EARLY DETECTION AND EARLY INTERVENTION IN PSYCHOSIS IN WESTERN EUROPE

Frauke Schultze-Lutter, Stephan Ruhrmann, Joachim Klosterkötter

Abstract

Prevention of mental ill health has been declared a major task by the European Commission; and an early detection and intervention in psychosis in terms of an indicated (secondary) prevention in persons already seeking help for mental problems is increasingly approached across Europe both on research as well as clinical level, a mixture of both dominating. The growing interest in this field of research across Western and Western-Central Europe becomes apparent in the rapidly increasing number of publications on this topic since the turn of the century that has nearly increased by the factor of 5. The 3 leading European countries in this are Germany, the United Kingdom and Switzerland.

Despite the very well reception of the 'prevention idea' by clinicians, researchers, relatives of patients with psychosis and clients and first promising results of early detection and/or early intervention studies, critics caution against the percentage of false-positive predictions by current prodromal criteria and the possibly unnecessary initiation of an antipsychotic psychological and/or pharmacological treatment along with its risks of unwanted side effects including early stigmatization. Supporters, however, argue that these short-comings will be overcome in the course of time and that the potential of new benign preventive interventions was just about to be discovered as well as caution against self-stigmatization by odd, eccentric behaviours and loss of functioning not recognized as part of an illness but attributed to the person him-/herself.

In future, joint efforts across clinical and scientific disciplines as well as countries will be required to enhance predictive accuracy, to develop broadly applicable and risk-adapted interventions, to provide help to all in need, to extend preventive efforts to other psychiatric disorders and to possibly reach the ultimate aim, a primary prevention of mental disorders.

Key Words: Early Detection – Early Intervention – Psychosis – Prodrome – Prevention

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Introduction

More than 27% of adult Europeans experience at least one form of mental ill health during any one year (Wittchen & Jacobi 2005). Of DSM-IV axis I disorders (American Psychiatric Association 1994), major depression (6.1%), specific phobias (6.1%) and somatoform disorders (6.3%) account for the highest estimated numbers of persons between 18 and 65 years of age in the general EU and EFTA population (301,7 million) affected by mental disorders within past 12 months; psychotic disorders, at 1.2%, affect an estimate of 3.7 million citizens in the EU within any 12-month period (Wittchen 2005, Wittchen & Jacobi 2005). At 0.035% per year not showing a high incidence of new cases in itself, the prevalence of schizophrenia, however, is relatively high due to the early age of onset and the often-chronic recurrent course (Rössler et al. 2005, Kirkbride et al. 2006).

Mental ill health costs the EU an estimated 3%-4% of gross domestic product (GDP), mainly through lost productivity; and mental disorders are also a leading cause of early retirement and disability pensions (EC 2005). Psychosis is one of the most burdensome and costly illnesses worldwide; and schizophrenia is listed as the 8th leading cause of disability-adjusted life years (DALYs) worldwide in 15 to 44 year-olds (Rössler et al. 2005).

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Since the 1960s, there has been considerable progress in the treatment and care of patients suffering from psychosis, with most efforts directed towards the severely ill and chronic ones. A decrease in costs - both direct and indirect - could be achieved, however, mainly by reduction of incidence and only moderately to minor by an improvement in prognosis and in community treatment, respectively (Rössler et al. 2005). Thus, a detection and - successful - treatment, i.e., the prevention, of psychosis prior to its first episode appears to be the main route to a substantial reduction of the overall burden linked to psychosis.

Starting from a brief retrospection of early concepts and fundamental works, the current paper tries to provide a general overview of current research and clinical activities and discussions around the early detection and treatment of psychoses in Western and Western-Central Europe.

Historical view

The observation that endogenous mental disorders, among them psychoses, rarely have a sudden onset and might be treatable prior to their full-blown expression had preceded even their description by Emil Kraepelin and Eugen Bleuler, as had the fact that they would be brought to the doctor's attention often too late. The term 'psychosis' and its synonym 'psychotic neurosis' was introduced into the psychiatric literature by the German forensic doctor Carl Canstatt in 1841 for psychic manifestations of a disease of the brain; as compared to the concept of neurosis that, before, had been summarized all diseases of the nervous system (Bürgy 2008). In the 1843 edition of his handbook, Canstatt wrote about psychoses and their treatment: "One observes such a high level of mental arousal in a great many individuals, who one cannot downright call insane, that real alienation is prompted by the slightest provocation. This we call the mental vulnerability, and most by chance causations, which call insanity into being, already come upon this pre-disposition. […] Where the ailment underlying the psychosis is recognized and is removable by doctor's action, where psychosis has not firmly struck its roots as an independent disease of the individuality, there, the causal indication fully claims its rights […] Yet more often causal indication lies beyond the scope of the doctor, and nothing else remains than direct combat of the psychosis" (p. 368f, translated by FSL).

About half a century later, Kraepelin's consideration of the so called 'formes frustes' of dementia simplex (Kraepelin 1896) and Eugen Bleuler's concept of 'latent schizophrenia' (Bleuler 1911) can be regarded as fundamental works on prodromal conditions. Both authors regarded episodes of frank psychosis only as the tip of the iceberg and assumed that mild forms of their fundamental symptoms and disturbances were rather widely distributed in the general population - culminating in relatives of schizophrenia patients, and often present for years prior to the first psychotic episode.

However, symptoms occurring in the prodromal phase of psychosis were thought too unspecific for a reliable early diagnosis by Kraepelin and Bleuler. A view long shared by the majority of both clinicians and researchers. Yet, some, e.g., the German psychiatrist Wilhelm Mayer-Gross, "wondered why, hitherto, one has so infrequently made use of the impressive experience that is represented by the first irruption of a thought disorder, a decrease in activity, an aberration in sympathy and other emotions into the healthy personality" (Mayer-Gross 1932, p. 296; translation by FSL). And his 1957 talk on the 'clinical diagnosis of early schizophrenia', the Scottish psychiatrist Hunter Gillies challenged the "apparently unspecific nature of the early symptoms [… that he believed to be] more specific than it would at first appear" (Gillies 1958, p. 47). To him, thought, affective and volitional disorders as well as autistic withdrawal presented "the most pathognomonic signs. But they must be looked for. During a lengthy interview they may emerge once only, or not at all. […] The early case does not show these [Bleuler's secondary symptoms] often, except in an embryonic form, and when they are present the diagnostic is obvious. […] It is, therefore, to the primary signs, and to the non-specific signs that precede even the primary signs, that we must direct our attention" (Gillies 1958, p. 50).

This had been done earlier by Klaus Conrad who had studied the beginning schizophrenia in 117 soldiers during the Second World War and, in 1958, published his *Gestalt* analysis of delusion. His work signifies the first attempt to systematically study the evolving psychosis in a larger sample and to identify a developmental phase model of early psychosis (Conrad 1958).

Fundamental works

Since the end of the 1970s, a growing number of publications from European groups prepared the ground for the idea of an early detection and intervention. These came, in particular, from:

- retrospective studies of the early course of schizophrenia (e.g., Bleuler et al. 1976; Gross & Huber 1985, 1986; Huber et al. 1979; Häfner et al. 1995, 2002; Klosterkötter 1992),
- clinical studies of the influence of the duration of untreated psychosis (DUP) on the course of the illness (see Marshall et al. 2005 and Perkins et al. 2005 for a review) and
- genetic high-risk, twin and birth cohort studies of risk indicators and vulnerability markers, especially from the United Kingdom and Scandinavian countries (e.g., Franzek & Beckmann 1998; Isohanni et al. 1997; Johnstone et al. 2000, 2005; Jones et al. 1998; Jones & Tarrant 2000; Kendler et al. 1996; Lawrie et al. 1999; Machón et al. 1983; Mednick et al. 1987; Parnas et al. 1993; Schulsinger et al. 1975; Suvisaari et al. 1999; Tienari et al. 1985a, b; Veijola et al. 2000-2001; see also Jones 2002 and Parnas & Carter 2002 for a review)

Furthermore, within the framework of basic symptom research, first attempts towards an identification of persons symptomatically at risk of psychosis were made (Süllwold & Huber 1986, Huber & Gross 1989, Huber 1995), and, in the late 1990's,

the first prospective early detection study of sufficient sample size and follow-up, the Cologne Early Recognition (CER) project (Klosterkötter et al. 2001, Schultze-Lutter et al. 2006), was concluded. The criteria derived in it (Schultze-Lutter et al. 2006, 2007a, b) increasingly complement the Australian 'ultra-high risk' (UHR) criteria (McGorry et al. 2003, Yung et al. 1998) in recent early detection and intervention studies conducted in Europe (e.g., Bechdolf et al. 2005a; Häfner et al. 2004; Klosterkötter et al. 2005; Ruhrmann et al. 2003, 2005, 2007; Simon et al. 2006).

The major impetus toward a prospective early detection and intervention research, however, was given by a study conducted in England - the Buckingham early intervention project (Falloon 1992, Falloon et al. 1996). This uncontrolled field study on adults who displayed signs and symptoms suggestive of schizophrenic disorders, DSM-III prodromal symptoms in combination with well established indicators of relapse, was the first to indicate that an early detection in combination with a comprehensive program of drug and psychosocial interventions was able to reduce the annual incidence in North Buckinghamshire within the study period (1984-1988) from the historical 7.4 (1974-1975) to 0.75 per 100,000 citizens (Falloon et al. 1996).

Clinical services

In Europe, such a combined clinical and scientific approach was only renewed in 1997 when, in Germany, the Cologne Early Recognition and Intervention Centre for mental crises (FETZ; Schultze-Lutter et al. 2008) started its work as the world's second early detection and intervention service.

Meanwhile, early detection and intervention programmes are operated in nearly all Western and Western-Central European countries (**Figure 1**), though they greatly differ. Whereas some programmes are predominantly research projects, e.g., the Detection of Early Psychosis (DEEP) project in Turku, Finland (Salokangas et al. 2004), others have a predominantly clinical focus, e.g., the Programma 2000 in Milan, Italy (http://www.programma2000.org). Most programmes, however, combine clinical and research efforts.

An outstanding role in the implementation of early detection in psychosis programmes within Europe has the United Kingdom. Following the implementation of 50 early intervention services for early first-episode psychosis that had been proposed and has received substantial funding by the National Health Service Plan (Department of Health 2000), attention has been increasingly shifted to the prodromal state, and many sites with an early intervention service have already extended their work to this state. For instance, in London the Outreach and support in South London (OASIS) service (Broome et al. 2005) that focuses on the prodromal state of psychosis has been established in addition to the Lambeth Early Onset (LEO) service (Power et al. 2007) aiming a reduction of the duration of untreated psychosis.

Working in partnership with the Royal College of General Practitioners, the Royal College of Psychiatrists and the British Psychological Society, the 'Care Service Improvement Partnership (CSIP)' on 'Early Detection in Psychosis' (http://www.earlydetection.csip.org.uk) of the NIS National Institute for Mental Health in England has created materials to highlight the best evidence and

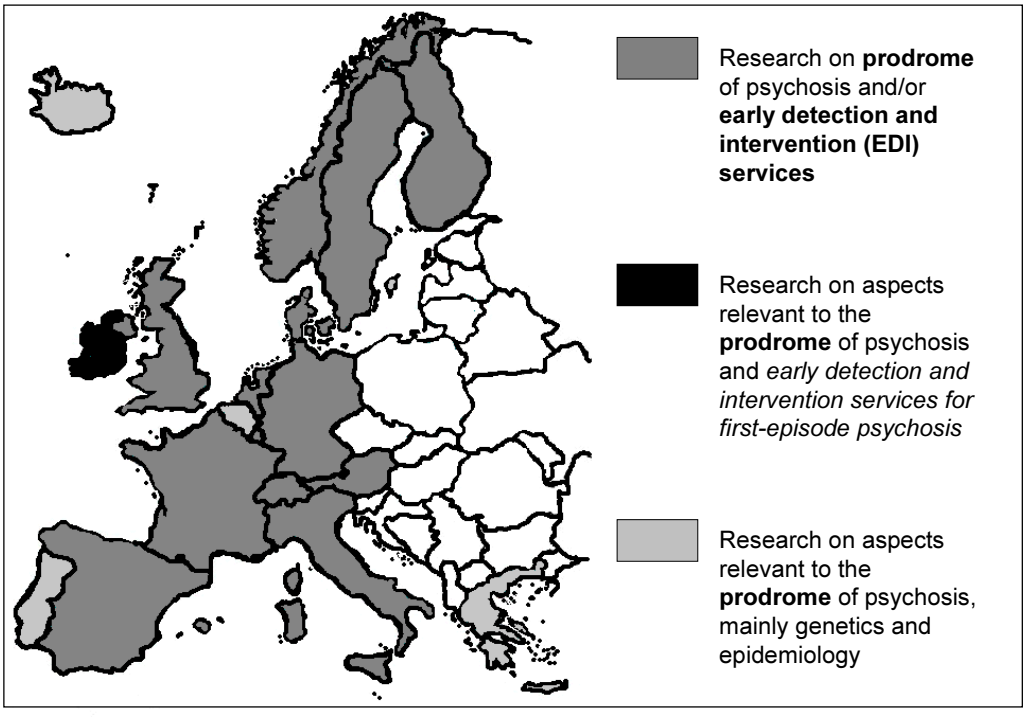

Figure 1. *Research and clinical early detection and intervention activities in Western European countries*

Figure 2. *Example of the UK initiative on early detection and intervention in psychosis: postcard for advertising the website and fact sheet for clients*

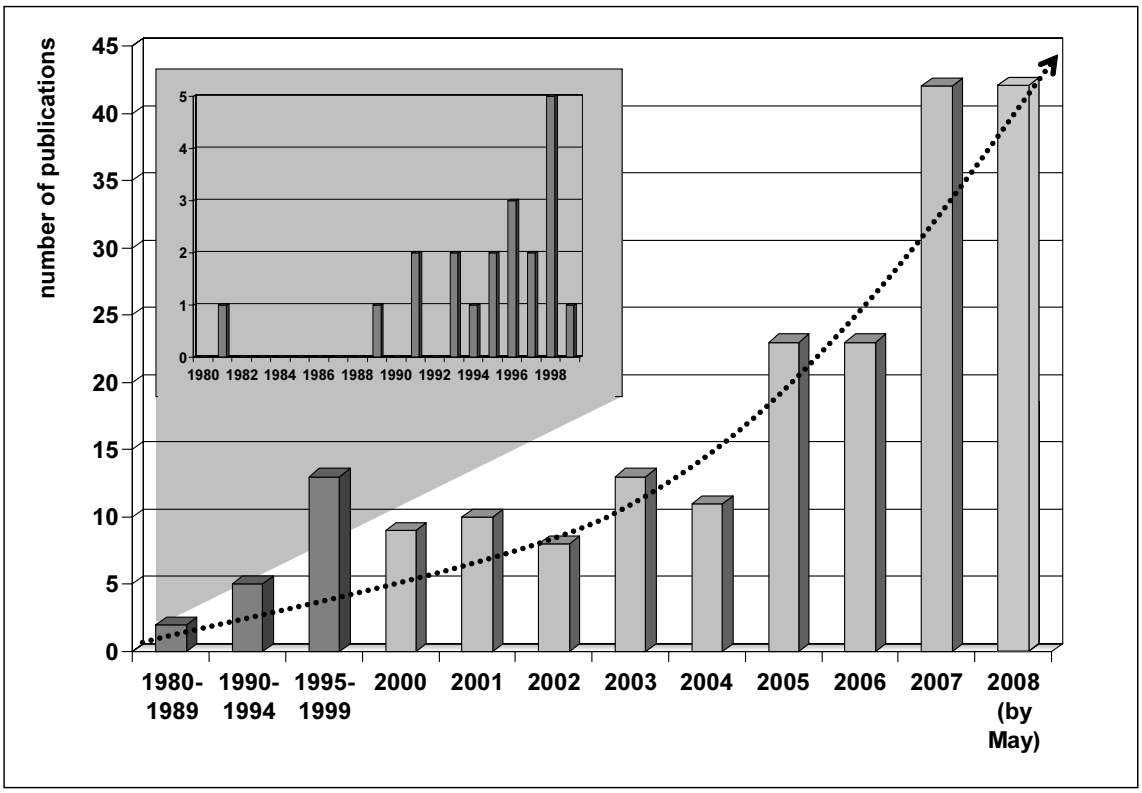

Figure 3. *Development in European journal publications on an early detection and intervention in psychosis*

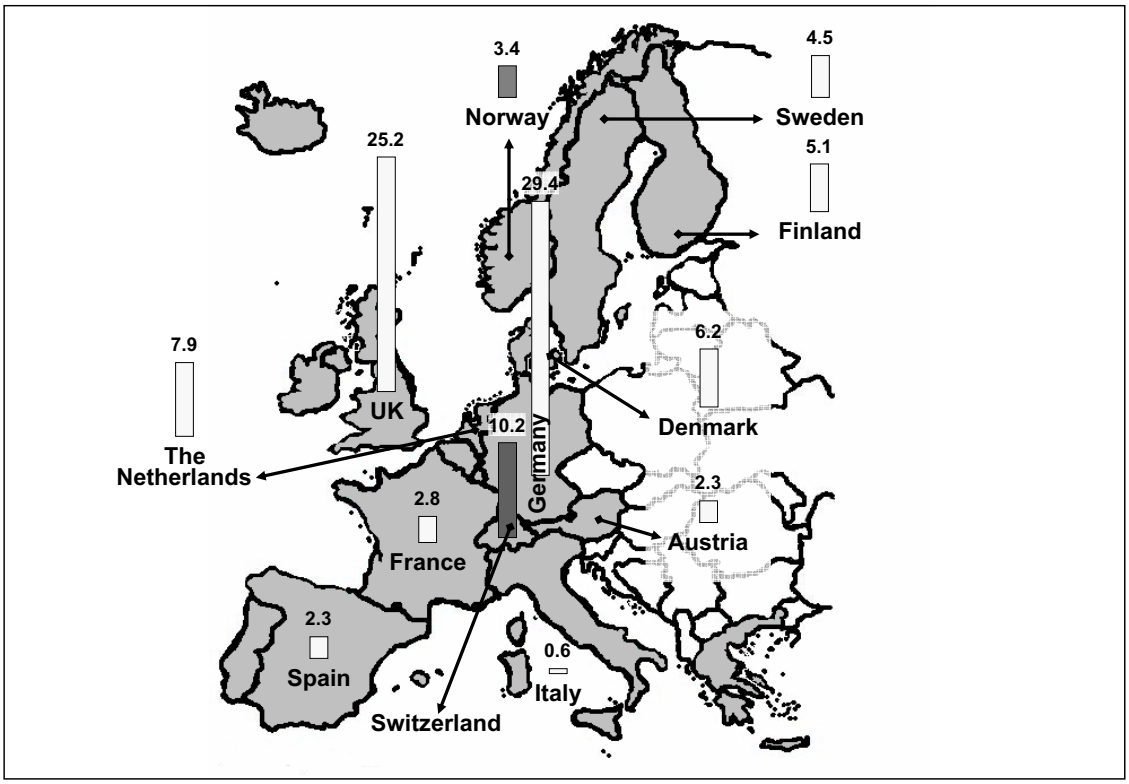

Figure 4. *Distribution of European journal publications on an early detection and intervention in psychosis across countries*

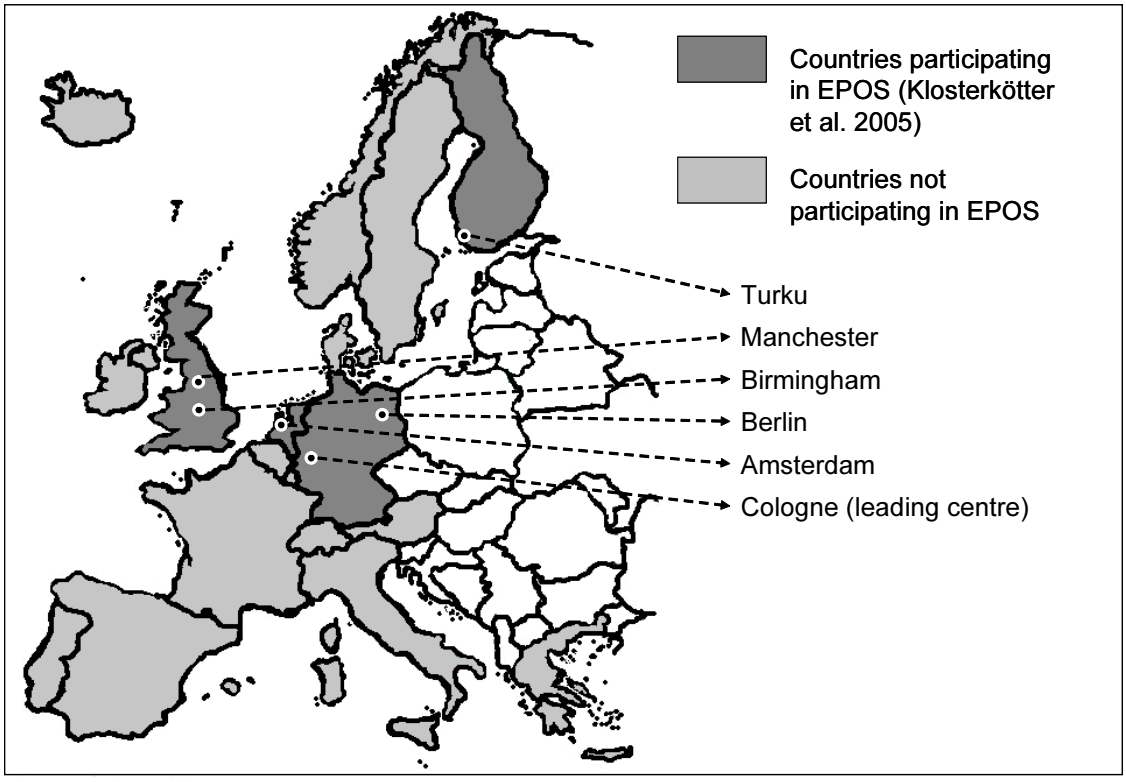

Figure 5. *Countries and centres participating in the first European study of prodromal psychosis, the European Prediction of Psychosis Study (EPOS; Klosterkötter et al. 2005)*

practice around the treatment of early psychosis, particularly focusing on the opportunity provided by detecting and treating those with an 'At Risk Mental State for psychosis'. Beside a report on the state of the art in early detection (http://www.earlydetection.csip.org.uk/silo/files/feb-2008-early-detection-report.pdf), the materials (for examples see **Figure 2**) include specific guidance for general practitioners and a set of fact sheets which summarise some of the main themes in the report and were designed to support practitioners from primary care, relevant community agencies and specialist mental health services in implementing an early detection of psychosis into their daily clinical work.

Research activity

Within the European research community, the growing interest in an early detection and intervention in psychosis prior to its first episode is evident in the increasing number of papers published within the last years (**Figure 3**). We searched PubMed, a service of the U.S. National Library of Medicine that includes over 17 million citations from MEDLINE and other life science journals for biomedical articles (http://www.ncbi.nlm.nih.gov/sites/entrez), for articles on the prodrome or prevention of psychosis of those the first author has a European affiliation. We used combination of the search term '*psychosis*' with each of the following terms: '*prodrome*', '*early detection*', '*prediction*', '*at risk*' and '*high risk*'. Furthermore, we narrowed our search to publications that already carried a focus on prodromal or preventive aspects in their title, i.e., we did not include papers relevant to the field but not especially focussing this aspect.

Altogether 177 papers from the initial EU and EFTA states (Iceland, Norway and Switzerland) were identified. Between 1990 and 2007, the number of papers on the prodrome of psychosis steadily increased from 0 to 42 per year (Figure 3). The leading countries in this were Germany and the United Kingdom with 52 and 45 papers, respectively, followed by Switzerland with 18 papers (**Figure 4**).

The papers covered the whole range of topics - from enhanced risk identification to an early detection, from psychopathological to neurobiological and imaging studies, from cross-sectional to longitudinal studies and from pure observational studies to randomized controlled intervention trials. Among the latter is a ground-breaking pilot study on the efficacy of omega-3-fatty acids as a neuroprotective substance in the prevention of first-episode psychosis that was carried out in Austria (Schäfer et al. 2007). Following the initial application of slightly modified treatment regimes that had proven efficient in frank psychosis, this study signifies the turn to alternative, new treatments tailored to the specificities of the prodromal states, i.e., the turn from an earlier to a truly preventive treatment.

European research policy

There is no health without mental health

This statement (EC 2005, p. 4) summarizes the European Community's (EC) basic attitude towards prevention of all mental disorders as issued in the Green Paper. Improving the mental health of the population: Towards a strategy on mental health for the European Union in 2005. In this, mental health is regarded as a resource which enables citizens to realise their intellectual and emotional potential and to find and fulfil their roles in social, school and working life. For societies in turn, good mental health of citizens were to contribute to prosperity, solidarity and social justice, whereas mental ill health were responsible for manifold costs, losses and burdens on citizens and societal systems including the often negative way in that society treats mentally ill and disabled persons. Despite improved treatment options and positive developments in psychiatric care, EU citizens with mental ill health or disability continued to experience social exclusion, stigmatisation, discrimination and/or the non-respect of their fundamental rights and dignity (EC 2005).

The mandate for action at EC level in the field of public health is defined in Article 152 of the EC-Treaty (http://europa.eu.int/eur-lex/en/treaties/selected/livre235.html) that instructs to ensure a high level of human health protection in the definition and implementation of all EC policies and activities. EC action is thereby meant to complement the independent national policies for improving health, for preventing illness, for providing health information and education as well as for reducing drug-related damage; cooperation between Member States is encouraged in these fields, not least by the EC's Framework Programmes for Research

Besides promoting the mental health of all citizens, improving the quality of life of people with mental ill health or disability and developing a mental health information, research and knowledge system for the EU, the European Commission proposed that as a major EU-strategy the addressing of mental ill health through preventive action (EC 2005).

In line with this, each of the last three Framework Programmes has addressed preventive aspects in psychosis research. Within the Fifth Framework Programme for research, technological development and demonstration activities (1998 to 2002), the European Prediction of Psychosis Study (EPOS; Klosterkötter et al. 2005) had been funded. Designed as a naturalistic follow-up study of potentially prodromal persons, it was carried out in 6 centres in four countries (**Figure 5**).

Within the Sixth Framework Programme, the call LSH-2005-2.1.3-4, 'Schizophrenia: from genotype to phenotype', aimed at a better understanding of the molecular aetiology and clinical phenotype of schizophrenia by identifying genetic and environmental determinants and their potential interaction in the development, severity and outcome of the disease. And within the current Seventh Framework Programme even two calls (HEALTH-2009-2.2.1-2 and -3) are on Schizophrenia with one of them especially related to its early stages:

HEALTH-2009-2.2.1-2: Identifying genetic and environmental interactions in schizophrenia. The project should aim at identifying genetic, clinical and environmental determinants playing a role in the development, severity and outcome of the disease in

man. Human studies on schizophrenic patients and their families should be at the core of the project. The project has also to include a translational component leading to the development of tools for early prediction, diagnosis, and monitoring of the disease.

Within the European psychiatric community, the significance of prevention is highlighted by the creation of a new section on 'Prevention of Mental Disorder' that was approved by the General Assembly of the Association of European Psychiatrists (AEP) in April 2008. This 18th section - 'Schizophrenia' is yet another section - will emphasize the expertise and activity of the AEP in the field of prevention (http://www.aep.lu/about/sections/index.html). The relevance of prevention in psychiatry is further underscored by the annual European Bristol-Myers Squibb Prevention Award in Psychiatry that has been established to recognize distinguished research in the field of prevention in psychiatric disorders, including psychosis, depression, anxiety and dementia.

Another new award particularly for research on or significant clinical efforts to the prevention of schizophrenic disorders carried out in Germany is the 'Gerd Huber-Preis' that has first been awarded in 2008.

Matters of dispute

Despite all progress and positive recognition, there are a couple of objections and unresolved issues related to an early detection and intervention in psychosis prior to its first psychotic episode that impede its broad implementation across Western Europe. And while some concluded from current studies that preventive efforts in psychosis were "not only necessary but also possible" (e.g., Schultze-Lutter 2004, p. 88) though further research was essential, others concluded from available data that it was "a waste of valuable resources" (e.g., David 2004, p. 111) at the expense of established cases of psychosis.

Emphasising the fact that, just having entered its second decade, early detection and intervention research was only at its beginning and far from having reached any conclusions yet, the supporters would argue that, already at this fairly early state of research,

1. current approaches to an early detection in terms of an indicated prevention identify persons at risk of psychosis reasonably well (e.g., Klosterkötter et al. 2001; Miller et al. 2002; Morrison et al. 2004; Phillips et al. 2000; Riecher-Rössler 2006; Ruhrmann et al. 2003; Schultze-Lutter et al. 2006, 2007b; Yung et al. 2004, 2005; see also Olsen & Rosenbaum 2006 for a review)
2. psychosocial deficits that are in most instances treatment-resistant in the wake of the first episode already develop in the prodromal and early course of the illness and should be prevented by early interventions (e.g., Häfner et al. 1995, 1999)
3. the first-episode of psychosis, if not prevented, may bring along irreversible brain morphological changes (e.g., Pantelis et al. 2003)
4. a substantial number of first-episode patients reported help-seeking for mental problems early in course (e.g., Köhn et al. 2004a,b)
5. at risk persons according to current prodromal criteria already suffer from a variety of social, psychological, neuropsychological and neurobiological problems and, consequently, are clearly in need for psychological and/or psychiatric treatment (e.g., Bechdolf et al. 2005b, Brockhaus-Dumke 2005, 2008; Broome et al. 2005; Gschwandtner et al. 2003; Koethe et al. 2006; Korkeila et al. 2007; Nieman et al. 2007; Pantelis et al. 2003; Parnas et al. 2001; Pukrop et al. 2006, 2007; Ruhrmann et al. 2008; Simon et al. 2006, 2007a; Schultze-Lutter et al. 2007c, d; Svirski et al. 2005)
6. ongoing information and awareness campaigns can facilitate early help-seeking and case detection, respectively (e.g., Joa et al. 2008; Larsen et al. 2006, 2007)
7. an early detection is well received by the families of patients who would have expected a range of positive consequences from an earlier diagnosis for themselves and their affected relative and who would have rarely feared an earlier stigmatisation for themselves or their affected family member as a result of an early detection of the illness (Lauber & Rössler 2003, Lauber et al. 2001)
8. treatment modelled on strategies established in psychosis (low-dose atypical neuroleptic treatment and/or cognitive-behavioural psychotherapy) seems to prevent or at least delay conversion to frank psychosis in persons symptomatically at risk of psychosis (e.g., Bechdolf et al. 2005c; McGlashan et al. 2006; McGorry et al. 2002; Morrison et al. 2004; Ruhrmann et al. 2005, 2007)
9. the early phase seems to enable alternative neuroprotective intervention strategies of little if any side effects, e.g., with omega-3-fatty acids, cannabidiol or very low-dose lithium (Berger et al. 2006, 2007; Leweke et al. 1999, 2004; Schäfer et al. 2007; Smesny et al. 2007; Sundram et al. 2004)
10. in case of success, a preventive approach to psychosis might offer a chance to positively change the public perception of the predictability and treatability of psychoses, thereby reducing public stigmatization and discrimination of those suffering from the disorder (WHO 2004)
11. and that an early detection and intervention might also help to prevent self-stigmatization by increasing empowerment early (Rüsch et al. 2005) and by preventing symptoms, which might lead to stigmatization and discrimination by others, e.g., odd and eccentric behaviour or significant psychosocial decline.

Opponents and sceptics of an early detection and (pharmacological) intervention in psychosis, on the other hand, argue that, at the current state of affairs,

1. even in help-seeking samples, i.e., within an indicated preventive approach, the predictive accuracy of prodromal criteria was insufficient, i.e., the risk of treating someone falsely considered as at risk of psychosis for a beginning psychosis was too high (e.g., Cougnard et al. 2005, Cougnard & Verdoux 2006, David 2004, Larsen et al. 2001)
2. if a universal prevention of psychosis at the population level would be attempted, e.g., "by

adding respiridone to the fluoride already put into drinking water" (p. 353), persons who would unnecessarily be treated would by far outnumber those with a potential benefit (Bentall & Morrison 2002)

3. epidemiological studies reporting that about one in ten persons would experience psychotic symptoms like delusions and hallucinations with the majority of them not seeking treatment (e.g., Bak et al. 2005; Bentall & Morrison 2002; Hanssen et al. 2005; Rössler et al. 2007; Verdoux & Cougnard 2006; Verdoux & van Os 2002; Verdoux et al. 1998; Stefanis et al. 2002, 2004a, b)
   (i) question the pathognomonic and pathologic significance of symptoms currently employed in prodromal criteria, in particular of attenuated (APS) and brief limited intermittent psychotic symptoms (BLIPS) as part of most widely used the UHR criteria that seem to be widely distributed in the general population,
   (ii) indicate a continuum between subjects from the general population and those with frank psychosis, thus rendering the introduction of a boundary between (prodromal) psychosis and normality a decidedly arbitrary process, and
   (iii) implicate that many persons can lead a happy and productive live despite being psychotic and, consequently, psychosis might not be dreadful for a significant number of those affected, that in turn meaning that an application of treatment with potential side-effects to avoid serious illness would not be not justified
4. psychosis - other than, for example, dental caries - was not a distinct clinical entity but a syndrome of ill-defined boundaries that suffers from the lack of well established etiological causes and the shortage of a coherent developmental model; thus it was not a feasible target of potentially harmful preventive measures such as neuroleptic treatment (Bentall & Morrison 2002, Grispini 2003)
5. risk-benefit and cost-benefit analyses of early detection programs were missing (Cougnard & Verdoux 2006)
6. focussing on early detection and intervention would violate some of the general medical principles, i.e., of the paramount of continuity of care, of the avoidance of doing undue harm and of treating the sickest first (David 2004)
7. preventive research suffers from a unchallengeable basic hypothesis assuming that, if early detection and intervention fails to work, not enough had been done or that the intervention had started too late (David 2004)
8. an early treatment carries the risk of somatic or psychological side-effects due to the use of antipsychotics or of labels such as 'early schizophrenia' or 'pre-psychotic', including the risk of a self-fulfilling prophecy and of an early and unnecessary stigmatisation (Larsen et al. 2001)
9. and that the prescription of antipsychotic medication would confirm the patients concerns that they were going mad, hence escalating their distressing appraisals and unhelpful coping strategies, which would be predicted by psychological approaches to understanding the transition to psychosis (French and Morrison 2004).

In summary, most arguments are related to the predictive accuracy of current criteria of the prodrome as well as the potential harm done with an early and potentially incorrect 'diagnosis' of a prodrome of psychosis and with 'antipsychotic' treatments of any kind initiated in the wake of such an early diagnosis.

Future directions

In line with the matters of dispute, the main focus in early detection and intervention research on psychoses in the nearer future will have to be on

- more specific prediction models and/or a staging of risk assessment by employing additional clinical and/or neurobiological features to reduce the proportion of false-positive predictions
- studies with longer follow-up periods to avoid distorted data by false false-positive predictions, i.e., by cases who had initially met prodromal criteria but not converted until conclusion of the study and, therefore, been classified as false-positive, but who will convert later on and, thus, in truth be true-positives
- larger samples and multi-site studies to allow controlling for overfit of prediction models, i.e., independent validation samples (Ransohoff 2004)
- a better understanding of the incidence and prevalence of potentially prodromal features in the general population when assessed in the same way as done in help-seeking clinical samples, i.e., within a professional clinical interview led by a trained psychiatrist or psychologist
- more sensitive criteria that are also able to capture cases of psychosis lacking positive symptoms, i.e, those with schizophrenia simplex or the disorganized subtype (Simon et al. 2007b)
- the development of group-specific sensitization programmes in order to reach not only about 30% (Köhn et al. 2004b) but the majority if not all persons who will develop a first-episode psychosis before the onset of psychotic symptoms (Simon et al. 2007b), thus decreasing the current sample bias in favour of early help-seeking persons (Schultze-Lutter et al. 2008)
- the development of safe and risk-adapted treatments - psychological and/or pharmacological - that are well-tolerated and well-accepted
- the conduction of risk-benefit and cost-benefit analyses of early detection and intervention programmes including a thorough assessment of direct and indirect costs.

To reach these aims and "overcome the pitfalls of schizophrenia prevention, optimal early detection systems need to be modeled as collaboration between youth and adult psychiatry and as networks across catchment areas. Failure to successfully combine the two areas would result in the prevention system again becoming highly selective." (Simon et al. 2007b, p. 102).

Once an early detection and intervention is sufficiently evidence-based, it should be implemented broadly into clinical guidelines and practice and paid for by health insurances. Yet before this can be done

across Europe, different types of programmes will have to be developed and again evaluated that fit the needs and possibilities of different settings in terms of (i) different health policies and funding schemes across European countries, (ii) different cultural or regional attitudes towards mental disorders and mental health care providers (iii) different mental health care providing institutions (e.g., private practice, day clinic, hospital or university hospital) and, last but not least, (iv) subgroups of patients with special needs or background (Schultze-Lutter et al. 2008). In addition, future early detection and intervention programmes will have to broaden their focus to other mental disorders to provide early support for those seeking it early in course of a non-psychotic disorder as already attempted in Northern France and Luxembourg. Such a an extension of preventive efforts might also pave the way towards the implementation of primary preventive efforts that, at present, are considered among the majority of supporters and opponents of an early detection and intervention alike as an unlikely aim due to the lack of specificity and the multitude of known risk factors of those each is of little predictive value in itself (Mäki et al. 2005). Yet, it had been argued that, at least theoretically, a primary prevention of psychosis might be possible in future (Suvisaari et al. 1999, Veijola et al. 2000, McGrath 2003) and "that trying to prevent schizophrenic disorders could be helpful, paradoxically, even if we could not reduce even one case of schizophrenia. As a matter of fact, risk factors for schizophrenia are not specific for this disease, but are relevant for a broad range of mental disorders. Even if we do not prevent schizophrenic disorders with primary, secondary or tertiary measures, our beginning to counteract well established risk factors for mental health (and promote protective factors) is an outstanding enterprise to promote health in the general population and reduce a broad spectrum of mental disorders" (Grispini 2003, p. 26).

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If not stated otherwise, the paper reflects the authors' personal views and knowledge. As such, it does not claim to give an exhaustive overview about all preventive efforts on psychosis within Western and Western-Central Europe. Local clinical services and papers not listed or under different key words in PubMed, in particular, might have escaped our attention.

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