

# Where should we put the focus of schizophrenia research in the next five years?

## Which research is to be prioritized in psychosocial therapies and rehabilitation?

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Prosser et al. (6) have argued in a recent editorial, that there is a false belief that psychotherapy is a psychosocial treatment whereas pharmacotherapy is a biological treatment. The authors argued that this assertion is not held out by cognitive neuroscience which suggests that both work on neurocognitive processes corresponding to complex functional disturbance and mental illness symptoms. In that perspective, future research to clarify treatment effects would have to combine biological, neurocognitive, imaging and social parameters with the ultimate aim of building effective systems of care.

In a recent debate, Kendall et al. (3) have taken issue with an editorial that commented on the 2014 NICE guideline on psychosis and schizophrenia, compared it with its equivalent 2013 Scottish guideline and retained that the NICE guideline was biased towards psychosocial treatments and against drug treatments. In response to that critique, Kendall et al. (3) argued that, in fact, the NICE guideline had more rigorous methodology than the Scottish guideline, and that the authors of the editorial appeared to have succumbed to bias themselves. This suggests that the issue of weighing the evidence on pharmacological and psychosocial interventions is complex and may be contentious. Therefore, valid methods of weighing the evidence and of translating guideline recommendations into mental health care practice should be prioritized.

In this comment, the following five specific topics are considered of importance in moving the field forward:

1. The case of supported employment (SE) in getting people with schizophrenia into competitive employment has been eloquently put in recent years by authors from the United States, and there is accruing evidence from other countries in support of this intervention that aims at direct labor market integration for people with psychosis who seek work and are offered ongoing support by both SE workers and community mental health teams. There have been recent efforts at weighing the evidence (Kinoshita et al. 2013). The focus, in research, should continue to be on rigorous testing in non-US settings and on identifying barriers to implementation in European labor market and mental health settings.
2. There is a shortage of high-quality research on how best to provide adequate housing to people with schizophrenia. The case of supported housing (SH) is eloquently put by studies such as the At Home/ Chez Soi project in Canada ([http://www.mentalhealthcommission.ca/English/system/files/private/document/mhcc\\_at\\_home\\_report\\_national\\_cross-site\\_eng\\_2.pdf](http://www.mentalhealthcommission.ca/English/system/files/private/document/mhcc_at_home_report_national_cross-site_eng_2.pdf)), and there is substantial implementation and research interest of SH-type models outside North America. Supported housing, a model combining a normal tenant role, focus on client control, social inclusion and in vivo learning with flexible community services and support should be tested in European settings. This would help move ahead in an area of research that has not received the research attention it deserves.
3. Recent psychosis and schizophrenia guidelines such as the NICE guideline have given much attention and strong recommendations regarding the provision of arts therapies in the treatment of people with schizophrenia (with a strong indication that art therapy may help alleviate negative symptoms). There has been a recent debate on the strength of this evidence (Kendall et al. 2016), and research efforts in this field should be maintained during the next five years. Also, it may help to concentrate more widely on a range of resource-oriented therapeutic models in psychiatry as pointed out in a conceptual review by Priebe et al. (5). This refers to therapeutic models that focus on utilizing patients' personal and social resources rather than reducing deficits. Models may include befriending (by non-professionals), client-centred therapy, creative music therapy, the open dialogue approach, peer support work, so-called positive psychotherapy, self-help groups, solution-focused therapy, systemic family therapy and therapeutic communities. Studying such models may help to identify key features characterizing effective care systems for people with psychotic disorders.

Die Psychiatrie 2016; 13: 158–159

4. It will be important to perform studies that help to identify the scope of eMental health interventions in the delivery of psychosocial interventions. A recent EPA guidance paper on eMental health interventions has presented a number of recommendations (2). It will be important to establish the scope of eMental health in fields such as, e.g., psychoeducation, self-help, peer support and illness management.
5. There are good reasons to monitor the effects of guideline recommendations on psychosocial interventions on both process (clinician/ team behavior) and patient outcomes. Current evidence suggests that the desired (process and patient) outcome effects of guideline implementation cannot be taken for granted, and thus, researchers in the field should strive for rigorous testing of individual measures and programmes implementing guidelines in routine care.

Above all and in concluding, implementation science has a high priority among our research tasks during the next five years as interventions that have shown to be efficacious are not necessarily put into practice. This clearly applies to psychosocial interventions (1). It applies, in particular, to low-and-middle income countries but it is vastly relevant to high-resource countries, too.

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## The ROAMER project – future directions and their implementation

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**R**OAMER (Roadmap for Mental Health Research in Europe) was a 3.5 year pan-European, multidisciplinary project. Its goal was to generate priorities for mental health and wellbeing research across Europe for the next 10–15 years. ROAMER involved academics (psychologists, biologists, psychiatrists, economists, political scientists) as well as service users, carers and families of people with mental health problems, healthcare providers, educators, social workers, policymakers and others. Full details of the project are given in Haro et al. (3).

ROAMER produced 6 research priorities (11). Applying these to schizophrenia yields some directions for the next 5 years:

- Interventions to prevent the development of schizophrenia and promote mental health among children, adolescents and young adults
- Focus on the causal/aetiological mechanisms of schizophrenia
- Developing and maintaining international and interdisciplinary schizophrenia research networks and shared databases
- Developing new and better interventions for schizophrenia, making use of recent advances in science, technology and practice (e.g. internet, mobile-based and blended treatments; ecological momentary assessments)
- Reducing stigma and making sure that people with schizophrenia, their families and carers are involved in decisions about future research

*Die Psychiatrie* 2016; 13: 159–161

- Systems-level research of the health and social systems used by people with schizophrenia, embedded within socioeconomic and cultural contexts

In addition to these recommendations, a number of issues specific to schizophrenia were raised over the course of the ROAMER project.

## Aetiology and diagnosis

While models that implicate a single biological or molecular cause for schizophrenia (e.g. the dopamine hypothesis) were useful in producing early treatments, these have been superseded by current knowledge of brain function, psychological function and symptomatology. Concepts such as the *connectome* have highlighted the importance of patterns of connected information processing in the brain (rather than just localising regional activity) and led to new models of schizophrenia (8). Similarly, use of symptom-cluster approaches to diagnosis have shown utility in developing treatment options beyond what might have been suggested by categorical diagnoses (5). Complementary analyses have clarified the role of perinatal environments and socioeconomic development in psychotic disorders (6). This reinforces the importance of preventative work and encouraging positive mental health.

Accumulating biological, cognitive and behavioural knowledge offers insight beyond diagnostic models that were informed solely by clinical observation. Future classifications and treatment decisions for schizophrenia would be well served by incorporating these insights.

## Treatments

There is a scarcity of new targets in developing pharmacological treatments. This has slowed the investigation of new molecules which could be useful for treating persistent (and especially negative) symptoms. Better aetiological understanding of schizophrenia is necessary to discover new treatment targets.

Antipsychotic drugs are associated with a variety of physical health problems, including movement disorders (13), weight gain and thyroid dysfunction (14). There is a pressing need for research that identifies the mechanisms by which these side-effects are produced. There is also a need to provide service users and their family and carers with information about the likely outcomes (and efficacy) versus side-effects of different treatments – whether these are medications, therapy or other interventions.

Psychological interventions are now evaluated systematically and with scientific rigour (9). This has shown the

efficacy of cognitive behavioural therapy for psychotic disorders (7, 12), but more research is needed – for example, into what factors best predict the most effective (and cost-effective) number of therapy sessions across different individuals (1). Advances in communication technology have afforded promising new avenues for psychological therapy (e.g. telepsychiatry, virtual reality and serious gaming), and these are also now in need of robust evaluation (2).

## Implementing research

A crucial aspect of developing new and better interventions is *implementation science*. This comprises research into factors determining the uptake of research evidence into policy, as well as the logistics of implementation (e.g. efficacy across different outcome measures, in different healthcare systems, etc.). As well as ensuring effective translation, implementation research is vital for developing evidence-based treatment and interventions for neglected aspects of schizophrenia. This includes negative symptoms, and comorbidity with physical symptoms, which are particularly common in people with psychotic disorders (4).

The recent RAND Mental Health Retrosight report (10) demonstrated that the greatest social and health benefits of schizophrenia-related research were achieved by interdisciplinary teams. Research networks allow for more effective and innovative research to be conducted by bringing together researchers across disciplines and countries, and pooling expertise and data. Europe is particularly well-suited to harnessing research networks for future schizophrenia research, as it is home to extensive national data registries of individuals diagnosed with schizophrenia and the treatments they receive. Coordinating such data across Europe would allow for powerful investigations of the efficacy of different forms of treatment.

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## Schizophrenia research priorities from the viewpoint of patients/relatives

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The significance of the knowledge and insights that the family/supporter can provide need to be recognised. The purpose of this document is to inform research towards the role of the family and supporter.

### Underpinning ethos for research supporting families

#### Recovery ethos

The belief by all that each person can have more active control over their lives by seeing how others have found a way forward. Inherent in this are the validation of individual strengths and experiences and the development of a response specific to and in the best interest of each individual.

#### Collaborative practice and shared learning

Recognizing the importance and benefit of shared experiences and learning within and between the different stakeholders.

*Die Psychiatrie* 2016; 13: 161–162

Informed choice and consent: Each individual has a right to self-determination and choice regarding their own lives. Sufficient and appropriate information along with the necessary support to use that information is made available to allow informed choice and consent.

### Support and interdependence

Families and supporters are an integral part of the support system. Good interventions for families promote better recovery. Equally, families and family members who provide support need support.

### Key areas for research

1. Support for families
2. The promotion of family/supporter/chosen advocate involvement in the service user's care
3. The provision of relevant information reflective of the family/supporter's needs
4. The provision of crisis support for the family/supporter
5. Supports for both the service user and the family/supporter as part of the discharge process

## 6. Involvement of the family/supporter in the care planning process

### Background

There is evidence that suggests that families often play an important role in the recovery of people with mental health problems. (3) and that family interventions can have a positive impact on service user outcomes, for example, rehospitalisation rates and adherence with medication (1, 4).

Family members and supporters report poor access to general information about mental ill health and limited information regarding the wellbeing and treatment of their loved one (3). They believe that their voice often goes unheard even when the actions of the health services directly impacts on the family and supporter. This is particularly apparent at critical times such as admission and discharge from hospital.

In addition, the trauma and challenge of supporting a person who experiences mental ill health can often be detrimental to the wellbeing and mental health of the individual supporter and the wider family for whom there may be limited information or supports.

All professionals working in mental health services are bound by law and their professional codes of practice to maintain strict confidentiality between themselves and those who use their service. The rights of the individual to his or her privacy and integrity is both recognised and respected within this document. Families and supporters do not want or need to know personal details. They are often the primary supporter of a loved one, particularly at times of crisis and they want and need to know what they can

do to support their family member's recovery in a constructive way.

There is growing recognition of the impact of supporting a person with mental illness on the family and supporters (3), and the need for a response that is inclusive of everyone's needs. The importance of the support offered by the family/supporter and their need for support to be able to perform this role is also recognised within this document.

In summary research on the needs of families should focus on the key themes outlined in this document. Such research should be participative and designed to inform improved service provision from the perspective of family members.

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## Which routes should psychopharmacological treatment research take in schizophrenia?

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**S**chizophrenia is a severe mental illness with numerous different symptoms. The complexity of schizophrenia and related spectrum disorders requires a sophisticated therapy and there are still unmet needs that should be addressed in research on therapy of schizophrenia.

Currently, an adequate therapy to reduce the risk of a severe chronic course of schizophrenia with relapses and a

lifelong vulnerability in the majority of patients is still a challenge. Moreover, most patients experience persisting impairments in their level of functioning, which hampers participation in different dimensions of life.

A database search was performed in DIMDI (Medline). The search period was 2005–2016 and focused on data from Germany respectively Europe. The keywords were “schizophrenia”, “therapy”, and “unmet needs”. The search was intentionally extensive in order to identify all suitable references. We identified 31 references that could be used

Die Psychiatrie 2016; 13: 162–163

to answer the question “Which routes should research on psychopharmacology therapy take in schizophrenia?” The most relevant references will be used in this short overview.

After a first-episode schizophrenia full and sustained remission is a major treatment objective (3). Within 1 year of antipsychotic treatment most first-episode patients reached a temporary state of symptomatic remission, but only 50% achieved sustained enduring remission. Moreover, at the onset of illness the rates of treatment resistance have been shown to be already around 10%–15% (4). Eventually 30% (2) – 60% (4) of patients with schizophrenia experience persistent positive psychotic symptoms despite appropriate antipsychotic treatment with adequate confirmation of treatment adherence. In addition, negative symptoms are a major treatment obstacle to enduring symptomatic remission in schizophrenia.

Patients with schizophrenia suffer from a wide spectrum of symptoms. Thus, treatment should be patient-individual and focus on the variety of symptoms of schizophrenia. Besides positive and negative symptoms the cognitive dysfunction is a core symptom of schizophrenia (6). Cognitive deficits are the best known predictor of impaired functional outcome in schizophrenic patients. Hence, there is a need to optimize cognitive training for patients with schizophrenia (6), but also to provide effective pharmacotherapeutic tools.

Non- or partial adherence with antipsychotic medication increases relapse and rehospitalisation rates in schizophrenia. The most frequent factor contributing to poor adherence is an orally administered every day medication, needing persistent support in taking the medication (7). Poor adherence is followed by impaired reduction of positive and negative symptoms and the concomitant occurrence of cognitive problems prevents symptomatic as well as functional remission. A study in German-speaking countries showed that besides patients' capabilities to manage their illness and social support the use of continuous antipsychotic medication reduced the risk of psychiatric readmission considerably (12).

Furthermore, adherence was predicted by the patients' attitude towards medication: a European multi-centre study demonstrated that there is a need to seriously consider and improve patient's attitude toward medication in

order to improve adherence (5). In addition, the choice of medication is influenced by the perception of the physicians towards medication (1).

A German study has highlighted new ways of routine patient care: individual patient care can be improved and deficits can be addressed by integrated care programs (10). Assertive community treatment embedded in an integrated care program proved to be more effective in terms of service disengagement and illness outcomes in patients with schizophrenia (8, 9). The implementation of treatment pathways brought about a robust change in efficacy (11).

In conclusion, research on psychopharmacology in schizophrenia should be focused on remission, treatment resistance, negative symptoms and main symptoms of schizophrenia like cognitive dysfunction. Furthermore, treatment concepts should consider improvement of adherence and implementation of integrated care programs.

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