Factors Facilitating Recovery in First-episode Psychosis

A Multi-Method Approach

by

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<div align="right">Jone Bjørnestad</div>

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Abstract

Background

Predictors of recovery are crucial to the successful tailoring of treatment in first episode psychosis. There is lack of service- user investigations with regard to factors driving recovery and experiences regarding antipsychotic treatment. Particularly clinically recovered service users are an under-researched subgroup. There are also few studies distinguishing the predictive effects of different social factors with regard to recovery.

Aims

Thus, the primary aim of this project was to identify factors facilitating clinical recovery during and after a first-episode psychosis. To achieve the main aim, we divided it into three secondary aims: *First*; we investigated factors facilitating clinical recovery seen from service-users' perspectives. *Second*; we investigated how clinically recovered service-users perceived using antipsychotic medication during and after a first-episode psychosis. *Third*; we tested separate dimensions of social functioning with regard to prediction of clinical recovery.

Method

A mixed method "exploratory sequential" inspired strategy was used: First we conducted two qualitative studies. Here, a thematic analytic approach within an interpretative–phenomenological framework was utilized. Twenty clinically recovered service users were interviewed. Analysis followed an established meaning condensation procedure. Both qualitative studies were based on the same data. In the third study a sample of first episode psychosis ($n = 186$) completed baseline measures of social functioning, as well as clinical assessments. In this study we used a hypotheses testing approach to identify specific social predictors

of clinical recovery. We hypothesized that first, satisfaction with social relations predicts clinical recovery; second, that frequency of social interaction predicts clinical recovery; and third, that the effect of friend relationship satisfaction and frequency will be greater than that of family relations satisfaction and frequency. We compared groups of recovered and non-recovered individuals using generalized estimating equations analyses.

Results

In the first qualitative study concerning factors driving recovery from service users perspectives analysis revealed a main theme; *Establishment of subjective self-agency*, and three subordinate themes; 1) *Environmental support and gentle pressure*, 2) *Individually tailored assistance*, 3) *Antipsychotic medication: relinquishing personal responsibility, and considerable side effects*.

The second qualitative study regarding experiences of antipsychotic treatment we identified five themes: 1) Antipsychotic drugs reduce mental chaos during the acute phase, 2) Non-stigmatizing environments were perceived to increase chances of successful use, 3) Antipsychotic drugs beyond the acute phase – considered to compromise the contribution of individual effort in recovery, 4) Prolonged use – perceived to reduce likelihood of functional recovery, 5) Antipsychotic medication was considered as a supplement to trustful relationships.

In study three, frequency of social interaction with friends was a significant positive predictor of recovery over a two-year period. Neither global perceived social satisfaction nor frequency of family interaction showed significant effects.

Conclusions

In the qualitative part of the investigation we suggest that an increase in sense of personal agency is a core mechanism driving recovery for

participants in the study sample. The facilitation of self-agency also seems pivotal for adherence when professionals present antipsychotic treatment as a treatment option. Findings indicate that interventions aiming to boost subjective and behavioral agency in service users might be of great benefit, particularly in combating negative symptoms of psychosis.

Acute phase antipsychotic treatment was mostly perceived as advantageous. However, costs were often seen as outweighing benefits beyond the acute stage. Findings clearly emphasize the need for a collaborative approach to be integrated across all phases of care. This study underscores the need to investigate sub-group differences with regard to long-term antipsychotic treatment.

In the quantitative part of the investigation we conclude that frequency of friendships are of particular clinical importance since it is a possibly malleable factor. Frequency of interaction may be affected through behavioral modification and therapy already from an early stage in the course, and thus increase recovery rates.

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1 Introduction

To improve the course and outcome in first-episode psychosis (FEP), service users, their families and support system need valid and applicable evidence-based knowledge of mechanisms facilitating recovery. However, research on recovery is still characterized by research designs that are likely to insufficiently identify key dimensions of such mechanisms, which probably have resulted in incomplete assessment of treatment needs and hence suboptimal treatment. A general problem with the a-priori hypothesis driven approach which dominates the traditional research literature, is that it is unsystematic regarding the generation of the hypotheses. The hypotheses may be derived from previous research, from theories or from idiosyncratic hunches of undisclosed origin from the researchers. (Alvesson & Sköldberg, 2009) Hence, the set of possible factors relevant to recovery may be insufficiently explored. In mature research fields, this is not necessarily a problem, but in the early phases, or when findings are inconsistent, systematic exploration is needed to ensure that important topics are covered. In this research project, we aimed to remedy this shortcoming by using a combined qualitative and quantitative approach. We began with two qualitative studies exploring service users' views regarding factors important to recovery and thereafter, based on hypotheses derived from these studies performed a quantitative approach testing our hypothesis using inferential statistics. We aimed to deliver clinically valid knowledge that increases the coherence between service users, their families and support system, as well as improved and systematic recovery-oriented treatment.

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2   Background

2.1   Psychosis

Psychotic disorders are among the leading causes of the total burden of disease worldwide and cause severe human suffering. (Rössler, Salize, van Os, & Riecher-Rössler, 2005) The cost of the disorder is substantial, as it largely affects young adults at the start of their careers and relationships. (Evensen et al., 2015; Johannessen, 2002) Descriptions of and approaches to psychosis have evolved throughout the past century, from Kreaplinian, characterizing psychosis as a brain disease with a gradually deteriorative and chronic outcome (Dementia Praecox), changing to seeing psychosis more as a reversible condition and one of many potential psychopathological outcomes with currently unknown origin. (Van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2009)

Psychosis is the collective term of a diverse group of psychiatric disorders characterized by reduced or absent reality-testing capability. (Helse- og omsorgsdepartementet, 2014; NICE, 2014) Symptoms that characterize psychotic disorders are often divided into three categories: 1) positive symptoms, such as hallucinations, delusions, disorganization, 2) negative symptoms, such as anhedonia, avolition and apathy, and 3) additional symptoms such as anxiety, depression and cognitive impairment (for example, attention- and memory difficulties).

Research on psychosis has mainly been focused on schizophrenia, which has a lifetime prevalence of *one* percent. (Peralta & Cuesta, 2007) Schizophrenia is described as a syndrome but is not a clearly defined condition. Diagnostic manuals (ICD-10/DSM-IV/V) distinguish between schizophrenia and related psychotic disorders as schizotypal disorder, paranoid psychosis, acute- and transient psychosis and schizoaffective disorders. In addition drug-induced psychoses and affective psychoses are classified outside the schizophrenia spectrum.

Psychotic disorders are associated with a high rate of comorbidity, increased risk of suicide, decreased physical health and mortality. (Hegelstad et al., 2012; Melle et al., 2006) Psychotic disorders have overall lifetime prevalence rates in excess of *three* percent, (Peralta & Cuesta, 2007) and the economic costs in Norway surpasses heart disease, all cancers and all rheumatic disorders combined. (Johannessen, 2002)

Currently, the stress-vulnerability model is the leading explanation model for psychosis, and points to a multifactorial causation with both genetic and environmental determinants. (Insel, 2010; Pescosolido et al., 2010) It is however unclear whether schizophrenia and other psychotic disorders are true nosological entities or whether they are part of a continuum with other mental disorders. (van Os, Kenis, & Rutten, 2010) A diagnosis of schizophrenia can be made based on various combinations of non-overlapping symptoms, and the high degree of heterogeneity in psychopathology, psychosocial functioning, progression and treatment response indicates that the aetiology of schizophrenia is complex or even that the diagnostic construct lacks validity. (Bentall, 2013; Read, Mosher, & Bentall, 2004; van Os, 2016) This debate has recently culminated with leading researchers stating that the term schizophrenia (as a categorical entity) is not valid, unscientific and may imply an unfounded pessimism regarding prognosis. (Murray, 2016; Selten, van Os, & Cantor-Graae, 2016) On the other hand, there is for the most part agreement regarding the phenomenology of psychotic symptoms and that these are both ecologically valid and has clinical value.

Most of our knowledge on the course and outcome of psychosis is derived from convenience samples from hospitals with chronic, treated incidence, or first-episode psychosis (FEP) patients, or a mixture of these. Collectively, these studies indicate that although the course and prognosis of psychosis have improved following the introduction of antipsychotic medication (Jablensky, 1997) and structured psychosocial

treatment, (Pilling et al., 2002) up to 80 % of patients with the most severe forms of psychosis, defined as high levels of positive symptoms and severe functional decline, still suffer a poor outcome. (Bottlender, Strauß, & Möller, 2010; Hopper & Wanderling, 2000; Jaaskelainen et al., 2013; Modestin, Huber, Satirli, Malti, & Hell, 2014) Poor outcome is associated with male gender, early age of onset, (Altamura, Bobo, & Meltzer, 2007) poor premorbid functioning, (MacBeth & Gumley, 2008) long duration of untreated psychosis, (DUP) (Marshall et al., 2005) substance abuse, (Lang, Kösters, Lang, Becker, & Jäger, 2013) unemployment, (Bond, Drake, & Becker, 2008) psychological trauma, (van Nierop et al., 2014) non-adherence to antipsychotic medication, (Leucht, Hierl, Kissling, Dold, & Davis, 2012) stress sensitivity, (Ulrich Reininghaus et al., 2016) deterioration of social network, (Gayer-Anderson & Morgan, 2013) cognitive deficits (Fusar-Poli et al., 2012; Aas et al., 2014) and prominent negative symptoms. (D. Perkins, H. Gu, K. Boteva, & J. A. Lieberman, 2005) However, research has yet to identify any consistent and replicable causal determinants of course or outcome. (van Os et al., 2010) Thus, although there has been significant progression regarding knowledge about factors driving psychosis and recovery, the research field of psychosis has not yet reached consensus regarding many major issues.

2.2   Recovery in psychosis

The recovery perspective has influenced how we think about treatment of people with severe mental disorders. (Hamm, Hasson-Ohayon, Kukla, & Lysaker, 2013; Leamy, Bird, Le Boutillier, Williams, & Slade, 2011) Regarding psychosis, recovery is on a superordinate level a process description of the symptomatic relief and increased functioning a person experiences after a psychotic episode. Parallel to the evolvement of a more optimistic view on prognosis the concept of recovery has gradually gained wider support among service-users, clinicians and researchers. This change partly results from an ambition from service-user led

organizations, which aim to change treatment approaches as well as politics. (Davidson, Schmutte, Dinzeo, & Andres-Hyman, 2008) With priorities such as increased user-involvement, shared decision-making and reducing an experienced power imbalance between service-users and professionals, the recovery movement is rapidly growing. A decisive factor in this development has been the increasing number of service-user investigations showing that people not only recover from psychotic symptoms, but that recovery involves a broader process with various objective and subjective outcomes. This includes the opportunity to live a life in line with subjective values and desires while having a mental illness. (Davidson, 2003) With regard to care, this perspective implies a greater emphasis on treatment relationships that are individually tailored, person-centred and which safeguards autonomy. (Davidson, Ridgway, Schmutte, & O'Connell, 2009) The recovery term is, however, inconsistently used and interpreted (Borg, 2007) and there is lack of consensus about the definition of recovery. (Slade et al., 2012) This currently makes it difficult to provide systematic recovery-oriented services. (Law, Morrison, Byrne, & Hodson, 2012)

2.2.1 Challenges with the concept of recovery

The two different ways of defining recovery are often conceptualized as personal recovery and clinical recovery; (Slade, 2009a) or recovery *in psychosis* and recovery *from* psychosis. (Davidson et al., 2008) On a continuum from non-recovered (on-going psychosis) to fully cured, clinicical recovery is positioned closer to cured then personal recovery. Thus, those achieving clinical recovery have always gone through at least one period of personal recovery. Viewing it this way, regardless of the on-going disagreement about the concept of recovery, clinical recovery will be the preferred outcome as it is closer to a fully cured condition.

The concept of clinical recovery (recovery *from*), a mainly research-derived concept, implies long-term stable symptomatic and functional

remission combined. (Liberman & Kopelowicz, 2002) Concerning the remission part, researchers increasingly use international standardized criteria; (Andreasen, 2006) no score of 4 or higher for the past six months on any of the following Positive and Negative Syndrome Scale (PANSS)(Kay, Fiszbein, & Opler, 1987) items: P1 (delusions), P2 (disorganized thought), P3 (hallucinatory behavior), N1 (affective flattening), N4 (passive social withdrawal), N6 (lack of spontaneity), G5 (bizarre posture), or G9 (unusual thought content). With regard to the functional part, typically a systematic functional measure is used (e.g. Strauss–Carpenter Level of Function Scale (Strauss & Carpenter Jr, 1977) together with a pre-defined time criteria (usually at least one year or more). (Liberman & Kopelowicz, 2002) These combined sub-scale based threshold criteria of remission and recovery are vulnerable to reliability imperfections, as errors in scoring e.g. the PANSS can lead to classification errors. Ultimately one single wrong score can determine which category a person is placed in (remitted/non-remitted and recovered/non-recovered). Particularly in cases of doubt (borderline cases) such thresholds, combined with validity and reliability issues are a concern.

Another challenge with the concept of clinical recovery is the high demands for improvement and functioning levels embedded in the concept. For many people, such a criterion will not represent a useful and realistic goal. Meta-analysis of psychosis populations show that only 9-21 percent achieves clinical recovery two years after a first-episode psychosis. Numbers are even lower in core-schizophrenia populations. Although higher levels are achieved later in the course the majority do not reach the criteria for clinical recovery. (Jaaskelainen et al., 2013) Given the status of treatment efficiency combined with the fact that psychosis populations have lower levels of academic and social premorbid functioning, (MacBeth & Gumley, 2008) and functional and social decline through both the prodromal phase (Robustelli, Newberry, Whisman, & Mittal, 2016) and the psychotic phase (Gayer-Anderson &

Morgan, 2013) the outcome of most not achieving clinical recovery is also the most plausible one. Particularly in sub-groups characterized by the lowest premorbid functioning, insidious onset and prominent negative symptoms, the outcome of clinical recovery unfortunately in many cases seem unlikely and thus also may be an ideal which may lead to more harm then good. Thus, as presented by the opponents of the concept of clinical recovery, the threshold for being assessed as clinical recovered seems, at least for a sub-group of service-users, as not reflecting a realistic developmental aim. However, apart for these issues, the measure of clinical recovery has positive aspects. This measure is research friendly as it is readily quantifiable and allows for replication. As there is currently no consensus about the concept of clinical recovery it may also be possible to set the measure of clinical recovery less strict regarding functioning levels and thereby make it a more realistic and ecological valid goal for a larger sub-group of service-users. From a community perspective clinical recovery is also applicable as it gives an objective estimate of employability and independent living skills, which is relevant to health-related and economic issues.

Personal recovery, (recovery *in*) on the other hand emphasizes the subjective dimension, seeing recovery as a personal meaning-constructing process defined by the service user with no objective threshold requirements of symptom relief or social and general functioning, nor predefined time-criteria. (Bellack, 2006; Davidson et al., 2008; Liberman & Kopelowicz, 2002) As with the concept of clinical recovery, the concept of personal recovery has clear political corollaries. The concept may serve to change the mental health system in a direction implying more reliance on service user defined measures and service-user informed services. This involves ensuring less discrepancy between service-users' experiences and the applied research-based measures, including measures of recovery. Personal recovery is advocated by service-user organizations to increase the ecological validity of the concept of recovery. (Leamy et al., 2011; Wykes, 2014) Critics of

personal recovery argue that the current lack of standardized criteria makes it difficult to fit this type of concept into the frame of generalizable research. (Liberman & Kopelowicz, 2005) They propose that an overly emphasis on the subjective dimension dilutes usefulness through less sample control and problems with replication and comparison. Further they argue that an ignorance of objective measures will prevent a valid and reliable foundation for treatment guidelines and thus obstruct refined and evidence-based health priorities.

2.2.2 Methodological challenges in recovery research and a possible solution

Different perspectives on recovery are also inscribed in a larger debate about preferred methodology, epistemology, ideology, and treatment paradigms, including the protracted and unresolved dispute between established qualitative and quantitative research schools regarding who have the most valid measures and approaches. (Alvesson & Sköldberg, 2009; McLeod, 2001; Slade, 2009b) A possible approach to resolve some of the methodological frictions between qualitative and quantitative approaches is to combine them in a mixed research design. (Creswell & Clark, 2011)

A backdrop for this claim is the current limited user involvement in the initial phases of research-project development, (Trivedi & Wykes, 2002; Wykes, 2014) leading to researcher-controlled research and reducing the contribution of service users. This happens despite that qualitative service-user investigations have proven to be fruitful in refining our understanding of quantitative findings, and to provide new knowledge about reasons for the success or failure of mental health services to treat severe mental illness. (Beck et al., 2012; Bellack et al., 2007; Davidson, Harding, & Spaniol, 2005; Leamy et al., 2011) These investigations have led to increased focus on the benefits of user involvement in order to improve treatment. Qualitative investigations also have the potential for leading to a transparent and ecological valid basis for hypothesis

generation. Nonetheless, due to limitations inherent in qualitative designs regarding their generalizability, a quantitative extension of the qualitative research format involving the use of standardized measures of recovery has been recommended. (Slade & Hayward, 2007) Multi-method designs combine this need for first-person perspectives with generalizability by testing hypotheses derived from qualitative methods using the inferential statistical logic of quantitative designs. (Creswell & Clark, 2011)

Bringing this back to the distinction between personal and clinical recovery such an approach seems to have the potential to bridge the service-user perspective (personal recovery) and the researcher driven approach (clinical recovery), integrating the mind-set of both schools. Hence, a multi-method design may contribute to improved operationalization of the concept of recovery while incorporating the perspectives of service users. In the long run this may make the concept of recovery both more researchable and ecological valid.

2.3 The social dimension of psychosis and recovery

Although there are divisive differences between the concept of personal and clinical recovery there are also uniting goods. Coherent with psychosis research in general, both schools recognize and suggest the social dimension as key to achieve recovery with emphasis on gaining or regaining full citizenship as the ultimate aim for the entire recovery process. (Davidson et al., 2001; Liberman, Kopelowicz, Ventura, & Gutkind, 2002)

On a superordinate level the social dimension in psychosis often involves developmental and social experiences, such as growing up in an urban environment, poverty, being part of a vulnerable sub-group and psychological trauma (Van os, 2010). For individuals genetically

vulnerable for psychosis such experiences are interlinked to increased probability of psychosis development. (van Os et al., 2010)

On a subordinate level the social dimension most often encompasses various elements of social functioning, such as work (preferably paid work), social meetings and status of living residence. Professionals and service-users coherently see these elements as central to quality of life and in functional recovery. (Davidson, Bellamy, Guy, & Miller, 2012) Empirical research has shown that reduced social network support is interlinked with the social deterioration many people experience throughout the course of illness. (Gayer-Anderson & Morgan, 2013) However, this negative development does in many cases start earlier; already in the prodromal phase (Robustelli et al., 2016) or even in childhood. (MacBeth & Gumley, 2008) Negative development has been shown to pre-date the onset of psychosis, (Gayer-Anderson & Morgan, 2013) and is associated with increased hospitalization rates and worse outcome. (Albert, Becker, Mccrone, & Thornicroft, 1998; Fraser, Berger, Killackey, & McGorry, 2006)

A supportive family, but even more so friendship networks (Davidson, Borg, et al., 2005; Davidson et al., 1999; Erickson, Beiser, Iacono, Fleming, & Lin, 1989; Morgan et al., 2008; Reininghaus et al., 2008) are however associated with better outcomes and more efficient use of health services, (Evert, Harvey, Trauer, & Herrman, 2003; Pinto, 2006) (Evert et al., 2003; Pinto, 2006) as well as a reduction in subjective loneliness, (Hawkley & Cacioppo, 2010) decrease in perceived social stigma, (Watson, Corrigan, Larson, & Sells, 2007) and better self-care functioning. (Evert et al., 2003) These are all examples of factors implying a relation between social support and social functioning, which is a core factor in psychosis. (van Os et al., 2010) There is also an association between supported socialization and improved social functioning, (Davidson et al., 2004) indicating a malleability in social capacities and highlighting social functioning as a promising target for tailored intervention. Both practical support and emotional friendships

buffer harmful impacts of stress exposure, (Davidson et al., 2004; Thoits, 2011) which might be causally linked with psychosis onset. (U. Reininghaus et al., 2016) Thus, care focused on social integration, increased social support and better social function seem to have potential to increase both personal and clinical recovery rates.

Several reviews have characterized the literature on the social dimension of psychosis as heterogeneous. (Albert et al., 1998; Buchanan, 1995; Gayer-Anderson & Morgan, 2013; Thoits, 2011) A main criticism concerns how studies have merged factors related to social interaction into one, or a few, global categories. This prevents a valid evaluation of their independent effects on outcome, including recovery. In addition, studies are often based on heterogeneous samples including both chronic and first-episode psychosis, limiting the generalizability of study findings. Ultimately, these issues leave knowledge gaps that may limit our ability to design helpful interventions. Thus, there seem to be a need to disentangle specific aspects of the social dimension, testing its separate parts and their contribution to outcome, including symptomatic remission and recovery.

2.4 Antipsychotic medication

Antipsychotic treatment has been widely used in psychosis treatment for several decades. Because of sedative effects and beneficial effects on positive psychotic symptoms, these medications were early suggested as the gold standard treatment of psychosis, leaving other treatment approaches relegated to secondary treatments or treatments that were offered in addition to antipsychotics. This picture largely remains unchanged today. (Sohler et al., 2016) Antipsychotic treatment is currently the generally recommended gold standard treatment for all phases of the psychotic syndrome, in the acute phase as well as throughout the protracted phases of maintenance and recovery. (APA, 2006; Kreyenbuhl, Buchanan, Dickerson, & Dixon, 2010; Sohler et al., 2016) Although antipsychotic medication has unequivocally proven

effective in acute and short-term treatment (Bola, Kao, & Soydan, 2011; Leucht, Tardy, et al., 2012) there is a lack of long-term, systematic double-blind controlled studies using clearly defined samples in terms of illness type, severity, and duration (Adams, Bergman, Irving, & Lawrie, 2013; Sohler et al., 2016) evaluating treatment effects as well as possible adverse effects. Most studies are short-term, with less then one-year follow-up. However, the majority of psychosis service-users use antipsychotics for several years, (Sohler et al., 2016) which illuminates a clear discrepancy between the current evidence base and clinical practise and guidelines. Several Cochrane reviews, applying strict quality criteria for including studies, support the claim that there is a lack of evidence regarding long-term use of antipsychotic medication. The conclusions are that the evidence base for short-term use of antipsychotics is weak while the evidence regarding long-term is more or less absent. (Adams et al., 2013; Asenjo Lobos et al., 2010; Leucht et al., 2013; Leucht et al., 2009; Saha et al., 2016)

This lack of long-term studies also implies a lack of studies investigating long-term side effects. Given possible adverse effects on brain function and structure, this issue is highly important. (Sohler et al., 2016) Additionally, most studies are financially supported by the pharmacy-industry, a multi-billion dollar enterprise, with clear earning incentives. The combination of lack of evidence for long-term positive effects, lack of documentation regarding negative side-effects and industry-financed research should be considered as alarming and worrisome.

Current long-term antipsychotic treatment is largely based on clinical experience and clinical judgment, which is what treatment is usually based on when hard evidence is absent. This practise has many potential pitfalls and increasing recognition of these shortcomings have resulted in a call for large-scale independent trials (Bola et al., 2011; Leucht, Hierl, et al., 2012; Saha et al., 2016) in order to create a new and improved evidence base to sufficiently understand the long-term

benefit/risk balance of antipsychotic drugs for different sub-groups of service-users. (Sohler et al., 2016)

There is however also a need for systematic investigation of service users' perspectives on using antipsychotic medications throughout the course of illness. Such perspectives are necessary to develop clinical relevant hypotheses for the suggested large-scale trials, and to illuminate implications for different subgroups of individuals. This also includes investigating how antipsychotic medication is perceived during and after the different phases of the course and how medications interact with other treatment approaches. As service-user investigations (Davidson, Borg, et al., 2005) show that recovery is more about functional aspects relative to symptomatic relief, investigations should focus broader and include examinations of how antipsychotic medication affects functional and social aspects of the recovery process. In this context, it is essential to acknowledge that for most individuals, functional recovery is often more protracted, and require more tenaciousness, compared with attainment of symptomatic remission. (Liberman & Kopelowicz, 2002; Slade et al., 2012) Thus, to investigate antipsychotic medications effects on functional and social recovery there is a clear need for long-term investigations, lasting beyond the achievement of symptomatic remission.

3   Summing up

Psychosis research has demonstrated numerous associations between clinical and demographical phenomena with course and outcome. Knowledge on causality, involving mechanisms driving and explaining these associations is scarce. The research is mainly based on quantitative approaches and in-depth investigations of the service-user perspective are few. To obtain hypotheses that capture the full range of relevant factors, the utilization of all relevant information sources is needed. In this regard both qualitative and quantitative approaches seem called for. A multi-method approach may resolve some of the methodological challenges within the field of psychosis.

The social dimension is relevant to most sub-fields of psychosis research, including recovery and antipsychotic medication. Most human functioning unfolds within a social context and perceived social exclusion is associated with poor health. For many service users, family contacts, friendship contacts and social network support deteriorate before, during and after psychosis. Research has demonstrated malleability of social capacities, making this field a promising target for tailored intervention. However, operationalizations of social factors are generally blurry. This makes it difficult to propose clear predictions of specific factor-effects, which in turn may impede the design of helpful intervention. Thus, there is a need for research which separates the social dimension and tests specific social factors and their effect on course and outcome, including recovery.

Clinical recovery is generally under-researched. Particularly service-user knowledge is scarce and there is need for research investigating factors both driving recovery and experiences of using antipsychotic medication. Individuals achieving clinical recovery may give useful knowledge about all phases of recovery, including periods of on-going

psychosis and decreased functioning but also periods characterized by fewer symptoms and good functioning.

Research on antipsychotic medication is generally characterized by lack of high-quality long-term investigations, but there is also little knowledge about people's first-person experiences. To better understand the long-term benefit/risk balance of antipsychotic drugs for different sub-groups of service-users but also to make antipsychotic treatment a safer and more efficient treatment there is call for both large-scale independent longitudinal trials as well as service-user investigations on how antipsychotic medication is perceived throughout the different phases of recovery. A main point here is that functional recovery generally is a more lengthy process then achieving symptomatic remission. Thus, long-term investigations are particularly needed to illuminate functional aspects of the recovery journey.

4   Aims

Primary aim

The primary aim was to identify factors facilitating clinical recovery during and after a first-episode psychosis.

Secondary aims

To achieve the main aim, we divided it into three secondary aims: *First*; we investigated factors facilitating clinical recovery seen from service-users' perspectives. In doing so, we aimed to systematically identify and describe specific, personally relevant experiences as well as environmental and treatment-related factors, which were perceived as explaining and facilitating recovery. *Second*; we investigated how clinically recovered service-users perceived using antipsychotic medication during and after a first-episode psychosis. *Third*; we disentangled factors in social functioning, and tested their separate effects on clinical recovery in a FEP sample during a two-year follow-up period.

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5 Methods

5.1 Common for both the qualitative and quantitative approach

A mixed research design

A multi method research design was used to overcome some of the limitations associated with both qualitative and quantitative designs when performed separately. We aimed to reduce researcher bias and enhance generalizability of our findings, while at the same time keep the service user-oriented perspective.

An "exploratory sequential" inspired strategy (Creswell & Clark, 2011) (p. 71) was used: First we conducted two qualitative studies, both investigating service user experiences. The first study was about factors driving recovery, the second regarding experiences of using antipsychotic medication. The exploratory sequential aspect was already present in-between these studies: The latter medication study was as a spin off from the first qualitative study, and was based on the same interview data: The collaborative analytic and interpretative process of the first qualitative study gave rise to new hypotheses and questions. These made us look through the data again with a focus on statements concerning antipsychotic medication.

The third study was quantitative, using a hypotheses-testing approach. The hypotheses were generated from the two qualitative studies. One of the main findings was that sensitive social pressure from friends was perceived as helpful for recovery. Another finding was that family relations were more often perceived as part of the aetiology of the illness, which possibly served to reduce or even hinder helping efforts and effects of such efforts. Friendships were conversely most frequently perceived as an unconditional good. On this basis we formed three

hypotheses concerning quality and frequency of friendship and family interaction tested in the third and quantitative investigation of this thesis.

Sample and recruitment

All study samples were recruited from the TIPS-1 study (N=281) and the on-going TIPS-2 study (N=400 approximately) (study 1 and 2), or from the TIPS-2 alone (study 3). These are two naturalistic follow-along FEP studies in south-Rogaland, Norway, including individuals from 1997, until 2014. Detailed descriptions of the inclusion criteria and methods can be found elsewhere. (Hegelstad et al., 2012; Joa et al., 2008; Stain et al., 2013)

Inclusion criterion for the TIPS-1 and TIPS-2 studies

Individuals who were included in these study met the following criteria: living in the catchment area (Rogaland county); age 15–65 years; meeting the DSM-IV criteria (as measured by The Structured Clinical Interview for the DSM-IV Axis 1 Disorders) (First, Spitzer, Gibbon, & Williams, 1995) for a first episode of schizophrenia, schizophreniform psychosis, schizoaffective psychosis, delusional disorder, brief psychosis, affective disorder with mood incongruent delusions, or psychosis not otherwise specified, and also from August 1, 2008 (TIPS-2) substance- and alcohol induced psychosis (excluded for the purpose of the present study); being actively psychotic as measured by the Positive and Negative Syndrome Scale (PANSS); (Kay et al., 1987) not previously receiving adequate treatment of psychosis; no neurological or endocrine disorders related to the psychosis; living in the catchment area, understands and speaks one of the Scandinavian languages; an IQ over 70; and being able and willing to sign an informed consent. Participants agreed to baseline assessment and follow-ups after 3 months, and 1, 2 and 5 years (also 10 years in TIPS-1).

Defining symptomatic remission and clinical recovery

Symptom remission was defined in accordance with international standardized criteria; (Andreasen, 2006) no score of 4 or higher for the past six months on any of the following PANSS items: P1 (delusions), P2 (disorganized thought), P3 (hallucinatory behavior), N1 (affective flattening), N4 (passive social withdrawal), N6 (lack of spontaneity), G5 (bizarre posture), or G9 (unusual thought content). Individuals were categorized as non-remitted if they reported any relapse, defined as deterioration of symptoms scored >3 on the relevant PANSS scales, during the previous 6 months.

Social functioning was measured by the subscales measuring work and social interaction of the Strauss-Carpenter Level of Function Scale (Strauss & Carpenter Jr, 1977) and the criteria of living independently: day-to-day living (independent living), role functioning (work, academic, or full-time homemaking), and social interaction. A score of 0 indicated very poor social functioning and 4 indicated adequate social functioning for the total period of the previous 12 months. Adequate social functioning was operationalized as a score of 4 in all three subscales for the total period of the previous 12 months.

Clinical recovery was operationalized as a single variable of "yes" for all patients who met criteria for both symptom remission and adequate social functioning.

5.2 Qualitative part

Research design

In qualitative research the aim is to understand and represent the experiences of people as they encounter, engage and live through situations. (Elliot, Fischer, & Rennie, 1999; Malterud, 1993) When trying to understand and investigate lived experiences, a qualitative approach is recommended as it generates a rich description of both local

contexts as well as subjective experiences. (Silverstein, Auerbach, & Levant, 2006; WHO, 2012)

For the qualitative part of the study we utilized a participatory thematic, reflexive analysis approach, (Binder, Holgersen, & Moltu, 2012; Boyatzis, 1998; Braun & Clarke, 2006) within an interpretative-phenomenological ontological and epistemological framework. (Gadamer, 1989; Heidegger, 1996) When employing a hermeneutical approach, in the process of understanding the context and experiences of the participants, the interpretative aspect is not only central, but also unavoidable. According to Gadamer (1989) the experiences of the participants can be approached more closely through a fusion of the researchers' and the participants' horizons, meaning that new understanding comes from a continuously developing, dynamic and reflexive dialog between participants and researchers. A central starting point in the phenomenological approach is the epistemological belief that important knowledge comes from individuals with lived experience of mental health problems, and that the central aim is to discover and interpret the meaning of such experiences. (Borg, 2007; Fossey, Harvey, McDermott, & Davidson, 2002) The focus is thus grounded in individual experiences, but at the same time it is acknowledged a comprehensive understanding of these experiences can only be achieved when examined within broader contexts. Hence, recovery was considered a social process as well as a personal and subjective phenomenon. (Veseth, Binder, Borg, & Davidson, 2012)

Service user involvement

To facilitate service-user involvement, the objectives and procedures in the qualitative part of this project were developed within the framework of user-involved research. (Borg, 2007; Trivedi & Wykes, 2002) Two fully recovered service users with lived experiences of psychosis and first-hand knowledge on clinical recovery processes were recruited from the local health trust (Helse Stavanger) to participate as co-researchers.

The objective of the first collaborative meetings was to develop and revise the interview guide used in the qualitative studies. The second part of this process was to collaborate on the interpretation of the findings and evaluate the project. One service-user joined the data analytic process (see *Analysis* in study 1 for details).

Reflexivity, scientific team and analytic cooperation

Pre-understandings include researchers' pre-existing experiences, hypotheses, perspectives, prejudices and frames of reference, which may influence any part of the research process. (Malterud, 1993) In line with reflexive methodology (Alvesson & Sköldberg, 2009; Binder et al., 2012) we outlined any personal and corporative issues which may have affected our interaction with the subjects or our interpretation of the data. Further we illustrated the method we used to deal with these challenges. The analysis team consisted of Bjornestad (team leader), Bronick, Veseth and Davidson, whom are trained clinical psychologists from various clinical and academic backgrounds, all with a particular interest in severe mental illness. Some differences were presented in theoretical and epistemological viewpoints, ranging from contextualism to Husslerian phenomenology.

On one hand we saw these differences as necessary to facilitate a rich description of the data, which often is required when examining an under-researched area. On the other hand, differences implied that the process of reaching coherent results, particularly in the interpretative analytic work, could be a challenge. Here, our reflexive approach guided us: As it was clear to us that such differences may have existed, we mapped differences in viewpoints in the preparatory phases of the study. Our timing here seemed crucial, as this allowed us to overcome possible disagreement by developing tailored decision rules to resolve disagreement ahead of analysis. We agreed on the following decision rules for the analytic process: 1) Have an open attitude and seek consolidation rather then conflict whenever differences were discovered.

2) Resolve minor disagreement utilizing the principle of parsimoniousness (i.e. Occam's razor: *when two competing theories make the same predictions, the simpler one is better)*. 3) To resolve major disagreement we applied A) an inductive principle using the raw data as a compass guiding us to the description of the phenomena at issue which seemed most true to the participants' lived experience. B) Then apply the principle of the best argument as described above.

Sample and recruitment

A sample classified as clinical recovered service users were recruited from the projects TIPS-1 (n=1) and TIPS-2 (n=19). We used the same cohort in both qualitative investigations. Participants were recruited consecutively at 2-, 5-, and 10-year follow-up sessions (calculated from inclusion date in TIPS-1 and TIPS-2). Twenty-seven eligible candidates were contacted; of these, four participants refused study participation and three were classified as non-recovered (subsequently after the actual interview), due to only 50 percent part-time work. Sample size was decided on the basis of stability of findings, reviewed after 15 and 17 participants (Hill, Thompson, & Williams, 1997). We stopped recruiting after 20 participants, as we considered the last three interviews not contributing with substantially new information. Exclusion criteria for the qualitative studies were: (1) Alcohol or substance abuse as primary diagnosis and (2) substance-induced psychosis. Service users with varied educational, occupational and social background were included. For demographic and clinical characteristics see Paper 1.

Interviews

A semi-structured interview guide was developed on the basis of a established qualitative procedure, (Miles, Huberman, & Saldaña, 2013) (p 25) literature on factors facilitating recovery, (Beck et al., 2012; Bellack et al., 2007; Davidson et al., 2001; Leamy et al., 2011; Leucht, Tardy, et al., 2012) and collaboration between researchers and two

recovered service users, focusing on the following possible contributors to recovery: 1) specific, personally-relevant experiences, 2) environmental factors and 3) treatment-related factors. To capture topics not adequately covered by the interview, an open-ended category was added to the end of each interview, in which participants could provide additional information that had not yet been elicited related to their recovery. Two pilot interviews were conducted with two clinical recovered service users. The interview guide was modified somewhat after these interviews, but the core-parts remained the same. The first author conducted all interviews: 17 interviews were conducted at Stavanger University hospital and three at participants' homes. Interviews were audiotaped and transcribed verbatim for the purpose of analysis (see paper 1 and 2 for interview question examples).

Analysis

We used a bottom-up, text driven approach, including an inductive meaning condensation procedure, involving the 6-steps as presented in Table 1 in Paper 1. The analytic approach was somewhat modified in study 2. Whether an inductive approach is feasible is an on-going debate. Some argue that regardless of holding a reflexive style, analysis will always be affected by the researchers' pre-conceptions. Thus a semantic approach implying an explicit e.g. epistemological stance is the only tidy and valid way of doing it. (Boyatzis, 1998) This can however also be seen as a continuum, which implies degrees of difference with regard to what extent the researcher is adopting a specific theoretical framework in the analytic process. (Alvesson & Sköldberg, 2009; Braun & Clarke, 2006; McLeod, 2001) The interpretative work will be affected by whether the researcher takes a clear e.g. Focaultianian stance versus a Heideggerian. A reflexive approach is in this regard an attempt to attenuate the ideological aspect and replace it with introspective reflection, and thereby reduce the impact of ideology, or at least make it more transparent how ideological pre-conceptions of the researcher

affect the interpretative process generating the study findings. However, the larger debate on this is beyond the scope of this thesis.

To strengthen the credibility of the study, the authors Bjornestad, Bronnick and Veseth conducted the 5-step procedure independently. In collaboration with remaining authors, all researchers compared their interpretations, agreed on themes with accompanying quotes, and validated the findings. Finally findings were revised and validated in collaboration with two auditors; (Hill et al., 1997) one independent, clinically recovered service user and one independent psychologist. Both received basic training in textual analysis prior to analysis and were given the instruction to read thoroughly through all interviews and write down their main assessments of what the interviews referred. Prior to the joint analysis meeting they were instructed to point out incorrect interpretations and thematic omissions in the researchers' findings, and to offer alternative interpretations of the data. In an analysis meeting (including auditors and researchers) first the auditors presented their findings followed by researchers presenting theirs. Data were then compared and discussed, applying the same decision rules as described above. Auditors' comments were written down and integrated in the finalization of the analysis. Finally, results were given auditors for comments before commissioning was completed.

5.3   Quantitative part

Aim

In this study, we aimed to test three hypotheses of specific social baseline predictors' effect on clinical recovery after two-year follow-up. See study 3 for details on hypotheses.

Sample

The study sample (n=186) was recruited exclusively from the TIPS-2 project. Study participation, dropout analysis, measures, clinical and demographic information are described in Paper 3.

Measures

Predictor variables

The selection and construction of the predictor variables was of particular importance in this study. With the backdrop of several reviews (Buchanan, 1995; Gayer-Anderson & Morgan, 2013; Palumbo, Volpe, Matanov, Priebe, & Giacco, 2015; Thoits, 2011) criticizing the use of unspecific and unclear global categories of social measures, we disentangled the conglomerate of social interaction into four specific measures using variables from the Lehman Quality of life Interview. (Lehman, Kernan, & Postrado, 1995) First, we conceptualized two dimensions of social functioning: Frequency vs. satisfaction, and friends vs. family. This gave rise to four combinations of social interactions for use in the statistical models, and yielded the opportunity to investigate systematically the relative importance of frequency of, versus satisfaction with family vs. friend interactions on clinical recovery. See paper 3 for details.

Outcome variables

Symptom remission was defined in accordance with international standardized criteria (Andreasen, 2006) as described earlier (p. 30).

Covariates

Model covariates were age, gender, baseline symptoms (PANSS positive, negative, depressive, excitative, and disorganized), DUPlog, time and substance abuse. Covariates were based on factors previous

studies had found to affect outcome, including symptomatic and functional remission. (Altamura et al., 2007; Bond et al., 2008; Lang et al., 2013; Marshall et al., 2005; D. O. Perkins, H. Gu, K. Boteva, & J. A. Lieberman, 2005; van Nierop et al., 2014) Number of covariates was however also a weighting process between different considerations, such as quality of previous evidence for the specific issue investigated, what our chosen statistical model could handle, possible multicollinearity and available data. Our choice fell on covariates, which consistently had affected both course and outcome.

The statistical technique of General Estimation Equations

The statistical technique of Generalized Estimating Equations (GEE) (Diggle & Kenward, 1994; Zeger & Liang, 1986) were used to estimate the effect of social interactions on recovery over the entire follow-up period (two years). This technique was applied for several reasons: GEE compensates for correlated longitudinal data and enable the analysis of the complete available data even when subjects have missing data at one or more measurement points. (Hanley, Negassa, & Forrester, 2003) This implies that the GEE may increase statistical power.

Recovery is a fluctuating phenomenon (Davidson et al., 2008; Liberman et al., 2002) and the rule is more often then the exception that individuals experiencing psychosis may have periods of psychotic relapse after they achieve their first period of recovery. Stable recovery usually occurs after some repetition of this pattern. The GEE estimated probability of recovery throughout year one and two, but also probability of recovery for both year one and two separately. Thus GEE models complex data of recovery well and at the same time capture important ecological aspects with regard to recovery as a fluctuating phenomenon.

The GEEs were set up as a binary logistic model, with a robust estimator and an unstructured covariance matrix. Time was defined as a categorical variable, yielding separate parameter estimates for each time-point. For

time, the reference category (coded 0) was the 2-year follow-up. Predictor variables and covariates were entered simultaneously in the GEE model as main effects, alongside the interaction terms of time with the hypothesis derived predictors.

Models tested

For social interactions as predictors of recovery, satisfaction with and frequency of social interactions were the dimensions investigated. Family versus friends were the two domains in which they were investigated. Hence, four variables were established as candidate predictors of recovery: Frequency of contacts with family, frequency of contacts with friends, satisfaction with family contacts, and satisfaction with friend contacts.

Model 1: In order to disentangle satisfaction versus frequency we analysed social frequency versus social satisfaction across both domains, friends and family, together. Frequency and satisfaction were entered as predictors (independent variables) of recovery (dependent variable).

Model 2: In order to investigate the relative importance of family versus friends, we entered satisfaction with friends versus satisfaction with family as predictors in the second model.

Model 3: In order to further investigate the relative importance of family versus friends, we entered frequency of contacts with friends versus frequency of contacts with family as predictors in the third model.

Model 4: From each of the fitted models, the significant predictors were included in a final analysis, excluding the other previously non-significant predictors, but still including the covariates.

Ethical Considerations

The present study was approved by the Regional Ethical Committee (2013/1246/REK sør-øst C). The Regional Committee has approved TIPS-1 for Medical Research Ethics Health Region II (#S-95189) and the Regional Committee for Medical Research Ethics Health Region East (#1.2007.2177). TIPS-2 is approved by Regional Ethical Committee (REK vest 015.03) and collaborates with TOP REK Øst (#493-03-01179, 630-04, 689-05250). With regard to the qualitative investigations, research indicates that interview studies may empower participants (Kitzinger, 1995) and enhance their feeling of self-worth. (Reason & Riley, 2008) Written informed consent was obtained from all participants in the study.

Funding

6 Findings

6.1 Summary paper 1

The paper is named "The central role of self-agency in clinical recovery from first episode psychosis", and presents findings from the first qualitative study. The aim was to investigate mechanisms of recovery after a first-episode psychosis as perceived by clinically recovered service users. In this study, we applied an interpretative-phenomenological approach, including a meaning condensation procedure, which culminated in one main theme and three related and subordinate themes: Main theme: *Establishment of subjective self-agency*. Subordinate themes: 1) *Environmental support and gentle pressure*, 2) *Individually tailored assistance*, 3) *Antipsychotic medication: relinquishing personal responsibility, and considerable side effects*. These findings were mainly discussed in the framework of the concept of self-agency- both in relation to how participants seemed to gain or regain self-agency after a period of psychosis, including individual contributions as well as the environmental and treatment contributions to the recovery process. Based on our analysis we suggest an increase in self-agency as a core mechanism driving recovery in the study sample, including those with prominent negative symptoms. Finally, we highlight that interventions with a focus on increasing self-agency may be particular beneficial for some sub-groups of individuals. This paper was published in *Psychosis - Psychological, Social and Integrative Approaches*.

6.2 Summary paper 2

The second paper is called: "Antipsychotic treatment – experiences of fully recovered service users". Here we investigate first-person accounts of clinically recovered service-users experiences of using antipsychotic medication during and after a first-episode psychosis, both from personal

and contextual perspectives. The interpretative-phenomenological approach led to five related themes: 1) *Antipsychotic drugs reduce mental chaos during the acute phase*, 2) *Non-stigmatizing environments perceived to increase chances of successful use*, 3) *Use of antipsychotic drugs beyond the acute phase – Considered to compromise the contribution of individual effort in recovery*, 4) *Prolonged use of antipsychotic drugs perceived to reduce likelihood of functional recovery*, 5) *Antipsychotic medication considered as a supplement to trustful relationships*. We conclude that antipsychotics are mostly perceived as an efficient treatment during the acute phase and also more broadly to achieve symptomatic remission. However, costs were often seen to outweigh benefits beyond this stage, particularly in relation to functional aspects of recovery. We discuss how these findings call for a collaborative approach of use and how tailored information about antipsychotics should be given early in the course, including different ways of presenting antipsychotic treatment to the service-user. This investigation highlights the need for further sub-group investigations of antipsychotic medication. The paper was published in *Journal of Mental Health*.

6.3   Summary paper 3

This paper was named: "With a little help from my friends" social predictors of clinical recovery in first-episode psychosis. Here we disentangled the social dimension and tested three specific hypotheses of social predictors of clinical recovery. We hypothesized that first, satisfaction with social relations predicts clinical recovery; second, that frequency of social interaction predicts clinical recovery; and third, that the effect of friend relationship satisfaction and frequency would be greater than that of family relations satisfaction and frequency. Only frequency of friend relationships was a significant predictor of clinical recovery. We discussed how the results may have been affected by the service-users' psychotic condition at baseline. Findings are also

discussed in the framework of the mere exposure effect. We suggest friendship frequency as a malleable factor, which can be modified through tailored intervention and thus increase recovery rates. The latter seems both testable and holds the potential of a cost-efficient intervention. This paper is accepted for publication in *Psychiatry Research*.

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7 Discussion

The main aim of this thesis was to investigate factors facilitating clinical recovery using a multi method research design. To achieve this, we sub-divided the project into three investigations: *First*; we investigated factors facilitating clinical recovery seen from service-users' perspectives, including specific, personally relevant experiences as well as environmental and treatment-related factors. *Second*; we investigated how clinically recovered service-users perceived using antipsychotic medication during and after a first-episode psychosis. *Third*; we investigated specific social predictors of clinical recovery using a quantitative approach. Due to the complexity regarding what drives recovery, a complete discussion requires a multi level perspective, including politics and public subsidy (money). As the main focus of this project was narrower, we will primarily discuss recovery in relation to our study findings and the potential clinical implications, which may be derived from these. In this regard the study findings allows for discussing recovery on two levels in particular: 1) A superordinate level concerning guidelines and implementation of treatment strategies. 2) A subordinate level regarding micro processes of human interaction. (Davidson & Johnson, 2014) This latter dimension is more rarely addressed in research, guidelines and implementation context. However, based on our findings, these processes seem essential to enable good implementation and increasing recovery rates. These to dimensions also highlight the need for both qualitative and quantitative research approaches in mental health research.

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8 Superordinate level – guidelines and treatment strategies

Early sensitive social pressure as a possible systematic intervention

In the third study of this thesis, dealing with social baseline predictors, we highlight the risk of social network deterioration already in phases prior to psychosis onset. (Gayer-Anderson & Morgan, 2013; Robustelli et al., 2016) Given this risk, together with proven benefits of early intervention (Marshall & Rathbone, 2006) and the indication that social frequency may be a modifiable treatment factor, (Davidson et al., 2004) it seems that a targeted, early intervention aimed to increase early social frequency of friendship contact may reduce the actual and perceived social deterioration often denoting psychosis.

Such an approach may be beneficial for several other reasons as well: It is plausible that frequent social contact increase subjective relational satisfaction by a *mere exposure effect.* (Zajonc, 1968) The exposure effect posits that individuals generally tend to develop preferences for objects and individuals as a consequence of familiarity. However, research shows that this effect requires and is reinforced by consistency in social relations, and conversely, is reduced if scattered among many. (Bornstein, 1989; Zajonc, 1968) Hence, increased social frequency, if consistently maintained, may in itself increase subjective satisfaction with social relationships. Further, in a longitudinal developmental perspective, (Kazdin, 2007) it is appropriate to treat the development of social relations as an evolving process. Time spent together is necessary to develop quality in any relation, and with a low frequency of interaction, the potential for such mutually satisfying social encounters is greatly reduced. Hence, it seems reasonable to assume that social frequency precedes, and is a prerequisite for, the development of social quality. Conversely, the lack of social frequency will diminish the potential for social interaction, and may ultimately lead to social

exclusion and possibly loneliness. This in turn may elicit, maintain and increase psychiatric difficulties. (Davidson et al., 2001; Hawkley & Cacioppo, 2010) Finally, frequent friendship interaction may lead to a sense of being precious to others outside the family, thus enhancing a perception of intrinsic value and capacity for independence and reciprocal social relations. All factors associated with subjective well being in severe mental illness. (Davidson, 2003; Marino et al., 2015) Merged together these findings highlights the potential significance of targeting frequency of social interaction in early psychosocial interventions for people with psychosis.

Findings from study three further suggest that this type of intervention may include individuals with a negative assessment of social quality, and individuals with an inclination for social withdrawal and isolation. Study findings indicate that these individuals also seem to have a positive effect of higher social frequency, making an argument that professionals perhaps should deemphasize the subjective assessments of relational qualities in the early customization of treatment and evaluation of treatment efficacy in the initial phase of the course.

Additional, we found in our qualitative investigation that sensitive pressure from family, friends and professionals was perceived as necessary to achieve full functional recovery. Hence, both the qualitative and quantitative approaches in this project coherently indicate that service-users not necessarily should dictate all treatment elements, particularly in the initial phase when symptom load is high, understanding of ones symptoms and distress may be challenging, and social withdrawal may seem a comfortable short-term strategy to master some of these difficulties. Although all studies in this project are related, they do represent two substantially different research methodological approaches. The latter strengthens the argument that sensitive and tailored pressure, aimed on what may be termed increased normative community participation, should be applied early to combat further social deterioration. Given the high symptom load and functional decline

that often characterize service-users in the early phases of psychosis, the responsibility for initiating this type of intervention should clearly be on professionals in collaboration with service-users, family members and their (broader) social network.

A possible systematic treatment approach – Self-agency treatment

In the first study concerning facilitating factors of clinical recovery, findings indicate that a traditional treatment approach with an extensive focus on risks, ill health, disease, treatment *delivered* by mental health professionals (Eriksson & Lindström, 2005; Harrow & Jobe, 2013) and extensive use of antipsychotic medication (Davis, Chen, & Glick, 2003; Harrow & Jobe, 2013) may be counterproductive for a sub-group of service-users. For the study sample, a robust sense of self-agency seemed necessary to achieve full social recovery. A self-agency deficit has been proposed as a core trait in schizophrenia, including loss of the ability to correctly attribute personal thoughts, internal speech, or covert or overt actions to oneself. (Jeannerod, 2009) It is also suggested that a sense of causal control is key to being able to feel accountability, or a responsibility for personal actions. (Bandura, 1997; Frith, 2014; Jeannerod, 2009) At present, chance most likely determines whether a systematic focus on self-agency promoting factors is present in social network support and treatment. These types of interventions are neither devoted explicit attention in current treatment guidelines. (NICE, 2014) We concluded by suggesting that future research might focus on new, self-agency restorative or building interventions, as well an increased emphasis of nurturing agency as part of existing interventions. Both psychosis research (Frith, 2014; Jeannerod, 2009) and related research on mental health, involving possible drivers of motivation (Bandura, 1997) suggest that this might be a fruitful approach.

Antipsychotic medication – a collaborative approach and systematic safeguards for use

An implication of the findings in study two, concerning antipsychotic medication is that treatment should be a collaborative approach, integrated across all phases of care. This implication is supported by previous research, (Borg & Kristiansen, 2004; Dixon, Holoshitz, & Nossel, 2016) and such an approach seems to be associated with increased adherence, a feeling of safety and improved trust and better collaboration between service-users and professionals. A systematic testing of a system wide implementation of safeguards and checkpoints to frequently monitor clients' experiences and wishes related to antipsychotic use seems called for.

All service-users were offered antipsychotic treatment, however six of them refused this type of treatment at baseline. Thus, this study shows that a sub-group of patients diagnosed with a psychotic disorder recovered from psychosis without using antipsychotic medication. This finding has at least two possible implications; 1) there is need to further investigate sub-groups of psychotic service-users to better assess and select type and duration of antipsychotic treatment. In this regard a starting point seems to be to differentiate clients who are stable and symptom free from others with persistent positive symptoms. This finding is in line with recommendations of previous research. (Andreasen, 2006; Harrow & Jobe, 2013; Wunderink, Nieboer, Wiersma, Sytema, & Nienhuis, 2013) Such an approach could be preventive, especially in relation to long-term use, where the potential for serious side effects are greater (Moncrieff, 2015). 2) There seem to be a basis to question the position of antipsychotic treatment as maintenance use treatment as a general recommendation. Thus, these findings challenge both international (NICE, 2014) and national (Helse- og omsorgsdepartementet, 2014) guidelines, which recommend antipsychotic treatment as a general, phase unspecific treatment as well

as the recommended treatment for all sub-groups of psychotic service-users.

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9 Subordinate level – Some of the micro level building blocks necessary to implement recovery oriented treatment strategies

The qualitative study findings indicate a strong relational basis in recovery. In particular a collaborative approach to antipsychotic medication, sensitive social pressure, good timing and tailored empathy from peers, family and professionals seem beneficial. The basis of these processes can be seen as operating on an *interpersonal micro level* (Davidson & Johnson, 2014):

The relational basis for sensitive social pressure

With regard to the psychotherapeutic basis of recovery, Safran and Muran (2014) highlight the dynamic character of the therapeutic alliance in psychotherapy. Alliance is understood as a continuously negotiated interaction between the therapist and the service-user. (Safran & Muran, 2000) They point out that the alliance in itself can be an important curative factor, which is in line with current research on healing factors in psychotherapy. (Norcross & Lambert, 2011; Norcross & Wampold, 2011; Wampold & Imel, 2015) Through the alliance negotiation, the service-user can assert her own needs, and experience these as taken into consideration, while at the same time she can be aware of and learn how to deal with the therapists' utterances. Trough this reciprocal relational process, which involves relational support, relational testing and relational training, the patient is provided with an opportunity to build and strengthen his own agency. (Safran et al., 2014) In our qualitative investigation these types of relations seemed to characterize both the psychotherapeutic alliance and relations in the social network. Instead of the service-user passively accepting the approach developed by others, they were gradually more and more involved as active agents or

collaborative partners in the development of a flexible approach tailored to their needs to fully recover. These findings are in line with a systematic review of qualitative literature, (Farrelly & Lester, 2014) concluding that the development of trust between psychosis patients and clinicians were facilitated by the therapists' ability to sensitively reinforce the autonomy and self-determination of the people they treated.

Qualitative findings of this project highlighted that these types of mutually respectful relations seemed a necessary interpersonal basis to utilize the strategy of sensitive social pressure. Also they seemed vital in clarifying the relation between the service-user, therapist and members of the social network regarding individual contributions, division of labour, expectations and responsibilities. The service-user was gradually held more accountable but at the same time a clear desire to help was conveyed. Here, timing seemed crucial both in the establishment of trust, but also to make pressure efficient. Sensitivity for how much the service user could take seemed pivotal, partly because approaches pushing the participants limit generally was seen as most efficient. This basis of trustful relations combined with sensitive social pressure seemed particularly efficient in combating the functional challenges of recovery, including negative symptoms.

Some of the interpersonal ingredients in a collaborative approach for efficient antipsychotic treatment

In the qualitative investigation a relational focus also seemed highly relevant for the antipsychotic treatment to be successful. Particularly this referred to the atmosphere where medication was offered, but also to how medication related information was communicated by professionals: In order to reduce service-users anxiety and negative prejudice associated with receiving a psychiatric diagnosis and antipsychotic treatment, (Hamilton et al., 2014; Kleim et al., 2008; MacDonald, Sauer, Howie, & Albiston, 2005), our findings, in line with previous research (Perkins et al., 2006) suggest that clients need to be well informed before initiating

antipsychotic treatment. Information appeared to best facilitate successful use when delivered in a manner to support and sustain self-recovery and perceived self-agency beliefs. This entailed presenting antipsychotic treatment as one of many tools supporting the person's recovery processes, rather than as the main and only way to recovery. Many participants described having had well-developed social networks prior to psychosis, and they believed that problems, including psychological ones were related to social situations and perceived maladjustment, e.g. social withdrawal as a result of bullying, social anxiety and lack of coping. Such problems were in turn described to have relational solutions, e.g. support from family, friends and psychotherapy, which was thought to improve resilience and build coping strategies. A perceived disproportionate focus on antipsychotic drugs from professionals was described as being in conflict with their idea of recovery as a social process, resulting in resistance, mistrust, and ultimately non-adherence.

Also, it seemed beneficial to focus on phase specific needs, e.g. linking successful antipsychotic treatment to the potential achievement of social and sustainable goals and functional aspects of recovery, such as paid competitive work. Our finding clearly emphasize that this type of information should be presented as soon as possible in the treatment course, as many participants reported, in line with previous research (Kane, Kishimoto, & Correll, 2013; McEvoy et al., 2007) discontinuing medication at a very early stage.

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10 Comments on the mixed method research approach

The first person perspective combined with inferential statistics
The two levels of analysis in this discussion (superordinate and subordinate) illuminate how a mixed approach may contribute with knowledge on both levels. In my opinion these levels are both relevant as they contribute with different as well as complementary knowledge. As argued, a mixed approach can make hypotheses generation a more transparent enquiry. Also, this approach may provide information regarding the "how" questions revealing necessary details about processes of recovery and how guidelines should be performed to have optimal impact on the service-user. Further, as the qualitative approach have challenges with generalizability the necessity of a quantitative extension seems required to test the generalizability of the qualitative findings. This bridging between research paradigms seems fruitful, both regarding the evaluation of treatment guidelines but also if the aim is to answer research questions broadly. Given the evidence grade of psychosis research in general, for me the latter seem crucial for further progression in this field.

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11 Strengths and limitations

Strengths

A strength in this project is that it illuminate a set of complex research questions from multiple perspectives. This is mainly due to the mixed method research approach. Coherent and convergent findings across methodologies strengthen study findings. (Alvesson & Sköldberg, 2009) Further the project's ability to provide in-depth knowledge about the service-user perspective is important to generate ecological valid and transparent hypothesis testable for quantitative investigations. Also, the qualitative approach seems a beneficial supplement to quantitative approaches to evaluate effects of treatment strategies and implementation of guidelines. The study approach of splitting the social dimension in study three (quantitative study) seems particularly promising for delivering new, and more specific knowledge regarding which single social factors should receive most attention when developing clinical treatment approaches to psychosis.

Limitations

In the qualitative part findings were context-dependent for the participants and setting in which the study was conducted. Possible significant meaning units may have been excluded as a result of a rich level of analysis. The study sample included a high percentage of participants diagnosed with episodic psychotic conditions expected to subside. Only two participants fulfilled core schizophrenia diagnostic criteria at the time of the interview. However, this distribution is expected when using clinical recovery as an inclusion criterion because the likelihood of becoming and remaining asymptomatic is greater for individuals with short-term and limited psychotic conditions. This does not, however, compromise the validity of the relevant findings regarding clinically recovered individuals, but particularly decreases generalizability for individuals suffering from the most severe and

prolonged psychotic conditions, such as schizophrenia. Also, all studies were performed in an early intervention area, meaning that participants received an extensive standardized treatment package. This may decrease generalizability to populations not covered by this type of health care. The timing of the interviews might make a possible bias and a limitation of this study. All participants had been in treatment for a minimum of two years before the interview. This might have resulted in recall bias. Further, in study 3 we left out covariates such as premorbid social functioning (Cannon-Spoor, Potkin, & Wyatt, 1982) as this variable were assessed to plausibly show multicollinearity with the predictor variables as both concerned social functioning and social interaction. Also we saw this covariate with several other potential pitfalls: First, we did not have data from relatives, meaning that the only available information source was study participants with active psychosis, as these data were collected at baseline. Due to the duration of untreated psychosis and uncertainty about the duration of the prodromal phase characterizing the sample, premorbid functioning data from childhood would have been the only data, which with certainly would not be possibly corrupted and overlapping with the psychotic phase. We assessed this mixture of being in a psychotic state combined with an assessment of childhood social memories to make the investigation of this variable prone for recall bias. Thus, although this variable could have strengthen the analysis by correcting for social functioning in childhood, which has been shown to affect outcome (MacBeth & Gumley, 2008) we assessed it to be to many potential pitfalls using it. Also, this being a hypothesis testing study, not a general model building inquiry this made the decision of leaving out premorbid social function from the model easier.

Furthermore, as this was the first study to do a clear and distinct split of the social dimension, testing specific social baseline predictors of clinical recovery, it was not straightforward process to choose relevant covariates. Although the statistical technique of General estimating

equations is robust, maybe the statistical model could have been simpler, using fewer covariates. This we do not know for sure.

Finally, in this study social satisfaction data were collected at baseline, and equivalent investigations at a later stage might have revealed different ratings of essentially similar social experiences. There is also a possibility that patients who experienced recovery also experienced change of social interaction, which may imply that changes in social interaction may be related to recovery.

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12 Implications for research and practice

As argued, the study finding of sensitive social pressure as a possible vital ingredient in clinical recovery, and the finding of increased social frequency as a significant baseline predictor of clinical recovery forms the basis for possible cost-efficient early interventions. As these phenomena are readily quantifiable, they seem well suited for objective tracking of progress and empirical testing.

Future research might investigate possible moderators to the association between frequency of friendship interaction and clinical recovery. Also, in- depth investigations of friendship relations might help reveal any unique relational qualities, which make them more particularly important to remission.

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13 Concluding remarks

Using a qualitative study approach, particularly in the initial phase of a research project or in a research area with limited knowledge seem beneficial both to reveal valid hypothesis and a more detailed level of knowledge important to service-users. Bridging the qualitative and quantitative methodological approaches within the same project seem advantageous to cover the phenomenon more thoroughly, but also helps overcoming some of the limitations with each study approach when conducted in isolation.

Regarding antipsychotic treatment, this project, in line with the general literature, emphasise medication as important in the acute psychotic phase and short-term treatment. However, the processes of recovery, particularly functional aspects seem to have a central social component dealing with factors other than the drugs alone. This finding advocates the need to better differentiate clients who are stable and symptom free from others with persistent positive symptoms of psychosis.

Splitting the social dimension allows for more specific and precise knowledge of which factors predicts and drives symptomatic remission. The study finding of increased frequency of friendship interaction seem promising as a basis for a testable intervention. We argue that this type of a more fine-grained approach in testing predictors possibly will allow for progression in the identification of factors and possible mechanisms driving both remission and recovery. Such pinpointing of effects seems to facilitate tailored care.

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"With a little help from my friends" social predictors of clinical recovery in first-episode psychosis

"With a little help from my friends" social predictors of clinical recovery in first-episode psychosis

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ABSTRACT

Social functioning is a conglomerate of factors central to clinical recovery after a first-episode psychosis. There is a lack of studies investigating the relative impact of factors related to social interaction. Disentangling these could facilitate improvement of psychosocial interventions. This study aims to investigate the impact of social interactions on two-year clinical recovery in first-episode psychosis, by examining frequency and satisfaction of relationships with family and friends. A baseline sample of 178 first-episode psychosis individuals were followed up over two years regarding social functioning and clinical status. We longitudinally compared those who were to those who were not recovered using generalized estimating equations analyses. Our results showed that frequency of social interactions with friends was a significant positive predictor of clinical recovery over a two-year period. Perceived satisfaction with relationships, and frequency of family interaction did not show significant effects. We conclude that interaction with friends is a malleable factor that could be targeted for early intervention. This would facilitate protective factors through the preservation of existing social networks and thus reduce the risk of disability associated with long-term psychosis. Findings indicate that even individuals with an inclination towards social withdrawal and isolation could benefit from this type of intervention.

1. Introduction

Clinical recovery can be seen as the ultimate outcome after a first-episode psychosis (FEP), implying long-term absence of psychotic symptoms and adequate social and vocational function (Liberman and Kopelowicz, 2002). Thus, early predictors of this type of recovery are highly relevant to investigate.

Social functioning is a core component of psychotic syndromes. Research interlinks early social, cognitive and emotional development to later social cognitive capacities, such as mentalization ability and theory-of-mind, considered vital to solid health and reversely, when impaired, a basis for early psychosis vulnerability, functional deterioration and worse outcome (Grau et al., 2016; Horton et al., 2015; MacBeth and Gumley, 2008; Ohmuro et al., 2016; van Os et al., 2010). Negative symptoms, operationalized as social withdrawal, apathy and avolition are also core feature of psychosis, associated with poor outcome and decreased social functioning (Kirkpatrick et al.,

2006; Parellada et al., 2015). Supportive family, but even more so, friendship networks (Davidson et al., 1999; Erickson et al., 1989; Morgan et al., 2008; Reininghaus et al., 2008) are however associated with better outcomes and more efficient use of health services (Evert et al., 2003; Pinto, 2006), as well as a reduction in subjective loneliness (Hawkley and Cacioppo, 2010) decrease in perceived social stigma (Watson et al., 2007), and better self-care functioning (Evert et al., 2003), all factors relating social support to social functioning. Research has demonstrated an association between supported socialization and improved social functioning (Davidson et al., 2004), thus indicating a malleability in social capacities and highlighting social functioning as a promising target for tailored intervention. Both practical support and emotional friendships buffer harmful impacts of stress exposure (Davidson et al., 2004; Thoits, 2011), which might be causally linked with psychosis onset (Reininghaus et al., 2016).

Several reviews have characterized the literature in this field as heterogeneous (Albert et al., 1998; Buchanan, 1995; Gayer-Anderson

and Morgan, 2013; Thoits, 2011). A main criticism concerns how studies have merged factors related to social interaction into one, or a few, global categories. This prevents a valid evaluation of their independent effects on outcome and clinical recovery. In addition, studies are often based on heterogeneous samples including both chronic and first-episode psychosis, limiting the generalizability of study findings. Ultimately, these factors leave knowledge gaps that may impede helpful intervention.

This study aims to disentangle some of the factors incorporated in the conglomerate of "social functioning", and testing their separate effects on clinical recovery in a FEP sample. To do so we developed three hypotheses of baseline predictors of clinical recovery:

1.1. Hypotheses

We hypothesized that first of all, satisfaction with social relationships predicts clinical recovery; secondly, that frequency of social interaction predicts clinical recovery; and third, that the effect of friend relationship satisfaction and frequency will be greater than that of family relationships satisfaction and frequency.

2. Methods

2.1. Sample

The sample was recruited from the on-going TIPS-2 study (Early Treatment and Intervention in Psychosis), a naturalistic follow-along FEP study in Rogaland, Norway, including a population-based cohort (350.000 individuals) of FEP individuals from January 2002, until August 2013. Detailed descriptions of the inclusion criteria and methods have been published elsewhere (Joa et al., 2008). Participants received treatment according to a two-year standard treatment protocol that included antipsychotic medication, supportive psychotherapy, and multifamily psycho-education. TIPS-2 was approved by the Regional Committee for Medical Research Ethics Health Region West, Norway (015.03). All participants provided written informed consent.

Individuals who were included in the study met the following criteria: living in the catchment area; age 15–65 years; meeting the DSM-IV criteria for a first-episode of schizophrenia, schizophreniform psychosis, schizoaffective psychosis, delusional disorder, brief psychosis, affective disorder with mood incongruent delusions, or psychosis not otherwise specified, and also from August 1, 2008 substance induced psychosis; being actively psychotic as measured by the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987): not previously receiving adequate treatment of psychosis; no neurological or endocrine disorders related to the psychosis; understands and speaks one of the Scandinavian languages; an IQ over 70; and being able and willing to sign an informed consent.

Six hundred and twenty eight individuals were eligible for inclusion. Of those, 265 (42,2%) declined to participate in the study. Thus, 363 patients were included. For the purpose of our statistical analyses we only included individuals with a minimum of one measurement of one- and/or two-year recovery status and a complete set of data for all predictor and covariate variables in the linear statistical analyses (n = 178) (Fig. 1). Those excluded (due to drop out n = 116; missing complete set of data for all predictor and covariate variables n = 69) did not significantly differ from those included on any baseline demographic or clinical characteristics (Age, Gender, PANSS scales (positive, negative, depressive, excitative, disorganized), GAF symptom, GAF function and Duration of untreated psychosis (DUP)). Attrition thus appears to be random, and the sample can be assumed to be representative with regard to baseline characteristics.

2.2. Clinical measures

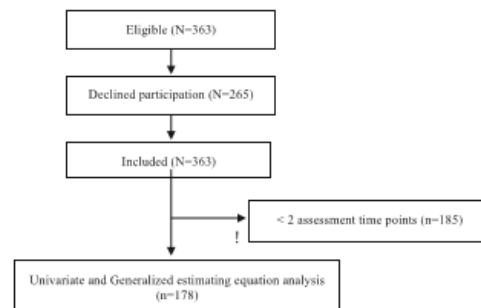The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-

Fig. 1. Flowchart – participant participation.

I) (First et al., 1995) was used for diagnostic purposes and symptom levels determined by mean and factor scores on the PANSS. In general, PANSS has been found to have good reliability and validity (Kay et al., 1988; Peralta and Cuesta, 1994). To determine group differences between recovered and non-recovered participants with regard to antipsychotic treatment and psychotherapy, we defined the following durations; weeks from inclusion to start of antipsychotic treatment and psychotherapy and weeks duration of antipsychotic treatment and psychotherapy.

Global functioning was measured by the Global Assessment of Functioning Scale (GAF) (APA, 1994). Scores were split into symptom (GAFs) and function (GAFf) subscales (Melle et al., 2004). The use of alcohol and other drugs was measured by the Clinicians Rating Scale (Drake et al., 1990). DUP was estimated as the time from onset of psychosis until the start of adequate treatment (Larsen et al., 2001). Onset of psychosis was considered to be the first appearance of positive psychotic symptoms, corresponding to a PANSS score of 4 or more on at least one of the following PANSS items; P1 (delusions), P3 (hallucinations), P5 (grandiosity), P6 (suspiciousness), and A9 (unusual thought content), for at least 7 days.

2.3. Social functioning measures

The brief version of Lehman's Quality of Life Interview (L-QoLI) (Lehman, 1996) was used to measure objective (frequency of face-to-face contact with family and friends) and subjective (satisfaction with family members and friendship contact) social functioning at baseline and at follow-ups, and to differentiate between family and friends in the past year. Measures were rated on a 5-point scale, ranging from 1 (terrible) to 5 (delighted) (Lehman et al., 1995). L-QoLI was also used to establish whether the participant was living independently, by dichotomizing the item concerning living situation into independent (score 1)/not independent (score 0). L-QoLI has demonstrated good validity and reliability both on objective and subjective scales (Lehman, 1996). The Strauss Carpenter Level of Functioning Scale (SCS) (Strauss and Carpenter, 1974) was administered to measure social contacts, paid competitive work and academic participation in the past year (measured at baseline and at follow-ups). Individual items on the SCS were rated on a 5-point Likert scale with higher values indicative of better functioning. Scores on both the L-QoLI and the SCS were based on interviews and all other available information (i.e. patient files, information from significant others if the study participant agreed) regarding functioning during the last year of the follow-up period.

2.4. Procedure

Trained personnel conducted baseline assessments within a week of contact. Raters were trained by rating pre-prepared case notes, asses-

sing videotaped interviews, vignettes and by attending clinical interviews as observers before entering the study assessment team. Good inter-rater reliability was achieved on major parameters in the research group in 2008 (Joa et al., 2008) and 2012. Reliability of measurements for DUP was 0.8 (ICC), and for diagnostic categories; $K = 0.9$ (Weibell et al., 2013). All participants included at baseline were set up for three-month, one-, two-, and five-year follow up evaluations. Baseline and follow up assessments (commonly lasting 2–3 h) mainly took place at Stavanger University Hospital, but sometimes at participants homes or other locations assigned by the participants.

2.5. Predictors

Predictor variables were baseline social and family relationships items from L-QoLI: a) Frequency of interaction with friends (Friends frequency), b) frequency of interaction with family (Family frequency), c) satisfaction with friend relationships (Friends satisfaction), and d) satisfaction with family relationships (Family satisfaction). These variables enabled us to independently test the contributions of family and friends.

2.6. Outcome measures

Symptomatic remission, functional remission and clinical recovery status were determined at two separate time points (1 and 2 years follow-up). Recovery status was determined by the following standardized, algorithmic-based approach:

2.6.1. Symptom remission

Symptom remission was defined in accordance with the international standardized criteria (Andreasen et al., 2005; van Os et al., 2006): no score at any time point of four or higher for the past six consecutive months on any of the following PANSS items: P1 (delusions), P2 (disorganized thought), P3 (hallucinatory behavior), N1 (affective flattening), N4 (passive social withdrawal), N6 (lack of spontaneity), G5 (bizarre posture), or G9 (unusual thought content). Fulfilling these criteria indicated symptom remission.

2.6.2. Functional remission

Social functioning was measured by the subscales measuring work and social interaction (SCS) and the criteria of living independently (L-QoLI): day-to-day living (independent living), role functioning (work, academic, or full-time homemaking), and social interaction. A score of 0 indicated very poor functioning and > 3 indicated adequate functioning. Participants had to have fulfilled these criteria for the last consecutive 12 months to obtain scores > 3 on the SCS. At the 12-month follow-up this is evidently impossible. Hence, for year one, participants had to have been in functional remission for 9 consecutive months (that is, between the 3- and the 12- months assessments). For the second year, the criterion of 12 consecutive months was sustained.

2.6.3. Clinical recovery

Clinical recovery was operationalized as a single variable of "yes" for all patients who met criteria for both symptom and functional remission. It should be noted that this operational definition does not imply that recovery is a static phenomenon, i.e. implying once recovered, always recovered. Thus, an individual may be recovered at 1 year but non-recovered at 2 years.

2.7. Statistical analysis

Analyses were carried out using SPSS, version 22. For the univariate analysis of baseline measures, comparing recovered to non-recovered participants, the recovered group was defined according to recovery status at the last available observation at 12 months or 24 months. Between-group differences were estimated employing Pearson chi-square tests for categorical variables, and unpaired two-tailed t-tests for continuous variables. Nonparametric statistics (Mann-Whitney U test) were applied for comparison of non-normally distributed data (Kolmogorov-Smirnov test). The DUP variable was log-transformed due to a severely skewed distribution. All tests were two-tailed, and Bonferroni corrections were carried out when appropriate. The choice of correction factor was made in each case based on the number of tests pertaining to each hypothesis, or number of variables in each category of parameters.

Generalized Estimating Equations (Diggle and Kenward, 1994; Zeger and Liang, 1986) were used to estimate the effect of social interactions on recovery over the entire follow-up period (two years). This technique compensates for correlated longitudinal data and enables the analysis of the complete available data even when subjects have missing data at one or more measurement points (Hanley et al., 2003). The GEE analyses were set up as binary logistic models, with a robust estimator and an unstructured covariance matrix. Time was defined as a categorical variable, yielding separate parameter estimates for each time-point. For time, the reference category (coded 0) was the 2-year follow-up. All models included the following covariates: Age, gender, baseline symptoms (PANSS positive, negative, depressive, excitative and disorganized), DUPlog, time and substance abuse; chosen on the basis of the literature. Predictor variables and covariates were entered simultaneously into the GEE model, alongside the interaction terms of time with the hypothesis-derived predictors.

For social interactions as predictors of recovery, satisfaction with and frequency of social interactions were the dimensions investigated. Family versus friends were the two domains in which they were investigated. Hence, four variables were established as candidate predictors of recovery: Frequency of contacts with family, frequency of contacts with friends, satisfaction with family contacts, and satisfaction with friend contacts.

Model 1: In order to disentangle satisfaction versus frequency we analysed social frequency versus social satisfaction across both domains, friends and family, together. Frequency and satisfaction were entered as predictors (independent variables) of recovery (dependent variable).

Model 2: In order to investigate the relative importance of family versus friends, we entered satisfaction with friends versus satisfaction with family as predictors in the second model.

Model 3: In order to further investigate the relative importance of family versus friends, we entered frequency of contacts with friends versus frequency of contacts with family as predictors in the third model.

Model 4: From each of the fitted models, the significant predictors were included in a final analysis, excluding the other previously non-significant predictors, but still including the covariates.

3. Results

Remission and recovery rates for one- and two-year follow up are outlined in Table 1. Baseline characteristics of individuals who were recovered at follow-up to those who were not are outlined in Table 2. Recovered individuals were more satisfied with both family and friend contacts, and had more frequent contact with friends at baseline,

Table 1
Recovery, symptomatic remission, and functional remission.

Characteristic	% (n/total N)	
	1-year	2-year
Recovery	14.4 (29/202)	24.0 (40/167)
Remission		
Symptomatic	34.2 (77/225)	47.0 (79/168)
Functional	27.2 (55/202)	30.5 (51/167)

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Table 2
Baseline characteristics across clinical recovery and non-recovery.

Characteristic	Total	[d] Not recovered	Recovered	P (E.S.)
Demographics (alpha = 0.0125)[*]				
Age at baseline mean (SD)	26.85 (10.73)	27.18 (11.22)	25.72 (8.86)	= 0.451 (0.136)
Female % (n)	46.10 (82)	80.50 (66)	19.50 (16)	
Male %	53.90 (96)	75.00 (72)	25.0 0(24)	= 0.382 (0.132)
Competitive Employment for > 20 h/wk % (n)	30.30 (54)	22.50 (31)	57.50 (23)	< 0.001 (0.671)
Regular School Participation	22.50 (40)	21.70 (30)	25.00 (10)	= 0.664 (0.066)
Living independently % (n)	94.40 (168)	76.20 (128)	23.80 (40)	= 0.080 (0.264)
Clinical status (alpha = 0.005)[*]				
GAF Symptom mean (SD)	31.88 (7.37)	31.62 (7.43)	32.80 (7.14)	= 0.364 (0.161)
GAF Function mean (SD)	41.19 (11.20)	40.38 (10.48)	44.05 (13.18)	= 0.064 (0.332)
PANSS mean (SD)				
Negative	2.16 (1.08)	2.22 (1.04)	1.97 (1.17)	= 0.196 (0.233)
Disorganized	2.03 (1.07)	1.97 (0.98)	2.25 (1.32)	= 0.145 (0.265)
Depressive	3.27 (1.04)	3.29 (1.05)	3.18 (1.03)	= 0.571 (0.102)
Positive	3.15 (0.82)	3.16 (0.82)	3.11 (0.80)	= 0.740 (0.060)
Excitative	1.58 (0.72)	1.57 (0.68)	1.62 (0.87)	= 0.722 (0.064)
Total	64.83 (14.42)	65.01 (12.75)	64.23 (19.29)	= 0.763 (0.055)
[a] Substance abuse % (n)	24.70 (44)	86.4 (38)	13.60 (6)	= 0.106 (0.244)
[b] DUP weeks median (Range, SD)	21.00 (0–2080, 223.39)	23.50 (0–2080, 245.75)	12.00 (0–416, 109.67)	= 0.129 (0.249)
[c] Core Schizophrenia % (n)	32.00 (57)	80.70 (46)	19.30 (11)	= 0.624 (0.104)
[d] Social functioning (alpha = 0.008)[*]				
Social satisfaction mean (SD)				
Family	4.77 (1.37)	4.77 (1.47)	4.79 (0.99)	= 0.926 (0.017)
Friends	4.61 (1.25)	4.49 (1.29)	5.06 (1.01)	= 0.010 (0.467)
Social satisfaction total	4.68 (1.03)	4.61 (1.09)	4.95 (0.74)	= 0.063 (0.340)
Social frequency mean (SD)				
Family	4.12 (0.82)	4.07 (0.87)	4.30 (0.63)	= 0.124 (0.280)
Friends	3.41 (1.06)	3.28 (1.13)	3.83 (0.68)	= 0.003 (0.542)
Social frequency total	3.69 (0.76)	3.60 (0.80)	4.02 (0.51)	= 0.002 (0.572)

E.S: Effect size (Cohen's D).
[*] Bonferroni adjusted alpha levels for each section of the table.
[a] Transformed to binary variables: Abuse defined as score of > 2 measured by the Clinicians Rating Scale.
[b] DUP: p-value and effect size is based on log-transformed DUP.
[c] Schizophrenia spectrum disorders: Schizophrenia, Schizofreniform and Schizoaffective disorder.
[d] Recovered/not recovered at last follow-up assessment.

compared to those who were not in recovery. They also more often had paid competitive work. We found no significant between-group differences for weeks from inclusion to start of antipsychotic treatment (p = 0.939; OR = 0.015) and psychotherapy (p = 0.416; OR = 0.156), or for weeks duration of antipsychotic treatment (p = 0.486; OR = 0.137) and psychotherapy (p = 0.189; OR = 0.242).

3.1. Predictors of clinical recovery

Table 3 shows the results of the adjusted generalized estimating equations (GEE) used to measure predictors of clinical recovery over the two-year follow-up. In total, four different models were fitted. In the first model, there were no significant interaction effects between any predictor variable and time; that is, social satisfaction and frequency developed similarly over time in both recovered and non-recovered individuals. We therefore removed all interaction terms for the next model. Here, social satisfaction did not predict recovery, while social frequency did. A model, in which friends and family satisfaction were included separately, indicated that only satisfaction with friends, not family, had significant effect. The same procedure was repeated for family and friends frequency, again, as separate predictors. Here, only frequency of contact with friends significantly predicted recovery. In the final model we included the predictor variables that had shown significant effects: friends satisfaction and friends frequency. Only friends frequency showed a significant effect. Thus, the final model included only the predictor variable friends frequency (outlined in Table 3). All models revealed significant main effects of Substance Abuse and Time.

Table 3
Model effect of generalized estimating equations on recovery status.

Characteristic	Test of model effects			Parameter estimates		
N = 178	Wald chi²	df	p	Odds ratio	Confidence interval (95%)	
Age	0.158	1	0.691	0.993	0.956	1.030
Gender (0:Male, 1:Female)	1.449	1	0.229	0.601	0.262	1.377
[a] Substance Abuse	4.265	1	0.039	0.342	0.124	0.947
[b] DUP	0.904	1	0.342	0.805	0.515	1.259
PANSS Negative	2.213	1	0.137	0.723	0.472	1.109
PANSS Disorganized	2.844	1	0.092	1.424	0.944	2.146
PANSS Depressive	< 0.000	1	0.994	0.998	0.663	1.504
PANSS Positive	0.519	1	0.471	0.821	0.480	1.404
PANSS Exitative	0.004	1	0.952	1.026	0.449	2.346
[d] Social Frequency Friends	8.503	1	0.004	1.803	1.213	2.679
[c] Time						
1 year	8.649	1	0.003	0.520	0.337	0.804

[a] Transformed to binary variables: Abuse defined as score of > 2 measured by the Clinicians Rating Scale.
[b] DUP: p-value and effect size is based on log-transformed DUP.
[c] Time reference category = 2 year follow up.
[d] Variables from Lehman Quality of Life Interview.

3.2. Sensitivity analysis

The recovery measure incorporates as a criterion that the individual should have interaction with friends in order to be classified as recovered. However, one of the strongest baseline predictors of recovery is a measure of friendship frequency. Thus, there is a

possibility that the effect of Friends Frequency on recovery is an artifact of preexisting social relationships. To remedy this possible explanation, we developed a modified recovery outcome measure without the criterion of friendship frequency; fulfilling criteria of symptomatic remission, day-to-day living (independent living) and role functioning (work, academic, or full-time homemaking), but *without* any friendship measure. The recovery assessment approach and statistical analyses were performed identically with the original procedure, testing our research hypothesis with the modified recovery outcome measure. Results did not differ significantly from the original analyses except for *Friends Frequency*, which had a marginally smaller effect (Wald chi^2; 7.581; df = 1; p = 0.006; OR = 0.593, 95% CI = 0.409–0.860).

4. Discussion

Our main finding was, in line with our hypothesis, that frequency of friendship interaction predicted clinical recovery during a two-year period. This effect was sustained even when we removed the friendship criterion from the recovery measure, indicating that the effect was not simply due to preexisting friendships. Contrary to our hypothesis, neither social satisfaction variables, nor frequency of social interaction with family members, contributed significantly to the prediction of recovery. Time and substance abuse were also significant long-term predictors of recovery in line with previous studies (Marshall et al., 2005; Perkins et al., 2005). The recovery rate of 24% in this study was in the upper range compared to other FEP samples (Jaaskelainen et al., 2013). Previous investigations has shown this to be associated with the early intervention focus in the region (Hegelstad et al., 2012).

The present study accommodates the criticism raised by reviews that collapsing diverse objective and subjective social measures into global categories limits our ability to draw general conclusions (Albert et al., 1998; Gayer-Anderson and Morgan, 2013). Positive effects on recovery related to social factors can in the present study be attributed to the independent contribution of frequency of interaction with friends. This finding underscores the necessity of using a more detailed operationalization of social phenomena to illuminate the possible mechanisms driving recovery.

The impact of frequency of social interaction on clinical recovery could be due to positive effects of both instrumental and emotional social support factors (Thoits, 2011). In a review regarding mechanisms linking social ties and support to physical and mental health, instrumental support has been proposed as one of the main factors facilitating coping with mental illness. Individuals suffering from FEP may have an increased chance of receiving such support when interacting frequently with friends. Further, the stress and burden of living with mental illness can be alleviated by emotional support from friends who can provide empathy and consolation (Law et al., 2016; Thoits, 2011).

Our findings echo previous findings showing that friends and peers outperform family members in facilitating a positive outcome in FEP (Davidson et al., 1999; Erickson et al., 1989; Morgan et al., 2008; Reininghaus et al., 2008). This may not be surprising as during adolescence, peers increasingly influence social life more than parents. Therefore friendship interaction may have greater transference with regard to coping with everyday challenges and development of age appropriate independence. However, family members are more consistent in their contact throughout the course of illness (Gayer-Anderson and Morgan, 2013), which may indicate that family members to a larger extent keep in contact regardless of the social skills of the individual. Interacting with friends may hence to a larger degree be an indicator of social skills. One could speculate that this be a confounder of the association between frequency of friend contacts and recovery. However, analyses indicated that the association was not merely an expression of preexisting social relationships.

The finding that frequency of friendship interaction predicted recovery in the absence of any significant effects of satisfaction with social interactions may appear puzzling. The implication is that although social interactions may be perceived as unsatisfactory, they nevertheless have beneficial effects. In line with this finding, previous research has found that baseline social withdrawal and anhedonia (Kirkpatrick et al., 2006) combined with perceptual and attribution disturbances (Frith, 2014), is related to a negatively biased and distorted view of social reality. Thus, the patients' subjective evaluation may not capture the full extent of the effects and qualities of social relationships in our study sample.

Further, frequent social contacts may over time increase subjective relational satisfaction by a mere exposure effect (Zajonc, 1968; Bornstein, 1989). The exposure effect is a tendency towards developing object preferences as a function of familiarity. Quality of relations, and satisfaction with them, would in this line of thinking develop as the number of contacts with the same people increase. This interpretation emphasizes the potential importance of targeting frequency of interaction in early psychosocial interventions.

4.1. Clinical implications

Our findings suggest the possibility of facilitating recovery through helping patients increase frequency of social contacts. Research has demonstrated an association between supported socialization and an increase in social interaction, thus indicating malleability of social frequency (Davidson et al., 2004). Further, as social frequency is readily quantifiable (Lehman, 1996), this factor is well suited for objective tracking of progress.

Given the comprehensive burdens associated with psychosis, including risk of deterioration of patients' social network (Gayer-Anderson and Morgan, 2013) and the general benefits of early intervention in FEP (Marshall et al., 2005), our findings form an argument that this type of intervention should be applied as early as possible in the course of illness. Our findings indicate that even individuals with a negative assessment of social quality, and individuals with an inclination towards social withdrawal and isolation, should be helped to engage in frequent social interactions.

One possible intervention could include systematically involving friends at an early stage of treatment by asking them to commit to regularly meet with the person. For those already experiencing social network deterioration a first step may be to help them reestablish their social network. For individuals with few or no friends an alternative may be a period of involving volunteers or peers paid in a part-time after school job, engaging the person in social contact. Although these approaches would need testing, if performed systematically and over time they could have a potential of alleviating subjective loneliness (Hawkley and Cacioppo, 2010) and reducing social stigma (Watson et al., 2007), both of which are associated with poor outcome. Importantly, interventions like this would induce the aforementioned exposure effect (Bornstein, 1989).

Future research might investigate possible moderators to the association between frequency of friendship interaction and clinical recovery.

4.2. Limitations

The main limitations of this study include non-participation and dropout. Of the eligible patients, 41.6% declined to participate at baseline, and 48.6% were lost to GEE analysis at two year follow up. This represents a loss of valuable information and may weaken the generalizability of our findings. However, we found no differences in baseline characteristics between included and non-included individuals. Attrition thus appears to be random, and the sample can be assumed to be representative with regard to baseline characteristics. The current study was performed in an early intervention area and participants were offered an extensive treatment package. This may decrease generalizability to populations not covered by this type of health care. Although adjusted for several research based covariates,

premorbid adjustment level was not adjusted for in the main analysis (GEE) due to our assessment that these variables possibly showed multicollinearity with the predictor variables. Social satisfaction data were collected at baseline, and equivalent investigations at a later stage might have revealed different ratings of essentially similar social experiences.

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