, and 3,418/9,882 (35%) in the HC group did not participate in the 46-year follow-up and the original study II. Among the cohort members with registered SZ diagnoses, both men ($p = 0.003$) and women ($p = 0.001$) who did not participate in the 46-year survey tended to have lower levels of education compared to the participants (Tables 16 and 17). Non-participating men with SZ diagnoses were less likely to be working than participating men with SZ ($p = 0.028$). Among individuals with OP, there were no statistically significant differences in any of the variables studied regarding participation. Among persons in the HC group, non-participants across genders had lower educational levels ($p < 0.001$ across genders) and were less likely to be working ($p < 0.001$ across genders) compared to the participants.

The results of the weighted analyses were highly similar to the results of the unweighted analyses. The detailed results of the weighted analyses are not presented as part of the thesis but can be found in the original publication II.

Table 16. Attrition analysis among men (Reprinted [modified] from study II © Authors [CC BY 4.0 license]).

Variable	Men								
	No psychosis			Other psychosis			Schizophrenia		
	Participants (n=2,961)	Non-participants (n=2,057)	p-value	Participants (n=42)	Non-participants (n=46)	p-value	Participants (n=29)	Non-participants (n=73)	p-value
Age at onset of psychosis, Md (IQR) (until 2012)				38.2 (31.3–42.0)	36.9 (28.4–40.3)	0.298	29.0 (24.6–38.1)	29.7 (24.8–34.1)	0.642
Educational level, n (%) (until 2015)			<0.001			0.297			0.003
Basic or below basic	222 (7.5)	342 (16.7)		8 (19.0)	9 (19.6)		3 (10.3)	25 (34.2)	
Secondary	1,485 (50.2)	1,131 (55.0)		22 (52.4)	30 (65.2)		17 (58.6)	42 (57.5)	
Tertiary	1,254 (42.4)	584 (28.4)		12 (28,6)	7 (15.2)		9 (31.0)	6 (8.2)	
Work situation, n (%) (2012)			<0.001			0.437			0.028[1]
Working	2,541 (87.4)	1,543 (78.1)		15 (38.5)	14 (30.4)		8 (28.6)	7 (9.7)	
Not working	365 (12.6)	433 (21.9)		24 (61.5)	32 (69.6)		20 (71.4)	65 (90.3)	

[1]P-value presented by Fisher's exact test

Abbreviation: Md, Median; IQR, interquartile range

Table 17. Attrition analysis among women (Reprinted [modified] from study II © Authors [CC BY 4.0 license]).

Variable	Women								
	No psychosis			Other psychosis			Schizophrenia		
	Participants (n=3,503)	Non-participants (n=1,457)	p-value	Participants (n=45)	Non-participants (n=42)	p-value	Participants (n=33)	Non-participants (n=43)	p-value
Age at onset of psychosis, Md (IQR) (until 2012)				37.6 (33.4–42.7)	37.0 (30.4–41.9)	0.253	31.4 (26.5–34.0)	29.3 (21.9–34.8)	0.268
Educational level, n (%) (until 2015)			<0.001			0.092			0.001
Basic or below basic	122 (3.5)	174 (11.9)		5 (11.1)	11 (26.2)		0 (0.0)	14 (32.6)	
Secondary	1,376 (39.3)	678 (46.5)		20 (44.4)	20 (47.6)		22 (66.6)	16 (37.2)	
Tertiary	2,005 (57.2)	605 (41.5)		20 (44.4)	11 (26.2)		11 (33.3)	13 (30.2)	
Work situation, n (%) (2012)			<0.001			0.321			0.268
Working	3,116 (90.3)	1,111 (79.4)		17 (40.5)	12 (30.0)		4 (13.3)	10 (23.8)	
Not working	335 (9.7)	289 (20.6)		25 (59.5)	28 (70.0)		26 (86.7)	32 (76.2)	

Abbreviation: Md, Median; IQR, interquartile range

7.3 Return to the labour market in schizophrenia and other psychoses (III)

7.3.1 Rates and reasons for disability pensions

In the NFBC1966 sample, 177/229 (77%) of persons with schizophrenia received disability pension for any reason (including somatic disorders) before 2016. Among individuals with other psychosis, 102/205 (50%), and of the non-psychotic group, 277/1,877 (15%) individuals had been on a disability pension.

170 (74%) individuals with SZ, 91 (44%) with OP, and 211 (11%) with NP had been on a disability pension for a psychiatric reason (Table 18), and only these individuals were included in further analyses.

7.3.2 Characteristics of the sample

Among individuals with SZ, 58% were men. Corresponding percentages of men were 45% for OP and 49% for NP. In all groups, the most common educational level was secondary education (51–52%). The proportions of basic or below basic educational level varied between 26–29%, and of tertiary level, between 19–22%. The mean age at the illness onset of psychosis was 29.8 years for SZ and 36.9 years for OP, the mean age of illness onset being 34.3 years for NP (Table 18).

Table 18. Characteristics of the sample (Reprinted [modified] from study III © Springer Nature).

Variable	Schizophrenia			Other psychosis			Non-psychotic psychiatric disorder		
	Disability pension for psychiatric reason (n=170)	No disability pension (n=53)	Total (n=223)	Disability pension for psychiatric reason (n=91)	No disability pension (n=109)	Total (n=200)	Disability pension for psychiatric reason (n=211)	No disability pension (n=1,604)	Total (n=1,815)
Gender, n (%)									
Man	99 (58.2)	31 (58.5)	130 (58.3)	41 (45.1)	59 (54.1)	100 (50.0)	104 (49.3)	761 (47.4)	865 (47.7)
Woman	71 (41.8)	22 (41.5)	93 (41.7)	50 (54.9)	50 (45.9)	100 (50.0)	107 (50.7)	843 (52.6)	950 (52.3)
Educational level[1], n (%)									
Basic or below basic	49 (28.8)	5 (9.4)	54 (24.2)	24 (26.4)	17 (15.6)	41 (20.5)	57 (27.0)	226 (14.1)	283 (15.6)
Secondary	89 (52.4)	25 (47.2)	114 (51.1)	47 (51.6)	59 (54.1)	106 (53.0)	107 (50.7)	807 (50.3)	914 (50.4)
Tertiary	32 (18.8)	23 (43.4)	55 (24.7)	20 (22.0)	33 (30.3)	53 (26.5)	47 (22.3)	571 (35.6)	618 (34.0)
Having children[2], n (%)									
No	123 (72.4)	26 (49.1)	149 (66.8)	38 (41.8)	36 (33.0)	74 (37.0)	85 (40.3)	331 (20.6)	416 (22.9)
Yes	47 (27.6)	27 (50.9)	74 (33.2)	53 (58.2)	73 (67.0)	126 (63.0)	126 (59.7)	1,273 (79.4)	1,399 (77.1)
Marital status[2], n (%)									
Not married	125 (73.5)	35 (66.0)	160 (71.7)	38 (41.8)	46 (42.2)	84 (42.0)	90 (42.7)	469 (29.2)	559 (30.8)
Married	20 (11.8)	10 (18.9)	30 (13.5)	22 (24.2)	27 (24.8)	49 (24.5)	62 (29.4)	729 (45.4)	791 (43.6)
Divorced or widowed	25 (14.7)	8 (15.1)	33 (14.8)	31 (34.1)	36 (33.0)	67 (33.5)	59 (28.0)	406 (25.3)	465 (25.6)
Age of illness onset, psychosis (years), Mean (SD)	29.8 (8.6)	32.4 (8.1)	30.4 (8.5)	36.9 (9.4)	36.4 (9.1)	36.7 (9.2)			
Md (IQR)	29.3 (23.1–35.5)	31.5 (26.5–38.0)	30.3 (24.1–36.6)	38.0 (33.6–44.3)	38.2 (28.5–44.2)	38.1 (30.7–44.3)			

Variable	Schizophrenia			Other psychosis			Non-psychotic psychiatric disorder		
	Disability pension for psychiatric reason (n=170)	No disability pension (n=53)	Total (n=223)	Disability pension for psychiatric reason (n=91)	No disability pension (n=109)	Total (n=200)	Disability pension for psychiatric reason (n=211)	No disability pension (n=1,604)	Total (n=1,815)
Age of illness onset, non-psychotic psychiatric disorder (years), Mean (SD)							34.3 (10.3)	38.2 (11.5)	37.7 (11.4)
Md (IQR)							36.5 (28.4–42.1)	42.1 (32.5–47.1)	41.3 (32.1–46.7)

[1]Until 2015, [2]Until June 2016

Abbreviation: SD, standard deviation; Md, median; IQR, interquartile range

The main diagnosis for receiving a disability pension in the SZ group was SZ for 115 (68%) individuals and OP or NP for 55 (32%) individuals. However, the majority of these 55 individuals in the SZ group had a diagnosis of psychotic disorder before receiving the disability pension. This information was based on other registers than those of the FCP and the SII. Among these 55 individuals, 29 (53%) had schizophrenia diagnosis and 14 (25%) had psychosis diagnosis other than schizophrenia in some other register before the initiation of the disability pension. Twelve (22%) individuals had a psychosis diagnosis in the registers only after receiving the disability pension. It is possible that at least some of these persons have had onset of psychosis before the initiation of the disability pension. However, none of these 12 persons were in the group who had returned to the labour market. In the other two groups, due to the unavailability of decimals of diagnoses (F-codes in ICD-10), it was not possible to separate whether the main diagnosis for receiving a disability pension was OP or NP.

Sixty-one percent of individuals with SZ, 90% of those with OP, and 90% of those with NP had only one disability pension period ($p < 0.001$, Table 19). The type of the latest disability pension was permanent full-time disability pension for 77% of individuals with SZ, for 68% of OP, and for 53% of NP. A fixed-term full-time disability pension was granted to 22% of individuals with SZ, 31% of OP, and 39% of NP. Few individuals had a partial fixed-term or partial permanent disability pension (Table 19). The difference in the type of the latest disability pension was statistically significant between SZ, OP and NP ($p < 0.001$).

Table 19. Characteristics of the disability pension (Reprinted [modified] from study III © Springer Nature).

Variable	Schizophrenia (n=170)		Other psychosis (n=91)		Non-psychotic psychiatric disorder (n=211)	
	n	%	n	%	n	%
Number of disability pension periods						
One	103	60.6	82	90.1	189	89.6
Two or more	67	39.4	9	9.9	22	10.4
Type of the disability pension received						
Permanent full-time disability pension	131	77.1	62	68.1	112	53.1
Fixed-term full-time disability pension	37	21.8	28	30.8	82	38.9
Partial permanent or fixed-term disability pension	2	1.2	1	1.1	17	8.1
Disability pension status at the end of the follow-up						
Disability pension ended due to death	19	11.2	7	7.7	12	5.7
Disability pension still running	136	80.0	67	73.6	139	65.9
Disability pension ended and alive (i.e., return to labour market)	15	8.8	17	18.7	60	28.4

7.3.3 Reasons for the discontinuation of the disability pension

Among persons with SZ, the disability pensions of 15 (9%) had ended due to a return to the labour market (Table 19). Corresponding rates for OP and NP were 17 (19%) and 60 (28%), respectively. The disability pensions of 19 (11%) individuals with SZ, 7 (8%) with OP, and 12 (6%) with NP had ended due to death. The difference in the reasons for the discontinuation of the disability pension was statistically significant between SZ, OP and NP ($p < 0.001$).

7.3.4 Return to the labour market

Among persons with SZ, 2/15 had returned to the labour market from a permanent full-time disability pension and 13/15 from a fixed-term full-time disability pension. Corresponding figures were 4/17 and 13/17 in OP, and 2/60 and 51/60 in NP. In NP, 7/60 had returned to the labour market from a partial permanent or fixed-term disability pension.

When analysing only those individuals who had been granted a permanent full-time disability pension, 2/131 (2%) with SZ, 4/62 (6%) with OP, and 2/112 (2%)

with NP were able to return to the labour market. Among individuals receiving a fixed-term full-time disability pension, 13/37 (35%) with SZ, 13/28 (46%) with OP, and 51/82 (62%) with NP were able to return to the labour market.

7.3.5 Predictors for return to the labour market

Predictors for return to the labour market in different groups are presented in Tables 20–22. Among individuals with SZ, individuals who were not married were less likely to return to the labour market compared to married individuals (OR: 0.22; 95% CI 0.06–0.76), and those with higher average school grades (OR: 2.02; 95% CI 1.09–3.75) and later age of onset of psychosis (OR: 1.07; 95% CI 1.02–1.11) were more likely to return to the labour market. Individuals having children were more likely to return to the labour market in OP (OR: 4.81; 95% CI 1.26–18.29) and NP (OR: 1.92; 95% CI 1.02–3.60), but not in SZ.

In all groups, the length of the latest disability pension period was significantly shorter (OR (95% CI) 0.60 (0.45–0.79) for SZ, 0.61 (0.45–0.81) for OP, and 0.61 (0.52–0.72) for NP) in those returning to the labour market compared to those with a disability pension still running. Regarding other predictors studied (i.e., gender, educational level, comorbid substance use disorder, age at the initiation of the latest disability pension period and proportion of time spent in psychiatric hospitalisation), there were no statistically significant differences in any of the groups.

Table 20. Predictors for return to the labour market by the age of 50 years (vs disability pension still running) in schizophrenia (Modified from study III © Springer Nature).

Variable	Schizophrenia			
	Return to labour market (n=15)	Disability pension still running (n=136)	OR (95% CI)	p-value
Gender, n (%)				0.680
Man[1]	9 (60.0)	74 (54.4)	1	
Woman	6 (40.0)	62 (45.6)	0.80 (0.27–2.36)	
Average school grades at the age of 16 years, Mean (SD)	7.8 (0.9)	7.3 (0.9)	2.02 (1.09–3.75)	0.026
Educational level[2], n (%)				0.754
Basic or below basic[1]	4 (26.7)	35 (25.7)	1	
Secondary	7 (46.7)	75 (55.1)	0.82 (0.22–2.97)	
Tertiary	4 (26.7)	26 (19.1)	1.35 (0.31–5.89)	
Having children[3], n (%)				0.218
No[1]	9 (60.0)	102 (75.0)	1	
Yes	6 (40.0)	34 (25.0)	2.00 (0.66–6.03)	
Marital status[3], n (%)				0.049
Married[1]	5 (33.3)	14 (10.3)	1	
Not married	8 (53.3)	111 (81.6)	0.22 (0.06–0.76)	
Divorced or widowed	2 (13.3)	11 (8.1)	0.55 (0.09–3.35)	
Comorbid substance use disorder[2], n (%)				0.113
No[1]	10 (66.7)	113 (83.7)	1	
Yes	5 (33.3)	22 (16.3)	2.57 (0.80–8.25)	
Age of illness onset, psychosis, Md (IQR)	33.3 (30.4–45.7)	29.1 (23.5–35.7)	1.07 (1.02–1.11)	0.005
Age at the initiation of the latest disability pension period, Md (IQR)	35.6 (28.0–41.6)	32.2 (25.5–40.1)	1.04 (0.98–1.11)	0.199
Length of the latest disability pension period (years), Md (IQR)	2.3 (1.1–6.7)	17.6 (10.2–25.0)	0.60 (0.45–0.79)	<0.001
Proportion of time (%) spent in psychiatric hospitalisation after illness onset[3], Md (IQR)	8.2 (12.9–35.1)	7.7 (2.3–18.0)	2.85 (0.64–12.65)	0.168

[1]Reference category, [2]Until 2015, [3]Status at the initiation of the latest disability pension period

Abbreviation: OR, odds ratio; CI, confidence interval; Md, median; SD, standard deviation; IQR, interquartile range

Table 21. Predictors for return to the labour market by the age of 50 years (vs disability pension still running) in other psychoses (Modified from study III © Springer Nature).

Variable	Other psychosis			
	Return to labour market (n=17)	Disability pension still running (n=67)	OR (95% CI)	p-value
Gender, n (%)				0.627
Man[1]	6 (35.3)	28 (41.8)	1	
Woman	11 (64.7)	39 (58.2)	1.32 (0.44–3.98)	
Average school grades at the age of 16 years, Mean (SD)	7.6 (1.0)	7.4 (1.0)	1.19 (0.68–2.07)	0.552
Educational level[2], n (%)				0.297
Basic or below basic[1]	2 (11.8)	21 (31.3)	1	
Secondary	10 (58.8)	32 (47.8)	3.28 (0.65–16.50)	
Tertiary	5 (29.4)	14 (20.9)	3.75 (0.64–22.10)	
Having children[3], n (%)				0.021
No[1]	3 (17.6)	34 (50.7)	1	
Yes	14 (82.4)	33 (49.3)	4.81 (1.26–18.29)	
Marital status[3], n (%)				0.688
Married[1]	6 (35.3)	17 (25.4)	1	
Not married	8 (47.1)	34 (50.7)	0.67 (0.20–2.23)	
Divorced or widowed	3 (17.6)	16 (23.9)	0.53 (0.11–2.49)	
Comorbid substance use disorder[2], n (%)				0.440
No[1]	13 (76.5)	44 (66.7)	1	
Yes	4 (23.5)	22 (33.3)	0.62 (0.18–2.11)	
Age of illness onset, psychosis, Md (IQR)	40.7 (34.7–44.1)	38.4 (33.0–44.5)	1.03 (0.97–1.10)	0.351
Age at the initiation of the latest disability pension period, Md (IQR)	38.7 (34.5–44.9)	39.0 (26.7–43.0)	1.05 (0.98–1.11)	0.150
Length of the latest disability pension period (years), Md (IQR)	1.8 (0.7–6.8)	11.2 (7.1–23.8)	0.61 (0.45–0.81)	<0.001
Proportion of time (%) spent in psychiatric hospitalisation after illness onset[3], Md (IQR)	2.2 (0.2–9.2)	3.8 (0.2–8.4)	4.62 (0.19–114.0)	0.350

[1]Reference category, [2]Until 2015, [3]Status at the initiation of the latest disability pension period

Abbreviation: OR, odds ratio; CI, confidence interval; Md, median; SD, standard deviation; IQR, interquartile range

Table 22. Predictors for return to the labour market by the age of 50 years (vs disability pension still running) in non-psychoses (Modified from study III © Springer Nature).

Variable	Non-psychotic psychiatric disorder			p-value
	Return to labour market (n=60)	Disability pension still running (n=139)	OR (95% CI)	
Gender, n (%)				0.939
Man[1]	29 (48.3)	68 (48.9)	1	
Woman	31 (51.7)	71 (51.1)	1.02 (0.56–1.88)	
Average school grades at the age of 16 years, Mean (SD)	7.2 (0.9)	7.2 (0.9)	1.06 (0.74–1.52)	0.740
Educational level[2], n (%)				0.227
Basic or below basic[1]	12 (20.0)	40 (28.8)	1	
Secondary	30 (50.0)	71 (51.1)	1.41 (0.65–3.05)	
Tertiary	18 (30.0)	28 (20.1)	2.14 (0.89–5.14)	
Having children[3], n (%)				0.044
No[1]	20 (33.3)	68 (48.9)	1	
Yes	40 (66.7)	71 (51.1)	1.92 (1.02–3.60)	
Marital status[3], n (%)				0.082
Married[1]	24 (40.0)	42 (30.2)	1	
Not married	22 (36.7)	75 (54.0)	0.51 (0.26–1.02)	
Divorced or widowed	14 (23.3)	22 (15.8)	1.11 (0.48–2.57)	
Comorbid substance use disorder[2], n (%)				0.150
No[1]	41 (71.9)	109 (81.3)	1	
Yes	16 (28.1)	25 (18.7)	1.70 (0.83–3.51)	
Age of illness onset, non-psychotic psychiatric disorder, Md (IQR)	35.4 (28.6–41.2)	37.9 (29.4–43.0)	0.99 (0.97–1.02)	0.688
Age at the initiation of the latest disability pension period, Md (IQR)	40.8 (36.3–44.8)	42.3 (35.2–45.3)	1.01 (0.97–1.04)	0.708
Length of the latest disability pension period (years), Md (IQR)	1.7 (1.0–3.1)	8.2 (5.3–15.3)	0.61 (0.52–0.72)	<0.001
Proportion of time (%) spent in psychiatric hospitalisation after illness onset[3], Md (IQR)	0.0 (0.0–1.9)	0.0 (0.0–1.4)	10.56 (0.44–254.8)	0.147

[1]Reference category, [2]Until 2015, [3]Status at the initiation of the latest disability pension period
Abbreviation: OR, odds ratio; CI, confidence interval; Md, median; SD, standard deviation; IQR, interquartile range

8 Discussion

8.1 Main findings

A summary of the aims and main findings of the studies is presented in Table 23.

Original study I was the first study to examine the effect of onset age on long-term outcomes of EOP by comparing outcomes among persons with onset before and at 18 years of age and between 18–22 years of age. The study presents a novel finding showing that persons with psychosis before the age of 18 years do not unambiguously have a poorer prognosis compared to those with onset age at 18–22 years. Instead, persons with earlier onset of psychosis (before 18 years) had better long-term socioeconomic outcomes. In relation to clinical outcomes, individuals with psychosis onset age at 18–22 years had more substance use disorders compared to persons with psychosis onset before 18 years, whereas the number of hospitalisations was similar irrespective of illness onset age.

In terms of educational level, having children, marital status, and substance use disorders, individuals with psychosis onset before the age of 18 years had relatively good outcomes which were similar to those with non-psychotic psychiatric disorder diagnosis before 18 years. Persons with EOP had more disability pensions compared to those with other early-onset psychiatric disorders.

Individuals with psychosis onset at the age of 18–22 years had overall worse long-term clinical and socioeconomic outcomes compared to persons with non-psychotic disorder onset at the age of 18–22 years and significantly unfavourable outcomes in terms of having children, marital status, and having substance use disorders in comparison to those with psychosis onset before 18 years of age.

Original study II was the first study to examine the distribution of typical employment trajectories in a general population birth cohort sample until midlife in relation to a lifelong history of SZ and OP. The results of the study show that approximately three-quarters of men and women with SZ and around half of individuals with OP had floundering employment trajectories, characterised by continuously high probabilities of unemployment and part-time work compared to any other trajectory. The risk of having a floundering employee trajectory versus other trajectories in midlife was distinctly elevated for individuals with SZ (33-fold odds for men and 10-fold odds for women) and OP (7-fold odds for men and 4-fold odds for women). These risks remained significant even when adjusted for well-established potential confounders.

Original study III showed that returning to the labour market in schizophrenia (9%) is possible, albeit rare. Returning to the labour market in other psychoses (19%) or non-psychotic psychiatric disorders (28%) tends to be more common. Returning to the labour market is more common after fixed-term than after permanent disability pension in all groups. Among people with SZ, being married, higher onset age of psychosis, and better average school grades predicted returning to the labour market. Having children predicted returning to the labour market among people with OP and NP. A shorter length of the latest disability pension was a predictor of returning to the labour market in all diagnostic groups.

Table 23. Summary of aims and main findings of the studies.

Study	Aim	Study sample	Main findings	Predictors of outcome
I	To study socioeconomic and clinical outcomes of early-onset psychiatric disorders (P, NP) with onset before 18 or at the 18–22 years of age.	Individuals with P<18y (n=41), P-18-22y (n=61), NP<18y (n=495), or NP18-22y (n=377)	Persons with P18-22y had overall worse clinical and socioeconomic outcomes compared to NP18-22y and poorer outcomes in terms of having children, marital status, and having substance use disorders compared to P<18y. Persons with P were more often on disability pensions compared to NP. Persons with P<18y had mainly similar socioeconomic and clinical outcomes compared to NP<18y.	
II	To compare 30-year employment trajectories among individuals with SZ, OP, and HC.	Individuals with SZ (n=62), OP (n=87), or HC (n=6464)	Most individuals with SZ (73–79%) or OP (51–52%) had a floundering employee trajectory. In HC, a traditional employee trajectory was most common in men (31%) and a highly educated trajectory in women (28%).	A history of psychosis was associated with elevated odds ratios for foundering trajectories in both men and women with SZ or OP when compared to HC.
III	To analyse the proportion and characteristics of individuals with SZ, OP or NP who return to the labour market after a disability pension.	Individuals with SZ (n=223), OP (n=200), or NP (n=1815)	9% of persons with SZ, 19% with OP and 28% with NP returned to the labour market.	In SZ, a later onset age of psychosis, being married, and better school performance, and in OP and NP, having children predicted returning to the labour market. A shorter length of the latest disability pension predicted returning to the labour market in all groups.

Abbreviation: P, psychosis; SZ, schizophrenia; OP, other psychosis; NP, non-psychotic psychiatric disorder; HC, healthy controls, i.e., individuals without psychiatric disorder; P<18y, psychosis onset before 18 years of age; P18-22y, psychosis onset at 18–22 years of age; NP<18y, non-psychotic psychiatric disorder onset before 18 years of age; NP18-22y non-psychotic psychiatric disorder onset at 18–22 years of age

8.2 Comparison with previous studies

8.2.1 Onset age and long-term outcomes in early-onset psychoses (I)

In both psychoses and non-psychotic psychiatric disorders, individuals with younger age at illness onset had more psychiatric hospital episodes due to their respective disorder. This may be explained by the longer follow-up time of those with younger onset age of illness. However, the difference in hospital episodes was statistically significant only between the NP groups. Younger age at illness onset has been linked with more hospitalisations in schizophrenia (Immonen et al., 2017). An Israeli study found a linear trend between onset age and hospitalisations in schizophrenia showing increased hospital use for people with earlier onset (Rabinowitz et al., 2016). However, a recent study reported that compared to adult-onset schizophrenia, people with early-onset schizophrenia have more inpatient days during the first years of illness, but long-term rates of inpatient treatment do not differ thereafter (Vernal et al., 2020). A recent meta-analysis reported that 55% of people with FEP were hospitalised during an average follow-up of seven years across different studies (Ajnakina et al., 2020).

The rates of persons without psychiatric hospital episodes due to psychosis in psychosis groups in this study (22–41%) align with the numbers of earlier studies showing that 21–34% of people with EOP are not in any psychiatric care in long-term follow-ups (Amminger et al., 2011; Boeing et al., 2007; Lay et al., 1997; Lay et al., 2000) and a study reporting that 69% of individuals with early-onset schizophrenia are rehospitalised after their 25th birthday (Hakulinen et al., 2019b). People with early-onset schizophrenia who do not need psychiatric outpatient or inpatient treatment after 25 years of age quite naturally have better educational, occupational, and social outcomes compared to individuals with a more chronic course of illness (Hakulinen et al., 2019b). In non-psychotic psychiatric disorders, the difference in the number of psychiatric hospital episodes between the age groups may also be explained by the Finnish legislation allowing wider criteria for involuntary hospital treatment for underaged persons.

The prevalence of substance use disorders in this study was principally higher in psychoses than in non-psychoses. This finding is in line with a previous study showing higher numbers of co-occurring substance use disorders among psychotic disorders than in other psychiatric disorders (Toftdahl et al., 2016). The higher

proportion of substance use disorders among people with later onset age of psychosis may be linked with the worse later outcomes for this age group found in this study. Substance use disorders are an increasing problem among persons with psychiatric disorders, particularly among those with psychotic disorders (Toftdahl et al., 2016). This study excluded psychoses due to substance use when defining the study groups.

Being woman has usually been associated with better outcomes in schizophrenia at the outset of the illness (Seeman, 2019) and with better outcomes of early-onset schizophrenia in some studies (Clemmensen et al., 2012). Thus, a higher number of women in the P<18y group (76%) compared to the P18-22y group (38%) may partly explain the differences in outcomes between the psychosis groups in the current study.

In relation to educational level, individuals with psychosis onset at 18–22 years had somewhat poorer outcome, with the highest number of persons with only basic or below basic level education (30%) and the lowest rate of tertiary education (13%) being achieved. In other groups, 16–24% of persons attained only basic level, and 23–28% achieved tertiary level. These findings align with previous studies reporting poorer educational outcomes for those with early-onset psychoses compared to other early-onset psychiatric disorders (Hakulinen et al., 2019a, Ringbom et al., 2022). However, in the current study, individuals with psychosis diagnosis at 18–22 years had poorer educational outcomes than those with psychosis onset before 18 years, contradicting previous studies of EOP (Diaz-Caneja et al., 2015) and studies comparing EOP to adult-onset psychoses (Vernal et al., 2020). This finding may be partly explained by this study focusing on the cut-off between traditional definitions for EOP and adult-onset psychosis (AOP) instead of comparing these two disorders with their most typical definitions.

The group of individuals with psychosis onset between 18–22 years of age included significantly more persons who were not in a relationship (95%) compared to other groups (66–75%). A recent Chinese study (Xu et al., 2020) found that 21% of individuals with early-onset schizophrenia (< 18 years old) had never been married whereas another study (Remberk et al., 2014) reported that among individuals with EOP, 11% were married and 36% were in a romantic relationship. The findings on the effect of onset age on later marital status in psychoses in this study differ somewhat from earlier studies linking later onset ages with being more often married (Ponnudurai et al., 2006) and better social outcomes (Immonen et al., 2017) in schizophrenia. Moreover, some studies have associated later onset age with better social functioning in early-onset psychoses (Diaz-Caneja et al., 2015).

The definition for the term early-onset psychosis varies across studies. This study included only persons with psychosis onset before 23 years of age, which affects the comparability of the current study with previous studies also including persons with adult-onset psychoses or studies including only persons with onset before 18 years of age.

With respect to offspring, individuals with psychosis onset at 18–22 years significantly more often did not have children (79%) when compared to other groups (52–59%). Some studies have reported an association between earlier onset of psychosis and reduced fecundity (McGrath et al., 1999). In schizophrenia, men usually have reduced fertility compared to women (Bundy et al., 2011). In this study, the unbalanced number of women (76% of persons with P<18y and 38% of those with P18-22y) in psychosis groups may have influenced the findings related to having offspring.

Disability pensions during the follow-up were more frequent among individuals with psychoses (37–46%) compared to those with other psychiatric disorders (12–14%). These results align with the previous studies that have reported early-onset schizophrenia being linked with a higher risk of being unemployed (Hakulinen et al., 2019a; Ringbom et al., 2022) and being outside the labour market (Hakulinen et al., 2019b) compared to other psychiatric disorders. Furthermore, a review of outcomes in EOP reported that better occupational functioning was predicted by older age at illness onset (Diaz-Caneja et al., 2015).

8.2.2 Employment trajectories in psychoses (II)

The results of the original study II align with previous studies which have demonstrated that individuals with schizophrenia are at an elevated risk of being outside the labour market (Hakulinen et al., 2019b). High proportions of people with SZ and OP presenting floundering employment trajectories indicate poor labour market attachment in these disorders (Virtanen P et al., 2011). The study supports previous findings on better occupational outcomes in individuals with OP than in SZ, but worse outcomes among these people than in individuals without psychosis (Hakulinen et al., 2019a; Hakulinen et al., 2020).

The rates of disability pension at age 46 among individuals with SZ (50% in men, 79% in women) and OP (33% in both men and women) in this sample were somewhat lower than the rates among individuals with SZ (80–89%) (Karpov et al., 2017; Perälä et al., 2008) and OP (69%) groups (Perälä et al., 2008) reported in

previous studies. The difference between current and earlier studies could be that individuals who have the most severe psychoses or receive disability pensions are less likely to participate in questionnaires, resulting in selection bias (Haapea et al., 2007). The results of attrition analysis pointed out a high proportion (90%) of non-participating men with SZ who were not working and both men and women participants with SZ (as in the HC group) often having higher educational levels compared to non-participants. Nevertheless, the results of the weighted analyses were similar to those of the unweighted analyses.

In terms of education, my findings of low proportions of people with psychoses in highly educated trajectories align with a recent meta-analysis (Dickson et al., 2020) showing that compared to individuals without SZ, those with SZ are less likely to enter higher education and attain significantly lower general academic achievement scores. Interestingly, when comparing school grades at age 16, both men and women with subsequent floundering trajectories and who became diagnosed with SZ during the follow-up had average school grades at least as high as those of men and women in the other employment trajectories, suggesting that success at school did not automatically lead to favourable employment in later life. It is notable that the age of the first occurrence of psychosis was lower for men and women with SZ than for those with OP. In this sample, people with earlier onset ages of psychosis were more likely to present floundering employee trajectories.

The median age at the first onset of psychosis in the study was high. This characteristic could be at least partly explained by the higher onset age among participants than non-participants as shown in the attrition analysis and by the higher number of individuals with OP compared to SZ among participants. Based on a recent meta-analysis, age at onset of OP is typically higher than in SZ (Solmi et al., 2022), as in this sample. Additionally, the use of register information in defining the age of onset in this study may affect the results, since the registers indicate the start of treatment instead of the onset of actual psychotic symptoms. The association between earlier onset age of psychosis and unfavourable occupational outcomes in SZ is unclear (Immonen et al., 2017; Tsang et al., 2010), but some studies have found a significant relationship between these characteristics. Nevertheless, later illness onset has been linked with many other favourable outcomes in SZ (Immonen et al., 2017).

Gender gaps in the labour market exist throughout the world (International Labour Office, 2017). The rates of floundering employees among individuals with SZ and OP in this study were similar across genders. Compared to men with SZ,

women with SZ were more likely to be pensioners, whereas among individuals with OP, the rate of pensioners was similar between genders.

Compared to those with OP, people with SZ were less likely to enter tertiary education and more likely to be single. Previous studies have reported poorer outcomes in people with SZ than in those with OP (Jobe & Harrow, 2005) and poorer outcomes in men with SZ and OP than in women with these disorders (Grossman et al., 2006). In terms of occupational outcomes in schizophrenia, some studies have found better outcomes for women than for men (Cotton et al., 2009, Seeman, 2019). Nevertheless, some studies have suggested better outcomes for men than for women in terms of paid employment in some regions of the world (Novick et al., 2016).

8.2.3 Return to the labour market in psychoses (III)

The proportion of persons with schizophrenia returning to the labour market found in this study is in line with the employment rates of 10–40% (Ajnakina et al., 2021; Huxley et al., 2021; Marwaha & Johnson, 2004) and with the unemployment rates of 89–94% found in previous studies (Hakulinen et al., 2019a). In addition, the recent Finnish RETIRE study found that only 10.5% of persons with a fixed-term psychiatric disability pension returned to work during the five years of follow-up (Pirkola et al., 2020).

Among psychiatric diagnoses, psychotic disorders typically have the poorest occupational outcomes after long-term work disability (Joensuu et al., 2019; Virtanen M et al., 2011). In parallel to few previous studies on return to work, the current study shows even lower numbers of returnees to working life (SZ 9% and OP 19% vs. 40–46% of persons with schizophrenia, schizotypal, or delusional disorder in Joensuu et al., 2019; Virtanen M et al., 2011). The difference compared to these previous studies can be explained by the fact that this study had a notably longer follow-up, the focus was on more severe stages of work disability, and by different settings, since the register of SII includes individuals with no lifetime attachment to working life because of disabilities occurring already at a younger age. In the Finnish disability pension system, permanent disability pensions are granted based on a significantly lower probability of regaining working ability compared to fixed-term disability pensions and long-term sick leaves. Virtanen M et al., 2011 used a broad definition of work disability including long-term sick leaves (> 90 days) and receipt of disability pensions without separating fixed-term

and permanent pensions. Following their recommendation, temporary and permanent disability pensions were handled separately in this study.

The sample of this study differed from samples in many previous studies because the most severe lifetime diagnoses detected from several registers were utilised. Whereas previous studies have studied the return to the labour market of individuals who have received disability pension due to diagnosis of schizophrenia or psychosis (regardless of their previous and forthcoming diagnoses in treatment settings), this study investigated the return to the labour market among those with lifetime schizophrenia or other psychosis. Thus, this study has explored a very good functioning outcome, i.e., return to the labour market, during life course among individuals with psychotic disorders.

In OP and NP, the proportions of permanent full-time disability pensions (68% in OP and 53% in NP) were somewhat lower than in schizophrenia. This may partly explain the higher proportions of persons who can return to the labour market compared to SZ. The total number of people with schizophrenia on a disability pension at some stage (77%) was also clearly higher than in OP (50%) and NP (15%).

In a systematic review, higher cognitive functioning was found to be a significant predictor of good vocational outcome among individuals with schizophrenia (Tsang et al., 2010). In this study, higher school grades at the age of 16 years predicted a return to the labour market. Better school performance has previously been associated with not being on a disability pension in schizophrenia in NFBC1966 (Lauronen et al., 2007). Higher school grades may be a proxy of cognitive reserve and functioning, and in this sense, these results are in line with previous studies (Tsang et al., 2010). Other predictors of good vocational outcome in the review by Tsang et al., 2010 included a lower level of negative symptoms, a higher level of education, social skills and support, a previous history of successful employment, use of different rehabilitation services, and younger age. According to extensive meta-analyses, the relationship between earlier age at illness onset and worse vocational outcomes in schizophrenia is not clear, although some studies have reported a significant relationship between the two (Immonen et al., 2017; Tsang et al., 2010). However, higher age at illness onset has been associated with many other good outcomes in schizophrenia (Immonen et al., 2017).

Previous studies have found that being married or cohabiting is a predictor of better vocational outcome (Tsang et al., 2010), and my results are in line with this finding. Being single has also been associated with worse occupational status in earlier follow-ups of NFBC1966 (Miettunen et al., 2007). In this study, having

children was a predictor of returning to the labour market in OP and NP, but not in SZ. Schizophrenia patients without offspring have been associated with having a more prolonged and severe course of illness than those with children (Ritsner et al., 1992), while the relationship between having offspring and outcome in other psychoses is less known. A shorter length of the latest disability pension was found to be a predictor of returning to the labour market in SZ, OP, and NP. Having long-term sick leave due to mental illness has previously been associated with increasing the risks of unemployment and disability pension (Hultin et al., 2012).

8.3 Strengths and limitations

8.3.1 Strengths of the study

NFBC offered a unique possibility to examine the outcomes of psychoses and non-psychotic disorders with an unselected, general population sample covering all branches of occupations and economy over a time period of 30 years in NFBC1986 and 50 years in NFBC1966.

The thesis managed to examine long-term outcomes of early-onset psychoses with over 30 years of follow-up, 30-year-long employment trajectories of psychoses from the ages of 16 to 45 years and return to the labour market in psychoses with data coverage over 50 years. Long-term follow-up studies are usually defined as follow-up periods exceeding five years; compared to those, the data coverage of the thesis was very long. Only few studies have analysed occupational or other outcomes of psychoses in very long-term follow-ups and no previous studies have analysed the employment patterns of individuals with psychoses in very long-term follow-ups. The length of the employment trajectory data in this study spanning four decades from the 1980s to the 2010s is internationally unique and offered a possibility to study labour market attachment in psychoses from early adulthood until midlife.

One of the study's strengths was the chance to not only study occupational outcomes of psychoses in general but also to analyse outcomes in SZ and OP diagnoses separately. The study was able to compare outcomes of SZ and OP to those of NP and HC. With respect to the gendered distribution of occupations, studying men and women separately in the original study II enabled to acknowledge the gender differences in longitudinal employment patterns in psychoses. Furthermore, analysing the outcomes of early-onset psychosis using age

as a categorical variable enabled to reveal different onset age-specific courses of the disorder. Previous studies have compared early-onset psychoses to adult-onset psychosis whereas the original study I focused on comparing the outcomes of EOP in two age categories. While previous studies have mostly drawn the line between EOP and AOP at 18 years of age based on the traditional definition of legal age, the original study I focused on the cut-off between EOP and AOP by stretching the upper age limit of EOP to 23 years so as to consider the brain development after 18 years of age.

A major strength of the study was the use of high-quality register data. Using register data offers certain advantages such as broad data coverage and powerful combinations of registers from different sources (Mellander, 2017). Psychotic illnesses influence individuals' functioning on many levels and thus, questionnaire-based research may suffer from sample bias and small response rates due to the difficult recruiting processes of psychotic individuals. False-positive psychosis diagnoses due to registration errors and varying diagnostic practices in outpatient settings have been reported (Vernal et al., 2018). By using data from multiple national registers in the case detection phase we were able to minimise the number of potential misdiagnoses. The universal, both earnings- and citizenship-based and comprehensively registered disability pension system of Finland offered an opportunity to study the course of pension periods very precisely. Unlike in previous studies, the data in the original study III also covered individuals who had not been able to enter working life due to early onset of illness or other reasons. This is an important viewpoint regarding psychoses which are among the top reasons for work disability in early adulthood. Due to this, the results of the original study III fully describe the psychiatric disability-related outcomes in all individuals with schizophrenia, other psychoses, and non-psychotic mental disorders in this population.

Another further strength was the possibility to minimise the effects of attrition and confounding factors by using attrition analysis and adjusting for well-established potential confounding factors in the thesis. Moreover, sensitivity analysis was utilised to exclude very early onset psychoses and non-psychotic psychiatric disorders in the original study I. Thus, it was possible to exclude some potential misdiagnoses of childhood and make the comparison between psychosis and non-psychoses more suitable.

8.3.2 Limitations of the study

The study has certain limitations. First, due to the long follow-up of NFBC studies, period effects should be noted. The differences in diagnostic practices and use of three diagnostic systems over the decades may have influenced the variation in the prevalence of different diagnoses and differences in grounds for granting disability pension. Especially after the 1990s, both views and funding possibilities on occupational rehabilitation changed. Rehabilitation became more working life oriented and possibilities for rehabilitation aimed at returning to the labour market increased. On the other hand, working life may have become more demanding socially, psychologically, and cognitively, making working opportunities more difficult, especially for those with schizophrenia. Moreover, variation in pension policies and employment levels between countries and at different times makes comparison of occupational outcomes with different studies difficult and has an impact on the generalisation of study results. In the future, the implementation of ICD-11 may result in further variation in the prevalence of psychotic disorders and some changes in psychiatric research.

The study results are derived from a Nordic welfare country providing access to health care, education, and social security for all citizens, so the results are best generalisable to other countries with similar labour market circumstances (Torp et al., 2020). However, the approach of focusing on the risk of experiencing the least favourable employment trajectories among individuals with psychoses is applicable across various countries and societies. Differences in treatment and rehabilitation practices between countries may lead to geographic variation in outcomes between different studies. Likewise, specific interventions used in some studies may cause variation in the outcomes across studies. However, the focus of the thesis was to study occupational and other outcomes of psychoses in general population sample with naturalistic study design.

The unbalanced number of men and women between the psychosis groups of the original study I may have influenced the findings by emphasising poorer outcomes for those with psychosis onset at 18–22 years of age due to a greater number of men in this group. Earlier studies have reported a greater number of early-onset psychotic disorders among males than females in Finland (Gyllenberg et al., 2010). Likewise, earlier onset ages of psychosis have been found for males than females (Solmi et al., 2022). Thus, the high number of women among those with psychosis onset before 18 years in the current sample may be at least partially

explained by coincidence. Another explanation for gender differences may be earlier help-seeking behaviour and detection in younger persons, especially among individuals with affective symptoms, which may be considered as a prodromal phase of psychosis (Filatova et al., 2017). Information on gender in all original studies was based on national population register information. However, due to societal changes it is important to notice that there is difference in studying gender and sex.

Besides gender, some other confounding factors such as substance use may have influenced the results between individuals with different ages of illness onset. The thesis excluded psychoses due to substance use which may be frequent especially in adolescence. This preference was due to the intention of focusing on non-organic psychotic disorders and making comparisons with previous studies more appropriate.

The sample of the original study II had higher-level educational and occupational functioning compared to the general population. Thus, potential selection bias limits conclusions of the study. Individuals with psychoses are typically overrepresented in jobs that are relatively easy to perform (Cohen et al., 2008; Marwaha et al., 2007; Yang et al., 2013). For that reason, the study's results may not be generalised to severely ill individuals with psychoses. However, the results of the original study II remained similar in the weighted analyses.

The small sample sizes, with respect to gendered trajectories and analysing SZ and OP separately, limit the statistical power of studies. The small sample sizes limited detailed examination of other than floundering trajectories in original study II. The small number of cases limited also statistical power when analysing the predictors in original study III and possibilities of studying potential predictors in original study I. Due to the small sample size of persons with psychoses in the original study I, it was not possible to study outcomes of early-onset psychoses between subclasses such as schizophrenia and other psychoses. Likewise, the sample sizes limited the possibilities for deeper investigation of the schizophrenia and other psychoses subgroups, such as psychotic depression. Due to sample sizes, certain categories of some variables such as socioeconomic or marital status were combined limiting more detailed analysing of these variables.

Various numbers of data were missing, which may have affected the results. For example, an important limitation was the potential lack of individuals with non-psychotic mental disorders in the original studies I and III. The registers used probably include the majority of individuals with psychosis (Miettunen et al., 2007; Perälä et al., 2007), and register data were complemented by self-reported lifetime-

psychosis diagnosis based on the follow-up questionnaires of NFBC1966 in the original study II. The focus of the thesis was on schizophrenia and other psychoses. However, individuals with non-psychotic psychiatric disorder treated solely in private sector or occupational health and those without any patient care relationship are not included in the registers and may thus have been missed. Also, the data collection of visits to specialised outpatient care did not start until 1998 when the NFBC1966 cohort members were over 30 years old. Thus, the prevalence of non-psychotic mental disorders may be underestimated. The prevalence of any mental disorder in the NFBC1966 (19.2%) is within the range of prevalence estimates (12.2–48.6%) found in a cross-national study (Andrade et al., 2000), but clearly lower than the lifetime prevalence in the Dunedin birth cohort study from New Zealand (85.8%) (Caspi et al., 2020). It is possible that some individuals with non-psychotic mental disorders may have had psychotic symptoms or a diagnosis, but these have not ended up in the registers used. Overall, registers used in the study had good data coverages and few missing data probably did not have significant effect on the results. Thus, imputations were not conducted.

The register data of the SII in NFBC1986 included only data on reimbursable medicines, but no data on disability pensions or sick days which were used in the original studies II and III utilising the NFBC1966. This limited not only case detection in original study I but also broader possibilities of studying various outcomes in NFBC1986. Furthermore, the disability pension data of the SII were available for the whole NFBC1966 only until the end of the year 2000. However, with regard to the register data availability, the study aimed to do its best to classify the subjects and measure the outcomes by using multiple national registers.

One problem across studies focusing on employment- and disability-related outcomes is in defining and measuring the outcome. Standard definitions or criteria for good occupational outcomes or being employed in schizophrenia research do not exist (Marwaha & Johnson, 2004). There is also a difference between returning to competitive work and returning to the labour market. Unfortunately, it was not possible to assess returning to work with the data available for this study. However, the study was able to evaluate the ending of disability pension due to psychiatric reasons and returning to the labour market with an unambiguous measure, showing clear differences between the diagnostic groups.

9 Conclusions

9.1 Main conclusions

The outcomes of early-onset psychoses are not similar for everyone. Illness onset before the age of 18 years does not necessarily associate with worse outcomes. The time between 18–22 years of age is an important period that may be disturbed by psychosis onset, which may lead to poor long-term socioeconomic and clinical outcomes going forward.

Schizophrenia and other psychoses are associated with an elevated risk for longitudinally poor occupational outcomes. This is reflected in most individuals as unfavourable employee trajectories, with unemployment and part-time work being common during working life until midlife, indicating weak labour market attachment among these disorders.

Although schizophrenia is associated with long-term work disability, it is possible to return to the labour market after being on a disability pension. Among individuals with other psychoses and non-psychotic disorders, returning to the labour market is somewhat more common than in schizophrenia.

The study was able to clarify occupational and other outcomes in psychotic disorders at three different stages of illness including onset, over the course of working life, and after years of disability pension. To conclude, compared to other psychiatric illnesses and to individuals without psychiatric disorders, these outcomes in psychoses are relatively poor. However, some individuals are able to attain better outcomes, reflecting the functional and occupational capacity of individuals with psychoses and emphasising the significance of developing interventions to fulfil that potential also in other individuals with psychotic disorders in the future.

9.2 Practical implications

Onset age has an important role in the psychosis onset phase and influences later outcomes. Among individuals with early-onset psychosis, typical adolescence-related developmental tasks such as the act of becoming independent, development of personality, and achieving age-dependent goals may be disturbed by the psychotic disorder and its consequences (McGorry et al., 2011). Furthermore, brain development is still ongoing in adolescence (McGlashan & Hoffman, 2000).

Individuals with later onset age of illness may have already transitioned to adult roles, including entering work and starting a family. The significance of onset age for later outcomes in psychoses is reflected in the original study I with psychosis groups having different long-term socioeconomic and clinical prognoses. One possible explanation for the differences in outcomes between persons with psychosis onset at different ages may originate from society. Due to legislation, underaged individuals typically take part in school health care, which may help in screening potential persons at risk of psychosis and hasten the arrangement of interventions for them. Individuals with psychosis onset at 18–22 years of age are in an important transitional phase in which they may no longer be involved in school health care, and since they have not yet entered working life, they are outside the occupational health care system. This may result in a longer duration of untreated psychosis and thus, poorer later outcomes for persons with onset age at 18–22 years of age. The poor prognosis of EOP found in the original study I emphasises the need for interventions to prevent adolescents from being waylaid from taking the usual steps that are typically completed in young adulthood. The results of the study indicate a specific need for interventions in outpatient settings for young adults at risk of psychosis or with psychosis within an important transition period between 18–22 years of age.

Returning to the labour market from disability pension in schizophrenia is not common. This is reflected in the high proportion of permanent full-time disability pensions (77%) granted to individuals with SZ, indicating a chronic and severe illness. On the other hand, this may reflect the thoughts of mental health care employees, i.e., that it is not possible to recover occupationally from schizophrenia (Marwaha et al., 2009).

Individuals with psychotic disorders often encounter barriers to gaining employment (Carmona et al., 2019; Marwaha & Johnson, 2004). However, many individuals with these disorders can do some type of work, and vocational rehabilitation should be offered actively for those who wish to work (Falkum et al., 2017). Vocational rehabilitation has many beneficial effects on mental health and well-being (Noordt et al., 2014). Working in schizophrenia is associated with other positive outcomes such as symptom levels, social functioning, self-esteem, and quality of life (Marwaha & Johnson, 2004). Positive associations between general functioning and personal recovery have been found (Van Eck et al., 2018). In terms of treatment, supporting the ability to study or work is an important goal because it

can further improve the functional, social, and clinical outcomes of psychosis (Tandberg et al., 2012).

Different types of rehabilitation services and interventions for individuals with psychosis exist with varying effectiveness (National Institute for Health and Care Excellence, 2020). Educational or vocational rehabilitation seems to improve attachment to school or work during early phases of psychosis (Correll et al., 2018). Increasing access to rehabilitation services is associated with better participation in employment (Carmona et al., 2019). However, based on a recent meta-analysis of randomised controlled trials, vocational rehabilitation is insufficient to ensure labour stability in psychoses (Carmona et al., 2017). The meta-analysis pointed to a need for more comprehensive approaches that address the functional deficits of people with schizophrenia from obtaining employment (Carmona et al., 2017).

The average time between the first psychiatric hospitalisation and disability pension in schizophrenia varies between 1 and 4 years (Cougnard et al., 2007; Kiviniemi et al., 2011; Miettunen et al., 2007). A short time frame between illness onset and exit from the labour market in psychoses emphasises the importance of treatment, interventions and vocational rehabilitation already in the early phases of psychotic illnesses. Some studies have found better longitudinal employment outcomes for individuals who have received early intervention services, but the association is not clear (Chan et al., 2019; Chan et al., 2020). Early interventions that aim for a quick return to work could prevent long-term exclusions from the labour market. Since in this study, returning to the labour market was possible also in later phases of illness and after long-term disability pensions, this kind of rehabilitation should be offered not only to all individuals in the early phase but also to those in later phases and during the illness course.

An investment in first finding employment and thereafter tailoring rehabilitation and treatment – the Individual Placement and Support approach – seems to increase the employment rates for individuals with longer-term mental health problems (Rinaldi et al., 2011). The IPS approach has been reported to be more effective than standard treatment particularly during the first months of intervention (Killackey et al., 2019). A preliminary report on the implementation of IPS in Finland has already been made (The Rehabilitation Foundation, 2018). Based on this report, certain challenges must be solved before the larger-scale implementation of IPS in the Finnish context (The Rehabilitation Foundation, 2018). However, promising development projects on the implementation of IPS as a service integrated into psychiatric treatment and rehabilitation already exist (Finnish Institute for Health and Welfare, 2022). The IPS model aims to improve

occupational outcomes in psychoses by using employment specialists who support psychotic individuals in all stages of the process of finding and maintaining employment (The Rehabilitation Foundation, 2018). By implementing the expertise of these employment specialists in psychiatric hospitals, it is possible to influence labour market attachment already in the early phase of psychotic disorders in the future.

Other promising projects also exist that can possibly be implemented as part of rehabilitation of psychotic disorders in Finland in the future. One of these, the TYÖOTE operational model, aims to improve co-operation between basic health care, specialist medical care, and occupational health care (Finnish Institute of Occupational Health, 2022). In this operational model, the occupational health care provider works as a case manager and assumes responsibility for coordinating individuals' treatment and rehabilitation in different health care units and takes care of the follow-up (Finnish Institute of Occupational Health, 2022). In this way, by utilising the competence of occupational health care, the project tries to make the employees' rehabilitation, treatment and return to work more efficient (Finnish Institute of Occupational Health, 2022).

Other community-based social interventions for individuals with severe mental illnesses and with a good level of evidence include the Housing First model of supported accommodation and family psychoeducation (Killaspy et al., 2022). Supported employment approaches combined with interventions such as job-related skills training and neurocognitive therapy can be applied to many individuals and are compatible with a wide range of occupational outcomes (Carmona et al., 2017). However, despite the considerable benefits of social interventions for mental health, they require multi-level stakeholder commitment and investment for successful implementation (Killaspy et al., 2022).

High risk of being outside the labour market for individuals with schizophrenia (Hakulinen et al., 2019a) leads to significant costs for society (Evensen et al., 2016). It is important to estimate whether current employment policies are effective in helping people with psychoses to find employment (Hakulinen et al., 2020). Furthermore, due to a high number of substance use among individuals with psychosis onset at 18–22 years of age, new integrated approaches combining addiction and psychiatric services for this age group are needed to ensure adequate interventions for those with dual pathology.

The results of thesis can be utilised to improve labour market attachment in individuals suffering from psychotic illnesses and can be applied when planning

treatment, vocational rehabilitation, and interventions for these individuals. The results underline the importance of vocational rehabilitation starting already during the early phases of psychotic illnesses. In the future, gender differences would be important to notice when planning rehabilitation for individuals with psychotic disorders.

The results of the study suggest that factors that have previously been associated with better outcomes in schizophrenia are also predictors of returning to the labour market. In the future, occupational rehabilitation could be planned and implemented especially for individuals with indicators of better possibilities to return to the labour market.

9.3 Recommendations for future research

To improve occupational outcomes for individuals with psychoses, in the future, it is important to study factors associated with return to the labour market and work in long follow-ups and large samples. More studies on the effectiveness of interventions and vocational rehabilitation are needed, with a particular focus on SZ and OP. Promising development projects aiming to improve occupational outcomes of psychotic disorders in Finland exist and, in the future, it is important to assess the effectiveness of these different models. Furthermore, more studies on long-term employment patterns among individuals with different psychotic disorders are needed. Due to onset age-related differences in the course and possible different forms of psychotic disorders, further studies focusing on different age groups are needed to clarify the prognosis and predictors of early-onset psychoses. Systematic reviews or meta-analyses focusing on the gender differences in occupational outcomes of psychoses would be needed to draw consistent conclusions on the effect of gender. Furthermore, more gender and sex differences research has been recommended to drive scientific discovery for all genders and sexes (Rich-Edwards et al., 2018).

Register data is a Nordic phenomenon (Mellander, 2017), and register-based studies on the occupational outcomes of psychosis are mainly concentrated in the Nordic countries with quite similar societies. In the future, combining current data with more recent data, such as information from the healthcare quality registers, can be used to gain a more comprehensive view on the outcomes of psychoses. However, register data offer only general viewpoints on individuals' functioning and occupational capacity but fail to provide a more comprehensive and consumer-oriented picture, which could have been collected with questionnaires. In the future,

it would be important to organise larger national or international (e.g., between Nordic countries) multicentre questionnaire studies to ensure adequate sample sizes with personal perspectives on functioning and work capacity. Occupational outcome research is a multi-dimensional concept that is carried out in many different fields of science. By increasing collaboration with these different fields such as psychology, economy, and sociology, we can gain a better understanding on the actual functional and occupational possibilities of individuals with psychotic disorders.

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Original publications

I Majuri, T., Haapea, M., Nordström, T., Säynäjäkangas, V., Moilanen, K., Tolonen, J., Ala-Mursula, L., Miettunen, J., & Jääskeläinen, E. (2022). Effect of onset age on the long-term outcome of early-onset psychoses and other mental disorders: a register based Northern Finland Birth Cohort 1986 study. *Manuscript.*

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III Majuri, T., Haapea, M., Huovinen, H., Nordström, T., Ala-Mursula, L., Penttilä, M., Martimo, K-P., Miettunen, J., & Jääskeläinen, E. (2021). Return to the labour market in schizophrenia and other psychoses – a register-based Northern Finland Birth Cohort 1966 study. *Social Psychiatry and Psychiatric Epidemiology, 56*(9), 1645–1655. https://doi.org/10.1007/s00127-020-02009-1

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