

STUDIES IN PATHWAYS TO CARE —
*duration of untreated psychosis and
its determining factors in early psychosis.*

Erling Inge Kvig, Cand Psychol

A dissertation for the degree of Philosophiae Doctor – May 2018

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Acknowledgements

This study was conducted between 2010 and 2014 at Nordland hospital, and UiT The Arctic University of Norway. Funding was provided by the Northern Norway Regional Health Authority.

Many people have offered support and intellectual stimulation over the years I have spent working on the study.

I am extremely grateful to my supervisors. Knut Sørgaard, the head of research at Nordland hospital, for inspiration and crucial support, and to Tor Ketil Larsen, for his kind and astute criticism, and especially the advice to take it «bird by bird»

I am indebted to the academic inspiration from the Health service researchers at Nordland hospital (especially Knut Sørgaard and Terje Øiesvold), the TIPS group (TK Larsen, Inge Joa and Robert Jørgensen), the Birmingham group (Max Birchwood and Swaran Singh). I am also indebted to Paul Møller and the «Hvidovre school of psychiatry» (Josef Parnas, Lennart Jansson, Peter Handest, Mads Henriksen and Julie Nordgaard), for the crucial inspiration of their work.

Special thanks to Steinar Nilssen for companionship and the many conversations during my training, and later when conducting this study.

Thanks to my co-researchers, Beate Brinchmann and Cathrine Moe. Also thanks to Lill Marta Lekanger for technical assistance, Sandy Goldbeck-Wood for feedback on the final manuscripts, and Tom Wilsgård for statistical assistance.

For many years, the staff at the library of Nordland hospital have provided me with with invaluable support and help in locating all those dirty old books. Special thanks to Ove Eide, Elin Strand and Kåre Dalhaug.

This study would have been impossible without the support from chief psychiatrist at the department of specialist psychiatry, Knut Kjerpeseth. Let me also express my gratitude to the support, patience and inspiration from colleagues and co-workers at the Regional Unit of Early Psychosis.

I am grateful to all the hospital wards, community practitioners and general practitioners participating in the study. And to all the brave patients for their invaluable participation in this study.

Thanks to all my friends (especially my brewing buddies and the Gockstock crew).

Finally, thanks to my family. Mom and Dad for all your support, my two daughters Benedikte and Charlotte, and to Veronica, for helping me to walk on, even when life came in the way.

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Summary

Many patients with a first episode psychosis (FEP) are treated late in their course of illness, and have a long duration of untreated psychosis (DUP). Treatment delay may be determined by both intrinsic (illness and patient related) and extrinsic (service and system related) factors. Although recent studies have documented substantial delay occurring after service entry, this component of DUP is largely unexplored in the literature.

In the present study we provide a descriptive epidemiology of the pathways to care of FEP patients in a Norwegian health care context, investigate the community level DUP, determinants of delay, and test whether treatment delay is co-determined by service and system related factors. To explore these issues we collected data from three different populations: 1) treated patients; 2) community practitioners; and 3) general practitioners.

Median DUP in this sample was 19.5 weeks. We found that service/system delay accounted for more than half of overall treatment delay. The intrinsic determinants of delay are highly idiosyncratic and there is great diversity in where and how patients present to services. In the service interval, referral delay and diagnostic delay was found to be important determinants. Referral decisions were dependent also on contextual factors, and the threshold for hospital referral was elevated in more peripheral areas. Diagnostic delay and misdiagnosis, perhaps related to an underestimation of the heterogeneity in early psychosis, also contribute to delay. In conclusion, we argue that DUP is a multidimensional construct implicating both intrinsic and extrinsic factors. Treatment delay is likely the result of an interplay of factors at different levels within a specific healthcare context.

By understanding where and why treatment delay occurs we may better able to design interventions to facilitate better earlier detection and treatment of psychosis. The findings in the present study highlight that an important target for early intervention is improving referral pathways and reducing the diagnostic delay in patients that are already receiving care from mental health services.

Sammendrag

Mange pasienter med en førstegangpsykose får behandling sent i forløpet og har en lang varighet av ubehandlet psykose (VUP). Forsinket behandling kan skyldes både indre (lidelse og pasient relaterte) og ytre (tjeneste og systemrelaterte) faktorer. Til tross for at nyere forskning har dokumentert at en stor del av forsinkelsen skjer mens pasienten mottar behandling i spesialisthelsetjenesten, så er denne komponenten av VUP lite utforsket.

Formålet med studien var å gi en epidemiologisk beskrivelse av behandlingsveier for pasienter med førstegangpsykose i et norsk helsetjenestetilbud, undersøke VUP på gruppenivå, undersøke årsakene til forsinket behandling, og å teste hypotesen om at forsinket behandling er medbestemt av tjeneste- og systemrelaterte faktorer. For å undersøke disse tema samlet vi inn data fra tre ulike populasjoner: 1) pasienter i behandling, 2) behandlere ved distriktpsikiatriske sentere, og 3) fastleger.

VUP hadde en medianverdi på 19.5 uker i dette utvalget. Vi fant at forsinkelse i helsetjenesten utgjorde mer enn halvparten av den totale forsinkelsen. Faktorene knyttet til indre faktorer var svært idiosynkratiske, og det er stor variasjon i hvor og hvordan pasienter kommer i kontakt med helsetjenesten. Viktige determinanter for forsinkelse i helsetjenesten var forsinket henvisning og forsinket diagnose. Beslutninger om å henvise var medbestemt av fysisk kontekst og terskelen for innleggelse var forhøyet i mer perifere områder. Forsinket diagnose og feildiagnose, muligens knyttet til at man undervurderer heterogeniteten i den kliniske presentasjon ved tidlig psykose, bidro også til forsinket behandling. På bakgrunn av disse funn fremholder vi at VUP er et flerdimensjonalt begrep som innbefatter både indre og ytre faktorer. Forsinket behandling forårsakes av et samspill mellom flere faktorer, på ulike nivåer, og er også bestemt av den fysiske konteksten.

En bedre forståelse av hvor og hvorfor forsinkelser i behandling skjer vil gjøre det mulig å uforme tjenester for raskere oppdagelse og behandling av psykose. Funnene i denne undersøkelsen understreker at et viktig mål for tidlig intervensjon er å bedre henvisningspraksis og å unngå forsinket diagnose for pasienter som allerede mottar behandling i spesialisthelsetjenesten.

List of papers

Paper I

Kvig, EI., Brinchmann, B., Moe, C., Nilssen, S., Larsen, TK., & Sørgaard, K. (2017) Geographical accessibility and duration of untreated psychosis: distance as a determinant of treatment delay. *BMC Psychiatry*, 17: 176.

Paper II

Kvig, EI., Brinchmann, B., Moe, C., Nilssen, S., Larsen, TK., & Sørgaard, K. (2017) "Lanthanic presentation" in first episode psychosis predicts long service delay: the challenge of detecting masked psychosis. *Psychopathology*, 50(4), 282-289.

Paper III

Kvig, EI., Moe, C., Brinchmann, B., Larsen, TK., & Sørgaard, K. (2017) Negotiating the boundaries of psychosis: A qualitative study of the service provider perspective on treatment delay in community mental health. *Early Intervention in Psychiatry*. Aug 23 (Epub ahead of print).

Paper IV

Kvig, EI, Brinchmann, B., Moe, C., Larsen, TK., & Sørgaard, K. (submitted) What do General Practitioners know about early psychosis? A survey of the diagnostic knowledge among gatekeepers to specialist mental health care in Northern Norway. *BMC Health Services Research*.

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Abbreviations

| | |
|---------|--|
| ANOVA | Analysis of Variance |
| CI | Confidence Interval |
| CMCH | Community Mental Health Center |
| CSSRI | Client Socio-Demographic and Service Receipt Inventory |
| DSM-IV | American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders, fourth edition |
| DSM-5 | American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders, fifth edition |
| DUP | Duration of Untreated Psychosis |
| GAF | General Assessment of Functioning |
| GLM | General Linear Model |
| GP | General Practitioner |
| HELFO | The Norwegian Health Economics Administration |
| ICD-10 | International Statistical Classification of Diseases and Related Health Problems, 10th revision |
| IGPS | International Study of General Practitioners and Early Psychosis |
| MD | Medical Doctor |
| NOS-DUP | Nottingham Onset Schedule - DUP version |
| OPCRIT+ | Operational Criteria checklist, enhanced version |
| OR | Odds Ratio |
| PAS | Premorbid Adjustment Scale |
| PANSS | Positive and Negative Syndrome Scale |
| SPSS | Statistical Package for the Social Sciences |
| TIPS | Early Treatment and Intervention in Psychosis |
| UHR | Ultra-high risk |
| WHO | World Health Organization |

1.0 Background

1.1 Why study treatment delay?

I had the great fortune, in my first job as a clinical psychologist, to get to work with people suffering from psychosis. My training was in psychotherapy, and my approach was very much talking to and trying to understand the patients through therapeutic interviews. I quickly learned that helping patients with psychosis is a team approach, collaboration with medical doctors, milieu therapist and other specialist, is a necessity. Most of the patients admitted to the ward received a schizophrenia diagnosis, and I found these patients particularly challenging and interesting to work with. It has been said that people with schizophrenia uses philosophy to understand the world, while people with autism uses mathematics. I think my own interest in philosophy made me intrigued by this and I found that the patients often had an interesting point of view on the world and our existence.

Although intrigued, I was also puzzled by the fact that many patients receiving the same diagnosis presented with very different symptoms and life-histories. The consultant psychiatrist assured me by saying that «If you have met one patient with schizophrenia, you have only met one patient with schizophrenia». Although patients presented very differently, one salient and common feature among our patients on the ward was that they often had experienced considerable delay in receiving help for their psychosis. An illness history representative for many of these patients is the following:

« A patient told me he began hearing voices inside his head at the age of thirteen. Initially he did not experience this as a mental health issue, his voices were friendly and only later become strange, destructive and experienced as a communication with another world. The patient had experienced bullying at school and he had symptoms of depression and anxiety at an early age. He had his first suicide attempt when he was 15 years old, and this prompted referral to a mental health professional. His symptoms were considered a consequence of bullying. He received different treatments for depression, social anxiety, substance abuse and obsessive-compulsive problems. At age 22 he was admitted to a specialized hospital ward for disabling OCD symptoms. After a prolonged admission with poor treatment response on CBT, a psychiatrist was incidentally asked to screen for psychotic symptoms. They discovered that the patient had constant verbal hallucinations since the age of 13, delusions about being able to influence other peoples, and delusions about his own body. His DUP was

13 years. He had at least 10 independent treatment contacts with mental health professionals before his psychotic symptoms were discovered».

My reason for conducting research on treatment delay in early psychosis is meeting patients such as this in my own clinical practice as a clinical psychologist. My early experiences made me curious about why this delay occur. Is it mainly due to the intrinsic factors of the illness (e.g., «lack of insight»)? Or is the mental health system also at fault? Can we prevent treatment delay? Several effective treatments for psychosis have been developed, e.g., medications, psychotherapy, milieu therapy, and supported employment. However, timely and accurate diagnosis is a prerequisite for the delivery of these effective treatment strategies. Therefore, it is important conduct research on treatment delay.

2.0 Introduction

2.1 Treatment delay and DUP

Early diagnosis and prompt treatment is a key focus in health care because of its association with morbidity and mortality. The improved outcomes seen in the last decades in illnesses such as cancer, infections and acute illnesses such as myocardial infarction, have come not only because of the development of new therapeutic methods, but also because of increased effort at early diagnosis and treatment (McGorry, 2015). The benefits of early diagnosis and treatment in these illnesses are widely acknowledged in both the public and research discourse.

Until recently, the same emphasis on early detection, diagnosis and treatment has not been considered essential in mental health care. Historically, and perhaps still predominately, late and slow intervention has been the rule. One important reason for this is that definite diagnosis in mental health takes time. For the majority of mental illnesses, a specific etiology is unknown and there are no definite biomarkers. Diagnosis relies on clinical descriptions, and the so-called operational criteria often specify a minimum duration before symptoms are considered clinically meaningful. In mental health, it has been common practice to monitor the illness, in order for it to «declare itself» (Larsen, McGlashan, & Moe, 1996). However, in the last few decades, research and practice within mental health have shifted from late treatment to focus on early detection and prevention of chronicity and disability (Byrne & Rosen, 2014). The construct of the duration of untreated psychosis (DUP), and research showing that lengthy treatment delay is an important predictor of outcome, has been important in this regard.

Although research documenting that duration of symptoms is a potential predictor of outcome was available already from the 1940s (Rupp & Fletcher, 1940; Henisz, 1966; Helgason, 1990), one of the first studies to highlight latency in treatment as a major problem in first episode psychosis was the Northwick Park study in the early 1980s (Johnstone, Crow, Johnson, & MacMillan, 1986). This study found a delay between the onset of the first symptoms to detection and treatment of more than a year for one quarter of the patients. The study also found a possible relationship between earlier treatment and improved outcome in terms of reduction of relapse after two years (Crow, MacMillan, Johnson, & Johnstone, 1986).

In the early 1990s (Loebel et al., 1992) published the first paper presenting the mean DUP as a predictor of outcome. Two different onset of illness intervals were measured in a cohort of 70 patients with schizophrenia or schizoaffective psychosis: 1) time between the first noticed behavioral changes and study entry (duration of untreated illness, DUI); 2) time between first experienced psychotic symptoms and study entry (duration of untreated psychosis, DUP). Both variables were found to be related to outcome in terms of level of remission, but only DUP was significantly associated with the outcome variable time to remission. Loebel et al (1992) thus emphasized the prognostic significance of acute symptoms in psychosis. In subsequent research, DUP has become one of the most studied predictors of outcome. Several meta-analysis published since 2001, have found at least modest associations between longer DUP and several short and long-term outcomes across several domains: severity of symptoms, remission rates, higher relapse risk, poorer treatment response; worse vocational and social functioning, poorer global functioning, and lower quality of life (Perkins, Gu, Boteva, & Lieberman, 2005; Marshall et al., 2005; Penttila, Jaaskelainen, Hirvonen, Isohanni, & Miettunen, 2014).

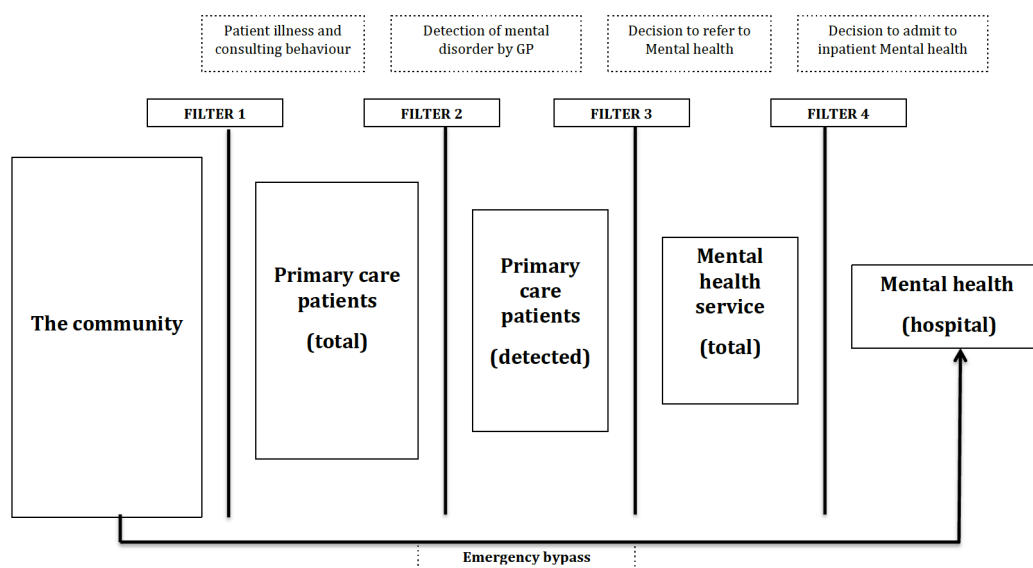
2.2 Early intervention and DUP

The finding that DUP is an important predictor of outcome has reinforced the relevance of early intervention programs. The highly successful Early Treatment and Intervention in Psychosis Study (TIPS) in Norway/Denmark demonstrated that community-level DUP can be reduced through multi-focus interventions involving mobile early detection teams, educational campaigns to the general public, newspaper, radio and cinema advertising, visits to schools, as well as seminars to healthcare professionals including general practitioners (Larsen et al., 2001; Melle et al., 2004). However, other early intervention studies have not been equally successful in reducing DUP (Lloyd-Evans et al., 2011). Studies have also demonstrated a great variability in DUP in different countries and healthcare contexts (Anderson, Fuhrer, & Malla, 2010). Improving the possibility of early intervention seems to require knowledge of where treatment delay occurs, as well as what causes treatment delays in a specific healthcare context. The first question is typically addressed in studies examining what has been termed «pathways to care» (Lincoln & McGorry, 1995), and the second in studies on the determinants of treatment delay (Compton & Broussard, 2011).

2.3 Pathways to care - where does delay occur?

Pathways to care are defined as «the sequence of contacts with individuals and organizations prompted by the distressed person’s efforts, and those of his or her significant others, to seek help as well as the help that is supplied in response to such efforts» (Rogler & Cortes, 1993), p.555. Studies of the pathways to care in early psychosis seeks to explore how differences in pathways translate into differences in DUP. The model first developed by Goldberg & Huxley (1980) has been important in this regard (see figure 1).

Figure 1: Pathways to care model



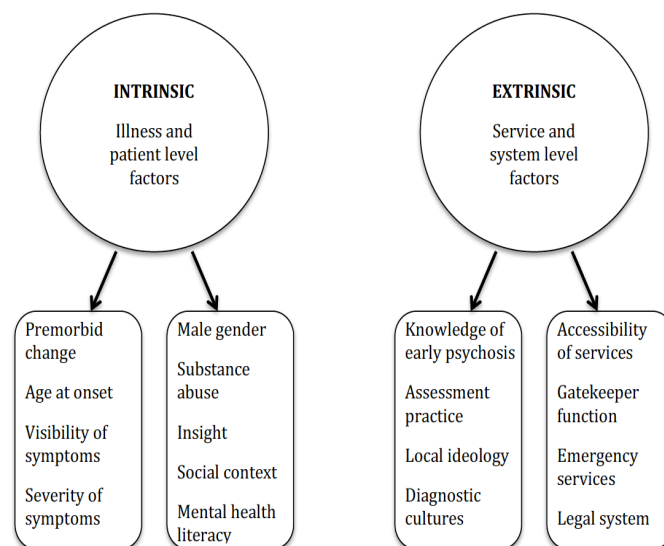
This model provides a comprehensive descriptive framework for understanding how people move into and through the mental health service system. The model suggests that the process of moving into the system involves passing through five service levels and four filters between the community and mental health care. Each service level represents a more specialized level of care than the previous one. Patients move between these levels via a series of selectively permeable filters that reflect decisions made by clinicians based on their consultations, diagnostic work and decision-making processes. In order to go from the community to primary care one must display illness and help-seeking behavior (the first filter); in order for mental illness to be detected by GPs or other primary care professionals he/she must detect the illness (second filter); in order to be seen by mental health services the GP must also be decide to refer (third filter); and to be admitted the mental health care professional must be decide to admit (fourth filter). This model and careful study of the

filtering process has proved useful in identifying the obstacles encountered by patients in accessing care (Volpe, Mihai, Jordanova, & Sartorius, 2015). Early studies on the pathways to care in first episode psychosis revealed that pathways are more varied and delays more extensive than for the common mental disorders (Lincoln & McGorry, 1995). This was partly explained as due to an increasing complexity in mental health services. Care is provided by a network of local and regional services, and in many cases emergency services and the criminal justice system are also involved in the pathways of early psychosis patients.

2.4 Determinants of DUP - what causes delay?

According to the overview given by Compton & Broussard (2011) the majority of studies thus far have focused on DUP as a predictor of outcome, and relatively few researchers have examined DUP as a dependent variable. However, knowledge of the determinants, or the factors that predict or relate to either short or long DUP, may be critical for service planners and initiatives aimed at reducing DUP. A large number of factors have been proposed and preliminary studied as determinants of DUP. There are however two basic groups of factors that seem to cause treatment delay in early psychosis (see figure 2).

Figure 2: Determinants of DUP



In the early studies of Loebel et al (1992) factors inherent to the patient's illness was seen as the most important determinants of outcome. While clinical features such as an insidious course of illness and lack of insight are most likely very important to treatment seeking and detection, other features such as availability and accessibility of services may equally impact

on treatment delay.

2.5 Critique of the DUP concept

Reduction of DUP, the time between onset of psychosis and start of treatment, is given priority in most early intervention programs. Nevertheless, the concept of DUP is still a matter of some controversy regarding both conceptual issues and the measurement of the DUP construct.

Upon finding a long mean DUP in a sample of first-episode schizophrenia, Larsen et al. (1996) commented that «new patients can emerge and function for a remarkable long time in the community with severe psychopathology» (p. 250-251). This phenomenon has been called «double bookkeeping» (Bleuler, 1950) or the «double ontological orientation» (Henriksen & Parnas, 2014), and refers to the «predicament (and ability) of simultaneously living in two different worlds, namely the shared social-world and a private, psychotic world» (p. 544). Studies on the phenomenology of psychosis have found that preceding the onset of psychosis, there is often a long period of time (the prodrome) where the patients experience a fundamentally altered self-world relation (with a loss of common sense, diminished presence, and solipsistic experiences), while remaining adapted to the social world (Parnas, Jansson, Sass, & Handest, 1998; Møller & Husby, 2000). Emerging psychotic symptoms are often understandable as progressive thematization of this underlying psychopathology, and do not appear as entirely new ego-dystonic and socio-dystonic «symptoms» associated with suffering. Professor Elyn Saks, herself suffering from schizophrenia, noted that «all my so-called symptoms were things I simply chose to think or do. I was choosing, e.g., to hold certain beliefs even though the evidence was not what would classically constitute «good evidence» - I had a special premium on the truth» (Saks, 2009), p. 972. The issue of onset dating is therefore also a conceptual issue, as it is highly dependent on what we take psychosis to be in the first place (Parnas, 2005). Thus, from the perspective of phenomenological psychopathology, dating the onset of psychosis would be impossible in many cases (Parnas, Nordgaard, & Varga, 2010). Although there are still unresolved issues on what we take psychosis to be (e.g., the discussion of the existence of a «psychotic continuum» (van Os & Reininghaus, 2016; Lawrie, 2016; Parnas & Henriksen, 2016)), the operational psychopathology of DSM-5 and ICD-10 currently define psychosis as simply a brief list of ostensive indicators (i.e., delusions, hallucinations, severe thought disorders, catatonia and negative symptoms). Acknowledging these conceptual difficulties, a

conservative definition of psychosis onset as an exacerbation of premorbid/prodromal tendencies and/or the emergency of new psychopathological phenomena («psychotic symptoms»), experienced by the subject as symptoms (i.e., ego-dystonic) or by carers as pathological changes (i.e., socio-dystonic), has been developed (Singh et al., 2005).

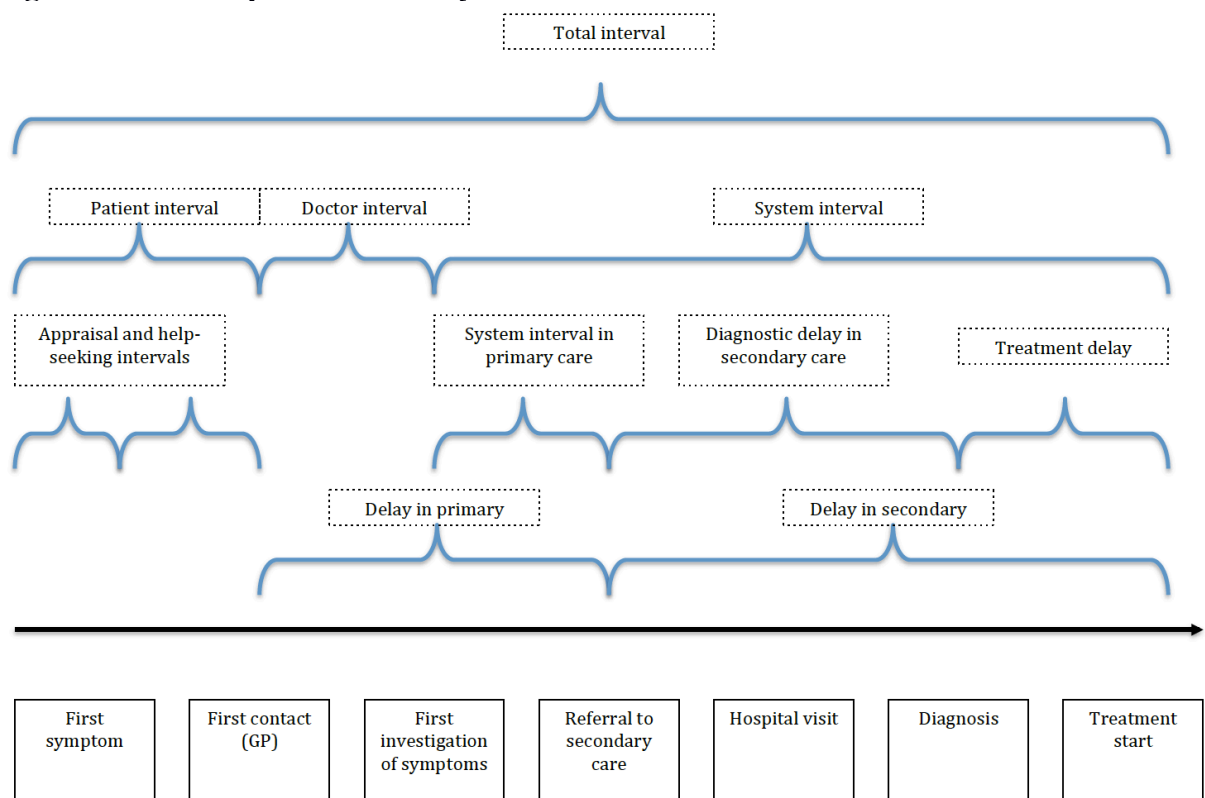
The technicalities of onset dating have been a topic of considerable attention, and as already noted seem highly dependent on what we take psychosis to be in the first place. Variability in criteria and methods used for measuring DUP could explain the heterogeneity in DUP across studies and healthcare contexts. However, in the research literature this discourse has led to a degree of consensus about its definition, and there are several structured psychometric scales developed for determining psychosis onset (Register-Brown & Hong, 2014). The DUP methodology proposed by Larsen et al (1996), where psychosis onset is defined as a certain cutoff score on subscales on a psychometric scale such as the Positive and Negative Syndrome Scale (Kay, Fiszbein, & Opler, 1987), has been important in the development of more structured methodology such as the Nottingham Onset Schedule used in this study (Singh et al., 2005).

Criticisms of the DUP construct have also been directed against the claim that it is an independent predictor of outcome (Bosanac, Patton, & Castle, 2010; Castle, 2012; Warner, 2013; Castle & Singh, 2015). These authors note that onset for the most severe patients may be insidious (Ho, Andreasen, Flaum, Nopoulos, & Miller, 2000; Morgan et al., 2006), and long DUP may therefore be inherent or inbuilt in the clinical presentation of severe forms of psychosis. Patients admitted acutely are more likely to have a brief, good prognosis psychosis, whereas those admitted late have a poorer prognosis. Thus, the relationship between DUP and outcome found in studies might be explained by a third variable, mode of onset. It has been claimed that DUP does not predict outcome, mode of onset predicts both DUP and outcome (Warner, 2013). According to these critics the success of early intervention efforts is largely the result of recruitment of people with inherent tendencies to better outcomes.

Responding to this criticism, Swaran Singh argues that the association between long DUP and a range of poor outcomes cannot be explained only by outcome being inbuilt into long DUP presentations, because several studies have shown that first contact with generic mental

health services risks increasing DUP (Castle & Singh, 2015). These studies show that generic services are responsible for more than a third of the total delay in first-episode psychosis (Norman, Malla, Verdi, Hassall, & Fazekas, 2004; Brunet, Birchwood, Lester, & Thornhill, 2007; Birchwood et al., 2013a). Further development of the conceptualization of DUP has therefore been proposed by Brunet et al (2007) and the «components of DUP» model. According to this model, DUP may be comprised of three different components: 1) Help-seeking delay (the interval between the onset of first symptoms and initiation of help-seeking); 2) Referral delay (the interval between first attempt to seek help and referral to mental health series) and 3) Mental health service delay (the interval between inception by mental health services and the commencement of appropriate treatment). Similar conceptualizations have been proposed by researchers on treatment delay in general medicine, particularly early cancer diagnosis (see figure 3). These researchers highlight the complexity of the concept of delay in health care, and importantly identify several intervals where obstacles to early treatment may occur (Olesen et al 2009).

Figure 3: The complexities of delay



In summary, several theoretical and technical issues have been raised regarding DUP. Important steps forward have been the developments of several structured and psychometric definitions of DUP, and conceptualization of DUP as comprising several intervals in addition to the patient interval. Further research on pathways to care, DUP and its determinants should focus on ascertaining different aspects of the service interval of treatment delay in first episode psychosis, controlling for the inherent/intrinsic variables such as mode of onset. In addition to research on the association between DUP and outcome, research documenting the usefulness of DUP as an indicator of the quality and efficiency of health care service/systems seems equally important (Mihai, Jordanova, Volpe, & Sartorius, 2016).

2.6 Overview of the literature

This section presents an overview of the research literature on pathways to care in early psychosis and determinants of treatment delay, followed by a summary of important themes.

2.6.1 Pathways to care and DUP

Relevant literature was searched from Medline (Ovid), PsychINFO (Ovid) and Embase (Ovid), using the following search strategy: duration of untreated psychosis OR therapy delay OR delay in treatment OR initiation of treatment AND psychosis OR psychotic disorders OR schizophrenia OR schizoaffective OR schizofreniform AND clinical pathway OR pathways OR pathways to care. The bibliographies of these papers and previously published reviews (listed in table 3) was also scanned to locate additional studies. Only quantitative studies specifically addressing descriptive analysis of pathways to care in relation to DUP were finally selected.

The following studies were reviewed in detail. First author, publication year, location, sample size, sampling source, methods used in data analysis, DUP, pathways indicators, and strength and limitations are presented in table 1. Relevant findings from this review are summarized briefly in the text.

Table 1: Original studies on pathways to care in relation to DUP.

| Authors, Year and Location | Study design | Participants, sources and analysis | DUP and pathways indicators | Strenghts and limitations |
|------------------------------|--------------------------------|---|--|--|
| (Johnstone et al., 1986), UK | Observational, cross-sectional | N = 253 % male =59 % schizophrenia (sz) | DUP = ≤ 8 weeks (w) (n=71), 8-24 w (n=62), 24-52 w | First to highlight delay as a problem. Cohort with 1 year |

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| | | = not stated (ns) Sample = catchment. Patient/family interview. Descriptive frequency analysis, bivariate. | (n=24), ≥ 52 w (n=66). First contact = GP Referral source = ns | delay. Noted some problems with non-consenters. |
| (Harrison et al., 1989), UK | Observational, case-control | N = 131 % male = 65 % sz = 68 Sample = catchment. Patient/family interview and medical records. Descriptive frequency analysis. | DUP = > 6 mo (52%) First contact = helping agencies Referral source = ns | First on afro-caribbean . WHO methodology. Possible information bias in family interviews. |
| (Jablensky et al., 1992), Denmark, UK, India, Ireland, Japan, Colombia, Nigeria, Czech Republic, Russia, USA | Observational, cross-sectional | N = 1379 % male = 55 % sz = ns Sample = multi-site. Patient interview, medical records. Descriptive frequency analysis. | DUP = ≤ 52 w (86%), ≤ 12 w (61%) First contact = psychiatrist Referral source = ns | Multi-site study. Rater reliability assessed. Different cultures and health systems. |
| (Cole, Leavey, King, Johnson-Sabine, & Hoar, 1995), UK | Observational, cross-sectional | N = 93 % male = 54 % sz = 62 Sample = catchment. Patient/family interview and medical records. Descriptive frequency analysis, Bivariate, Logistic regression. | DUP = ≥ 4 (84%) First contact = GP Referral source = na | Retrospective and recall error, statistical power, lack detailed analysis of GP decision. |
| (Lincoln, Harrigan, & McGorry, 1998), Australia | Observational, quantitative and qualitative data, | N = 62 % male = 65 % sz = 52 Sample = specialized service. Patient interview. Descriptive frequency analysis | Mean DUP = 38.9 w First contact = GP Referral source = ns | Retrospective and recall bias, use of WHO encounter form. |
| (Larsen, Johannessen, & Opjordsmoen, 1998), Norway | Observational, cross-sectional, and discussion of 3 case studies with long DUP. | N = 34 % male = 70.6 % sz = 100 Sample = specialized. Patient interview Descriptive frequency analysis, bivariate, logistic regression | Median DUP = 54 w First contact = GP, surgeon, psychologist (3 cases) Referral source = ns | Small sample, few covariates in regression model. |
| (Burnett et al., 1999), UK | Observational, cross-sectional. Comparing ethnic groups. | N = 100 % male = 65 % sz = 100 Sample = catchment. | Median DUP = ns First contact = GP Referral source = ns | Retrospective analysis, not equal groups, recruitment area not |

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| | | Patient/family interview and medical records. Descriptive frequency analysis, bivariate, logistic regression. | | representative for UK population. |
| (Bhugra et al., 2000), Trinidad/UK | Observational, cross-sectional. Comparing ethnic groups. Two samples. | N = 46/38 % male = 57/74 % sz = 100/100 Sample source = psychiatric/criminal. Patient/family interview and medical records. Descriptive frequency analysis, bivariate. | Median DUP = ns First contact = primary care/psychiatrist Referral source = ns | Two sites, no interrater reliability tests, gender distribution different. |
| (Garety & Rigg, 2001), UK | Observational, cross-sectional survey with 1y follow-up | N = 21 % male = 76 % sz = 100 Sample source = psychiatric, catchment. Medical records. Descriptive frequency analysis. | Median DUP = ns First contact = inpatient Referral source = police | Utilized case finding procedures, findings consistent with other studies, retrospective. |
| (Skeate, 2002), UK | Observational. Cross-sectional | N = 42 % male = 76 % sz = 100 Sample = catchment Patient interview. Descriptive frequency analysis, ANOVA. | Median DUP = 15.4 w First contact = GP Referral source = ns | Investigates help-seeking, ordinal DUP, retrospective recall bias. |
| (Fuchs & Steinert, 2002), Germany | Observational, cross-sectional | N = 50 % male = 60 % sz = 100 Sample = catchment, inpatient. Patient interview Descriptive frequency analysis | Median DUP = 8 w First contact = psychiatrist Referral source = | Paper in German, retrospective assessment. |
| (Addington, Van Mastrigt, Hutchinson, & Addington, 2002), Canada | Observational, cross-sectional | N = 86 % male = 66 % sz = 100 Sample = specialized. Patient/family interview. Descriptive frequency analysis. | Median DUP = 27 w First contact = GP Referral source = emergency clinic | Retrospective data. |
| (Scholten & Malla, 2003), Canada | Observational, cross-sectional | N = 134 % male = 74 % sz = 84 Sample = specialized. Patient/family | Median DUP = 19.4 w First contact = ns Referral source = outpatient | Observational, no statistical significances |

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| | | interview and medical records. Descriptive frequency analysis. | | |
| (Yamazawa et al., 2004), Japan | Observational, cross-sectional, two hospital sites compared | N = 83 % male = 42 % sz = 100 Sample = outpatient Medical records. Descriptive frequency analysis, bivariate. | Median DUP = 20 w First contact = direct referral Referral source = police/legal | DUP calculated from date in medical records, only core schizophrenia included |
| (Fuchs & Steinert, 2004), Germany | Observational, cross-sectional | N = 66 % male = 59 % sz = 100 Sample = inpatient. Patient interview. Descriptive frequency analysis, bivariate. | Median DUP = 8 w First contact = psychiatrist Referral source = ns | Retrospective data, but using structured methods, selection bias because only inpatients included |
| (Kohn et al., 2004), Germany | Observational, cross-sectional | N = 80 % male = 73 % sz = 100 Sample = inpatient. Patient interview. Descriptive frequency analysis. | Median DUP = 28.6 w First contact = psychiatrist Referral source = ns | Paper in German, possible selection bias, only inpatients included. |
| (Norman et al., 2004), Canada | Observational, cross-sectional | N = 110 % male = 80 % sz = 76 Sample = specialized. Patient/family interview and medical records. Descriptive frequency analysis, bivariate. | Median DUP = 21.1 w First contact = emergency clinic Referral source = ns | Structured interviews used, investigated two components of delay, |
| (Cognard et al., 2004), France | Observational, cross-sectional | N = 86 % male = 64 % sz = 62 Sample = inpatient. Patient interview. Descriptive frequency analysis, bivariate, logistic regression. | Median DUP = 28 First contact = psychiatrist Referral source = ns | Regression model, median split DUP, possible selection bias because only inpatients, retrospective but multiple sources |
| (Chiang, Chow, & Chan, 2005), China/Hong Kong | Observational, cross-sectional | N = 35 % male = 40 % sz = na Sample = specialized. Patient/family interview. Descriptive frequency analysis, bivariate. | Median DUP = 17.4 w First contact = social worker Referral source = telephone med. | Structured interview, retrospective and possible recall bias, cross checks with other data, small sample |
| (Gill, Koh, & | Observational, cross- | N = 38 | Median DUP = 12 w | Small sample, |

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| Jambunathan, 2005), Malaysia | sectional | % male = 58 % sz = 76 Sample = inpatient. Patient interview. Descriptive frequency analysis. | First contact = inpatient Referral source = ns | skewed outcome, retrospective and possible recall bias, urban sample may limit representativeness |
| (Morgan et al., 2005), UK | Observational, cross- sectional | N = 462 % male = 58 % sz = 74 Sample = catchment. Patient/family interview and medical records. Descriptive frequency analysis, bivariate, logistic regression. | Median DUP = 9 w First contact = GP Referral source = GP | Regression models fitted, with interaction terms, reliance on case notes for a subset of participants. |
| (Chong, 2005), Singapore, a/b | Observational, cross- sectional | N = 112/287 % male = 37/55 % sz = 100/33 Sample = psychiatric, specialized. Patient/family interview. Descriptive frequency analysis, bivariate, linear regression using log transformation. | Median DUP = 48 w First contact = patient/family Referral source = ns | Long DUP, used regression model, retrospective and possible recall bias. |
| (Pek, Mythily, & Chong, 2006), Singapore | Observational, cross- sectional | N = 334 % male = 52 % sz = 68 Sample = specialized. Patient interview. Descriptive frequency analysis, bivariate. | Median DUP = 16 months First contact = family Referral source = ns | Did not use structured instruments to assess DUP, possible recall bias. |
| (Addington & Addington, 2006), Canada | Observational, cross- sectional | N = 373 % male = ns % sz = 75 Sample = specialized. Patient interview. Descriptive frequency analysis, ANOVA. | Median DUP = 19 and 39 weeks First contact = ns Referral source = inpatient | Compared referral sources, longer DUP in outpatient, |
| (Compton, Esterberg, Druss, Walker, & Kaslow, 2006), USA | Observational, cross- sectional | N = 25 % male = 76 % sz = 88 Sample = inpatient. Patient/family interview and medical records. Descriptive frequency analysis. | Median DUP = 32.9 w First contact = mental health Referral source = psychiatrist | First report on pathways in US, structured assessment with one assessor, small sample. Sample not representative. |
| (Platz et al., 2006), Switzerland | Observational, cross- sectional | N = 104 % male = 75 | Median DUP = ns First contact = GP | Prodromal clinic study, structured |

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| | | % sz = ns Sample = specialized. Patient/family interview. Descriptive frequency analysis. | Referral source = ns | assessment of variables, retrospective data and possible recall bias, not manifest psychosis. |
| (Turner, Smith-Hamel, & Mulder, 2006), New Zealand | Observational, cross-sectional | N = 182 % male = 72 % sz = 55 Sample = specialized. Patient interview and criminal records. Descriptive frequency analysis, bivariate. | Median DUP = 4.2 w First contact = inpatient Referral source = inpatient | Representative as recruitment from only clinic in catchment area, retrospective data and recall bias. |
| (Bechard-Evans et al., 2007), Canada | Observational, cross-sectional | N = 98 % male = 69 % sz = 81 Sample = specialized. Patient/family interview and medical records. Descriptive frequency analysis, bivariate, ANOVA, linear regression with log transformation. | Median DUP = 13.1 w First contact = emergency Referral source = ns | Structured assessment, components of DUP analysed, epidemiological representative sample. Many statistical tests performed (familywise error). |
| (Wong, 2007), Hong Kong | Observational, cross-sectional | N = 58 % male = 34.5 % sz = ns Sample = specialized. Family interview. Descriptive frequency analysis. | < 247 w (72%), 24-52 w (12%, >52 w (16%) First contact = social worker Referral source = ns | Interviews with caregivers, convenience sample, structured interviews, retrospective data. |
| (Chien & Compton, 2008), USA | Observational, cross-sectional | N = 76 % male = 68 % sz = 100 Sample = inpatient. Patient/family interview and medical records. Descriptive frequency analysis, bivariate. | Median DUP = 27.7 w First contact = inpatient Referral source = inpatient | Association of mode of onset on DUP and pathways variables. Possible information bias and recall bias because of retrospective data. |
| (Cratsley, Regan, McAllister, Simic, & Aitchison, 2008), UK | Observational, cross-sectional | N = 59 % male = 68 % sz = 66.1 Sample = specialized. Medical records. Descriptive frequency analysis, bivariate, linear regression. | Median DUP = 91 days First contact = ns Referral source = outpatient | Referral route by inpatient liaison and home treatment, related to lower DUP. Small sample and multiple testing. |
| (Razali & Mohd Yasin, 2008), Malaysia | Observational, cross-sectional, comparison of | N = 60 % male = 80 % sz = 100 | Median DUP = ns First contact = traditional healers | Not representative sample, retrospective data and recall bias. |

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| | psychosis and epilepsy referral pathways. | Sample = outpatient. Patient/family interview. Descriptive frequency analysis, bivariate. | Referral source = ns | |
| (Temmingh & Oosthuizen, 2008), South Africa | Observational, cross-sectional | N = 21 % male = 52 % sz = 76 Sample = inpatient. Patient/family interview and medical records. Descriptive frequency analysis, bivariate, ANOVA, effect sizes. | Median DUP = 18 w First contact = GP Referral source = GP | Small sample. Recruitment from inpatient, may not be representative. Retrospective data and recall bias. |
| (Naqvi, Hussain, Zaman, & Islam, 2009), Pakistan | Observational, cross-sectional | N = 93 % male = 59 % sz = ns Sample = inpatient. Patient interview. Descriptive frequency analysis, bivariate. | Median DUP = 14.8 months First contact = psychiatrist Referral source = ns | Data from developing country. Convenience sampling from tertiary hospital. Structured assessments. Possible recall bias. |
| (O'Callaghan et al., 2009), Ireland | Observational, cross-sectional | N = 142 % male = 62 % sz = 74 Sample = specialized. Patient/family interview. Descriptive frequency analysis. | Mean DUP = 82 w First contact = GP Referral source = ns | Analysis of components of delay. Representative sample. Retrospective data and recall bias. Multiple sources. |
| (Sharifi et al., 2009), Iran | Observational, cross-sectional | N = 91 % male = 58 % sz = 74 Sample = inpatient. Patient/family interview. Descriptive frequency analysis, bivariate, linear regression with log transformation. | Median DUP = 11 w First contact = psychiatrist. Referral source = family or health professional. | Data from admitted patients in Iran, Retrospective data with possible recall bias. Multiple sources of data. Not structured assessments. |
| (Archie et al., 2010), Canada | Observational, cross-sectional | N = 200 % male = 78 % sz = 100 Sample = specialized. Patient/family interview and medical records. Descriptive frequency analysis, bivariate, logistic regression. | Median DUP = 22.1 w First contact = physician Referral source = ns | First study of ethnic variation in Canada. Urban study. Structured assessment, Retrospective data. |
| (Shin et al., 2010), | Observational, cross- | N = 18 | Mean DUI = 13 | First study from |

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| Korea | sectional | % male = 72.2 % sz = 0 (ultra-high risk (UHR) sample) Sample = specialized. Patient interview. Descriptive frequency analysis. | months First contact = family, teacher or internet. Referral source = ns | Korea, on adolescents. UHR sample. Small sample. |
| (Lund et al., 2010), South Africa | Observational, cross-sectional | N = 152 % male = 73 % sz = 66 Sample = inpatient. Patient/family interview and medical records. Descriptive frequency analysis. | Median DUP = ns First contact = GP Referral source = ns | Inpatient sample, several exclusion criteria. Retrospective data, but multiple sources. |
| (Boonstra et al., 2012), Netherlands | Observational, cross-sectional | N = 182 % male = 76.9 % sz = 48.9 Sample = specialized. Patient interview. Descriptive frequency analysis, bivariate, GLM to assess confounding. | Median DUP = 8.9 w First contact = GP Referral source = ns | Analysis of components of DUP. Uses NOS-DUP. Rural and urban sample. Retrospective data, but structured assessment and multiple sources. |
| (Lihong et al., 2012), Japan | Observational, cross-sectional | N = 108 % male = 47 % sz = 100 Sample = inpatient and outpatient. Medical records. Descriptive frequency analysis, bivariate, linear regression with no transformation. | Median DUP = 10.5 months First contact = inpatient Referral source = family | Long DUP. Both inpatient and outpatient, representative sample. Only medical records used. Did not include premorbid function in regression, confounding. |
| (Anderson, Fuhrer, Schmitz, & Malla, 2013), Canada | Observational, cross-sectional | N = 324 % male = 69.8 % sz = 71.3 Sample = specialized Patient/family interview and medical records. Descriptive frequency analysis, bivariate, logistic regression. | Median DUP = 16.4 w First contact = emergency Referral source = emergency | Study of determinants of negative pathways and subsequent engagement. Recruitment to specialized service, may not be representative. Retrospective data, but structured assessment and multiple sources. |
| (Ghali et al., 2013), UK | Observational, cross-sectional | N = 1024 % male = 65 % sz = na Sample = specialized. Patient interview. Descriptive frequency analysis, | Median DUP = 11.5 weeks (treatment DUP), 16 weeks (service DUP) First contact = GP and emergency Referral source = ns | Ethnic variation in early intervention context. Reports on service DUP. Reports on selection bias, sampling bias, measurement bias |

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| | | bivariate, ANOVA, multivariate regression adjusting for covariates. | | (recall) and missing data analysis. |
| (Birchwood et al., 2013a), UK | Observational, cross-sectional | N = 343 % male = 73 % sz = 66 Sample = specialized. Patient/family interview and medical records. Descriptive frequency analysis, bivariate, log transformation, ANOVA. | Median DUP = 50 days First contact = ns Referral source = community mental health | Reports on components of DUP. Greatest contribution from service delay. 30% non-consenters. Retrospective data, possible recall bias. |
| (Cocchi et al., 2013), Italy | Observational, prospective over 11 years. 110 FEP and 96 UHR patients. | N = 206 (110 FEP/96 UHR) % male = 82 (FEP) % sz = ns Sample = catchment. Patient/family interview and medical records. Descriptive frequency analysis, bivariate. | Mean DUP = 160.5 days for 110 FEP patients. First contact = public/private mental health center Referral source = ns | UHR and FEP patients followed for 11 years. |
| (Adeosun, Adegbohun, Adewumi, & Jeje, 2013), Nigeria | Observational, cross-sectional | N = 138 % male = 39.9 % sz = ns Sample = inpatient. Patient interview. Descriptive frequency analysis. | Median DUP = 38 w First contact = traditional/religious healers Referral source = ns | Understudied population. Good interrater reliability Structured assessments were not used, recall bias unknown, . |
| (Fridgen et al., 2013), Germany | Observational, cross-sectional, UHR and FEP patients. | N = 61 (UHR), 37 (FEP) % male = 59/67.6 % sz = ns Sample = specialized. Patient interview. Descriptive frequency analysis, bivariate. | Median DUI = 3.4 years, DUP = 12 months (FEP) First contact = family/relative Referral source = medical institutions | Retrospective data and possible recall bias. Small sample size and limitations on statistical analysis. Patients may be treated in private practice, may not be representative sample. |
| (Ehmann et al., 2013), Canada | Observational, cross-sectional | N = 104 % male = 67 % sz = 55 Sample = specialized. Patient/family interview. Descriptive frequency analysis, bivariate. | Median DUP = 30.5 w First contact = community service Referral source = ns | Comparison of community and inpatient pathways. Recruitment from several sources. |
| (Bhui, Ullrich, & Coid, 2014), UK. | Observational, cross-sectional | N = 480 N male = 294 N sz = 165 | Median DUP = 3 months First contact = | Investigating which pathway is related to shorter DUP. Large |

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| | | Sample = catchment. Patient interview and medical records. Descriptive frequency analysis, bivariate, Poisson regression. | primary care (GP) Referral source = ns | sample. Structured instruments. Retrospective data and cross-sectional design. |
| (Odinka et al., 2014), Nigeria | Observational, cross-sectional | N = 360 % male = ns % sz = ns Sample = catchment, inpatients. Patient interview. Descriptive frequency analysis, bivariate, logistic regression. | Median DUP = 48 w First contact = faith based healers Referral source = ns | Culturally influenced beliefs on the causes of schizophrenia may contribute to treatment delay. Possible confounders noted as limitation. |
| (Singh et al., 2015), UK. | Observational, cross-sectional | N = 123 % Male = 74 % sz = 71.8 Sample = catchment Patient/family interview and medical records Descriptive frequency analysis, bivariate, adjusted logistic regression. | DUP = ≤ 6 mo = 39.4%, > 6 mo = 61% First contact = ns Referral source = ns | First study examining ethnic variations in pathways to care and how they are influenced by illness attributions and other confounders. Small sample, possible selection and information bias noted as limitations. |
| (Tomita et al., 2015), South Africa. | Observational, cross-sectional | N = 57 % male = 64.9 % sz = 45.6 Sample = inpatient. Patient interview. Descriptive frequency analysis, bivariate, adjusted poisson regression. | Median DUP = ns First contact = general hospital Referral source = ns | Traditiona health practitioners often contacted during pathways and related to treatment delay. |
| (Chesney, Abdin, Poon, Subramaniam, & Verma, 2016), Singapore | Observational, cross-sectional | N = 900 % male = 49.7 % sz = 42.9 Sample = Patient/family interview and medical records. Descriptive frequency analysis, bivariate, linear regression. | Median DUP = 5 months First contact = specialist health, inpatient Referral source = ns | Large study. Some patients treated in private practice, possibly not included. Tertiary treatment center, may possibly have selection bias. Potential information bias noted. |

Summary:

This review includes studies from many different countries and diverse healthcare contexts. Several pathways indicators are reported on, although most frequently reported is point of entry and which contact made the referral to mental health services. A main finding

is that the pathways to care taken by FEP patients is largely dependent on the specific healthcare context. In most European studies the General Practitioner (GP) is the first contact, in the US and Japan hospitals are often the first contact, in China/Hong Kong social workers are contacted, while in many developing countries a traditional healer is the first contact after the onset of psychosis. The importance of geographical region as a determinant of pathways, indicate that differences in social, cultural and specific healthcare system are important determinants of the pathway taken.

Regarding DUP there is also great variability in reported median values. This ranges from 4 weeks in a study from New Zealand (Turner et al., 2006), to 48 weeks in a study conducted in Nigeria (Odinka et al., 2014). This may also be related to issues of representativeness. Several studies are based on special samples and not units with catchment area responsibilities. This makes generalizability to ordinary clinical samples difficult. In addition, few studies report on the rate of patient refusals, also important for analysis of representativeness. Although the patient delay/interval is noted to contribute significantly to DUP in many studies, several recent studies from European countries report significant service/system delay. In some studies, this delay contributes almost as much as the patient interval. The reasons for this delay is unclear.

This review raises several important questions. Given the importance of healthcare context, are there also local and regional differences? Can difference in geographical context influence pathways and treatment delay? The GP is an important point of entry, but do they recognize the early presentation of psychosis? When do they decide to refer? A recent finding is that delay after entry to mental health services is sometimes considerable, what are possible the reasons for this delay?

2.6.2 Determinants of DUP

The literature before 2008 has already been reviewed by (Compton & Broussard, 2011). The search term «duration of untreated psychosis» and «determinants», «predictors» and «correlates» was used to locate additional original research and review articles. Only quantitative studies specifically addressing predictors of DUP were eventually selected.

The following studies were reviewed in detail. First author, publication year, location, sample size, DUP, methods used in data analysis, significant determinants of DUP, and

strengths and limitations are presented in table 2. Relevant findings from this review are summarized briefly in the text.

Table 2: Original studies on the determinants of DUP

| Authors, Year and Location | Participants, DUP (median), and analysis | Significant determinants of DUP | Strengths and limitations |
|---|---|---|---|
| (Larsen et al., 1998), Norway. | N = 34 DUP = 54 w Descriptive frequency analysis, bivariate, logistic regression. | Demographic (older age at admission, unemployment, few friends), Function (low GAF score), Clinical (active social avoidance). | Small sample, few covariates in regression model. |
| (Verdoux et al., 1998), France. | N = 59 DUP = 12 w Descriptive frequency analysis, bivariate, logistic regression. | Demographic (low education level), Family/social (family history of psychiatric hospitalization), Function (low GAF). | Possible selection bias, but tested in subsidiary study. Retrospective data, no standardized assessment. |
| (Møller, 2000), Norway. | N = 19 DUP = ns Descriptive frequency analysis. | Mode of onset. | Comparison long and short DUP (cutoff 6 mo). Mode of initial psychosis development |
| (Drake, 2000), UK | N = 248 DUP = 12 w Descriptive frequency analysis, log transformation, ANOVA. | Family/social (social integration, coping, lack of insight, avolition, preoccupation, hostility) Clinical (PANSS total, positive, general psychopathology, low SFS). | Inpatients, retrospective data, possible selection and information bias. |
| (Barnes, 2000), UK. | N = 53 DUP = 26 w Descriptive frequency analysis, bivariate. | Demographic (older age at admission). | Small sample, few variables included, retrospective data. |
| (Skeate, 2002), UK. | N = 42 DUP = 15.4 w Descriptive frequency analysis, ANOVA. | Clinical (avoidance), Pathways (inconsistent visits to GP). | Small sample, retrospective data. |
| (Kalla et al., 2002), Finland/Spain. | N = 86 DUP = 8 w Descriptive frequency analysis, bivariate. | Function (poor global, labor incapacity), Clinical (schizophrenia diagnosis), Mode of onset. | Two different samples, urban and rural, inpatient and outpatient, variation in diagnostic practice. |
| (Haley, Drake, Bentall, & Lewis, 2003), UK. | N = 50 DUP = 8 w Descriptive frequency analysis, ANOVA. | Clinical (internal locus of control). | |
| (Yamazawa et al., 2004), Japan. | N = 83 DUP = 20 w Descriptive frequency analysis, bivariate. | Demographic (unemployment). | Data on variables from records, no structured assessments. |
| (Chen et al., 2005), China, Hong kong. | N = 131 DUP = 20 w Descriptive frequency | Function (less secondary school), Family (no family history of | Retrospective, but structured assessments. |

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| | analysis, bivariate, logistic regression. | schizophrenia), Clinical (schizophrenia diagnosis), Mode of onset. | |
| (Chong, 2005), Singapore. | N = 112 DUP = 48 w Descriptive frequency analysis. Linear regression model fitted. | Demographic (single marital status, male gender), Function (tertiary education). | Long DUP, used regression model, retrospective and possible recall bias. |
| (Peralta, Cuesta, Martinez-Larrea, Serrano, & Langarica, 2005), Spain. | N = 100 DUP = 157.6 w Descriptive frequency analysis, logistic regression. | Function (poor work/academic support). | Retrospective data (recall bias) and inpatient sample. |
| (Pek et al., 2006), Singapore. | N = 334 DUP = 16 w Descriptive frequency analysis, bivariate. | Demographic (single marital, unemployment), Function (lower GAF), Clinical (schizophrenia diagnosis, lower level insight), Pathways (police involvement). | Did not use structured instruments to assess DUP, possible recall bias. |
| (Morgan et al., 2006), UK. | N = 495 DUP = 9 w Descriptive frequency analysis, bivariate, Cox regression. | Demographic (unemployment), Family/social (no family involvement in help seeking), Mode of onset. | Both inherent and contextual in model, noted possible confounders. |
| (Moss, Fleck, & Strakowski, 2006), USA. | N = 195 DUP = ns Descriptive frequency analysis. | Religion (protestant). | |
| (Bechard-Evans et al., 2007), Canada. | N = 98 DUP = 13.1 w Descriptive frequency analysis, ANOVA, linear regression with log transformation. | DUP HS: Demographic (age at onset), Clinical (schizophrenia diagnosis, psychomotor poverty), Premorbid (lower PAS social), DUP R: Demographic (ethnicity- non caucasian), Age at onset, Clinical (disorganization). | Structured assessment, components of DUP analysed, epidemiological representative sample. Many statistical tests performed (familywise error). |
| (Clarke, Browne, McTigue, Gervin, & 2007, 2007), Ireland. | N = 166 DUP = 20 w Descriptive frequency analysis. | Function (social withdrawal) Clinical (diagnosis of schizophrenia/schizofreniform). | |
| (Large, Nielssen, Ryan, & Hayes, 2008), Western countries | N = 5849 DUP = 79.5w/55.6w Descriptive frequency analysis, bivariate and linear regression with log | Health system (obligatory dangerous criterion in mental health laws). | Several limitations noted. Could not control for possible confounders. |

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| | transformation. | | |
| (Goulding et al., 2008), USA. | N = 34 DUP = 38.1 w Descriptive frequency analysis, bivariate. | Family/social (lower family strength total + accord sub scale. | Small sample, cross-sectional assessment and retrospective bias. |
| (Compton, Chien, Leiner, Goulding, & Weiss, 2008), USA. | N = 73 DUP = 23.4 w Descriptive frequency analysis, cox regression. | Family/social (family involvement in help-seeking) Mode of onset. | Inpatients, retrospective data. But consensus assessments. |
| (Compton et al., 2009)a, USA. | N = 42 DUP = 24.5 w Descriptive frequency analysis, Cox regression. | Health service (lack of insurance, financial problems, barriers to help-seeking). | Inpatients, small sample, non-consenters and information bias. |
| (Compton, Goulding, Gordon, Weiss, & Kaslow, 2009)b, USA. | N = 42 DUP = 24.5 w Descriptive frequency analysis, Cox regression. | Family/social (lower family strength, lower family coping, perceived caregiver strain) Clinical (higher insight). | Inpatients, small sample, non-consenters and information bias. |
| (Nishii et al., 2010), Japan. | N = 150 DUP = 6 months Descriptive frequency analysis, bivariate. | Mode of onset. | Inpatient sample, urban area, retrospective data. |
| (Broussard et al., 2013), USA. | N = 180 DUP = ns Descriptive frequency analysis, linear regression. | Function (prior incarceration), Clinical (premorbid cannabis use, level of alcohol use, level of childhood/adolescence maltreatment), Mode of onset. | Narrow demographic sample (generalizability) and in subset could not estimate mode of onset. |
| (Apeldoorn et al., 2014), Netherlands. | N = 852 DUP = <1 month Descriptive frequency analysis, ordinal logistic regression. | Demographic (male gender, migration status), Age at onset. | Large sample, representative, standardized assessments. Retrospective bias. |
| (Kini, Tharayil, Prabhavathy, & Haridas, 2015), India. | N = 45 DUP = ns Descriptive frequency analysis, bivariate. | Brief DUP related to lower age, higher educational status, acute onset, higher negative symptoms or general psychopathology. | Small sample. No structured assessments of DUP. Retrospective data. |
| (Okasha et al., 2016), Egypt. | N = 100 DUP = 36.93 months Descriptive frequency analysis, linear regression. | Demographic (age, residence, being illiterate) Family (negative family history), Clinical (PANSS positive and negative scores; severity), Age at onset, Mode of onset. | Cross sectional, retrospective and recall bias. |
| (Hastrup, Haahr, Jansen, & Simonsen, 2017), Denmark. | N = 1266 DUP = > 12 months (32.8%) Descriptive frequency analysis, multinomial regression. | Demographic (male gender, rural status- living in peripheral municipality), Clinical (cannabis use), Age at onset. | Large study, differences in DUP assessments possible, errors across units/regions. |

Summary:

The reviewed studies demonstrate that there is strong evidence for several intrinsic (illness/patient level) predictors of DUP, and only a few studies substantiating the importance of extrinsic (service/system level) predictors. Demographic variables (e.g., unemployment), clinical variables (e.g., schizophrenia diagnosis), proxy variables for social network (living alone, low family support), premorbid status (poor social and global function), age at onset (adolescence onset) and an insidious mode of onset are all important determinants and associated with longer DUP. Particularly the three predictors premorbid change, age at onset and mode of onset have a robust evidence base (Brunet & Birchwood, 2010).

Few studies have specifically investigated service or system level variables. One study found lack of insurance as a predictor (Compton et al., 2009a), while another study found that service systems with an obligatory dangerous criterion in relation to involuntary treatment was associated with longer DUP (Large et al., 2008). Several of the reviewed studies suggest that inefficiency on the part of the service provider (e.g., lack of knowledge of early psychosis, diagnostic delay) is possibly related to longer DUP.

There are very few studies specifically addressing service or system level predictors of DUP, although several suggest that inefficiency on the part of the service providers can potentially delay treatment. Can how assessments are conducted in mental health care contribute to treatment delay? Can the structures of health services and the location of treatment facilities contribute to treatment delay?

2.6.3 Reviews on pathways to care studies

Table 3 summarizes previous meta-analyses and reviews regarding pathways to care in relation to DUP. These reviews highlight the challenges in comparing studies due to methodological differences and contextual factors. Recent reviews emphasize the importance on differentiating the components of delay, which may have different determinants and require specific strategies of intervention.

Table 3: Reviews and meta-analysis of pathways to care and DUP

| Authors, Year | Number of studies | Main topic of review | Conclusion | Comments |
|---------------------------|---|--|---|-------------------------------------|
| (Lincoln & McGorry, 1995) | Non-systematic review of studies between 1977-1995. Six studies | Pathways to care in first episode psychosis. | Evidence of extensive delays. Understanding of help-seeking and | Non-systematic review. Few studies. |

| | | | | |
|---------------------------|---|--|---|--|
| | highlighted. | | referral pathways limited. Studies suggest factors affecting access to treatment are important. | |
| (Lincoln & McGorry, 1999) | Non-systematic review of studies | Pathways to care in early psychosis. | Authors emphasize complementing the clinical-epidemiological perspective with data on consumer experiences. Highlights promoting early access by making services more accessible and user friendly. | Non-systematic review. Few studies. Highlights accessibility. |
| (Singh & Grange, 2006) | 15 studies reviewed (between 1989-2005). | Pathways to care studies and methods for assessing the pathways to care construct in first episode psychosis. | Several measures are used, but none with established psychometric properties. Lack of theoretical and conceptual framework. Conflict between empirical study of healthcare utilization and its predictors, and the patients narrative of gaining access to health care. | Systematic review, but meta-analysis impossible because of heterogeneity in measurements used. |
| (Norman & Malla, 2009) | Non-systematic review of studies | The nature and determinants of pathways. Determinants of delay. Interventions evaluated for effectiveness in reducing delay. | Highlights factors related to service providers in determining delay. Emphasize on efforts at developing better early intervention. | Highlights different components of delay. Lacuna in research on delay in rural areas. |
| (Anderson et al., 2010) | 30 studies reviewed (period between 1985-2009). | The nature and determinants of pathways to care in first episode psychosis. | First contact after onset of psychosis is most often a physician (GP, psychiatrist, outpatient mental health). Referral source (to mental health) is most often emergency services (emergency clinic, crisis team, inpatient). | No meta-analysis because of clinical, statistical and contextual heterogeneity. Descriptive synthesis of data. No validated tool for measuring pathways to care construct. |

| | | | | |
|---|---|---|---|--|
| | | | No consistent result on determinants of pathways. No consistent results on impact of pathways on treatment delay. | |
| (Anderson et al., 2010) | 7 studies | Meta-analysis of studies examining ethnic variations in pathways to care at first episode psychosis. | Evidence for ethnic differences in likelihood of involuntary admission. Effect modification of socio-demographic factors noted. | Ethnic variation is an important determinant of pathways. |
| (Brunet & Birchwood, 2010) | Non-systematic review of studies. | Duration of untreated psychosis and pathways to care. | Reviews evidence for the importance of specialized services for first episode psychosis. Highlights local audits to identify pathway barriers and to target interventions. | Reviews robust evidence for the "three factors" (poor premorbid functioning, gradual development of early signs, and adolescent onset) as determinants of DUP. |
| (Boydell, Stasiulis, Volpe, & Gladstone, 2010) | 31 papers identified by systematic search of databases. | Descriptive review of qualitative studies in first episode psychosis. | Majority of studies concern patients in community settings. Studies exist on patients, their families and service providers. | Several studies on the subjective experience of illness, help-seeking and receiving help. Lack theoretical framework, and there are methodological problems. |
| (Compton & Broussard, 2011) | 18 studies specifically addressing predictors of DUP | Overview of studies reporting on potential determinants of DUP. Review of studies specifically addressing predictors. | Classification of predictors in 6 categories: Demographic, Premorbid and onset, Illness, Family level, Societal, Health service/system level. More sophisticated statistical modeling needed, controlling for several factors in samples. | Less research on the determinants of DUP. Provides a conceptual model, useful for later studies. |
| (Schaffner, Schimmelmann, Niedersteberg, & Schultze-Lutter, 2012) | 25 studies | Overview of international studies. Highlights help-seeking behavior and predictors of DUP. | Evidence of DUP at about one year. On average 3 help-seeking contacts before adequate treatment. Negative factors on all levels (patient, social and | Reviews studies from 1986-2009. Paper in German. |

| | | | | |
|---|------------------------------|---|---|---|
| | | | system level). | |
| (Volpe et al., 2015) | 8 studies | Systematic review of studies on the pathways to care for adult patients using standardized methodology. | Found significant differences among different countries and regions within the same country. The role of primary care and gatekeepers are highlighted. | Mean help-seeking delay was 10.5 weeks, system delay was 5.8 weeks, and total delay was 16.3 weeks. First-contact was a general practitioner for 39 % of cases. |
| (Murru & Carpiniello, 2016) | Selective review of studies. | Overview of studies on DUI and DUP. | DUP associated with outcome, comorbidity and response to treatment. Research should evolve from a unidimensional to a multidimensional DUP construct. | DUI and DUP are multidimensional constructs that imply both intrinsic (mode of onset) and extrinsic (access to services) factors. |
| (Gronholm, Thornicroft, Laurens, & Evans-Lacko, 2017) | 40 studies. | Systematic review of stigma and pathways to care in UHR and FEP populations. | Included both quantitative and qualitative studies. Presents a meta-synthesis and overview of the complex ways stigma influence help-seeking and service contact in UHR and FEP patients. | Stigma related processes is important determinant of delay in help-seeking and DUP. |

2.7 What is still unclear?

This literature review of international studies indicates that many patients with early psychosis are detected and treated late in their course of illness. Treatment delay can occur prior to and after service entry, and be determined by both intrinsic (illness and patient level) and extrinsic (service and system level) factors. The service/system interval of DUP is largely unexplored, even though recent studies have documented its importance. The Norwegian healthcare context, in its rural configuration, offers a unique opportunity to investigate these aspects of the DUP. Similarities in socioeconomic, demographic between catchment areas, and absence of private providers and a national healthcare system helps rule out many confounders. This specific health care context has been the context several previous health service studies, reviewed by Hansen & Øiesvold (2004). No previous studies on DUP and its determinants have been conducted in this setting. Therefore, it was interesting and important to conduct this study.

3.0 Aims of the thesis

We wanted to provide a descriptive epidemiology of the pathways to care in first episode patients in Nordland county, investigate the community-level DUP in this population, explore potential reasons for delay occurring after service entry, and test whether treatment delay is co-determined by service and system level factors. By understanding where and why treatment delays occur we may be better able to design interventions to facilitate earlier detection and treatment.

The specific aims were:

1) To assess clinical, help-seeking and pathways indicators in treated patients in Nordland county. To explore the associations between geographical accessibility of specialist psychiatric acute wards and overall DUP, and the association between mode of initial presentation and service delay, controlling for other known risk factors.

2) To study the service providers perspective on the reasons for treatment delay in community mental health. To explore the challenges service providers experience in engaging patients with FEP, and what they are doing to meet this.

3) To study General Practitioners with a gate-keeping function to specialist care in a rural part of Northern Norway. To explore the level of diagnostic knowledge and referral practices to mental health services.

4.0 Material and methods

4.1 Study design

The theoretical model indicates that treatment delay can occur at different intervals. As we wanted both a descriptive epidemiology of the general pattern of pathways, and more in-depth information on the different intervals, a mixed methods design including both quantitative and qualitative research methods was chosen (Creswell, 2014). Data was collected from three different populations.

4.2 Study populations

4.2.1 Sample 1: Treated patients

Study population

The population for Papers I and II consisted of consecutive recent onset psychosis patients (aged 16-35 years) in contact with mental health services in the county of Nordland in northern Norway, during September 2010 - September 2013. According to epidemiological studies, the treated incidence rate for the population at risk (16-35 years) is 12-16 per 100 000/year (Jablensky et al., 1992). According to these estimates, in Nordland county, with a population of 240,000, the eligible study population would be between 86 and 115 persons.

Study sample

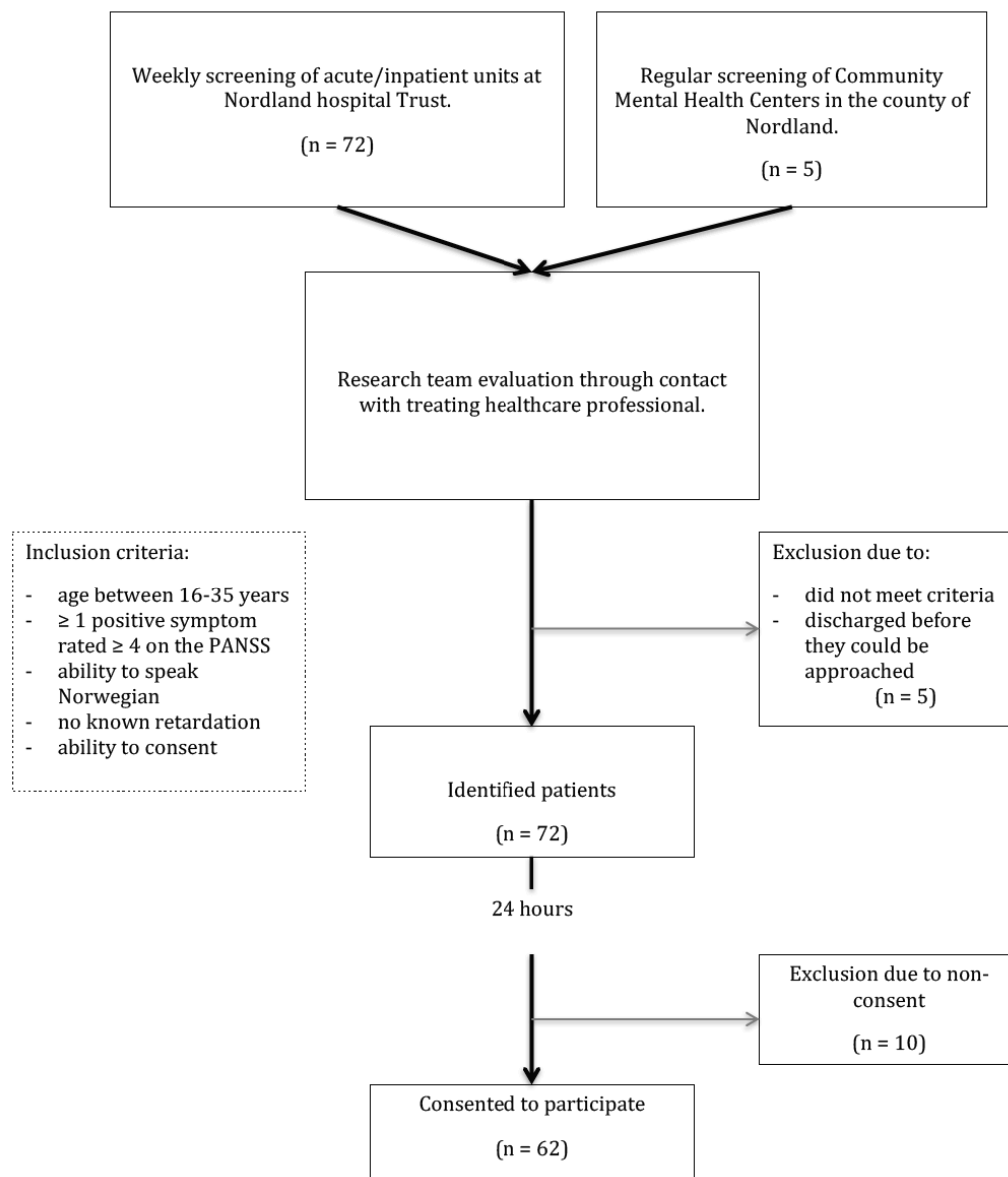
During the study, 77 patients were referred and 72 were asked to participate (2 patients did not meet inclusion criteria and 3 were discharged before they could be approached). Overall 62 (86 %) of these patients agreed to participate. The patient sample is characterized in Paper I, p. 5. The treated incidence rate based on our sample is 10 per 100 000/year. This somewhat lower incidence rate could be due to deficient case finding procedures, a lower incidence number in rural areas (McGrath et al, 2004), or lower availability and use of mental health services in this region.

Recruitment and sampling procedures

Participants were recruited from inpatient/acute wards at the Central hospital and 7 Community Mental Health Centers (CMHC) located in Nordland county. The acute wards were screened weekly, and the community centers were contacted regularly for recent onset psychosis patients. In cases where the screening procedure identified potential participants, the treating health care professional was contacted the same or following day for evaluation of inclusion/exclusion criteria, and if the patient could be approached by the research team. No patients were acutely ill when interviewed. If their treating health care professional assessed that patients were too unwell to participate, they were contacted again after stabilization or initiation of treatment.

Eligible patients were approached with information about the study (appendix 2a), and given 24 hours to decide if he/she wants to participate in the study. Written informed consent was obtained to administer the clinical assessments (appendix 2b).

Figure 4: Sample selection for treated patients



Refusers

Background information on non-responding patients were collected during screening. Only information on age (year of contact minus the year of birth), gender, municipality (zip code) and referral source was collected. Comparison between responders and refusers is

shown in table 4.

Table 4: Comparison of consenters and refusers

| | Consenters (n = 62) | Refusers (n = 10) | P ¹ value |
|------------------------|---------------------|-------------------|----------------------|
| Age, mean (s.d.) | 23.6 (4.8) | 25.6 (5.4) | 0.23 |
| Male gender (%) | 71 | 50 | 0.19 |
| Rural living place (%) | 53.2 | 70 | 0.32 |
| Inpatient referral (%) | 100 | 0 | - |

¹ Comparisons were calculated using Chi square tests for proportions and t-tests for means.

Materials and data collection

Interview schedule

Participants were assessed using a battery of standardized assessments, including the Client Socio-Demographic and Service Receipt Inventory (CSSRI, (Chisholm et al., 2000)), the Nottingham Onset Schedule-DUP version (NOS-DUP, (Singh et al., 2005)), the Gater Encounter form (Gater et al., 1991), the Premorbid Adjustment Scale (PAS,(Cannon-Spoor, Potkin, & Wyatt, 1982)), the Route Timeline (Birchwood et al., 2013a), and the OPCRIT+ checklist (Rucker et al., 2011). The assessment battery is presented i paper I, p. 2-3, and in appendix 3a-c.

Design of materials

The assessment procedure was constructed with three parts: a pre-interview schedule, a semi-structured interview and a post-interview schedule. In addition, research diagnoses were assigned through a best estimate consensus procedure (described in paper I, p. 3 and paper II, p. 2).

Pre-interview: Before approaching the patient, information recorded in the Preliminary Assessment Form of the NOS-DUP and the CSSRI was completed. The treating health care professional was the informant for this part of the assessment schedule.

Semi-structured interview: A timeline was constructed based on a social history interview (Lyketsos, Nestadt, Cwi, Heithoff, & Eaton, 1994) and used as a life calendar where memory cues (key events and anchor dates) were used to cross-check other themes (Belli, 1998). Ratings were made on premorbid function (the PAS), the development of symptoms, lifetime

psychopathology, the four crucial dates of the NOS-DUP (onset of non-diagnostic symptoms, first psychotic symptom, first episode of psychosis and treatment compliance), help-seeking/consulting behavior, and the responses to these effort (the Gater encounter form). A card sort procedure was used to identify emerging non-specific and psychotic symptoms during the course of illness. The interview lasted from 1.5 to 2 hours.

Post-interview: Different sources of information was later used to triangulate the information, resulting in more depth of information than could be obtained by interviews alone. Sources of information used was case notes, medical records, referral letters from GPs, telephone interviews with key or family informant, and interviews with the treating health care professionals. A visual route timeline detailing the treatment history and help-seeking/consulting behavior was constructed. During this phase, all the encounter forms were sequenced chronologically and the relevant pathways number was added. Finally, each contact was coded in relation to the phase in which help was sought.

A mid-point dating rule was used to date onset of symptoms and encounters (Perkins et al., 2000). When a participant can not specify the exact month and or year a symptom or an encounter began, the midpoint takes the middle date for the range given by the participant. E.g. the mid-point for winter (December, January, February) is January, the mid-point for sometimes in 1999 is July 1999, and if given only the month this is taken to mean the middle day of that month, i.e. the 15th.

For the OPCRIT+ ratings, all data from assessments, referral letters and case notes from medical files were available to the principal investigator and an experienced psychiatrist blinded to the individual characteristics of the participant. The OPCRIT+ rating form was independently completed by both raters, and subsequently subjected to consensus discussions.

Data entry

A scoring manual and paper entry form were designed for all data. Data were entered using a single-entry approach with two different people to eliminate errors. The software package, SPSS, version 21 for Macintosh, was used for data entry and data analysis. Cleaning, recoding and calculating derived variables was performed using SPSS.

Data analysis

The main statistical analysis performed in Paper I and II are described in the following.

Exploring and transforming variables

Distribution of outcome

In Paper I the primary outcome variable was overall DUP whereas in Paper II the primary outcome was the service delay component of DUP. In the preliminary analysis, the distribution of both outcome variables, were explored. The commonly found skewed DUP distribution was also found in this sample. The normality assumption of parametric statistical tests was therefore violated, and necessitated the use of non-parametric tests. For the analysis, we made a categorical division by defining an outlier cohort using the median split as cutoff. In paper II, service delay was also transformed into a dichotomous variable using a median split.

Transforming variables

For the statistical analysis, several variables were transformed. This is presented in Paper I on p. 3-4, and in Paper II on p. 3.

Bivariate analysis

Predictors were chosen on the basis of previous studies on the determinants of DUP. Non-parametric test were used in bivariate analysis of outcome and predictors, using Chi squared and Kruskal-Wallis test for categorial variables, and Mann-Whitney U and Spearman rho for continuous variables.

Multivariable statistical analysis

Constructing the model

Multivariable logistic regression models were constructed in both Paper I and Paper II, to test the association between predictors and outcome variables, alone and adjusted for other known predictors of DUP. The assumptions for logistic regression, linearity between continuous predictors and outcome, independence of errors (overdispersion), and multicollinearity were checked before performing the analysis (Field, 2013). We also performed multiway cross tabulations of all categorical independent variables, checking that each cell had greater than 1 and no more than 20% are less than 5, to ensure we did not have

incomplete information from the predictors.

The predictors with known clinical importance and the variables of interest were entered in bivariate analysis with the outcome variables. Non-parametric tests were used in bivariate analysis. All tests were two-tailed with a significance level of .05.

In constructing the regression models, we first included one predictor at a time, analyzing fits with the estimated coefficients, standard errors and the likelihood ratio test for the significance of coefficient. Predictors were then entered hierarchically (blockwise entry).

Assessing model fit/strength of covariates

Model fit and strength of covariates was assessed using R statistics, the likelihood ratio test and Wald statistics. In Paper I and II Hosmer & Lemeshow, Cox & Snell and Nagelkerke statistics were also reported.

Regression diagnostics

The following regression diagnostics were performed in Paper I and II. Examination of residual statistics (Cook's distance, Leverage, Standardized residuals, DFBeta values) were used to examine influential cases and outliers. Linearity of logit was examined by the interaction between the continuous variable and outcome. Test for multicollinearity was performed by a linear regression analysis with the same outcome and predictors.

Interaction terms

Interaction was checked by adding an interaction term to the final model. Testing for interaction was done in Paper I and is presented in Paper I (p. 4). If the interaction term was non-significant, according to Wald statistics and likelihood ratio test, it was dropped from the reported model.

4.2.2 Sample 2: Community practitioners

Study population

The population for Paper III was service providers working in one of 7 Community Mental Health Centers (CMHC) in Nordland county during the study period 2010-2011. Two of the sites had the same administration, but was situated at two different locations. The population comprised both adult and child and adolescent mental health services. The sites served populations of 13 000 to 74 000 people, and the number of municipalities served varied between 4-9. The service providers had different professional backgrounds: medical doctors, psychiatrists, psychologist, nurses and others with at least 3-year educations in health care. Each site employed between 45 to 100 healthcare professionals, involved in outpatient, inpatient and ambulatory services.

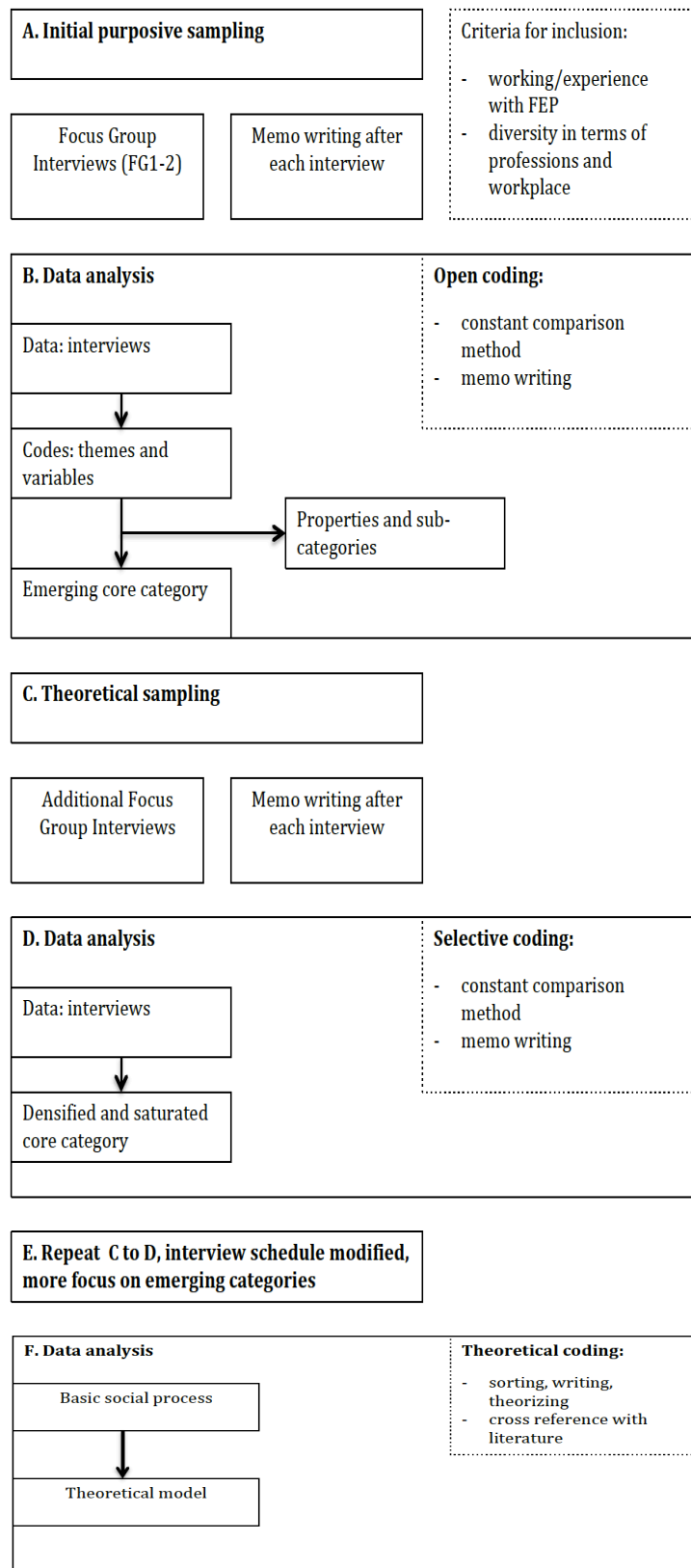
Study sample

The study sample comprised 33 healthcare professionals. The characteristics of the participants are presented in Paper III, p. 3. Each focus group interview had 2-7 participants. In most groups, there was diversity in terms of age, gender, professional background and work place (i.e. adult or child and adolescent mental health).

Recruitment and sampling procedures

An invitation letter was sent by e-mail to center leaders where we asked each to suggest from 5-8 participants for each focus group (appendix 2c). We used a purposeful sampling procedure, asking the leaders to suggest participants who had a special interest and regularly worked with patients experiencing FEP. We also asked that the suggested participants were diverse in terms of age, gender, professional background and workplace. In addition to the invitation letter, an interview guide with several predetermined themes, a declaration of consent, and information booklet on the different parts of the research project was included in the e-mail (appendix 2d and 4b). The invitation letter and declaration of consent was drafted according to the recommendations of the Regional Ethics Committee (appendix 1). A member of the research team telephoned center leaders one week after the letter was sent, and made specific appointments for conducting the focus group interviews. All the focus groups were conducted at the CMHCs.

Figure 5: Sampling procedure for community practitioner sample



Materials and data collection

Interview guide and design of materials

An interview guide was developed for the initial focus group interviews. We based this on an interview guide used in a similar qualitative research project conducted in Birmingham, The National Eden Project (Birchwood et al., 2013b). As this project was evaluating the implementation of Early Intervention Services in Birmingham, UK, several changes had to be made to make it useful in our setting. Our basic research question was more open ended, and not concerned with evaluating a specific service approach. We stated the research question as: «what are the challenges that providers experience in assessing patient status and engaging them during the early phases of psychosis?», and «what are healthcare professionals doing to meet this?».

Questionnaire

A questionnaire detailing information on gender, age, professional background and years of experience (appendix 4a), was administered to participants before each focus group together with the declaration of consent (appendix 2d).

Data collection

Focus groups were conducted by a main moderator (first author of Paper III) and an assistant moderator/observer (second author). The moderators role was to facilitate the interaction between participants, stimulate debate, and encourage elaborations and to ensure that all participants took part in the discussion. The assistant moderator made field notes and observations during the interview. The focus groups lasted from 90 to 120 min. We used items in the interview guide as probes for discussions. The same interview guide was used for the first, second and third interview, but was revised as the core category emerged from the data analysis. Theoretical sampling was used to sample new data that could test or fill out emerging codes and categories.

Data entry

All the interviews were audio recorded and transcribed immediately after they were completed by a research assistant. Audio files and transcripts were entered into the NVivo 9 software package for analysis.

Data analysis

The sampling and data analysis process is summarized in table 5. In accordance with grounded theory methodology, data collection and analysis proceeded simultaneously (Glaser & Strauss, 1967). An initial purposive sampling procedure was used. We asked center leaders to recommend participants to the focus group interviews based on their interest in and experience with early psychosis patients. The transcripts and memos written after each interview was analyzed immediately after they were completed. For an example of a case based memo, see appendix 6a, and for an example of theoretical memos see appendix 6b. The grounded theory method uses three levels of coding: open, selective, and theoretical. The levels are consecutive and sequential. After the three first interviews open coding was employed. Interview transcripts were dissected into discrete components through a line-by-line reading, and categories were labelled by the participants own words (see appendix 6c for a list of open codes after the first three interviews). During this coding process, the constant comparison method and theoretical memoing was used (Glaser & Strauss, 1967).

In the open coding phase the constant comparison method was first used to compare selections of data with each other to find similarities or dissimilarities. When further interviews were analyzed, new selections of data were compared to existing categories to see if these confirmed or disconfirmed existing data. Memo writing was conducted simultaneously with the coding process. At this stage this involved reflections on the data and conceptualizations. Memos, in the form of texts, diagrams, and figures were written during the comparative process. This process of memo writing also yielded ideas on where to sample new data (Glaser, 1998). As categories began to fill, become «densified» and core categories are identified, the process of theoretical sampling ensured that new data contributed to the development of theory (Glaser, 1978). In further focus group interviews, the interview guide was slightly changed to explore similarities and important differences regarding the emerging codes and categories.

As a core category developed, representing the participants major concern, the next phase of coding, selective coding, involved re-reading of the already conducted interviews, conducting new interviews, and focusing the research process more on data that were relevant to the emerging concepts. A core category was abstracted from several sub-categories. Sampling and coding continued until densification and saturation, where no new data resulted from further coding or data collection.

The final stage, theoretical coding, we utilized theoretical memoing and sorting of categories to create a theoretical model that presented the key concepts and how they related to each other. A literature review was performed after the substantive theory was formulated. We searched the literature using PubMed, PsychINFO and Embase, using «negotiation» or «negotiating» as keywords. Papers where «negotiating» was considered a core process were selected for further analysis. Comparison and conceptualizations from this literature was used in memos during theoretical coding. An example of the research process from raw data to the theoretical concepts is illustrated in table 5.

During data analysis consensus discussions within the research team and with supervisors was used throughout. This was important to ensure that the analysis remained open to the participants own explanations rather than the researcher’s preconceptions.

Table 5: Examples of the data process coding

| Raw data | Open coding | Selective coding | Final concepts |
|---|---|---|---|
| At the same time...If you say no to treatment it can often be a very rational choice. You have that right, where you can say no, and I have to respect that and pull out of the case. But there are no absolutes here. I think in many cases we need to be more assertive rather than pull out. We may have to reach out more, make contact again, or at least be sure if the person has made his choice on reasonable or rational reasons. But I have tried to make these calls if I sense that it is not only, "because I dont feel like it". The reason can be that I can't do it or I don't manage it. And when I make the call, I sense a relief in the patient because they don't open the mail you see and they say I really don't know who you are. So, I don't think it is wrong to reach out a bit more, make those calls. If we are very worried, somebody has expressed concerns about a person, maybe from their relatives, then you may have to knock on their door. In some cases. But in these cases, I think you should have a...it should be highly likely that the person is very ill. | A relation first, then finding out. To make contact Relationship competency Go slow approach | Enabling: The person first needs to decide if he is a help-seeker. HCP invites, and gives a choice. Help-seeking is an intentional and active process. | NEGOTIATING STATUS: enabling personalizing participating |
| We can't be too limited by routines about who can be accepted for treatment. Some of our patients does not strictly have the right to prioritized help, but they still have a concerning mental state given their age and have functional decline and disturbing symptoms. So we have to be flexible,.. and we are also flexible about working hours. We can meet after hours or go on a home visit after hours. We do not want that to become routine, but we have to sometimes because that is what the patient or their relatives want. It depends also on how acute the situation seems... | Not enough to meet only at the office Need an unconventional approach It demands a different approach Flexibility Adapted treatment | Personalizing: Reciprocating the patients trust. Adapting to the patients needs. May involve "throwing away the book". | |
| Approach. Yes we have maybe...In engaging patients it often begins with their economy. Very often they have chaos in their life and especially in terms of economy. It makes them very distressed and it is very difficult to navigate. They have student loans, their bank does not understand them or they don't know how to cooperate with them, and they have Nav, with their decision letters, and they are not easy to understand. They feel it is very difficult to make contact with their case manager and they don't understand what he says to them, Or they don't know what to ask for. When we meet a new patient...It can often be a very good situation. That they experience chaos in their economic situation. Then we can come in...And we can sort of be a navigator in this situation. Helping them out, but also helping them to help themselves..with what is most important right now. So, it is very often like that with the patients we have here | You need to be a useful person Offer help where he is One to one contacts Focus on strenghts and resources A broad view A generic approach | Participating/broadiening In his entire lifeworld To his distress, rather than diagnosis To focus not only on present state, but also future needs | |

4.2.3 Sample 3: General practitioners

Study population

The population for paper IV consisted of certified MDs working as GPs in Nordland county. Data was extracted from The Norwegian Health Economics Administration (HELFO, <http://www.helfo.no>). As of November 2010, there were 199 GPs registered in Nordland. For the reminder letter sent out in May 2011, 19 of these were removed from the list owing to retirement, while 39 had been added. Overall, the study population consisted of 219 eligible GPs.

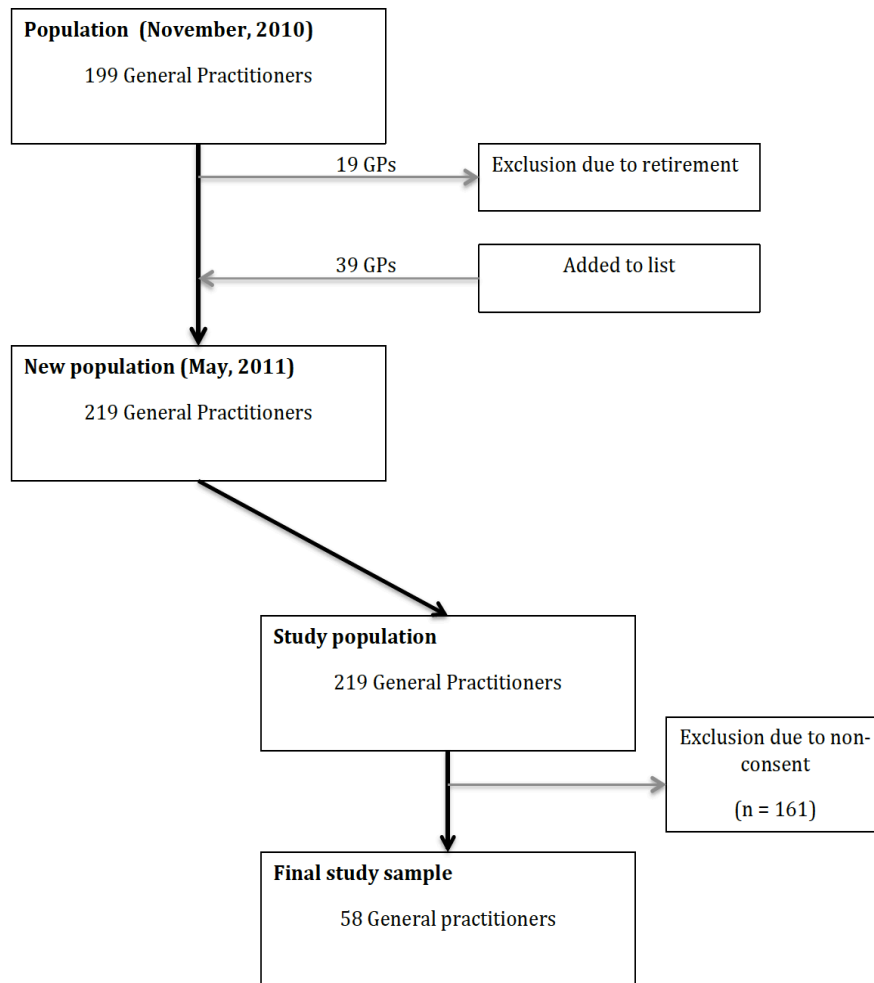
Study sample

A low response rate was expected in this study. A total of 58 of the 219 GPs in the eligible study population responded to the invitation to participate, equaling a response rate of 26.5 %.

Recruitment and sampling procedures

The first invitation to participate in the study and a paper version of the questionnaire was sent by post November 2010 (appendix 2e and 5b). In May 2011, we again extracted information on GPs practicing in Nordland county from the HELFO site. A first invitation was sent to the new GPs and a reminder to the other GPs in May 2010 (appendix 2f). A reminder to the 39 newly added GPs was sent in October 2011.

Figure 6: Sampling procedure for General Practitioners sample



Non-responders

Information on GPs working in Norway was collected from HELFO and several other public sources (Statistics Norway (<https://www.ssb.no/en/>); Norwegian Medical Association (<http://legeforeningen.no>)). According to data provided by these sources, mean age of GPs in Norway is 46.86 years, 41.7 % of GPs are woman, and 57 % have a speciality in general medicine.

Compared to the data from HELFO our participants were representative in terms of age (sample GP age was 46.53 years) and speciality (sample GP speciality in general medicine was 65.5 %). Comparison of the distribution of gender could not be performed because of too many missing data in our sample.

Materials and data collection

Questionnaire

The questionnaire is presented in paper IV, p. 6-7.

Design of materials

It is well known that GPs in Norway are busy and overloaded with invitations to participate in clinical studies. The material was therefore designed as a short 4-page questionnaire (appendix 5b). A pre-paid and pre-addressed envelope for returning the questionnaire was included in the invitation/reminder letters.

Data entry

The data file was prepared by a research assistant, using a single-entry approach. Cleaning, recoding and calculating the derived variables was done by the principal researcher.

Data analysis

The main statistical analysis performed in Paper IV are described in the following.

Exploring and transforming variables

Distribution of outcome

Only 2 items regarding «diagnostic knowledge» and 4 apriori selected background variables were analyzed. The primary outcome variable was derived from the diagnostic knowledge items utilizing a scoring system developed for the original Swiss survey in 2001 (Simon et al, 2001). The scoring system and distribution of the outcome variable is presented in Paper IV, p. 7-8.

Transforming variables

The following variables were selected apriori because of they have been found related to diagnostic knowledge of early psychosis among GPs in the previous studies using the same questionnaire and scoring system:

- Experience with psychiatry: was derived from item 27, dichotomized into yes or no.
- Experience with treatment of psychosis: was derived from item 3, with 4 possible

categories (none, 1-2years, 3-5 years, or \geq 5years)

- Experience as a physician: was derived from item 23, we used a median split (median = 19 years) to create a dichotomized variable.

- Rural practice setting: was derived from item 28, dichotomized into yes or no.

Characteristics of these variables are shown in Paper IV, table 1.

Bivariate comparisons

The association between diagnostic knowledge and the 4 experience variables were explored using χ^2 -tests (experience with psychiatry, experience as a physician and rural/urban practice setting), and Mann-Whitney U-tests (Experience with treatment of psychosis). In addition to comparisons with the GP sample in the International Study of General Practitioners and Early Psychosis (IGPS) were made using χ^2 -tests for categorical variables and t-tests for continuous variables.

5.0 Ethics

5.1 Ethical concerns in Paper I and II

In Paper I and II, we collected person-sensitive information on patients in a vulnerable situation undergoing treatment in mental health care. We considered the following ethical considerations: 1) are patients in treatment for a recent onset psychosis competent to consent to participation in a research project? and 2) are patients unduly pressured to participate if the first request is made by their treating healthcare professional? Regarding the first concern, the Helsinki declaration § 9 (World Medical Association, 2013) states that consent to participate in research should be «informed, voluntary, expressed and documented». The same principle is expressed in the Act on Medical and Health Research, § 17 (Act 2008-06-20 no.:44, 2014). Patients were recruited from both the acute wards and the CMHC, but most patients were inpatients at the time of inclusion, and most were experiencing psychotic symptoms (delusions, hallucinations, disorganized thought and catatonic symptoms). Recent research has documented that even in patients experiencing psychotic symptoms, competency to consent can still be preserved (Anderson & Mukherjee, 2007). According to these studies the presence of cognitive symptoms and disorganization are more detrimental to capacity to consent than psychotic symptoms. Regarding the second concern, the Act on Medical and

Health Research § 13, states that consent to participate in research must be made voluntary. We were concerned that the dependency between patient and treating health care professional could influence the patient decision.

To address these ethical concerns, the process of informing the patients about the study included several steps. All patients were only approached by the research team once the treating healthcare professional had made an assessment of the patient's clinical state as stabilized, according to both clinical and individual parameters. After screening for new patients, potential participants were noted in a research log (age, gender, place of living, name of treating healthcare professional). The treating healthcare professional was contacted the same day for evaluation if inclusion criteria were met. In patients eligible for inclusion, the healthcare professional was contacted weekly until it was possible to approach the patient with information on the study. In the recruitment process it was not uncommon that we had to wait weeks or months before approaching the patient. We also stated clearly to the treating healthcare professional that information on the study and getting consent must happen independently of the treatment situation. Information on the study was thus only given by the research team. Information was given orally and in writing. The patient was approached again 24 hours after receiving information on the study, and was asked to consider their participation in the study. The interviews were conducted with a sensitive and emphatic interview style.

5.2 Ethical concerns in Paper III and IV

In Paper III and IV, we did not collect person sensitive information, and the studies were more concerned with decision making processes in the mental health services. In Paper III we asked community practitioners about decisions in the assessment and engagement of patients with early psychosis, whereas in Paper IV we asked GPs about decisions in evaluating and referring early psychosis patients to mental health care. Studies of decisions and not persons are considered as research on health services, a field that does not fall under the Act on Medical and Health Research (Act 2008-06-20 no.:44, 2014). The conduct of these part studies still adhered to ethical principles of protecting the dignity, rights and welfare of participants.

6.0 Results - main findings from the study, the paper abstracts

Paper I: Geographical accessibility and duration of untreated psychosis: distance as a determinant of treatment delay.

Background: The duration of untreated psychosis is determined by both patient and service related factors. Few studies have considered the geographical accessibility of services in relation to treatment delay in early psychosis. To address this, we investigated whether treatment delay is co-determined by straight-line distance to hospital based specialist services in a mainly rural mental health context.

Methods: A naturalistic cross-sectional study was conducted among a sample of recent onset psychosis patients in northern Norway (n=62). Data on patient and service related determinants were analysed.

Results: Half of the cohort had a treatment delay longer than 4.5 months. In a binary logistic regression model, straight-line distance was found to make an independent contribution to delay in which we controlled for other known risk factors.

Conclusions: The determinants of treatment delay are complex. This study adds to previous studies on treatment delay by showing that the spatial location of services also makes an independent contribution. In addition, it may be that insidious onset is a more important factor in treatment delay in remote areas, as the logistical implications of specialist referral are much greater than for urban dwellers. The threshold for making a diagnosis in a remote location may therefore be higher. Strategies to reduce the duration of untreated psychosis in rural areas would benefit from improving appropriate referral by crisis services, and the detection of insidious onset of psychosis in community based specialist services.

Paper II: "Lanthanic presentation" in first episode psychosis predicts long service delay: the challenge of detecting masked psychosis.

Background/Aims: Studies of pathways to care in first episode psychosis have documented a substantial treatment delay occurring after entry to mental health services. An initial presentation with neurotic rather than psychotic symptoms is common in first episode

psychosis. The term "lanthanic patient" has been used to refer to patients presenting with a reason for help-seeking that is unrelated to the underlying pathology. The aim of this study is to explore whether a lanthanic presentation is related to prolonged service delay.

Methods: The sample comprises 62 patients with recent onset psychosis. Data on socio-demographic, clinical, help-seeking and pathways indicators were collected using a comprehensive semi-structured interview schedule.

Results: Service delay accounted for more than half of the overall treatment delay. An initial presenting complaint of neurotic symptoms was related to prolonged service delay. The effect remained after controlling for other potential risk factors of service delay.

Conclusion: Anomalous experiences of pleasure, desire or motivation are common in emerging psychosis. These difficulties are often misinterpreted as complaints of depression and anxiety by health professionals. The presence of such symptoms can introduce a focal vision in health professionals on the immediate presented rather than the underlying psychopathology, and lead to under-detection of psychosis.

Paper III: Negotiating the boundaries of psychosis: a qualitative study of the service provider perspective on treatment delay in community mental health.

Aim: Evidence shows that many patients are detected and treated late in their course of illness, and that substantial delay occurs even after entry to mental health services. Although several studies have examined the service user and carer perspectives on treatment delay, few have explored the issue from the service provider perspective. The aim of this study was to broaden our understanding of treatment delay by exploring the service provider perspective on reasons for treatment delay in community mental health services.

Methods: A qualitative study using data from focus group interviews with 33 healthcare professionals in community mental health care. Interview data were digitally recorded and transcribed verbatim, and analysed using a grounded theory approach.

Results: Service providers perceived divergent or conflicting perspectives as the main challenge in early psychosis. Clinical negotiation was chosen as the main term describing the interactions between patients and healthcare professionals: This was observed in three

overlapping areas: (i) Negotiating the patient's status as help-seeker; (ii) Negotiating the place and conditions of treatment; (iii) Negotiating the meaning of distressing experiences and the timing of treatment options.

Conclusions: This study suggests that delay in initiation of treatment for psychosis in community mental health is related to clinical challenges of early disengagement from services and diagnostic uncertainty. Service providers found negotiating the therapeutic relationship and patient-centered flexibility more useful in ensuring engagement than an assertive outreach approach. Diagnostic uncertainty was resolved through watchful waiting using a distress-overload conceptualization in assessing changes in mental state and service needs.

Paper IV: What do general practitioners know about early psychosis? A survey of the diagnostic knowledge among gatekeepers to specialist mental health care in Northern Norway.

Background: General practitioners (GPs) have an important role in many health care systems. In countries where GPs act as gatekeepers to specialist services, efforts towards early intervention of psychosis depends largely on prompt recognition of the early symptoms in primary care. Several studies have documented great variability in the knowledge of GPs regarding this. In this study, we wanted to investigate GPs knowledge of the symptoms of early psychosis in a health care context with a gatekeeping function located in a rural area of northern Norway.

Methods: The study design was a cross-sectional questionnaire survey of GPs (n = 58) working in the county of Nordland in northern Norway. Data on diagnostic knowledge and a priori selected explanatory variables were analysed.

Results: We found that the GPs in this sample had adequate knowledge of the frank psychotic symptoms, whereas the more insidious signs of early psychosis were under-identified. There was a significant variability in diagnostic knowledge, but no association with experience or rural status were found. Compared to international samples, the surveyed GPs had significantly lower diagnostic knowledge of early psychosis.

Conclusions: The GPs in this sample reported that they collaborated closely with specialist in the diagnosis and treatment of early psychosis. GPs may use a more global judgement of psychopathology, and patients are quickly referred for further assessment. This may in part explain their lower diagnostic knowledge. Implications for primary and specialist care levels are described.

7.0 Discussion of methodology

Bias can be defined as «systematic errors in the design and conduct of a study» (Szklo & Nieto, 2012) p. 109. Essentially, there are two types of bias: selection bias and information bias.

Selection bias is defined as "distortions that result from procedures used to select subjects and from factors that influence participation in the study" (Porta, 2014), p. 225. Information bias can be defined as "a flaw in measuring exposure, covariate, or outcome variables that results in different quality (accuracy) of information between comparison groups" (Porta, 2014), p. 128.

The validity of a study is the degree to which inferences drawn from a study are warranted when account is taken of the study methodology and characteristics of the participants (Porta, 2014). Internal validity concerns the degree to which a study is free from bias, whereas external validity concerns the degree to which the results of a study can be generalized to the study population or other populations.

The possibility of bias might threaten the conclusions drawn in this study. In this section, I will discuss the possible threats of bias throughout the research process as described in section 4. I will also discuss potential confounding, specific statistical problems, and methodological issues specific for qualitative research.

7.1. Study design

We used a mixed methods design, or more specifically a «convergent parallel mixed methods» design (Creswell, 2014). This design is characterized by collecting both

quantitative and qualitative data at roughly the same time, and integrating these to provide a comprehensive analysis of the research problem. We chose this method because we wanted to be able to describe general patterns of pathways to care and DUP in quantitative terms, combined with more in-depth inquiries about why the observed patterns arise in the service interval of DUP. The literature review revealed that few studies have investigated the service interval of the DUP. It was our opinion that modeling the research design on previous studies of pathways to care studies were unlikely to increase our understanding of this field. Therefore, we decided to also conduct a more in-depth inquiry of GPs and the referral pathway, and a qualitative study of community practitioners and challenges in engaging and diagnosing first episode patients. It was also our contention that general patterns, what kind of contacts patients have in their pathways, and the relationship between variables at different levels are best captured by quantitative methods, while the process view is probably best captured by more in-depth inquiry, using both quantitative and qualitative research methods.

7.2. Study population

A recent review of the research literature showed that most studies on pathways to care in early psychosis have been conducted in settings with at least moderate population density (Norman & Malla, 2009b). Although there has been great diversity in terms of different countries and health care systems, less was known about settings with lower population densities. This gap in knowledge made it important to conduct this study. However, in terms of representativeness and generalizability to other populations, there are potential limitation.

In sample 1 (treated patients) the study population is a mainly rural population where differences in accessibility of services vary, and this may have impact on the treated incidence. Several studies have indicated lower incidence of psychosis in rural areas (McGrath, Saha, Chant, & Welham, 2008; Pedersen & Mortensen, 2001), although reasons for differences are not known. We also used an exclusion criteria in terms of age (16-35 years), and this may have excluded patients with late onset psychosis. Recent studies indicate that woman commonly have a later onset, with a second peak occurring at 40 years (Ochoa, Usall, Cobo, Labad, & Kulkarni, 2012).

In sample 2 (community practitioners) there are possibly local differences in Community Mental Health Centers in Norway, and this may potentially limit generalizability (Bjorbekkmo et al., 2009). This is noted in Paper III, p. 8.

In sample 3 the study population was GPs working in Nordland county. Many practices were in rural areas with varying accessibility of specialist services. Research indicate that patients with psychosis have more contact with their GP in smaller municipalities (Sørgaard et al., 2003; Hetlevik, Solheim, & Gjesdal, 2015). Limitation are noted in Paper IV.

7.3. Study sample

Participants to studies are often included on reasons of convenience rather than scientific reason ensuring representativeness. In this study possible selection bias during recruitment might have skewed the sample, and in the following I will discuss these issues.

Sample 1: Treated patients:

The study was conducted in a central hospital in the county of Nordland. All the patients admitted to the wards in the hospital were screened weekly by the research team for eligibility to the study. With such intensive follow up on the wards few cases were likely to be missed. The same intensity of follow up among the local CMHCs dispersed in the large geographical area of Nordland was impossible. This made recruitment among the local centers difficult, and may have introduced bias because hospitalized cases are usually not representative of all cases, the so called «Berkson bias» (Szklo & Nieto, 2012). It is possible that hospitalized patients have more complex psychiatric problems than non-hospitalized patients. On the other hand, psychosis is associated with major consequences such as social dysfunction, inability to work or to go to school, and it is possible that the level of dysfunction means that most patients are in fact admitted in the course of their illness. Although mental health systems differ, and the threshold for admitting patients may vary, there are studies indicating that up to 80% of patients with psychosis are admitted to hospital, especially during the early course of their illness (Sipos, 2001; Wade, Harrigan, Harris, Edwards, & McGorry, 2006). However, to ensure that patients not admitted to our primary recruitment sites, also could be included in the study, we designed a special recruitment strategy towards the CMHC in Nordland county (Eaton, Hall, Macdonald, & McKibben, 2007). This involved conducting workshops on psychosis and training in identifying psychotic symptoms in each center during the first year of the study, and also recruiting contact persons in the centers responsible for screening referred patients. Healthcare professionals working within the child and adolescent centers were also invited to participate in these workshops. The contact persons were telephoned regularly (monthly) for discussions

on possible new cases.

Most studies lose a significant number of cases because participants refuse to give informed consent. This is called, "non-response bias" by Bhopal (2016). The rate of non-response varies in studies, but expected rate is 30-40 per cent. This may introduce bias, because non-responders are likely to differ from responders. We therefore collected information on age, gender, social circumstances and referral source, to conduct a response analysis. Analysis of refusers were presented in section 4. We found no significant difference between responders and refusers.

Sample 2: Community practitioners

As stated in section 4 we used an initial purposive sampling procedure in recruiting participants in sample 2. This may introduce selection bias. In accordance with Grounded theory methodology, generalizability is investigated by conducting further studies and checking the transferability of concepts. These limitations are noted in Paper III, p. 8.

Sample 3: General Practitioners

A low response in surveys of GPs are common due to lack of time and perceived unimportance (Cummings, Savitz, & Konrad, 2001). Varying interest in mental health, the low prevalence of psychosis in rural areas, and the topic of diagnostic knowledge and referral practices could have caused GPs to be reluctant to participate. We therefore used several strategies to increase response rate (VanGeest, Johnson, & Welch, 2007). The questionnaire was short, only 4-pages with 30 items, and with each letter we included a stamped return envelope and a signed endorsement letter from the medical director and chief of psychiatry at the hospital (appendix 5a). In order to not introduce selection bias in the reminder process, only one reminder letter was sent ensuring to treat all GPs equally. The response rate was still low (26 %), and this must be taken into account when interpreting the results. Responders are perhaps more interested in mental health and psychosis, and the diagnostic knowledge among non-responders may be even lower than reported.

7.4. Materials

According to Szklo & Nieto (2012) information bias results from either imperfect

definition of study variables or flawed data collection procedures. Possible information bias will be discussed in terms of validity and reliability issues in the respective samples.

Sample 1: Treated patients.

The primary outcome in Paper I and II was DUP, and this was defined as the period of time between the onset of psychosis and the initiation of adequate treatment. In DUP research this general definition is largely agreed upon, but there is however a large variability in how this construct is quantified (Register-Brown & Hong, 2014). The primary measurement instruments in our study was the NOS-DUP (Singh et al., 2005). The NOS-DUP is designed to provide a standardized and reliable way of recording early changes in psychosis and identifying time points ("4 crucial dates") for measuring DUP. The most important time points are DUP onset and endpoint:

- DUP onset: In NOS-DUP, the DUP onset is operationally defined with 1) specific symptoms defined by a well-known assessment instrument (Positive and Negative Syndrome Scale, PANSS, (Kay et al., 1987)), 2) severity rating based on the anchors of the PANSS (rated at least 4), and 3) the symptom must have "lasted throughout the day for several days, or several times a week, not being limited to a few brief moments" (Larsen et al., 1996). A decision rule called the "mid-point dating rule" (Perkins et al., 2000) was used when the patient could not specify the exact date, the midpoint takes the middle date for the range given by the subject (midpoint for July is the middle of that month, i.e. the 15th).
- DUP endpoint: In NOS-DUP, defined as the, "date when treatment is commenced at clinical adequate dose for which there is evidence of compliance", where clinical adequate dose is further defined as a dosage "equivalent to 2-3 mg haloperidol" and compliance is defined as "evidence that medication is being taken at 75% or above, the prescribed dosage; and for 75% of the prescribed time, or above" (Polari et al., 2011).

Clear and operational definitions of the study variables minimize problems associated with validity and the possibility of information bias and misclassification. The validity of DUP estimates is however rarely mentioned in DUP research (Maurer & Häfner, 1995; Friis & Larsen, 2003). Future research will benefit from efforts to standardize DUP measurements for example with structured methods such as NOS-DUP. With a gold standard of DUP measurement, validity issues using concurrent criterion validity assessments would benefit

our understanding of the validity of the concept.

Observer bias occurs when there is a "systematic difference between a true value and the value actually observed due to observer variation" (Porta, 2014). In our study patients are interviewed individually using the NOS-DUP, and this information was used, together with information from charts and family members, by the investigator to assign values on rating scales. In the study, three different investigators collected the information and performed the ratings. This may introduce systematic bias, for example if one rater usually tends to be more generous when assigning values than the others. To prevent this problem a comprehensive training and consensus procedure was implemented. Before data collection commenced, the three investigators had training sessions with the developers of the NOS-DUP scale. In these sessions the investigators rated case vignettes and later discussed the ratings to arrive at similar scores. As the NOS-DUP also uses a well-known psychiatric assessment instrument, the PANSS, independent training sessions on the use of this instrument was also conducted before beginning data collection. The group scored several training tapes, including a tape made by the developer of the PANSS, to reach a more stable level of agreement. During data-collection the group of investigators had regular sessions (1/week) for quality assuring data. In these sessions, transcripts of the interviews and other information gathered by using the NOS-DUP procedure was presented, and rated independently by the investigators. The ratings were compared and when disagreement occurred. The information was reviewed again and discussed to reach agreement. This consensus rating procedure is possible to use in a small study like this with few included cases, but would be too time-consuming in larger studies (Klein & Ouimette, 1994). As the period for data collection was quite long in this study, to further quality assure the data and minimize bias, calibration and training sessions were conducted at regular intervals. In these sessions the group of investigators way of using the rating scales was tested by comparing with expert raters from other studies or research groups.

Reliability issues is also present in the procedure used to assign psychiatric diagnosis to the patients included in the study. Psychiatric diagnoses are based on cross-sectional and longitudinal symptom review. There are no objective tests that yield definite diagnosis. Patients in our study were recruited from acute wards, often shortly after a psychotic episode, and the available information were primarily the acute presentation of symptoms. Often there is rather incomplete information about longitudinal symptoms (Spitzer, 1983). The previously

described OPCRIT+ procedure was therefore used in this study to assign diagnoses retrospectively on the basis of information from charts after their psychiatric condition is stabilized, and also longitudinal information has been recorded in charts (Azevedo et al., 1999; Fennig, Craig, Lavelle, Kovasznay, & Bromet, 1994). This information was collected by the research team, and later rated by an expert blind to information on treating clinician-generated diagnosis.

Sample 2: Community practitioners

For the focus-groups we used an interview guide, constructed using a template from a similar qualitative study conducted in Birmingham, The National Eden Project (Birchwood et al., 2013b). The following questions were selected (Norwegian translation in parenthesis):

- Have there been any changes in the way service responds to the needs of young people during it's development? (Hvordan er tjenesten hos dere organisert for å imøtekomme behovene til unge førstegangs psykotiske?)
- Do you think psychologist, OTs, ASWs, psychiatrist or other non-nursing professions should have a caseload? Or should they be available to all service users according to their needs, that is «floating» in and out of cases - as required? (Har ulike profesjoner ulike roller? Hvordan fordeles oppgaver?)
- Have demographic and/or geographic features caused any difficulties? (På hvilken måte har geografiske eller demografiske faktorer innvirkning på hvordan tjenesten er organisert?)
- What are the main ways that you engage clients with your service? (Hvilke utfordringer har dere med å engasjere pasienter i sin egen behandling?)
- Has your EIS been involved in the development of new relationships or partnership agreements, or other changes in links that your EIS has with other sectors and services? (Hvilke instanser samarbeider dere med?)
- Are there any concerns about referral pathways? (Hvilken praksis har dere for henvisning? Hvilke faktorer er av betydning for når og hvor pasienten henvises til videre behandling?)

To these items we also added some questions regarding assessment practices, how transitions from child and adolescence services to adult services were made, what specific challenges they had in their work, and asked if they could describe their experience with a recently identified patient with early psychosis (appendix 4b).

Concerns in these interviews was the so-called Hawthorne effect. The Hawthorne effect was described by Landsberger (1958), and describes the tendency for people to do things to please the researcher, which results in artificial results. The moderator had to be mindful of this effect, by stimulating debate and ensuring that all participated. After the first interview, we noticed that participants were too fixed on the interview guide, even more than the moderator, and we therefore removed this from the table in later interviews.

Sample 3: General Practitioners

The questionnaire used in the GP survey was the Norwegian version of the validated questionnaire used in the multi-centre International Study on General Practitioners and Early Psychosis (Simon et al., 2009). This questionnaire was also used in an original Swiss survey in 2001 (Simon, Lauber, Ludewig, Braun-Scharm, & Umbricht, 2005), and has been used in an Irish sample as well (Gavin & Cullen, 2006). That the questionnaire was previously validated and used in several samples, ensured that the content validity of the questionnaire was satisfactory. A concern in this survey was that the responders could over-report socially desirable behaviors, while under-reporting socially undesirable ones (Krumpal, 2011). Anonymity ensured by the coding procedure, and the fact that the questionnaire was self-administered rather than administered by an interviewer, may have reduced social desirable answers.

7.5. Confounding

Szklo & Nieto (2012) defines confounding as a "situation in which a non-causal association between a given exposure and an outcome is observed as a result of the influence of a third variable" (Szklo & Nieto, 2012). The possibility of confounding is especially likely in cross-sectional observational studies, where participants has not been randomly allocated. Confounding can be controlled for by stratification or adjustments in multivariable analyses. In the analysis of possible extrinsic (service/system level) determinants of DUP, thought to be potential targets for early intervention efforts, intrinsic (illness/patients level) factors needed to be considered concurrently. We performed multivariable analyses in Paper I and II, controlling for known risk factors of DUP.

7.6. Statistical considerations

DUP, and its components (patient and service interval), was the outcome variable in Paper I and II. In most samples this variable has skewed distribution. Many studies therefore use a categorical division of this variable in statistical analysis. These categorizations often make use of cutoff points of <3 months, <12 months, etc. (e.g., Apeldoorn et al., 2014). Another alternative is using a log-transformed DUP to approximate normality (Birchwood et al., 2013a) or use non-parametric statistical tests to compare across the entire distribution of DUP.

As there is not adequate evidence for any clinically meaningful threshold or any agreed upon cutoff point (Marshall et al., 2005), and transformed variables can be difficult to interpret and translate into practice, we chose to use the sample median as a cut point in dichotomizing the outcome variable. A problem with this is of course that different studies have different cut-point, which can make comparisons difficult. Recent developments such as using «curve fitting approaches» (Hannigan, Bargary, Kinsella, & Clarke, 2017) or «quantile regression» (Guloksuz et al., 2016), are promising alternatives but were not described in the literature until recently (2016-17).

7.7. Considerations in qualitative research

We chose qualitative methods in the in-depth study of community practitioners and the process of engaging first episode patients. The reason for this choice was that although previous studies have found substantial delay in community care, few studies have keyed in on specific reasons for delay in the community context. Therefore, it was impossible to explore this matter in a more objective manner using already validated and reliability tested questionnaires or interview schedules. Qualitative research, however, is vulnerable to allegations of subjectivity and speculative analysis, and this might threaten its internal validity. In quantitative research reliability is inherently to the research instruments, whereas in qualitative research reliability is more a matter of procedural quality. Several choices in terms of ensuring minimal impact of bias were made in the research process (e.g., transparency throughout the process, documenting the steps taken, and triangulation between researchers).

Transparency in terms of sampling, data collection and analysis is an important first step in ensuring internal validity in qualitative research. In Paper III, and further in section 4 of this thesis, the research process is therefore described thoroughly by exposing each step and inclusion of several illustrating examples. Grounded theory methodology specifies a series of consecutive and sequential coding process, where each stage guides the following steps (Giske & Artinian, 2007). The coding process is illustrated by examples in section 4.

Another step towards ensuring internal validity of the study was the use of triangulation throughout the research process. Team discussions within the research team and with supervisors both after conducting interviews and during the process of data analysis, were used to explore different angles, viewpoints and specialist knowledge from the field.

An important strategy in Grounded Theory methodology is searching for negative or deviant cases in order to modify the emerging theory in light of new data. The 4 criteria of «fit, relevance, workability and modifiability» (Glaser, 1978; Glaser, 1998) are specified as essential criteria in evaluating a theory. Fit refers to the constant fitting and refitting of categories to the data, and relevance is about the grab a theory has for participants in relation to the core problem in the area of study, and these criteria are important to the validity of a theory. Workability is concerned with the ability to predict and interpret what is happening, whereas modifiability is about the potential for development of a theory in light of new ideas and data. The finding of differing opinions on the decision to admit patients with a first episode psychosis is an example of a negative case, but was used to modify the theory. Yet it is important to note that others may have interpreted this as an atypical case inconsistent with the interpretation provided.

Missing from this study is the perspective of the patients on the clinical encounter, as we did not interview any patients in order to confirm our interpretation of this encounter as conflicted. Other studies however, have confirmed that patients disengage from treatment contacts, confirming that the issue of disagreement on goals and focus areas are important reasons. It is however a shortcoming that this could not be explored in this particular health context, and thus represent an important area for continuation of this work.

Reflexivity concerns the researchers position and point of view on the results of a study (Malterud, 2001). The research team all worked in the central hospital, and had no experience

with community practice. This posed a problem because the field of study was entirely unknown. To address this, we utilized the results from another study, the National Eden Project, and used translation of parts of their interview schedule. Although the field of community practice was unknown, we had experience with first episode psychosis patients and this could have affected the collection and interpretation of the data. There is the risk that familiarity with the clinical challenges of early psychosis could make us blind to other aspects of the situation. Working explicitly at distancing, and focusing also on the unique contextual factors was important in this regard. Sympathy and admiration for the difficulties in the task at hand, could potentially influence the interpretation. The reflective detachment was helped by including the entire research team and supervisors in interpretation of the data. Team discussion after conducting interviews introduced different experiences, and provided a more balanced assessment of data. The main supervisor had extensive knowledge of community psychiatry through several research projects, and this complemented the interpretative process. The potential bias of reflexivity might however be present in the final analysis of the data, and this is noted in the paper.

7.8. Conclusion

In conclusion, there is little evidence of information bias, and the conduct of the study created no major selection bias. The samples were considered representative of their study populations. We believe overall that the study has reasonable internal and external validity.

8.0 Discussion of main results

The main findings are discussed in the respective papers. This discussion will elaborate on some common themes, and how these relate to the current discourse and findings in the field.

8.1. Topography of the pathway

One of the early reviews of pathways to care in early psychosis used the geographical metaphor of «topography» when introducing this field of study (Lincoln et al., 1998). Topography is commonly understood as the study of shapes and features of surfaces, and their depiction in maps. The metaphor is useful because it indicates that although the

mapping of key nodes (e.g., first contacts, referral sources) are important, the concept also encompasses the importance of contextual factors (i.e., the entities or objects that surrounds the key nodes). This has been an important theme running through all the papers in this study. In this section, we will report on the general patterns of the pathways to care (the «topography»), and in later sections supplement this with contextual information gathered from the in-depth studies.

8.1.1 Point of entry

Point of entry refers to the care pathway contact from whom help was first sought after the onset of psychotic symptoms. In the sample of treated patients, we found that for the majority the point of entry to health services was a GP (39 %). Following GPs as first contact, was an emergency clinic (23 %). The high level of GP involvement in the initial pathways was expected as a consequence of their gatekeeping function in the Norwegian healthcare system. It is also consistent with other studies conducted in European countries (Johnstone et al., 1986; Cole et al., 1995; Burnett et al., 1999; Skeate, 2002; Morgan et al., 2005; Platz et al., 2006; O'Callaghan et al., 2009; Boonstra et al., 2012; Ghali et al., 2013; Bhui et al., 2014). The pattern of first contact observed between different studies support the claim that first contacts are not random and are highly dependent on the specific cultural, social and health care context. A systematic review of pathways studies also showed regional trends in terms of first contacts (Anderson et al., 2010). In European countries, the largest proportion of first episode patients has GPs or other physicians as first contacts, whereas in North America emergency services is often the first contact. In many Asian and some of the developing countries, non-physicians are often first contacts.

First contacts are important targets for early intervention efforts. The finding of regional trends between studies highlights the importance of local audits in order to target interventions more effectively. Our findings suggest that in the Norwegian healthcare context, in addition to targeting GPs, emergency services could also be an important target for early intervention efforts because a substantial number of patients have their first contact with these services.

8.1.2 Referral source

Referral source refers to the contact who suggested or arranged contact with mental health services. Most patients in the sample of treated patients had a non-acute specialist referral (71 %), and this constituted GPs, lay or self-referral and patients already in specialist services. In this sample, 27 % had an acute specialist referral either by GP or the emergency clinic. Similarly to findings regarding point of entry, comparisons between different studies have found that referral source is also highly dependent on social, cultural and health care context (Anderson et al., 2010). Important differences are observed in systems operating with either open referrals or through gatekeepers mechanisms. In European systems, often with gatekeeper mechanisms, physicians are the referral source for a large proportion of patients, whereas in North American jurisdictions emergency services have been found to be referral source for the largest proportion of patients.

The high proportion of referral through non-acute pathways in this study partly reflect the strong gatekeepers function of GPs in the Norwegian health care system. Still, quite many patients were referred through acute pathways. Referral by emergency services is often interpreted as a potential negative pathway associated with poor engagement with health services and dissatisfaction with treatment (Compton, 2005). Although there are probably complex and interacting factors responsible for acute referral pathways, the heterogeneity of psychotic presentations is also important. Psychosis, and particularly schizophrenic psychosis, is often depicted as insidious, chronic illness with a natural deteriorating course. However, long term studies show that in schizophrenia there is a great diversity in types of onset (acute, insidious,), course (single episode, phasic, chronic), psychopathology and outcome (Häfner, 2014). Our finding that 42 % in the sample of treated patients had an acute mode of onset (onset definable within 1 month) is partly due to this diversity, although this number also includes patients with other non-schizophrenic psychotic disorders. Clinical studies indicate that between 10-20 % of patients with schizophrenia spectrum disorders have an acute onset (Häfner, 2014). Most of the acute referrals in this sample were to the acute wards in hospitals (87 %), making this the most rapid and effective pathway to care in terms of DUP, which is consistent with several other studies (Bhui et al., 2014; Birchwood et al., 2013a; Boonstra et al., 2012; Cheung, Roper, & Purdon, 2013).

Lastly, the accessibility of specialist services in a specific health care context is also an

important determinant of findings on referral sources in studies. This was the topic investigated in Paper I and will be discussed in later sections.

8.1.3 Final port

The average number of treatment contacts before receiving antipsychotic therapy in the sample of treated patients was 4, ranging from 1 to 13. For most patients, the final port or the contact responsible for commencement of appropriate treatment, was at an acute or inpatient unit at the general hospital (71 %). This is consistent with others studies finding that as many as 80 % of patients are admitted within the first years after onset of psychosis (Sipos, 2001; Wade et al., 2006).

Patients who were admitted at first mental health contact had shorter DUP than those receiving community mental health care, consistent with findings in other studies (Bechard-Evans et al., 2007; Birchwood et al., 2013a; Boonstra et al., 2012). Patients in contact with specialist mental health services at psychosis onset (26 %) had longer DUP, replicating the finding of (Boonstra et al., 2012). Community mental health deal with a wide range of mental health problems. These data indicate substantial delay occurring in community mental health.

8.2. What happens in the patient interval?

We defined the patient interval as the interval between onset of psychosis and the first presentation to a professional health contact (Chien & Compton, 2008). This theme was investigated most thorough in Paper II, although relevant findings on this theme was also presented in Paper III, from the community practitioners perspective.

8.2.1 Intrinsic factors and help-seeking

Our findings are in line with previous research on the importance of «the three intrinsic factors» of treatment delay: mode of onset, age at onset and premorbid function. Reviewing the literature on determinants of DUP (Brunet & Birchwood, 2010) has stated that «the more these three factors are present (poor premorbid functioning, gradual development of early signs and adolescent onset), the longer may be the DUP» (p. 10). In patients with poor premorbid function, the early symptoms may be confused with the ongoing difficulties with

adjustment (Larsen et al., 1998), if symptoms develop slowly they may be seen as features more or less habitual for the person (ie. «ego-syntonic») and mask the appearance of psychosis (Møller, 2001), while presentation during adolescence may cause «difficulties of identifying the psychosis signal from the psychopathological noise of adolescence» (Birchwood et al., 2013a), (p. 63).

In accordance with previous studies we found the three intrinsic factors related to long DUP (described in Paper I and II), replicating the findings from numerous studies on the importance of these factors (Larsen et al., 1998; Verdoux et al., 1998; Møller, 2000; Kalla et al., 2002; Larsen et al., 2004; Norman et al., 2004; Chen et al., 2005; Peralta et al., 2005; Morgan et al., 2006; Pek et al., 2006; Bechard-Evans et al., 2007; Schimmelmann, Conus, Cotton, McGorry, & Lambert, 2007; Compton et al., 2008).

The factors may influence both the patient and service interval (Bechard-Evans et al., 2007), although the association between patient characteristics and delay in help-seeking behavior have been highlighted in recent literature (Compton & Broussard, 2011). In general, young people tend not to seek professional help (Rickwood, Deane, & Wilson, 2007). In an epidemiological sample conducted in a Norwegian context, with highly available services free of charge, only one third sought help for common mental health problems even when the symptom load was experienced as high by the person (Zachrisson, Rödje, & Mykletun, 2006). In early psychosis, this tendency is compounded by the intrinsic factors, making help-seeking initiated by the person themselves an unlikely event. Our finding that 68 % in the treated patient sample did not seek help themselves is consistent with this. For the majority (43.5 %) help was initiated by family members, replicating the finding in other studies (Archie et al., 2010; Cheung et al., 2013; O'Callaghan et al., 2009; Cocchi et al., 2013). Only 21 % in this sample reported seeking help themselves.

The in-depth study of treatment delay in community mental health (Paper III) similarly found that early psychosis patients were often experienced as ambivalent and reluctant in terms of help-seeking. Community practitioners stated that service disengagement related to non-attendance and treatment drop-out, were important factors responsible for prolonging treatment delay. Another factor highlighted in Paper III was the importance of social context on the help-seeking process. Consistent with the finding in the treated patients sample, the informants stated that help-seeking in early psychosis patients was often a family decision

rather than an individual decision or choice. The community practitioners reported that referrals in small communities was often made informally by family members or others, before formal help-seeking was initiated by the patient or his/hers significant others. Similar findings have been reported in research on help-seeking behavior in young people (Rickwood et al., 2007). A possible explanation on how social context influences help-seeking is that people often consult with their social network, or lay referral system, seeking provisional validation before consulting a healthcare professional and professional validation (Ogden, 2012). Several studies have found that poor social networks, or variables proxy to social network (e.g., living circumstances, relationship status, employment) are related to longer DUP (Larsen et al., 1998).

The level of prodromal help-seeking was also high in this sample, with 43.5 % seeking help during that phase of illness, a finding in line with other studies (Rietdijk et al., 2011; Addington et al., 2002; Platz et al., 2006). Consistent with this, we found that a substantial proportion of patients (26 %) were already in treatment for other mental health problems at the time of psychosis onset. Most of these patients were receiving treatment from community-based specialist services (75 %). In Paper II we found that initial help-seeking in 43.5 % of treated first episode patients is for non-specific symptoms and concomitant problems. These findings are consistent with other studies, reporting that the trigger for help-seeking is often symptoms of depression and/or anxiety, rather than attenuated or psychotic symptoms (Falkenberg et al., 2015; Schultze-Lutter et al., 2015). Thus, for a group of patients, despite seeking help for their mental health, their help-seeking behavior can mask the underlying psychopathology, and their psychosis is not picked up by healthcare professionals in mental health. These findings suggest that the help-seeking delay in early psychosis is highly idiosyncratic and difficult to unravel in individual patients (Connor et al., 2016). Underestimating the heterogeneity in first presentations in early psychosis, may be an important reason for prolonged treatment delay in the mental health services.

8.3. What happens in the service interval?

We defined the service interval as the interval between first professional health contact, and the onset of treatment (Chien & Compton, 2008). In Paper II we reported on a substantial service interval, contributing 54 % to overall treatment delay. According to the model specified by Goldberg & Huxley, two crucial moments in the pathways to care are 1) the GPs

recognition of mental illness and decision to refer, and 2) the mental health professionals recognition of psychosis and decision to treat or admit. Referral decisions were investigated in Paper I and IV, while challenges in recognizing psychosis were investigated in Paper II and III.

8.3.1 The context of referral decisions: gatekeeping and geographical accessibility

Deinstitutionalization has greatly improved access to mental health services, but at the same time introduced an organizational complexity of services. In most health care contexts, mental health services are provided by a network of local and regional services, and the effectiveness of this system depend on referral mechanisms. In many European countries, the conventional pathway to specialist care is through the GPs, and this was the topic of the in-depth study of GPs in Paper IV.

Given the importance of GPs as gatekeepers to all specialist care in the Norwegian healthcare context, efficiency is highly dependent on the diagnostic knowledge and referral practices of GPs. The main finding was that, similarly to other studied GP samples, GPs were generally aware of some of the early features of early psychosis, but these were reported less often than more obvious psychotic symptoms such as delusions and hallucinations (Simon et al., 2005; Simon et al., 2009; Verdoux, Cougnard, Grolleau, Besson, & Delcroix, 2006; Gavin & Cullen, 2006; Holub & Wenigová, 2010).

However, GPs in the Nordland sample reported high rates of referral to specialist mental health services, and also reported using such referrals to corroborate diagnosis. These finding are in line with other studies of a close collaboration between GPs in Norway and the specialist level (Hetlevik & Gjesdal, 2010). One interpretation of these findings is that GPs in this sample have lower knowledge of early psychosis features because they refer patients with mental health problems early for diagnostic assessments. Referral decisions are perhaps framed more in terms of dichotomous options such as treatment vs wait-and-observe, serious vs not-serious, and referral vs no-referral. As argued by Stolper et al (2011), diagnostic and referral decisions among GPs, often involving early and undifferentiated presentations, are made according to gut feelings of «there is something wrong here» thus playing a prognostic rather than a diagnostic role (Dinant, Buntinx, & Butler, 2007). Research on GPs clinical reasoning indicate that contextual information, or everything a healthcare professional knows from his/her patient apart from the signs/symptoms, are major determinants of the decision-

making process (Stolper et al., 2011).

The influence of context on referral decisions was also the topic of Paper I. The primary aim of deinstitutionalization was the reduction of the number of beds, and the introduction of the policy of «lowest level of effective care» (LEON principle). Thus, in most health care context the threshold for admission is high, with some variability between countries/regions on whether it is offered only for patients who pose emergency problems or patients who need treatment (e.g., for psychosis). In Paper I we found support for the hypothesis that the location of treatment facilities, in terms of geographical distance to psychiatric acute wards, has an independent effect on treatment delay. Distance to community mental health was unrelated to delay. The influence of geographical accessibility on utilization rates has been documented in other areas such as out-of-hours emergency clinics (Raknes, Hansen, & Hunskaar, 2013) and referral rates to general hospitals (Burns, Wholey, & Huonker, 1989). This study is to our knowledge the first to report on distance to acute care as a determinant of DUP.

Clinical decision-making is influenced by both clinical and non-clinical factors (Hajjaj, Salek, Basra, & Finlay, 2010). In clinical practice, referral decisions are made according to traditional clinical criteria, but equally influential are non-clinical factors such as the characteristics of the patient (e.g., a chaotic life style), characteristics of the healthcare professional (e.g., diagnostic knowledge, knowledge of referral pathways), or characteristics of the health care context (e.g., geographical location, ideological policies). Our findings indicate that contextual information is an important determinant of referral decisions in early psychosis. In terms of GPs referral to specialist care, highly available local specialist services translates into fast referrals, perhaps reflecting a culture of collaboration between GP and specialist levels of care in the Norwegian health care context, and the use of contextual information (e.g., the patient context) to inform decisions.

Effects on context on referral decisions were also observed in the timing of hospital referrals, and longer straight-line distance to hospitals significantly delayed referrals. In early psychosis, the mentally ill person often lack insight and is not able to evaluate different treatment options. As such, the person is at the mercy of the clinical decision making and referral behavior of the healthcare professional. Increasing awareness of the potential role of non-clinical factors in clinical decision-making and referral decisions could be an important target in efforts to reduce treatment delay, especially in more sparsely populated areas.

8.3.2 The context of recognizing psychosis: assessment practices and late treatment response

Recognizing psychosis, especially in its early phases, is inherently difficult because patients often present with symptoms that are non-specific, ambiguous, or they have an unusual symptom presentation (Brunet, Birchwood, Lester, & Iqbal, 2006; Preti, Cella, & Raballo, 2014; Boonstra, Wunderink, Sytma, & Wiersma, 2008). This was evident in Paper III where community practitioners noted that diagnostic uncertainty could be an important determinant of delay. Informants expressed that patients present with ambiguous symptoms or «symptoms of everything», often resolved by watchful waiting until diagnostic clarity could be attained. Similarly, a main finding in Paper II was that the presenting complaint in many first episode patients was for non-specific or concomitant problems rather than psychotic symptoms. For patients presenting to GPs with a «lanthanic presentation», psychotic symptoms were only identified in 30 % when reaching the specialist level (first mental health contact).

Furthermore, we found that a neurotic onset was related to treatment delay, specifically to the service component of DUP. Although other studies have also documented treatment delay related to diagnostic uncertainty (Norman et al., 2004; Brunet et al., 2007; Boonstra et al., 2008), our findings indicate a delay specifically related to the mode of presentation. Thus, more easily recognizable, but non-specific symptoms, such as anxiety, depression, substance use or distress, can mask underlying psychosis and contribute to treatment delay. The early psychiatrists concept of pseudo-neurotic forms of schizophrenia seems relevant here (Hoch & Polatin, 1949; Strahl, 1980; Connor, Nelson, Walterfang, Velakoulis, & Thompson, 2009). However, in recent decades, the only source of psychopathological knowledge for most mental health care professionals is the DSM/ICD manuals. In these manuals symptoms which overlap categories have been removed, and it is therefore a novelty for some clinicians to learn that symptoms such as depression and various anxiety disorders are often a part of psychotic disorders (Parnas, 2015).

Our interpretation of these findings was that service delay could be related to inadequate assessment practices and lack of knowledge of the science of psychopathology. The recognition of psychosis involves a cognitive activity on the part of healthcare professionals weighing cross-sectional and longitudinal clinical data, with an eye to contextual information such as the gestalt of the patient (Parnas, 2012) and actuarial data (Ruhrmann, Schultze-

Lutter, & Klosterkötter, 2010). It has been argued that current diagnostic practices is often reduced to a «associative event» (Parnas, 2015). If a patient complains of feeling down the diagnosis is depression, complaints of difficulties in concentration and attention immediately suggests ADHD, and if complaints of difficulties in social interactions are presented the diagnosis of Aspergers syndrome dominates the cognitive field. This impressionistic approach to the diagnostic process is likely to lead to misdiagnosis and late treatment response. Diagnostic work is also influenced by over-reliance on research-based structured assessment methods that are likely to lead to more missed diagnosis (Nordgaard, Revsbech, Sæbye, & Parnas, 2012), and the influence of various «diagnostic cultures» (e.g., discounting psychotic symptoms by renaming them «dissociative») (Nordgaard et al., 2017).

8.4. DUP as a multidimensional construct - delay as co-determined

The theoretical model used in this study conceptualize DUP as multidimensional construct. Treatment delay is determined by factors at different levels. At the intrinsic level are the illness/patient related factors shaping help-seeking behavior, and at the extrinsic level are the service/system related factors shaping the response to this behavior. The composition of local health contexts - what services are available, how accessible they are, how consultations, diagnostic work and decision-making processes are made - will set parameters on the potential routes to care and provision of treatment. Thus, DUP is not a stochastic event, but is co-determined, and we need to understand both intrinsic and extrinsic factors, and their interaction, in determining the points of entry into the healthcare system. Many studies of determinants of DUP have not taken into account the potential influence of the service/system context on shaping the pathways to care (Morgan, Mallett, Hutchinson, & Leff, 2004)

To quantify the influence of the several intrinsic and extrinsic factors on DUP, we used multivariable statistical models in Papers I and II. Previous research has established three important intrinsic factors associated with DUP: premorbid change, age at onset and mode of onset. These were adjusted for in the statistical models estimating the association between predictors and outcomes.

In Paper I we tested the hypothesis that the extrinsic (service/system) variable, geographical accessibility, was an independent predictor of treatment delay, by statistically adjusting for the intrinsic factors in the model. We found support for this hypothesis and our

interpretation is that «perceived access» is lower in remote areas, and can potentially lead to longer DUP. We also suggested that this effect might be stronger if the patient has an insidious onset, further delaying detection and referral. The finding that living in a peripheral area is associated with prolonged DUP has also been found in a recent Danish study (Hastrup et al., 2017).

In Paper II we tested the hypothesis that in first episode patients presenting to health services with a non-psychotic initial complaint, a lanthanic presentation, will have a long service delay, after adjusting for the intrinsic factors. We found support for this hypothesis and our interpretation is that assessment procedures in mental health often are impressionistic and have a focal vision on the first verbalization of the patient, thereby failing to detect the underlying psychopathology.

More sophisticated modeling and probability analysis is needed in DUP research. Future studies should use more sophisticated statistical regression models, to quantify the association between predictors of interest and DUP, while controlling for the effects of patient level predictors known to be associated with DUP.

9.0 Conclusions

The aim of the present study was to provide a descriptive epidemiology of where treatment delay occurs, and explore what causes treatment delay in this specific healthcare context. Our findings indicate that, although recent research has elucidated several important determinants of the patient interval, the heterogeneity of psychosis, diversity of symptoms, and the highly idiosyncratic ways patients present to services, is probably underestimated by many healthcare professionals. Thus, the initiation of help-seeking is highly dependent on the social context, first contact may be GPs, emergency clinics or the criminal justice system, complaints may be for psychotic or non-specific symptoms, and there is great variability in the routes taken before receiving adequate care.

The present finding of substantial delay occurring within specialist mental health services is in line with recent studies in other health care contexts. Aspects of the referral pathway and diagnostic delay are important determinants of this service/system interval.

We found that referral decisions are highly dependent on the context of the decision-making process. Perceived availability and accessibility of specialist services among GPs in Norway translate into timely specialist referral. When GPs suspect mental health issues, perhaps utilizing contextual information and «gut feelings» to evaluate severity, prompt referrals are made, and collaboration between GPs and specialist in the assessment and treatment in mental health problems is well established. We also found context effects in hospital referrals. The threshold for hospital referral depend not only on clinical factors, but also on non-clinical factors (e.g., personal knowledge of referrers, contextual information on the patient, and institutional factors such as ideology and healthcare policies). Our findings highlight that the location and nature of hospital facilities may also cause elevated thresholds.

Our findings also indicate that failure to detect psychosis, delayed diagnosis and misdiagnosis, are important reasons for delay within healthcare services. The great diversity in onset, course, and psychopathological profile, often makes diagnostic work challenging. In early psychosis, a neurotic onset is not uncommon. Patients may present with more easily recognizable symptoms such as depression, anxiety, and substance abuse, masking the underlying psychotic psychopathology. Underestimating this heterogeneity in first presentations, and the use of impressionistic assessment practices and «associative diagnosis» are proposed as possible explanations for this delay.

In conclusion, we argue that DUP is a multidimensional construct implicating both intrinsic and extrinsic factors. Treatment delay is likely the result of a dynamic process shaped by an interplay of intrinsic and extrinsic factors within a specific health care context. The finding of a substantial service/system delay has several implications. Although increasing the general mental health literacy in youths by educational campaigns is important for reducing delay in help-seeking, the gain will be largely undone if the service/system delay is not also reduced. An important target for early intervention is therefore improving referral pathways and reducing delayed diagnosis in patients that are already receiving care from mental health services.

10.0 Further perspectives

10.1 Improving referral pathways

A strategy to reduce treatment delay would benefit from implementing specialized services for further assessment and initiation of treatment for early psychosis. Adequate and accessible outpatient and inpatient resources are needed. The routes to health care are highly diverse in early psychosis, and patients may access services in a number of ways. Improving referral pathways, keying in on GPs, emergency clinics and generic community mental health, could be effective in reducing the service component of DUP. In real-world settings referral decisions will be influenced by both clinical and non-clinical factors. Referrers knowledge and perceived accessibility of specialized services is vital for a referral to occur, especially in more sparsely populated areas

The proposed multidimensional model of DUP suggest that the impact of patient level determinants may vary depending on the specific context. Thus, the effect of spatial distance is perhaps more likely in patients presenting with an insidious or a neurotic onset. Strategies to improve appropriate and urgent referral, including hospital referral, for further assessment also in these cases should be an important target.

10.2 Improving diagnostic practices

Psychosis should be a differential diagnosis in the evaluation of every referral, regardless of the presenting complaint. Underestimating the heterogeneity of psychosis and its diversity of presentations is important for understanding how delay within mental health occurs.

The findings in this study encourage a more comprehensive assessment of in patients presenting to mental health services. Psychosis is a complex and heterogeneous disorder, and every possible psychopathological phenomenon can occur during its course. Teaching of an adequate interview approach and the science of psychopathology are needed. In addition, mental health practitioners need to be aware of the concept of differential diagnosis and potential influences on the diagnostic process. Proper diagnostic work involves familiarity with the prototypical structure of psychopathology, a phenomenological perspective, knowledge of diagnostic hierarchies and the concept of spectrums, and most importantly, being exposed to an academic, rigorous and peer-shared reflection.

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Paper I

Kvig, EI., Brinchmann, B., Moe, C., Nilssen, S., Larsen, TK., & Sørgaard, K.

Geographical accessibility and duration of untreated psychosis: distance as a determinant of treatment delay.

BMC Psychiatry (2017), 17: 176.

PubMed: PMID 28486982

Paper II

Kvig, EI., Brinchmann, B., Moe, C., Nilssen, S., Larsen, TK., & Sørgaard, K

"Lanthanic presentation" in first episode psychosis predicts long service delay: the challenge of detecting masked psychosis.

Psychopathology (2017), 50(4), 282-289.

PubMed: PMID 28797004

Paper III

Kvig, EI., Moe, C., Brinchmann, B., Larsen, TK., & Sørgaard, K.

Negotiating the boundaries of psychosis: A qualitative study of the service provider perspective on treatment delay in community mental health.

Early Intervention in Psychiatry (2017). Aug 23 (Epub ahead of print).

PubMed: PMID 28836376

Paper IV

Kvig, EI, Brinchmann, B., Moe, C., Larsen, TK., & Sørgaard, K.

What do General Practitioners know about early psychosis? A survey of the diagnostic knowledge among gatekeepers to specialist mental health care in Northern Norway.

Submitted to *BMC Health Services Research* (2018, April)

Appendices

1. Regional Ethics Committee notification

2. Invitation and consent forms

- a. Invitation to participate for treated patients (hospital and CMHC versions)
- b. Consent form for treated patients
- c. Invitation to participate for community practitioners
- d. Consent form for community practitioners
- e. Invitation letter to general practitioners
- f. Reminder letter for general practitioners

3. Materials for treated patients sample

- a. Nottingham Onset Schedule – DUP, Norwegian translation
- b. Gater Encounter Form, Norwegian version
- c. Route timeline

4. Materials for community practitioners sample

- a. Questionnaire on community practitioner background
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5. Materials for general practitioners sample

- a. Endorsement letter
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6. Examples of memos and coding process in community sample

- a. Case-based memo
- b. Theoretical memo
- c. Open codes after three interviews
- d. Theoretical coding - sorting

Appendix 1

Regional Ethics Committee notification



UNIVERSITETET I OSLO

DET MEDISINSKE FAKULTET

Seksjonsleder Knut W. Sørgaard
Nordlandssykehuset
Fagavd
8092 Bodø

**Regional komité for medisinsk og helsefaglig
forskningsetikk Sør-Øst D (REK Sør-Øst D)**

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Nettadresse: www.etikkom.no

Dato: 30.10.09

Deres ref.:

Vår ref.: 2009/1426

2009/1426 Varighet av Ubehandlet Psykose i Nordland

Vi viser til søknad av 07.09.09 om godkjenning av ovenfor nevnte forskningsprosjekt.

Prosjektleder er dr. philos, psykolog Knut W. Sørgaard.

Forskningsansvarlig er Nordlandssykehuset HF, avd. Bodø.

Prosjekttema:

Pasienter med psykoselidelser har en lang varighet av ubehandlet psykose (VUP), typisk mellom 1-2 år. Denne studien skal man undersøke tre kilder til forsinkelse i behandling for pasientgruppen; 1) Pasient- eller sykdomsrelaterte forsinkelser, 2) Forsinkelse i henvisning fra primærhelsetjenesten og 3) Forsinkelser i spesialisthelsetjenesten. 120 pasienter skal inkluderes i studien.

Komiteen har vurdert søknaden og godkjenner at prosjektet gjennomføres med hjemmel i helseforskningsloven § 10, jf. forskningsetikkloven § 4.

Tillatelsen er gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknaden og protokollen, og de bestemmelser som følger av helseforskningsloven med forskrifter. Komiteen anbefaler imidlertid at det i informasjonsskrivet gjøres noe bedre rede for hva en telemedisinsk konsultasjon innebærer.

Dersom det skal gjøres endringer i prosjektet i forhold til de opplysninger som er gitt i søknaden må prosjektleder sende endringsmelding til REK. Vi gjør oppmerksom på at hvis endringene er vesentlige må prosjektleder sende ny søknad, eller REK kan pålegge at dette gjøres.

Forskningsprosjektets data skal oppbevares forsvarlig, se personopplysningsforskriften kapittel 2, og Helsedirektoratets veileder for «Personvern og informasjonssikkerhet i forskningsprosjekter innenfor helse- og omsorgssektoren», <http://www.norsk-helsenett.no/informasjonsikkerhet/bransjenormen/Personvern%20og%20informasjonsikkerhet%20i%20forskningsprosjekter%20v1.pdf>

Tillatelsen gjelder til 31.12.2016. Av dokumentasjonshensyn skal opplysningene bevares inntil 31.12.2021. Opplysningene skal lagres aidentifisert, det vil si atskilt i en nøkkel- og en opplysningsfil. Opplysningene skal deretter slettes eller anonymiseres.

Prosjektet skal sende sluttmelding, se helseforskningsloven § 12, senest 31.06.2017.

Vedtak:

Komiteen godkjenner at prosjektet gjennomføres i samsvar med det som framgår av søknaden

Vedtaket var enstemmig

REK har gått over til elektronisk saksbehandling og fått ny saksportal:

<http://helseforskning.etikkom.no>. Vi ber om at svar på merknader og henvendelser til REK sendes inn via denne portalen eller på epost: post@helseforskning.etikkom.no. Vennligst oppgi REKs saksnummer.

Med vennlig hilsen

Stein A. Evensen (sign.)
Professor dr.med.
leder

Ingrid Middelthon (sign.)
komitésekretær

Brevet er godkjent elektronisk

Appendices 2a-f

Invitation and consent forms

Appendix 2a

Invitation to participate for treated patients

Invitasjon til deltakelse i forskningsprosjektet:

”Varighet av Ubehandlet Psykose & Behandlingsveier i Nordland”

Bakgrunn og hensikt

Dette er en invitasjon til å delta i forskningsprosjektet ”Varighet av ubehandlet psykose og behandlingsveier i Nordland”. Målet med studien er å finne ut hvilke erfaringer deltakerne har med hjelpeapparatet, både i hjemkommunen og på sykehuset, og om de opplevde å få hjelp når de trengte det. Vi er også interessert i å lære mer om hvordan psykiske problemer påvirker ulike livsområder, som for eksempel skole, arbeid, venner og familieliv.

Studien gjennomføres av en forskningsgruppe bestående av doktorgradsstudent Erling Kvig, og to forskningsassistenter Beate Brinchmann og Cathrine Moe. Veiledere for studien er forskningsleder ved Nordlandssykehuset Knut Sjørgård, samt professor Tor K Larsen (Universitetet i Stavanger) og PhD Grigory Rezvy (Nordlandssykehuset).

Hva innebærer studien?

Vi vil be om at en person fra forskningsgruppen kan få intervjuet deg. Intervjuet vil foregå i avdelingen eller på vårt kontor, og vil vare i omtrent to timer. Vi ønsker å vite noe om din oppvekst, hvordan du har opplevd å få psykotiske symptomer, hvordan du har oppsøkt hjelp for disse og hvilken behandling du har fått. Under intervjuet vil vi bruke en tidslinje for å tidfeste ulike hendelser i livet ditt og intervjuet vil bli tatt opp med båndopptaker. I forkant av intervjuet vil vi snakke med din behandler eller lese i journal for bakgrunnsopplysninger om tidligere behandling.

Hva skjer med informasjonen om deg?

All informasjon blir anonymisert. Dette betyr at alle opplysninger blir behandlet uten navn og fødselsnummer eller andre gjenkjennende opplysninger. En kode knytter deg til dine opplysninger gjennom en navneliste. Denne navneliste blir forsvarlig oppbevart.

Det er kun autorisert helsepersonell som er knyttet til prosjektet som har adgang til navnelisten, og som kan finne tilbake til deg. Informasjonen som innhentes slettes 5 år etter at studien er avsluttet.

Det vil ikke være mulig å identifisere deg i resultatene av studien når disse publiseres.

Frivillig deltakelse

Det er frivillig å delta i studien. Du kan når som helst og uten å oppgi noen grunn trekke ditt samtykke til å delta i studien. Dette vil ikke få konsekvenser for din videre behandling. Om du nå sier ja til å delta, kan du senere trekke tilbake ditt samtykke uten at det påvirker din øvrige behandling.

Intervju med foreldre eller en nærstående person

Dersom du tillater det vil vi be om et intervju med dine foreldre. De vil bli intervjuet pr. telefon og få spørsmål om deres erfaring av din sykdom og hvordan dere søkte hjelp. Deltakelse i studien er ikke avhengig av om du samtykker til dette.

Samtykkeerklæring

Hvis du ønsker å delta i studien ber vi om at du leser og underskriver samtykkeerklæringen som ligger vedlagt. Dersom du ikke ønsker å delta vil vi takke deg for din tid.

For mer informasjon om studien

Se hjemmesiden til Enhet for Nysyke med Psykose (ENP) ved Nordlandssykehuset

www.nlsh.no/enp/
(klikk på fanen for "Forskning")

Har du spørsmål til studien, eller ønsker å trekke deg, ta kontakt med oss

Erling Kvig/ Beate Brinchmann / Cathrine Moe

telefon 75501532 / 75501533

e-post : enp@nlsh.no

Forskningsgruppen er ansatt ved Enhet for Nysyke med Psykose,
Rehabiliteringsavdelingen
Nordlandssykehuset HF, psykisk helse og rusklinikken

Invitasjon til deltakelse i forskningsprosjektet:

”Varighet av Ubehandlet Psykose & Behandlingsveier i Nordland”

Bakgrunn og hensikt

Dette er en invitasjon til å delta i forskningsprosjektet ”Varighet av ubehandlet psykose og behandlingsveier i Nordland”. Målet med studien er å finne ut hvilke erfaringer deltakerne har med hjelpeapparatet, både i hjemkommunen og på sykehuset, og om de opplevde å få hjelp når de trengte det. Vi er også interessert i å lære mer om hvordan psykiske problemer påvirker ulike livsområder, som for eksempel skole, arbeid, venner og familieliv.

Studien gjennomføres av en forskningsgruppe bestående av doktorgradsstudent Erling Kvig, og to forskningsassistenter Beate Brinchmann og Cathrine Moe. Veiledere for studien er forskningsleder ved Nordlandssykehuset Knut Sjørgård, samt professor Tor K Larsen (Universitetet i Stavanger) og PhD Grigory Rezvy (Nordlandssykehuset).

Hva innebærer studien?

Vi vil be om at en person fra forskningsgruppen kan få intervju deg. Intervjuet vil foregå på poliklinikken eller hjemme hos deg, og vil vare i omtrent to timer. Vi ønsker å vite noe om din oppvekst, hvordan du har opplevd å få psykotiske symptomer, hvordan du har oppsøkt hjelp for disse og hvilken behandling du har fått. Under intervjuet vil vi bruke en tidslinje for å tidfeste ulike hendelser i livet ditt og intervjuet vil bli tatt opp med båndopptaker. I forkant av intervjuet vil vi snakke med din behandler eller lese i journal for bakgrunnsopplysninger om tidligere behandling.

Hva skjer med informasjonen om deg?

All informasjon blir anonymisert. Dette betyr at alle opplysninger blir behandlet uten navn og fødselsnummer eller andre gjenkjennende opplysninger. En kode knytter deg til dine opplysninger gjennom en navneliste. Denne navneliste blir forsvarlig oppbevart.

Det er kun autorisert helsepersonell som er knyttet til prosjektet som har adgang til navnelisten, og som kan finne tilbake til deg. Informasjonen som innhentes slettes 5 år etter at studien er avsluttet.

Det vil ikke være mulig å identifisere deg i resultatene av studien når disse publiseres.

Frivillig deltakelse

Det er frivillig å delta i studien. Du kan når som helst og uten å oppgi noen grunn trekke ditt samtykke til å delta i studien. Dette vil ikke få konsekvenser for din videre behandling. Om du nå sier ja til å delta, kan du senere trekke tilbake ditt samtykke uten at det påvirker din øvrige behandling.

Intervju med foreldre eller en nærstående person

Dersom du tillater det vil vi be om et intervju med dine foreldre. De vil bli intervjuet pr. telefon og få spørsmål om deres erfaring av din sykdom og hvordan dere søkte hjelp. Deltakelse i studien er ikke avhengig av om du samtykker til dette.

Samtykkeerklæring

Hvis du ønsker å delta i studien ber vi om at du leser og underskriver samtykkeerklæringen som ligger vedlagt. Dersom du ikke ønsker å delta vil vi takke deg for din tid.

For mer informasjon om studien

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Rehabiliteringsavdelingen
Nordlandssykehuset HF, psykisk helse og rusklinikken

Appendix 2b

Consent form for treated patients

Samtykke til deltakelse i forskningsprosjektet

”Varighet av Ubehandlet Psykose & Behandlingsveier i Nordland”

Jeg bekrefter å ha fått muntlig og skriftlig informasjon (informasjonsskriv 02.09-2010-versjon 1) om studien.

Jeg er også informert om at jeg kan si nei til å delta uten at det vil påvirke videre behandling, og at jeg når som helst kan velge å trekke meg fra studien.

Jeg ønsker å delta i studien

(signert av prosjektdeltaker, dato)

(signert av forsker, dato)

Jeg samtykker til at mine pårørende kan kontaktes for deltakelse i studien

(signert av prosjektdeltaker, dato)

Navn, adresse og telefonnummer på pårørende som kan kontaktes:

Appendix 2c

Invitation to participate for community practitioners

Invitasjon til deltakelse i forskningsprosjektet

"Varighet av Ubehandlet Psykose & Behandlingsveier i Nordland"

Bakgrunn og hensikt

Dette er en invitasjon til å delta i forskningsstudien "Varighet av ubehandlet psykose og behandlingsveier i Nordland". Formålet med studien er å øke vår kunnskap om når og hvordan mennesker med psykoselidelser kommer i kontakt med hjelpeapparatet i Nordland fylke. Kunnskap om årsaker til forsinkelser i behandlingsveier i et ruralt område som Nordland, vil også kunne belyse om det er systematiske forskjeller i forhold til mer urbane områder, og om det kan være behov for andre typer strategier for å redusere varighet av ubehandlet psykose.

Studien gjennomføres av en forskningsgruppe bestående av doktorgradsstudent Erling Kvig, og to forskningsassistenter Beate Brinchmann og Cathrine Moe. Veiledere for studien er forskningsleder ved Nordlandssykehuset Knut Sjørgård, samt professor Tor K Larsen (Universitetet i Stavanger) og PhD Grigory Rezvy (Nordlandssykehuset). Deler av studien inngår også i mastergradsprosjekt i klinisk sykepleie for Cathrine Moe, der professor Berit Brinchmann (Høgskolen i Bodø) er veileder.

Som del av denne studien ønsker vi å få vite hvordan tjenestetilbudet hos dere er organisert for å hjelpe unge mennesker som opplever psykotiske symptomer, hvilke faktorer som påvirker tjenesten, hvilke utfordringer dere har og hva som skal til for at dere kan gi det tilbudet dere ønsker. Videre ønsker vi å høre om hvilke instanser dere samarbeider med og hvilke rutiner dere har for henvisninger, samt hvordan dere planlegger og gjennomfører overgang fra BUP til DPS.

Hva innebærer studien?

Vi vil be om å få gjennomføre et fokusgruppeintervju hos dere. Intervjuet vil foregå i et egnet rom hos dere, og vil vare i 1-2 timer. Intervjuet vil bli tatt opp på bånd. Vi ønsker deltakere som har erfaring med å jobbe med unge nysyke psykotiske fra BUP og DPS. Vi ønsker rundt 5-8 deltakere der det gjerne er fordeling mellom kjønn og profesjoner (lege, psykolog, sykepleier, sosionom).

Hva skjer med informasjonen?

All informasjon blir anonymisert. Dette betyr at alle opplysninger blir behandlet uten navn eller andre gjenkjennerende opplysninger.

Det er kun personell som er knyttet til prosjektet som har adgang til datamaterialet, og det vil ikke være mulig å identifisere deltakere i resultater av studien når disse publiseres. Informasjonen som innhentes slettes 5 år etter at studien er avsluttet.

Frivillig deltakelse

Det er frivillig å delta i studien. Man kan når som helst og uten å oppgi noen grunn trekke samtykke til å delta i studien. Studien er godkjent av etisk komité.

Dersom noen hos dere ønsker å delta vil vi be om underskrivelse av samtykkeerklæring samt svar på et kort demografisk spørreskjema der vi ber om kjønn, alder og profesjonsbakgrunn. Man kan når som helst trekke tilbake samtykke, uten å oppgi noen grunn. Samtykkeskjema og spørreskjema vil bli delt ut i forkant av gruppeintervju. Ytterligere informasjon om hva studien søker å finne svar på samt temaguide til fokusgruppe ligger vedlagt.

Vi vil takke deg for din tid til å lese igjennom denne informasjonen, og håper det vil være av interesse å delta.

For mer informasjon om prosjektet ta gjerne kontakt med:

Erling Kvig/ Beate Brinchmann/ Cathrine Moe

Enhet for Nysyke med Psykose (ENP),

Nordlandssykehuset HF, psykisk helse og rusklinikken

Telefon 75501532/ 75501573

E-post enp@nlsh.no

Med vennlig hilsen

Erling Kvig

Beate Brinchmann

Cathrine Moe

Appendix 2d

Consent form for community practitioners

Samtykke til deltakelse i forskningsprosjektet

“Varighet av Ubehandlet Psykose og Behandlingsveier i Nordland”

Formålet med prosjektet er å øke vår kunnskap om når og hvordan mennesker med psykoselidelser kommer i kontakt med hjelpeapparatet i Nordland fylke.

Som en del av denne studien vil det gjennomføres fokusgruppeintervju ved DPS. All informasjon fra intervjuet blir anonymisert. Dette betyr at alle opplysninger blir behandlet uten navn eller andre gjenkjennende opplysninger.

Det er kun personell som er knyttet til prosjektet som har adgang til datamaterialet, og det vil ikke være mulig å identifisere deltakere i resultater av studien når disse publiseres. Informasjonen som innhentes slettes 5 år etter at studien er avsluttet.

Det er frivillig å delta i studien, og man kan når som helst og uten å oppgi noen grunn trekke samtykke til å delta i studien. Studien er godkjent av etisk komité

Jeg bekrefter å ha lest informasjon om studien og ønsker å delta i fokusgruppeintervju og svare på demografisk spørreskjema.

(dato, signatur av prosjektdeltaker)

Appendix 2e

Invitation letter to general practitioners

Invitasjon til deltakelse i forskningsprosjektet

”Varighet av Ubehandlet Psykose & Behandlingsveier i Nordland”

Bakgrunn og hensikt

Dette er en invitasjon til å delta i forskningsstudien ”Varighet av ubehandlet psykose og behandlingsveier i Nordland”. Målet med studien er å øke vår kunnskap om når og hvordan mennesker med psykoselidelser kommer i kontakt med hjelpeapparatet i Nordland fylke.

Studien gjennomføres av en forskningsgruppe bestående av doktorgradsstudent Erling Kvig, og to forskningsassistenter Beate Brinchmann og Cathrine Moe. Veiledere for studien er forskningsleder ved Nordlandssykehuset Knut Sørgård, samt professor Tor K Larsen (Universitetet i Stavanger) og Dr.med Grigory Rezvy (Nordlandssykehuset).

Hva innebærer studien?

Vi vil be deg om å svare på spørreskjema som vil bli tilsendt på e-post. All informasjon er anonymisert, og slettes 5 år etter at studien er avsluttet. Det er kun personell som er knyttet til prosjektet som har adgang til informasjon.

Det vil ikke være mulig å identifisere deg i resultatene av studien når disse publiseres.

For mer informasjon om studien

Se hjemmesiden til Enhet for Nysyke med Psykose (ENP) ved Nordlandssykehuset

www.nlsh.no/enp/forskning

Har du spørsmål til studien, eller ønsker å trekke deg, ta kontakt med oss

Erling Kvig/ Beate Brinchmann / Cathrine Moe

telefon 75501532 / 75501533

e-post : enp@nlsh.no

Appendix 2f

Reminder letter to general practitioners

INVITASJON TIL DELTAKELSE

Dette er andre utsendelse av invitasjon til å delta i forskningsstudien "Varighet av ubehandlet psykose og behandlingsveier i Nordland".

Dersom du tidligere har svart på undersøkelsen ønsker vi å takke deg og ber om at du ser bort fra denne invitasjonen.

Vi vil be deg om å svare på det vedlagte spørreskjema. På første side fyller du inn det tall som blir din kode i kodesystemet for anonymisering. Fyll så inn dine svar, før du returnerer skjema i vedlagt svarkonvolutt. Takk for din deltakelse.

For mer informasjon om studien

Se hjemmesiden til Enhet for Nysyke med Psykose (ENP) ved Nordlandssykehuset

www.nlsh.no/enp/
(klikk på fanen for forskning)

Har du spørsmål til studien, eller ønsker å trekke deg, ta kontakt med oss

Erling Kvig/ Beate Brinchmann / Cathrine Moe

telefon 75501532 / 75501533

e-post : enp@nlsh.no

Appendices 3a-c

Materials for treated patient sample

Appendix 3a

Nottingham Onset Schedule, Norwegian version

NOS DUP

Nottingham Onset Schedule – Duration of Untreated Psychosis

NORSK UTGAVE

Originalpublikasjon: Singh, SP, Cooper, JE, Fisher, H et al (2005) Determining the chronology and components of psychosis onset: the Nottingham Onset Schedule (NOS). Schizophrenia Research, 80: 117-130.

Norsk oversettelse av Erling Inge Kvig, Cathrine Moe og Beate Brinchmann, Nordlandssykehuset, Psykisk helse og rus, Rehabiliteringsavdelingen

ID #: _____ Født: _____ Kjønn: _____

Dato: ____ / ____ / ____

Nåværende psykiatrisk diagnose: _____

Dato for innleggelse/kontakt psykisk helsevern: _____

Intervjuer: _____

Samtykkeskjema underskrevet: _____

3: NOS INTERVJU

ADMINISTRERING: Intervjuet gjennomføres ved baseline.

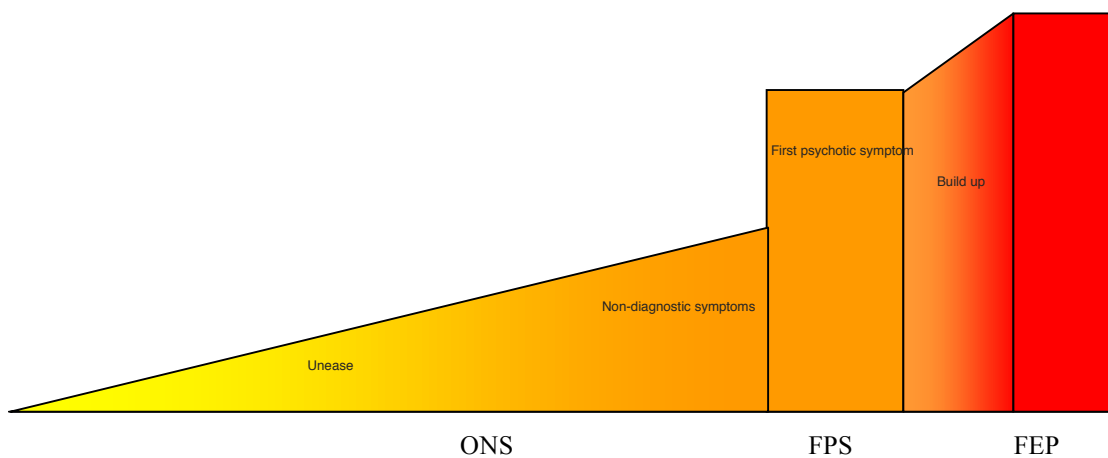
FORMÅL: Å kartlegge de ulike tidspunkt i debut av psykose.

Innledning

The Nottingham Onset Schedule-DUP version (NOS-DUP) er et kort, semistrukturert intervju for å kartlegge flere tidspunkt ved debut av psykose.

Begrepet debut i NOS: Debut er definert som perioden mellom de første rapporterte/observerte forandringer i mental tilstand/atferd til utvikling av psykotiske symptomer (overgang inn i/til psykose). Debut kan fremtre som:

- fremtredelse av symptomer som angst, depresjon, irritabilitet osv.
- fremtredelse av svekkelser, i form av psykologiske, kognitive, sosiale eller atferdsmessige svekkelser
- fremtredelse av uvanlig eller bisarr atferd
- funksjonsnedsettelse på det mellommenneskelige, sosiale, utdannings- og yrkesmessige områder
- fremtredelse av psykotiske symptomer
- overgang til psykose (utvikling av vedvarende psykotiske symptomer)



Debut er begrepsmessige definert som bestående av:

- et prodrom, som begynner med debut av ikke-diagnostiske symptomer (ONS)
- fremtredelse av positive psykotiske symptomer (FPS); og
- oppbygging av symptomer som fører til første psykotiske episode (FEP)

Overgangen til psykose er det punktet der symptomene når tilstrekkelig varighet og intensitet til å gi en sikker diagnose på en psykotisk lidelse. *Tilstrekkelig varighet* er definert som at symptomene forekommer på de fleste dagene i minst en uke. *Tilstrekkelig intensitet* innebærer at symptomene har en betydelig innvirkning på personens fungering. Et slik symptom vil gi en skåre på 4 eller mer på PANSS.

NOS tillater flere måter å definere DUP på: fra start av prodromet til oppstart av behandling (varighet av ubehandlet sykdom); fra fremtredelse av første psykotiske symptom til start av behandling; og fra dato for sikker diagnose til start av behandling.

DEFINISJONER I NOS:**DEBUT AV IKKE DIAGNOSTISKE SYMPTOMER (ONS)****Definisjon:**

Prodrom er definert som "sykdomsfasen før fremtredelse av klare psykotiske symptomer".

Prodromet består av

- 1) debut av ikke-diagnostiske symptomer (ONS), og
- 2) de første (avblekede/forbigående) psykotiske symptomer.

Debut av prodromalsymptomer inkluderer vanligvis ikke-spesifikke forstyrrelser i stemning, tenkning, atferd, persepsjon og fungering. For at slike symptomer skal bli vurdert som en del av den psykotiske lidelse, må symptomet vedvare uten oppnåelse av tidligere premorbid fungering, før gjennombrudd av psykose.

**Merk at en person kan beskrive lav sosial kontakt og tilbaketrekning som del av sin væremåte i barne- og ungdomsalder, men først senere uttrykke at de har mistet interesser for vennskap. Kun en åpenbar forverring av slike karakteristika skal defineres som symptom på prodromale tilstander.*

Operasjonalisering:

Debut av prodromet har to faser:

- P1 er en periode med "ubehag"
- P2 er "ikke-diagnostiske symptomer".

Et symptom kan defineres som "ubehag" hvis det var utvetydig tilstede, men ikke av en slik alvorlighetsgrad at det kan oppfylle kriteriet til å fylle skåren 1 på SCAN (WHO, 1992). Enhver høyere skåring vurderes som et ikke-diagnostisk symptom, fremfor ubehag.

Når det gjelder måling av DUP, er de to subkomponentene av prodromet regnet som en fase, og debut av prodromet er vurdert som "debut av de første rapporterte/observerte forandringer i stemning og atferd" (= debut av ikke-diagnostiske symptomer, ONS).

Sjekklisten og kortstokk for prodromalsymptomene er gruppert og inkluderer forstyrrelser i stemning, tenkning, atferd og persepsjon

FØRSTE PSYKOTISKE SYMPTOM (FPS)

Definisjon:

Første psykotiske symptom (FPS) defineres som "tilstedeværelse av et eller flere positive psykotiske symptom".

Slik NOS definerer FPS kan det også bestå av "avblekede" og/eller "forbigående" psykotiske symptomer, som eventuelt kan øke i intensitet og varighet til de når et psykotisk nivå.

Operasjonalisering:

Pre-psykotiske manifestasjoner av psykotiske symptomer er vurdert som prodromal hvis:

KORTVARIG FORBIGÅENDE PSYKOSE:

En **skåring på 4 eller mer** på Positive and Negative Syndrome Scale (PANSS) ledd P1 Vrangforestillinger, P3 Hallusinatorisk atferd eller en **skåring på 5 eller mer** på P2 Tankemessig desorganisering

PLUSS

Symptomene er tilstede i mindre enn én uke, eller forsvunnet uten antipsykotisk medikasjon

AVBLEKEDE SYMPTOMER:

En **skåring på 3** på P1 Vrangforestillinger, eller en **skåring på 2-3** på P3 Hallusinatorisk atferd, eller en **skåring på 3-4** på P6 Mistenksomhet/Forfølgelsesidéer, eller en **skåring på 3-4** på P2 Tankemessig desorganisering.

Morrison, Bentall, French, Walford, Kilcommons, Knight, Kreutz, Lewis (2002) Randomised controlled trial of early detection and cognitive therapy for preventing transition to psychosis in high-risk individuals. Study design and interim analysis of transition rate and psychological risk factors. *British Journal of Psychiatry*, 181 (suppl. 43), 78-84.

FIRST EPISODE PSYCHOSIS (FEP)

Definisjon:

Første episode psykose er definert som "tydelig påvist tilstedeværelse av vrangforestillinger, hallusinasjoner, førsterangssymptomer, katatone symptomer eller tankeforstyrrelser"

Overgangen til psykose er det punktet der symptomene når tilstrekkelig varighet og intensitet til å gi en sikker diagnose på en psykotisk lidelse.

Operasjonalisering:

Tilstrekkelig varighet er definert som at symptomene forekommer på de fleste dagene i en uke eller mer (Larsen 1996)

Tilstrekkelig intensitet innebærer at symptomene har en betydelig innvirkning på personens fungering.

Når et symptom tilfredstiller varighet og intensitetskriteriet, er dato for episodens debut (mnd/år), den dato når symptomet først inntreffer på terskelverdien av varighet/ intensitet.

Debut dato for FEP (estimert av forsker) er definert som datoen når:

FØRSTE EPISODE PSYKOSE:

En skåring på 4 eller mer på Positive and Negative Syndrome Scale (PANSS) ledd P1 Vrangforestillinger, P5 Storhetsidéer, P6 Mistenksomhet/Forfølgelsesidéer, P3 Hallusinatorisk atferd or G9 Uvanlig tankeinnhold, i konteksten av manifeste psykotiske symptomer.

Symptomene må ha vart hele dagen i flere dager eller flere ganger i uken i flere uker. Ikke begrenset til noen korte øyeblikk.

PLUSS

Symptomene må ha vært tilstede i en periode på to uker eller mer. (ta høyde for remisjon som følge av behandling) for å bli vurdert som debut av psykose.

ETTERLEVELSE AV BEHANDLING (TC)

Definisjon:

Etterlevelse av behandling er definert som "datoen for når behandling er påbegynt i en klinisk adekvat dose som etterleves"

Operasjonalisering:

Etterlevelse er definert som "at pasienten tar sin medisin med sikkerhet i minst 75% av tiden og i minst 75% av den anbefalte dose".

Etterlevelse kan antas hvis pasienten følges opp av hjemmesykepleien eller på sykehus, og det ikke foreligger noen historie på mangelfull etterlevelse. Når en pasient initialt har hatt mangelfull etterlevelse, er dato for start av behandling det tidspunkt pasienten begynner å ta medisinen sin.

ETTERLEVELSE AV BEHANDLING

Dette er definert som datoen når *antipsykotisk behandling påbegynnes i klinisk adekvat dosering* der det er *evidens for etterlevelse*, som:

1a er ved eller over anbefalt dosering anbefalt av IRIS retningslinjer (se vedlagt liste)

OG

1b fortsetter for en periode på minst 1 mnd. Etterlevelse er vurdert i henhold til overnevnte kriterier.

Ekvivalente antipsykotikum doser:

| antipsykotikum | Daglig dose |
|-----------------|-------------|
| chlorpromazine | 100 mg |
| clozapine | 50 mg |
| haloperidol | 2–3 mg |
| loxapine | 10-20 mg |
| pimozide | 2 mg |
| sulpiride | 200 mg |
| thioridazine | 100 mg |
| trifluoperazine | 5 mg |
| risperidone | 2-3 mg |

* "IRIS guidelines recommend a dosage equivalent to 2-3mg haloperidol. Equivalent dosages were obtained from the BNF (pg 173). The dosage for risperidone however is an exception, as IRIS specify a dosage of 2-4mg".

GJENNOMFØRING OG SKÅRING AV NOS INTERVJUET:

i) NOS er laget for å bli administrert:

- med en pasient og en informant,
- så nært som mulig til tidspunktet for debut av lidelse.
- etter at anamnese og psykisk status presens er gjennomført.

Intervjuet gjennomføres i henhold til den overordnede strukturen i NOS, men rekkefølgen for de ulike delene vil være avhengig av de nøkkeldatoer og sentrale hendelser som foreløpig er stadfestet. Intervjuer har betydelig grad av frihet i fremgangsmåte.

Den som blir intervjuet bør være i stand til å konsentrere seg og være oppmerksom i intervjusituasjonen samt kunne gi informert samtykke.

ii) Gjennomføring av Preliminary Assessment Sheet (PAS):

Forsikre deg om at foreløpige nøkkeldatoer og sentrale hendelser er nedtegnet i PAS før intervju med pasient. PAS fylles ut på bakgrunn av journalnotater og andre informasjonskilder før gjennomføring av intervju. Identifiser symptomer og livshendelser og betydningsfulle datoer, diagnoser, medikamentforeskrivninger, historikk på etterlevelse eller bivirkninger, og tegn på remisjon. Ha PAS med deg og benytt det som en intervjuguide.

| PRELIMINARY ASSESSMENT SHEET | | |
|------------------------------|--|-----------|
| DATE | Presentation | NOS phase |
| | | (PC) |
| Christ mas -05 | <i>Studying at university, reports being normal up to the end of term. Started feeling like couldn't cope, started feeling restless. Mother thought it was due to being over-tired.</i> | ONS |
| Dec -06 | <i>Family suffered a bereavement, AE decided to take a break away from university. He felt that couldn't cope. He went back to university, it started again. Started feeling like he couldn't cope and feeling restless. Low in mood. Mother believed it was due to the bereavement and the SAD (seasonal affective disorder). Mother called the GP, AE didn't want to go on medication. Due to past fears about his father, Doctor prescribed him medication. AE didn't take his medication. He was advised to speak to his doctor at the university.</i> | |
| Oct -08 | <i>Went abroad on holiday, his mood worsened, felt self destroyed and low in energy. At some point he reported to his mother that he had seen flashing lights/floating shades in front of his eyes.</i> | FPS |
| June/ Aug -09 | <i>Started experiencing sleep disturbances, started sleeping in mother room. Felt scared about something.</i> | |
| 24 aug/ early sept. | <i>Sleep disturbances was becoming more irregular. He started to become fixated on his dad; was hearing voices telling him something about his dad. Receiving special messages from God about his dad's health. Believed the voices were telling him to go outside of the house, and knock on neighbours doors.</i> | FEP |
| 27.09. 09 | <i>Section 2, Sheffield</i> | TC |

- iii) **Begynne intervjuet:** Forklar først for intervjupersonen at du allerede vet noe om hvordan lidelsen deres startet, og at du nå ønsker å sjekke noen detaljer for å sikre at vi har fått den riktige rekkefølgen på ting. For eksempel:

“Jeg er interessert i å finne ut mer om hvordan du følte deg og hvilke ting som skjedde med deg i de ulike stadiene av lidelsen din. Jeg er spesielt interessert i å få belyst hvordan du følte deg i den tidlige fasen, før det ble riktig åpenbart for deg og din familie at det var noe galt”

Identifiser, sammen med intervjupersonen, noen få nøkkeldatoer og sentrale hendelser som står tydelig frem, og som kan knyttes til debut av lidelsen. Etabler et så tydelig og klart bilde som mulig av komponentene til psykosedebut rundt disse. Når du er sikker på at intervjupersonen forstår formålet med intervjuet, begynn med enten den sikreste eller den første dato eller hendelse i PAS skjemaet, og still f. eks spørsmålet:

“Det står her i notatene mine at du først kom i kontakt med helseapparatet den (nevn dato). Hvordan følte du deg på det tidspunktet?”

“Følte du at det var noe galt med deg?”

“Hvilken type opplevelser hadde du?”

“På hvilken måte var du annerledes enn sånn som du brukte å være”

“Så, hvis vi jobber oss bakover i tid fra det tidspunktet, når var siste gang du følte at du var sånn som du brukte å være”

Under intervjuet er det viktig å minne intervjupersonen på at debut av lidelsen innebærer en betydelig forverring fra premorbid fungering og at personen ikke senere gjenvinner sitt tidligere funksjonsnivå.

- iv) **Første del, åpne spørsmål:** Hvis NOS etterfølger et anamnestic intervju, kan intervjuet f. eks introduseres med noe som:

“Du har fortalt tidligere at du visste at Mafiaen var etter deg og skulle skade deg. Det begynte cirke to uker før jul. Nå ønsker jeg at vi kan se på hva som foregikk før dette, og hvordan du følte deg frem til dette begynte å skje”

Hvis NOS ikke etterfølger et anamnestic intervju bør intervjuer bruke første delen av intervjuet til å finne ut av intervjupersonenes positive psykotiske symptomer og datere dem. Intervjuer bør så innhente informasjon ved bruk av åpne spørsmål:

“Hvis vi går tilbake til det tidspunkt der du følte deg bra og det gikk bra for deg, hva var det første som skjedde... hva var den første forandringen du merket?”

Når forekomsten av et symptom har blitt bekreftet, kan dato klargjøres, om nødvendig, med direkte spørsmål.

Det kan være nyttig å gjenta den informasjonen som er gitt for å forsikre seg om at informasjonen er nøyaktig. Feks;

“Så du husker at du var på ferie i Kypros i august, men ca to uker etter oppstart av studier i september, så beskriver du at du følte deg bekymret og nedfor på grunn av høy arbeidsbelastning. Dette opptok deg så mye at du ikke fikk sove før klokken 3 på natten. Stemmer dette?”

- v) **Bruk av sjekklister:** Dette innbefatter sjekklisten i NOS for prodromalsymptomer. Disse listene er ikke utømmende, men er kun ment som illustrasjoner. Du kan bruke en kortstokk, der hvert kort har et symptom skrevet på og legg disse foran pasienten. Du kan be dem om å velge de kortene som stemmer med deres erfaringer og forsøk å finn tidspunktene disse intraff.

Utforsk alle relevante ikke-psykotiske symptomer med direkte spørsmål hvis nødvendig:

“ Vi har vært gjennom ting ganske detaljert, men jeg vil gjerne forsikre meg om at vi ikke har glemt noe så jeg vil nå spørre deg om noen spesifikke ting”.

Feks.: “Har du noengang hatt følelsen av å være rastløs, ute av stand til å slå deg til ro?”

- vii) **Oppstart av behandling:** Få bekreftelse fra pasienten om de bruker medisin eller ikke. Undersøk når medisinen først ble foreskrevet. Hvis nødvendig, bruk foreskrivningsdato fra PAS som utgangspunkt.

Få informasjon om:

- Type antipsykotika
- Dose
- Foreskrivningdato
- Dato for etterlevelse (minimum 75% etterlevelse)

. Sjekk om medisinen ble tatt som foreskrevet.

“ f.eks Noen kan fortelle at de ikke er så interesert i å ta medisinen sin for en eller annen grunn. Hva føler du om å bruke medisin? Har du noen gang hatt lyst til å la være å ta medisinen innimellom?”

- v) **Utfylling av NOS:** Informasjon kan nå overføres til oppsummeringsarket. Prodromet inkluderer alle ikke-psykotiske symptomer som har vært tilstede i prodromalfasen; første psykotiske symptom refererer til tidspunktet for utvetydig forekomst av positive symptomer, uavhengig av symptomenes varighet.

OPPSUMMERINGSSKJEMA FOR NOS

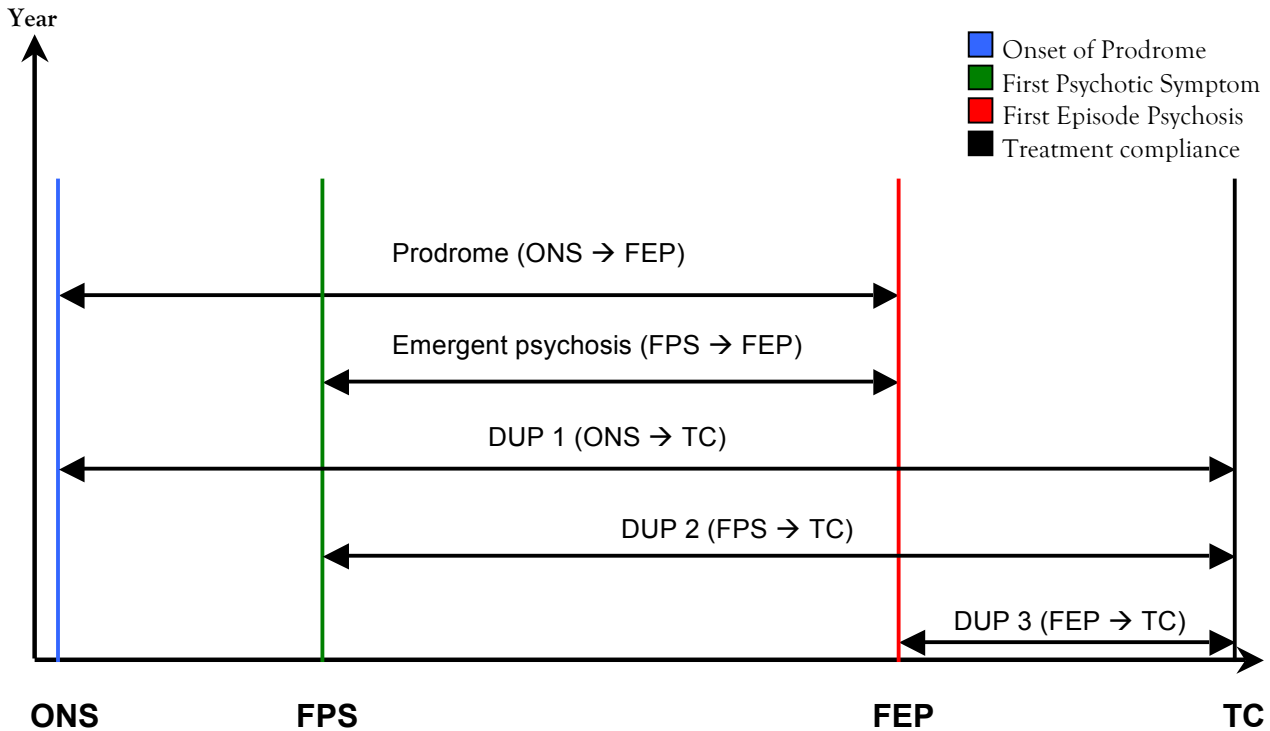
| NOTTINGHAM ONSET SCHEDULE: DUP VERSJON | | |
|--|---|----------|
| DATO | Presentasjon | NOS fase |
| | Notes Patients account Carers account | (PC) |
| | | ONS |
| | | FPS |
| | | FEP |
| | | TC |

UTREGNING AV NOS SYKDOMSPERIODER

| | The 4 crucial dates De 4 avgjørende datoer | Medical records Behandler | Client Pasient | Family Familie | Consensus based estimate Estimert dato |
|------|---|------------------------------|-------------------|-------------------|---|
| ONS | Onset of non-specific symptoms Debut av ikke diagnostiske symptomer | | | | (dato dd/mm/åå) |
| FPS | First psychotic symptom Første psykotiske symptom | | | | (dato dd/mm/åå) |
| FEP | First Episode Psychosis Første episode psykose | | | | (dato dd/mm/åå) |
| TC | Treatment Compliance Etterlevelse av behandling | | | | (dato dd/mm/åå) |
| | NOS illness periods NOS sykdoms periode | | | | (N ^o of days) Antall dager |
| P | Prodrome Prodrom | FEP - ONS | | | |
| DEP | Duration of Emergent Psychosis Varighet av | FEP - FPS | | | |
| DUP1 | Duration of Untreated Illness (DUI) Varighet av ubehandlet sykdom | TC - ONS | | | |
| DUP2 | Duration of Untreated Emergent Psychosis Varighet av ubehandlet | TC - FPS | | | |
| DUP3 | Duration of Untreated Manifest Psychosis Varighet av ubehandlet psykose (sikker diagnose?) | TC - FEP | | | |

* The time period from FEP to TC (DUP 3 above) is recommended as standard measure of DUP (see Larsen et al, 1996).

NOS tillater at DUP blir definert på flere ulike måter:



vii) Praktiske tips:

- Vær fleksibel og tilpass intervjueteknikk til intervjuperson. Noen ganger kan det være lettere å jobbe bakover fra det første positive psykotiske symptom viste seg, til begynnelsen av prodromet.
- Datoer vil ofte være unøyaktige til tross for at man forsøker å relatere det til bursdager, jul, sommerferie eller viktige hendelser i personens liv. Begynnelse, midten av, eller slutten av en måned vil ofte være det nærmeste estimatet, og ofte vil personen heller ikke klare å være så nøyaktig. Hvis noen angir en måned uten nærmere informasjon, tolk dette som midten av den måneden, f.eks den 15. Sommer defineres som juni, juli og august, høsten som september, oktober og november, vinter som desember, januar og februar og høst som mars, april og mai. Midt på sommeren vil derfor være juli, midt på vinteren vil være januar etc.
- Symptomer kan være flyktige og periodiske. Prodromale symptomer kan begynne for så å forsvinne for en tid. Debut av symptomer er det tidspunkt der symptomer begynner og tidligere funksjonsnivå ikke gjenvinnes til tross for at symptomene kommer og går. I noen tilfeller, spesielt med fremtredende negative symptomer ved debut, kan det være vanskelig å identifisere en tydelig debutdato. Det er viktig å konsultere familiemedlemmer og utforske når personen begynte å vise en tydelig avvik fra tidligere vanlige premorbide fungering.
- *Gjennombrudd* av psykose er det punktet der symptomene når den varighet (minst en uke) og intensitet som påvirker personens fungering.

Referanse: Singh, SP, Cooper JE, Fisher H et al Determining the chronology and components of psychosis onset: the Nottingham Onset Schedule (NOS). *Schizophrenia Research* 2005, vol 80, p 117-130

Appendix 3b

Gater Encounter Form, Norwegian version

Behandlingsvei nr.**A) Sykdomsfasen**

| | | | | | |
|----------|--------------------------------|----------|---------------------------------|----------|------------------------------|
| 1 | Ikke diagnostisk symptom (ONS) | 2 | Første psykotiske symptom (FPS) | 3 | Første episode psykose (FEP) |
| 4 | Remisjon | | | | |

B) Hvem ble kontaktet?

| | | | | | |
|-----------|--------------------------------------|-----------|-------------------------------------|-----------|-------------------------------|
| 1 | Fastlege | 2 | Kommunal psykiatrtjeneste | 3 | NAV (sosial) |
| 4 | Religiøs kontakt | 5 | Akutmottak (113) | 6 | Privatpraktiserende psykiater |
| 7 | Politi | 8 | Psykiatrisk sykehus, 3 linje | 9 | DPS, sengavdeling |
| 10 | Legevakt | 11 | DPS, poliklinikk, ambulansetjeneste | 12 | Privatpraktiserende psykolog |
| 13 | Terapeut innen alternativ behandling | 14 | Neurolog | 15 | Andre (spesifiser) |
| 16 | Kommunale tjenester | 17 | BUP | 18 | Andre (spesifiser) |
| 19 | Kriminalomsorgen | 20 | Venner | 21 | Familie |
| 22 | Healer | 23 | Lærere | 24 | PPT |
| 25 | Kommunal hjemmetjeneste | 26 | Psykooseam | 27 | Religiøse institusjoner |
| 28 | | 66 | Ikke kjent | | |

B2) Hvilken form for kontakt

| | | | | | |
|-----------|------------|----------|-----------------|----------|------|
| 1 | personlig | 2 | Telefonkontakt | 3 | Brev |
| 4 | Via SMS | 5 | Interne/ e-post | 6 | Amet |
| 66 | Ikke kjent | | | | |

C) Når ble denne tjenesten kontaktet?

Estimer til begynnelsen/midten/sluttet av måneden hvis det ikke angis en nøyaktig dato)

____/____/____ (dd/mm/åååå)

C2) Hvem møtte til avtalen?

| | | | | | |
|-----------|------------|----------|----------------------------------|----------|-----------------------|
| 1 | Ingen | 2 | Pasienten | 3 | Familie medlem(mer) |
| 4 | Venn(er) | 4 | Pasienten og familie medlem(mer) | 6 | Pasienten og venn(er) |
| 66 | Ikke kjent | | | | |

D) Hvem foreslo å oppsøke hjelp?

| | | | | | |
|----------|---------|----------|---------------------|----------|----------|
| 1 | Pasient | 2 | Familie medlem(mer) | 3 | Venn(er) |
|----------|---------|----------|---------------------|----------|----------|

| | | | | | |
|----------|--|----------|------------------------------------|-----------|------------------|
| 4 | Henvist fra tidligere kontakt nr _____ | 5 | Pasienten og familie medlem(mer) | 7 | Arbeidskollegaer |
| 8 | Hentet av polititil tvangsinleggelse | 9 | Kontaktpersonen oppsøkte pasienten | 66 | Ikke kjent |

E) Hvilke problemer oppsøkte pasienten/pårørende hjelp for?

F) Hvordan vil du (forskeren) vurdere symptomene til pasienten på dette tidspunkt?

| | | | | | |
|----------|----------------------|-----------|---------------------------|----------|------------------|
| 1 | Psykotiske (psykose) | 2 | Ikke-spesifikke symptomer | 3 | Uklare symptomer |
| 4 | Nærpsykotisk | 66 | Ikke kjent | | |

G) Ble det foreskrevet/administrert medikamenter?

| | | | | | |
|----------|--------------------|----------|---------------|----------|------------------|
| 0 | Nei | 1 | Antipsykotisk | 2 | Anti-depressiver |
| 3 | Andre (spesifiser) | 4 | Ikke kjent | | |

H) Var det etterlevelse av behandling?

| | | | | | |
|----------|-----|----------|----|----------|-----|
| 0 | Nei | 1 | Ja | 2 | N/A |
|----------|-----|----------|----|----------|-----|

I) Ble pasienten henvist til andre tjenester?

| | | | | | |
|----------|---|-----------|---------------------------|----------|---|
| 0 | Nei | 1 | Tilbys behandling ved DPS | 2 | Henvist til DPS, men ikke fått tilbud om behandling |
| 3 | Henvist til annen instans. Kontakt nr _____ | 66 | Ikke kjent | | |

J) Ble andre tiltak, råd eller henvisninger tilbudt?

| | | | | | |
|-----------|----------------------------------|----------|------------------------------|-----------|--|
| 0 | Ingen | 1 | Veiledning/ råd/støtte | 2 | Regelmessige møter/ Utadretter oppfølging |
| 3 | Polikliniske samtaler | 4 | Religiøse handlinger | 5 | Kontroll av fysisk helse |
| 6 | Tvangsinleggelse | 7 | Frivillig innleggelse | 8 | Religiøs henvendelse |
| 9 | Ble mer aktiv i religiøs praksis | 1 | Endret livsstil/ aktiviteter | 11 | Ble bedt om å prøve alternativ behandling (f.eks akupunktur/homøopati) |
| 12 | Kulturell handling | 1 | Andre (spesifiser) | 66 | Ikke kjent |
| 14 | Tilbudt oppfølgings avtaler | 3 | | | |

K) Syntes det/taker(e) denne kontakten var nyttig?

| | | | | | |
|-----------|------------|----------|-----|----------|-----|
| 0 | Ja | 1 | Nei | 2 | N/A |
| 66 | Ikke kjent | | | | |

Appendix 3c

Route timeline

Appendices 4a-b

Materials for community practitioners sample

Appendix 4a

Questionnaire on community practitioner background

Spørreskjema til deltakere i fokusgruppe i forskningsprosjektet
"Varighet av Ubehandlet Psykose i Nordland"

Kjønn _____

Alder _____

Profesjon _____

Ansiennitet _____

Appendix 4b

Interview guide for community practitioners

Temaguide

- 1. Hvordan er tjenesten hos dere organisert for å imøtekomme behovene til unge førstegangs psykotiske?**
- 2. Har ulike profesjoner ulike roller? Hvordan fordeles oppgaver?**
Hvilken rolle har sykepleierne spesielt?
- 3. På hvilken måte har geografiske eller demografiske faktorer innvirkning på hvordan tjenesten er organisert?**
- 4. Hvilke utfordringer har dere med å engasjere slike pasienter i sin egen behandling?**
- 5. Hvilke rutiner har dere for utredning og diagnostisering?**
- 6. Hvilke instanser samarbeider dere med?**
- 7. Hvilken praksis har dere for henvisning? Hvilke faktorer er av betydning for når og hvor pasienten henvises til videre behandling?**
- 8. Hvordan planlegges og gjennomføres overgang fra BUP til DPS?**
- 9. Hvilke utfordringer har dere?**
- 10. Kan dere fortelle om nylige erfaringer fra behandling av en pasient med førstegangs psykose?**

Appendices 5a-b

Materials for general practitioner sample

Appendix 5a

Endorsement letter

ET BEDRE HELSETILBUD TIL PSYKOSEPASIENTEN

Som avdelingssjef ved Rehabiliteringsavdelingen ved Nordlandssykehuset i Bodø er jeg opptatt av at psykosepasientene i Nordland skal få best mulig behandling. Av erfaring vet vi at denne pasientgruppen har behov for sammensatte tjenester, der innleggelse i sykehus for tidlig diagnostikk og igangsetting av adekvat behandling, ofte inngår som en del av tilbudet.

Jeg er opptatt av at tilbudene ved Rehabiliteringsavdelingen skal være best mulig tilpasset de behovene som fastleger og lokale tjenester har for denne pasientgruppen. I arbeidet med å forbedre oss har vi derfor satt i gang et forskningsprosjekt rettet mot å finne ut av hva som er viktig for at pasientene skal få rett behandling, til rett tid, på rett sted.

Studien "Varighet av ubehandlet psykose og behandlingsveier i Nordland" har som mål å øke vår kunnskap om, når og hvordan, mennesker med psykoselidelser kommer i kontakt med hjelpeapparatet i Nordland fylke. Denne studien vil være viktig for videre utvikling av vårt behandlingstilbud.

Fastlegene er helt sentrale for at psykosepasienten skal få et bra helsetilbud, og derfor vil det ha stor betydning at fastleger i Nordland deltar i denne studien for å synliggjøre behov og eventuelle mangler i dagens tjenestetilbud.

Jeg håper du kan sette av noen minutter til å besvare det vedlagte spørreskjema slik at vi sammen kan gi et bedre helsetilbud til psykosepasienten.

Med vennlig hilsen



Knut Kjerpeseth

Avdelingsoverlege, Nordlandssykehuset



Otto Mathisen

Fagdirektør, Nordlandssykehuset

Appendix 5b

IGPS questionnaire, Norwegian version

23. Hvor mange år er det siden du fullførte medisinsk embetseksamen?

år

24. Vennligst oppgi din alder

år

25. Har du deltatt i noe undervisning om schizofreni eller tegn ved psykose siste måneden?

nei ja, vær så snill å angi navn, plass og dato for undervisning:

26. Hva er din spesialitet?

allmennmedisin indre medisin annen/ ikke spesialist

27. Var psykiatri en del av din spesialisering?

Ja Nei

28. Praktiserer du i by- eller utenombyregioner?

By uten universitet By med universitet Utenomby/region

29. Har du hørt om TIPS (tidlig intervensjon ved psykose)-prosjektet?

Ja Nei; gå til spørsmål 30

dersom ja; hvordan har du hørt om TIPS?

Ordtale i media Foredrag

Deltakelse på kurs Annet; angi hvordan: _____

30. Er du interessert i ny informasjon om tidlig behandling av psykoser?

Ja Nei

dersom ja; hva kunne du tenke deg å være med på?

Kvalifikasjonskurs Seminar på DPS/Sykehuset Få tilsendt informasjon Ha besøk på kontoret

Annet; angi hva: _____

VUP & Behandlingsveier i Nordland

Undersøkelse av behandlingspraksis ved
begynnende psykose i allmennhelsetjenesten

Kodesystem for anonymisering av dine svar:

Mors fødselsdato (eksempel 28.06.1930)

2 8

Mors fødselsår (eksempel 28.06.1930)

3 0

Fars fødselsdato (eksempel 04.12.1925)

0 4

Ditt kjønn (m eller k)

**Vi vil takke deg for din tid og ditt meget viktige samarbeid,
for å hjelpe oss i å forbedre intervensjon ved førstegangs psykoser.**

FOREKOMST I DIN PRAKSIS

1. Tenker du at en førstegangs psykose vil starte med tidlige varsel signaler?

- Ja Nei

2. Hvor mange pasienter med en kjent psykose diagnose gir du psykiatrisk behandling i din praksis årlig?

- Ingen 1-2 3-5 6-9 ≥ 10

3. Hvor mange pasienter behandler du i din praksis årlig hvor du har mistanke om begynnende psykose?

- Ingen 1-2 3-5 ≥ 5

4. Hvor mye tid bruker du vanligvis til konsultasjon med en pasient ved mistanke om begynnende psykose?

- < 10 min 10-20 min 20-30 min > 30 min

5. For å kunne beregne hvor mange pasienter ved mistanke om begynnende psykose som mottar konsultasjoner i allmennpraksis, vil vi gjerne at du indikerer det totale antall pasienter du behandler i din praksis årlig.

pasienter

6. Hva er den årlige fordeling i aldersgrupper som mottar behandling i din praksis?

< 18 år _____ % 18-35 år _____ %
36-65 år _____ % > 65 år _____ %

SAMHANDLING MED ANDRE

7. Blir pasienter med mistanke om begynnende psykose behandlet av deg alene eller i samarbeid med andre spesialister eller institusjoner? (bare ett svar tillatt)

- Behandlet utelukkende i min praksis.
- Tilfeldigvis konsultasjon med spesialister for utredning/rådgiving, henvisning til en spesialist for stadfesting av diagnose og for å etablere medisinering. Oppfølging skjer i min praksis.
- Har overlatt behandling til spesialist/ psykiater i poliklinikk.

8. Blir pasienter med en psykose behandlet av deg eller i samarbeid med andre spesialister eller institusjoner? (bare ett svar er tillatt)

- Behandlet utelukkende i min praksis
- Tilfeldigvis konsultasjon med spesialister for utredning/rådgiving, henvisning til en spesialist for stadfesting av diagnose og for å etablere medisinering. Oppfølging skjer i min praksis

9. Er du fornøyd med ditt samarbeid med spesialisthelsetjenesten?

Ikke fornøyd 1 - 2 - 3 - 4 - 5 Veldig fornøyd

10. Vi er interessert i å vite om du støter på problemer i den psykiatriske behandlingen av pasienter med psykose. (bare ett svar er tillatt)

- Ingen problemer
- Søk med problematisk atferd (for eksempel aggresjon, stoffmisbruk) hos pasienten med psykose. Både klarer jeg og ønsker å forsette med den psykiatriske behandlingen i min praksis
- På grunn av problematisk atferd (for eksempel aggresjon, stoffmisbruk) hos pasienten med psykose, så ønsker jeg ikke å forsette med den psykiatriske behandlingen i min praksis
11. Med tanke på behandling av tidlige psykoser, hvilke psykiatriske tjenester ønsker/trenger du i din region? (mer enn ett svar tillatt)
- Kontinuerlig opplæring
- Et spesialisert mobilt team for utredning i din praksis
- Spesialisert, tverrskol henvisning eller konsultasjons service (poliklinisk/konsultasjon på klinikkaavdeling)

DIAGNOSE

12. Hvilke symptomer støter du mest på når du skal vurdere din mistanke om en begynnende psykose? (mer enn ett svar tillatt)

- Hallusinasjoner/vrangforestillinger Stoffmisbruk
- Sosial tilbakevending Søvnproblemer
- Psykosomatiske plager Depresjon/angst
- Suicidalitet Svimmelhet
- Tilbakegang i sosial funksjon Bissar oppførsel
- Konflikter med foreldre, lærer, arbeidsgiver

13. Hva gjør du vanligvis for å stadfeste diagnosen?

- Personlig historie Laboratorieteste
- Familie historie Ultralyd
- Observasjon over måneder Neurologisk utredning
- Observasjon over flere dager og uker Nevropsykologisk utredning
- Andre undersøkelser (CT og liknende) Konsultasjon med/henvisning til en spesialist
- Informasjon fra beyrdingstule andre (familie/arbeidsgiver/skole) Direkte spørsmål til pasient om relevante symptomer

BEHANDLINGSPRAKSIS

14. Hva slags behandling vil du anbefale til en pasient ved mistanke om en førstegangs psykose episode (uavhengig om du behandler pasienten selv)? (mer enn ett svar tillatt)

- Psykoterapi og familierapi
- Farmakoterapi
- Observere og avvante

15. Hvis du medisinere, hva slags medikasjon bruker du vanligvis for pasienter ved førstegangs psykose episode som du behandler i din praksis, og hva er doseringen du bruker?

_____ (navn) _____ mg/d

_____ (navn) _____ mg/d

_____ (navn) _____ mg/d

_____ (navn) _____ mg/d

16. Hvor lenge ville du fastholdt den antipsykotiske medikasjon etter en førstegangs episode hos dine pasienter?

- Noen dager 3-4 uker 1-6 mnd
- 6-12 mnd 12-24 mnd 3-5 år
17. Hvor lenge ville du fastholdt den antipsykotiske medikasjonen ved gjentatte episoder hos en pasient med remisjon etter en episode?
- Noen dager 3-4 uker 1-6 mnd
- 6-12 mnd 12-24 mnd minst 3-5 år

18. Hvor høy vurderer du tilbakefallsrisikoen til å være for en ubehandlet pasient i løpet av det første året etter en psykose episode?

_____ %

19. Hvilke er de to klinisk mest relevante bivirkningene i forbindelse med langvarig antipsykotisk behandling du støter på?

- Ekstrapyramidale symptomer Seksuell dysfunksjon
- Tardive dyskinesier Galactorrhea
- Sedasjon Tåkesyn
- Svimmelhet Tørr munn
- Vektøkning Hjertemerkat
- Hematologiske bivirkninger Effekt på lever enzymer
- Metabolske bivirkninger (diabetes, forhøyning av serum lipider)

VURDERING AV PROGNOSE

20. Basert på din erfaring, hvordan vurderer du prognosen til behandlede pasienter etter en førstegangs psykose episode? (bare ett svar tillatt)

- Prognosen kan være god, en episode med opprettholdelse av psykososial fungering er mulig
- Flere episoder med mulig opprettholdelse av psykososial fungering
- Flere episoder med progressiv tilbakegang av psykososial fungering og dårlig sykdomsprognose

21. Tor du det er mulig å forebygge psykose ved å starte behandling i prodromalfasen?

- Ikke mulig Mulig av og til Mulig i de fleste tilfeller

22. Hvordan vurderer du virkningen av tidlig intervensjon (for første psykiotiske episode) med tanke på utviklingen av psykose?

- Ingen innvirkning
- Moderat innvirkning
- Stor innvirkning

Appendices 6a-d

**Examples of memos and
coding process in community sample**

Appendix 6a

Case-based memo

Case based memo

H: Det stemmer veldig godt med for det her vi har lest om at det er sånne praktiske orden, praktiske ting er veldig sånn god innfallsvinkel spesielt det her med økonomi at å få pasientene til å se at det er nyttig og komme dit. Og det har han her fortalt om det her å ta en kjøretur og alle de her spontane samtalene at de er de beste samtalene som man har.

Syntes de var så flink å sette ord på det.

I: Det var de

H: Det var 1 ting han her om «at de kommer inn til oss med hele livet sitt i en plast pose» og de aner ikke hva som er oppi der. Det var utrolig sånn fin illustrasjon på det.

I: Det er mange fine sitater å ta vare på.

H: Ja jeg har liksom satt utropstegn med det

I: Det er også noe med det der med det som de setter ord på at de her pasientene, kanskje spesielt de her første gangs psykotiske, de kommer inn med hele livet i kaos. Ikke bare har de symptomer, men det er altså ingenting som fungerer rundt og alt på en måte har «dotte» helt i fra hverandre. Og det du begynner med det er kanskje ikke, du burde ta en medisin som gjør at alt ordner seg.

H: Nei å møte opp til samtale 1 gang i uken

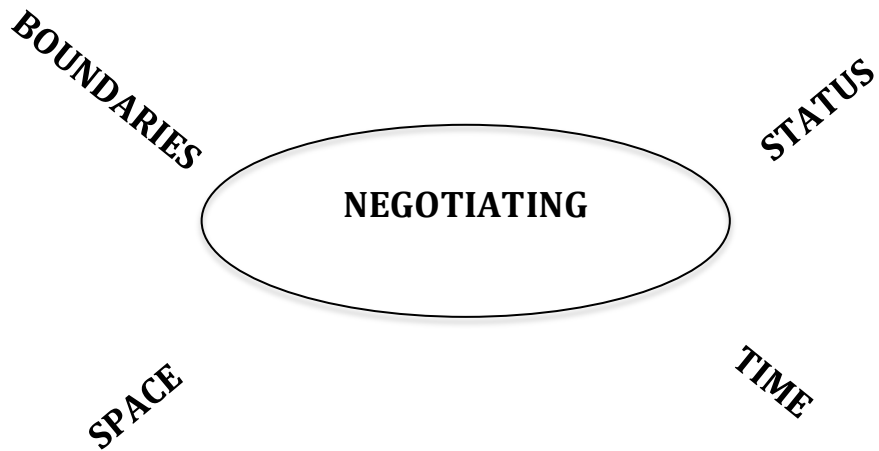
I: Ja du må liksom begynne litt i en annen ende, men man må jo nøste seg opp til man kommer dit at de får hjelp også de psykiske, man kjenner det jo igjen eller vi kjenner jo det igjen. Og de tenker sånn her og har erfart

H: Det var litt fint det hun sa om at, at medisin er viktig men man trenger ikke ha det trenger ikke å være det første man gjør. Det her at man kan gå på dag avdelinger også å være i og på en måte bli trygg der og være i trygge omgivelser begynne kanskje med en lite dose også øke på. At det er rom for å ja holde ut og vente litt. Heller det enn å sette i verk sånne dramatiske tiltak.

Appendix 6b

Theoretical memo

Theoretical memos



NEGOTIATING IN THE PATIENTS WORLD:

- "dive into the patients world"
- space: geographical challenges
- time: crisis resolution and crisis as opportunity
- status: ambivalence in help-seeking/disengagement
- boundaries: uncertainty and absolute psychosis

Appendix 6c

Open codes after three interviews

Open codes after three interviews

| | |
|-----------------------------------|---|
| å skape kontakt | absolutt psykose problematikk, akutt |
| allmennpsykiatrisk fokus | ambulant team modell |
| ambulante tjenester | andre grupper som trenger intensiv oppfølging |
| avstand | Behandlings-pessimisme |
| behov for innleggelse | Bemannings-problemer |
| bredt blikk | bruk av sentralsykehus funksjoner |
| BUP tenkning | BUP VOP samarbeid |
| dagenhet | de små kommunene |
| drøftingsforum | en til en kontakt foretrekkes |
| faglig oppdragelse | fleksibilitet |
| fokus på utredning | fokusere på ressurser |
| fordelen med å være liten | geografi utfordringer |
| gå sakte tilnærming | hele forløpet |
| hjemmebesøk | husregler |
| ikke nok med samtale på kontor | individual behandling |
| interesse | kollega samarbeid |
| kommune oppgaver | kommunens bed |
| kommunikasjon mellom enheter | kontakt innad |
| krav på poliklinikkene | krever en annen tilnærming |
| krisevakt | kronifiserte forløp |
| kunnskapsnivå på legevakt | lav terskel tilbud |
| lite erfaring med psykose | lokal organiseringsmodell |
| lokale senger | mer behandlings-optimisme idag |
| miljøterapi | møter ikke opp |
| må også være nytteperson | nærhet |
| omfattende behandling | oppsøkende |
| oppsøkende behandlingsteam | pasienter med rødflagget |
| pasienter som ikke kan legges inn | pasientfelle |
| poliklinikk er nevrosearbeid | poliklinisk tilnærming |
| politisk føring | problemer med å være små |
| psyk team | psykiater i kommunen |
| psykose blir for snevert | psykose rehab team |
| psykosedamene | psykosepasienten ikke prioritert |
| psykoseteam | pådrivere |
| pågående | rehabiliteringsteam |
| Rehabiliterings-tenkning | relasjon først og så finne ut av |
| relasjonskompetanse | samhandling med 1 linje |
| sitte å vente | sømloese tjenester og samhandling |
| spennende | spesialiseringsfokus |
| spesialistdekning | systemisk tenkning |
| team modeller | team og roller funksjoner |
| team tilnærming | tidlig intervensjon |
| tidlig oppdagelse | tilby hjelp der og da |
| tilpasset behandling | to behandlere |
| tverrfaglig team | ufordrende pasienter |
| uklare tilfeller | ukonvensjonell tilnærming |
| ute dager | utredningskompetanse |
| veiledning til hverandre | ventetid etter henvisning |
| vil ikke ha kontakt | å jobbe indirekte |
| å legge seg på vent | |

Appendix 6d

Theoretical codes - sorting

Theoretical coding - sorting

| Negotiations | Status | Space | Time |
|--------------|---|---|---|
| | Vil ikke ha kontakt, utfordrende pasienter, individuell behandling, krav på poliklinikk, psykosepasienter ikke prioritert, pådrivere, interesse, spennende | Møter ikke opp, ikke nok med samtale på kontor, poliklinikk er nevrosearbeid, poliklinisk tilnærming, spesialistfokus, husregler, faglig oppdragsel, miljøterapi | Lite erfaring psykose, kronifiserte forløp, tidlig oppdagelse, mer behandlingsoptimisme i dag, behandlingsspesimisme, tidlig intervensjon |
| | Enabling Relasjon først og så finne ut, å skape kontakt, relasjonskompetanse, gå sakte tilnærming, nærhet og distanse (promoting help-seeking) | Moving Oppsøkende behandling, ute dager, ambulant team modell, ambulante tjenester, psyk team, psykiater i kommunen, geografi utfordringer, dagenhet, hjemmebesøk, psykoseteam, psykosedamene, lokal organiseringsmodell, lokale senger | Sensing distress Uklare tilfeller, pasienter med rødflagget |
| | Sharing Må også være en nytteperson, tilby hjelp der og da, en til en kontakt, fokus på ressurser | Linking/bridging Veiledning til hverandre, kollegasamarbeid, drøftingsforum, kontakt innad, kommuneoppdager, samhandling, kommunens bed, kom. Mellom erk, | Strategizing Hele forløpet, sitte og vente, å legge seg på vent, krisevakt |
| | Broadening Bredt blikk, allmennpsykiatrisk fokus, psykose for snevert, rehabiliteringstilnærming, fleksibilitet, ukonvensjonell tilnærming, krever en annen tilnærming, omfattende behandling, tilpasset behandling, team modell, team tilnærming, to behandlere, tverrfaglig team, | Net-working Team og roller, BUP tenkning, å jobbe indirekte, systemisk tenkning, sømløse tjenester, BUP_VOP, fordeler med å være liten, de små kommunene | Deciding Absolutt psykoseproblematikk, akutt |
| | | Transferring Bruk av sentralsykehus, behov for innleggelse, pasienter legges ikke inn, spesialistdeknning, bemanning, pågående | Naming Fokus på utredning, utredningskompetanse |

