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The World Psychiatric Association (WPA)

The WPA is an association of national psychiatric societies aimed to increase knowledge and skills necessary for work in the field of mental health and the care for the mentally ill. Its member societies are presently 135, spanning 117 different countries and representing more than 200,000 psychiatrists.

The WPA organizes the World Congress of Psychiatry every three years. It also organizes international and regional congresses and meetings, and thematic conferences. It has 66 scientific sections, aimed to disseminate information and promote collaborative work in specific domains of psychiatry. It has produced several educational programmes and series of books. It has developed ethical guidelines for psychiatric practice, including the Madrid Declaration (1996).

Further information on the WPA can be found on the website www.wpanet.org.

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Report on the implementation of the WPA Action Plan 2008-2011

MARIO MAJ

President, World Psychiatric Association

This report summarizes the main activities conducted by the WPA in implementation of its Action Plan 2008-2011, approved by the General Assembly in September 2008 (1,2).

WPA contribution to the development of ICD-11

WPA Member Societies have participated in the WPA-World Health Organization (WHO) Global Survey of Psychiatrists' Attitudes Towards Mental Disorders Classification, whose results have been published in *World Psychiatry* (3) and are expected to significantly influence the ICD revision process. Each Society has received a file with its own raw data and the results of the analysis of those data. Several Societies are producing papers based on those results.

Many WPA officers or experts have been appointed as chairpersons or members of ICD-11 Working Groups. The chairpersons include W. Gaebel (Working Group on Psychotic Disorders), M. Maj (Working Group on Mood and Anxiety Disorders), P. Tyrer (Working Group on Personality Disorders), L. Salvador-Carulla (Working Group on Intellectual Disabilities), and O. Gureje (Working Group on Somatoform Disorders).

The WPA President is a member of the ICD-11 International Advisory Board.

World Psychiatry is one of the main channels through which the international psychiatric community is following the ICD-11 development. A special article authored by the ICD-11 International Advisory Board, summarizing the philosophy of the entire process, has been published in the journal (4). A report by the Working Group on Intellectual Disabilities appears in this issue (5). Several papers produced by the Working Group on Mood and Anxiety Disorders will be collected in a special supplement to the journal. Forums on various topics relevant to ICD-11 development have been published or are scheduled for publication in the journal (e.g., 6-11).

Several WPA Member Societies and experts are being or will be involved in ICD-11 field trials and in the various translations/adaptations of the diagnostic system.

The WPA is actively contributing to the process of harmonization between the ICD-11 and the DSM-5.

WPA programme on disasters

The WPA contribution to the management of mental

health consequences of major disasters has had, during the triennium, two components: a) training and sensitization of psychiatrists; b) intervention when a major disaster occurred.

The first component has been implemented through a series of train-the-trainers workshops and sensitization courses.

The train-the-trainers workshops aimed to train psychiatrists of the various regions of the world (with a special focus on those at highest risk) to address the mental health consequences of disasters, so that they can become themselves trainers for other mental health professionals in their regions and represent a resource for their countries when a new disaster occurs.

The first of these train-the-trainers workshops was co-organized with the WHO in Geneva in July 2009 (12). Among the participants were psychiatrists who subsequently had a leading role in addressing the mental health consequences of disasters in their countries, including Y. Suzuki (who is currently coordinating mental health interventions in the prefecture of Sendai, Japan) and U. Niaz (who coordinated mental health efforts on the occasion of a recent disaster in Pakistan). Further train-the-trainers workshops have been held in Bangladesh, China, Russia, Egypt, Brazil and Argentina.

The sensitization courses aimed to call the attention of psychiatrists worldwide to the mental health consequences of disasters and to update them about strategies of prevention and intervention. These courses have been held within all major WPA meetings in 2010 and 2011.

The intervention component of the WPA strategy has been implemented in different ways, depending on the peculiarities of the various disasters.

In 2010, on the occasion of the Haiti emergency, the WPA partnered with its Member Societies and relevant Scientific Sections and with the WHO in recruiting psychiatrists who were well trained, able to speak French and Creole, and willing to spend a prolonged period of time in the area of the emergency. A report by Dr. K. Ravenscroft, who was recruited through this mechanism and served for many months in Haiti, has been published in *World Psychiatry* (13).

In 2011, on the occasion of the Japan emergency, the WPA has partnered with the Japanese Society of Psychiatry and Neurology in building up an intervention and research project focusing on the nuclear component of the disaster, which is going to be funded by the Japanese government. Dr. E. Bromet, a prominent international expert of mental health consequences of nuclear disasters, has acted as an

advisor in the preparation of the project. Two papers related to this initiative have appeared in *World Psychiatry* (14,15).

World Psychiatry

World Psychiatry, the WPA official journal, is the most widespread psychiatric journal in the world, reaching more than 33,000 psychiatrists in 121 countries, and being for many thousands of them the only accessible international psychiatric journal (16).

The journal is published regularly in seven languages: English, Spanish, Chinese, Russian, French, Arabic and Turkish. Individual papers or abstracts are translated in further languages, including Japanese, Polish, Romanian and Italian, and posted on the WPA website (www.wpanet.org) and/or those of the relevant WPA Member Societies.

The journal has now an impact factor of 5.562, ranking 9 out of 126 psychiatric journals.

All issues of the journal can be freely downloaded from PubMed Central and the WPA website.

WPA guidance papers

The WPA has produced during the triennium four guidance papers on issues of great practical interest to psychiatrists worldwide, never covered in the past by international guidelines. Each guidance paper has been developed by an international task force, translated into several languages, posted on the WPA website and published in *World Psychiatry*.

The papers deal with steps, obstacles and mistakes to avoid in the implementation of community mental health care (17); how to combat stigmatization of psychiatry and psychiatrists (18); mental health and mental health care in migrants (19); and protection and promotion of mental health in children of persons with severe mental disorders (20).

WPA research fellowships

The WPA has implemented during the triennium a programme of one-year research fellowships for early-career psychiatrists from low or lower-middle income countries, in collaboration with internationally recognized centers of excellence in psychiatry.

These centers included the Department of Psychiatry and Western Psychiatric Institute and Clinic, University of Pittsburgh Medical Center, Pittsburgh, PA, USA; the Institute of Psychiatry, King's College, London, UK; the University of Maryland School of Medicine, Baltimore, MD, USA; the Orygen Youth Health Research Centre, University of Melbourne, Australia; and the Mood Disorders Programme, Case Western Reserve School of Medicine, Cleveland, OH, USA.

Six early-career psychiatrists (three from Asia, two from

Africa and one from Latin America) have been selected on the basis of calls for applications posted on the WPA website. They have committed themselves to apply in their country of origin what they learn through this initiative. Interim or final reports by these fellows about their experience are available on the WPA website.

WPA-funded research projects

The WPA has funded during the triennium several collaborative research projects, selected on the basis of international calls posted on the Association's website.

These projects deal with the factors facilitating or hampering the choice of psychiatry as a career by medical students; stigmatization of psychiatry and psychiatrists; depression, demoralization and functional impairment in cancer patients; intensive metabolic monitoring and care of patients with schizophrenia; and social inclusion of patients with severe mental illness.

Interim reports on the progress of these projects are available on the WPA website.

WPA educational products and sets of recommendations

The WPA has produced with Wiley-Blackwell, during the triennium, a series of books dealing with the recognition, epidemiology, pathogenesis, cultural aspects, medical costs and management of the comorbidity of depression with diabetes, heart disease and cancer (21-23).

Three sets of slides based on these books have been produced and disseminated to Member Societies. The slides on depression and diabetes are available on the WPA website in 17 languages (English, French, Portuguese, Spanish, Italian, Estonian, Croatian, German, Swedish, Azeri, Bosnian, Romanian, Czech, Russian, Indonesian, Bangla and Japanese). The slides on depression and heart disease and those on depression and cancer are available in 8 languages.

The WPA has also developed an educational module on physical illness in patients with severe mental disorders, which has been published in two parts in *World Psychiatry* (24,25) and posted on the Association's website. The module has been or is being translated into several languages. Two sets of slides based on this educational module have been produced and posted on the Association's website.

An international task force has developed during the triennium a WPA template for undergraduate and postgraduate education in psychiatry and mental health, which has been posted on the WPA website and is being translated in several languages.

Special sections of the Association's website have been devoted to continuing education of psychiatrists, education of the general public on mental health issues, and description of successful experiences in the mental health field.

The WPA Committee on Ethics has developed a set of

recommendations for relationships of psychiatrists, health care organizations working in the psychiatric field and psychiatric associations with the pharmaceutical industry. This document has been published in *World Psychiatry* (26) and posted on the WPA website.

An international task force has produced a set of WPA recommendations on best practices in working with service users and family carers. This document appears in this issue of the journal (27).

WPA train-the-trainers workshops and educational courses

The WPA organized in 2009 and 2010 a series of train-the-trainers workshops aimed to contribute to the integration of mental health care into primary care in Nigeria and Sri Lanka. These workshops were conducted in collaboration with the national governments. They targeted nurses and clinical officers working in dispensaries and health centers, and were followed by a phase of supervision of participants (28). Detailed reports on the workshops are available on the WPA website.

Educational courses dealing with issues of great relevance to psychiatric practice have been organized by the WPA in Abuja, Nigeria; Sao Paulo, Brazil; Dhaka, Bangladesh; St. Petersburg, Russia; Beijing, China; Cairo, Egypt; Yerevan, Armenia; and Istanbul, Turkey.

Workshops on leadership and professional skills for young psychiatrists have been co-sponsored by the WPA in Singapore, Nigeria and Turkey.

WPA Early Career Psychiatrists Council

A WPA Early Career Psychiatrists Council has been established during the triennium. Its members have been appointed by WPA Member Societies and subdivided into five geographic areas (Europe I, Europe II, Asia/Australasia, Africa and Middle East, Americas), each with a coordinator.

The Council has produced papers and documents for *World Psychiatry* (29) and the WPA website; organized symposia on the occasion of several scientific meetings; carried out surveys; participated in the translation and adaptation of the WPA slides on depression and physical diseases.

The first personal meeting of the Council took place during the 15th World Congress of Psychiatry.

WPA press releases

During the triennium, the WPA has produced periodically press releases on topics relevant to mental health. Among those which have resulted in a wide media coverage are the releases focusing on two papers published in *World Psychiatry*: the report on the Iraq Mental Health Survey (30), covered in articles appearing in the *International Her-*

ald Tribune, the *New York Times* and the *Washington Post*, and the paper on income-related inequalities in the prevalence of depression and suicide behaviour (31), covered in an article in *USA Today*.

One more press release which led to a significant media coverage was that related to the WPA International Congress held in Florence in April 2009, focusing on the relationship between sleep problems and suicide, and resulting in articles published in the *Guardian* and the *Daily Telegraph*.

Other WPA-WHO collaborative activities

The WPA has implemented during the triennium several other initiatives in collaboration with the WHO (32).

In October 2009, the WPA and the WHO co-organized in Abuja, Nigeria a Policy Roundtable bringing together ministers of health, senior policy makers and professional leaders of the nine African countries identified in the WHO's Mental Health Gap Action Programme (mhGAP) as needing intensified support to scale up mental health services: Burundi, Cote d'Ivoire, Democratic Republic of Congo, Ethiopia, Ghana, Kenya, Liberia, Malawi and Nigeria. The outcome of the roundtable was the development of road maps for mental health care in those countries.

WPA experts contributed to the production of the WHO's mhGAP Intervention Guide and the WHO's Atlas of Resources for the Prevention and Treatment of Substance Abuse.

Other activities in partnership with Member Societies

Many WPA Member Societies participated in the WPA Survey on Strategies to Reduce the Treatment Gap for Mental Disorders, whose results were published in full in *World Psychiatry* (33) and will be summarized in a paper in *The Lancet* (34).

The WPA has assisted during the triennium many of its Member Societies in their interactions with national institutions concerning policy matters or refinement of educational curricula. Papers describing this collaboration have been published in partnership with the Czech Psychiatric Association, the Hungarian Psychiatric Association, the Brazilian Association of Psychiatry and the Portuguese Association of Psychiatry.

The WPA has organized during the triennium scientific meetings in all continents, always in partnership with its Member Societies (35). The 15th World Congress of Psychiatry, organized in partnership with WPA Member Societies in Argentina, has been the most attended congress in the history of the Association.

Many Congresses of Member Societies have been co-sponsored by the WPA and/or have included Symposia or CME Courses co-organized with the WPA. WPA leaders

have met officially with leaders and/or members of Member Societies on the occasion of many national congresses, to discuss local priorities and provide advice. On several occasions, WPA leaders and leaders of Member Societies have held joint press conferences or participated in talk shows.

In several WPA scientific meetings, seminars were organized in which leaders of selected Member Societies illustrated the structure and activities of their associations to representatives of other Member Societies, answered their questions and provided advice on specific issues.

The WPA has implemented during the triennium an initiative to support the development of national psychiatric journals in low- and middle-income countries. A task force has worked with editors of selected journals to strengthen their chances of being indexed in international databases (36). Several journals whose editors participated in this project have recently achieved indexation.

Financial support to the Action Plan

The activities of the Action Plan have been supported by a consortium of industry and non-industry donors. The donors have had no input on the contents of the Plan and the selection of people participating in its implementation. No activity within the Action Plan has been mono-sponsored.

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Prediction and prevention of schizophrenia: what has been achieved and where to go next?

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In modern medicine, vigorous efforts are being made in the prediction and prevention of diseases. Mental disorders are suitable candidates for the application of this program. The currently known neurobiological and psychosocial risk indicators for schizophrenia do not have a predictive power sufficient for selective prevention in asymptomatic patients at risk. However, once predictive basic and later pre-psychotic high risk symptoms of psychosis develop into the five-year initial prodrome, the impending outbreak of the disease can be predicted with high accuracy. Research findings suggest a differential strategy of indicated prevention with cognitive behavioral therapy in early initial prodromal states and low dosage atypical antipsychotics in late initial prodromal states. The most important future tasks are the improvement of the predictive power by risk enrichment and stratification, as well as the confirmation of the existing and the development of new prevention strategies, with a stronger focus on the etiology of the disorder. In addition, the prediction and prevention approach would benefit from the inclusion of risk symptoms in the DSM-5 criteria.

Key words: Schizophrenia, risk factors, early course, basic symptoms, high risk symptoms, risk staging, differentiated prevention

(World Psychiatry 2011;10:165-174)

Since the traditional clinical paradigm has been replaced by the modern molecular one, medicine set off into new directions. “Prediction”, “prevention” and “personalization” are the programmatic key words of this new approach. Like other medical disciplines, psychiatry has broadened its focus from diagnosis and treatment to the detection and estimation of the risk of disease development, the prediction of its onset and strategies to avoid its manifestation (1-4).

Although treatment of schizophrenia has greatly advanced over the last decades, a significant number of patients continue to take an unfavorable chronic course (5,6). This makes schizophrenia the leading cause for permanent occupational disability among people under 40 years of age in Germany (7), and the 8th most common cause for disability adjusted life years (DALYs) lost among the 15 to 34-year olds worldwide (8), despite its low prevalence. Moreover, schizophrenia involves tremendous direct and indirect societal costs (9) and a huge burden on patients and their families (8,10).

It is becoming increasingly clear that schizophrenia is a complex disorder with polygenic heredity and that its pathogenesis is greatly influenced by interactions between different genes and between genes and environment. Associations to variants of the genes for dysbindin and neuregulin-1, the genetic locus G72 and the DAOA (D-amino acid oxidase activator) gene have now been repeatedly confirmed. As with all other complex diseases, research is focusing now on characterizing the polygenetic predisposition and clarifying its influence on the development of the phenotype (11). Research methods range from molecular genetics via proteome research to cell biology, neurophysiology, brain structural and functional imaging and neuropsychology. With all these methods, several indicators for an increased risk of schizophrenia have been identified. However, the currently recognized neurobiological risk factors are not sufficiently predic-

tive to allow the development and application of “selective” prevention measures targeting asymptomatic persons at risk. For neuropsychological risk factors, this has just become evident in the large-scale attempt of the North American Prodrome Longitudinal Study (NAPLS) group to improve their multivariate model by integrating the examined neurocognitive variables (12).

There are also established environmental risk factors for schizophrenia, such as pregnancy or birth complications, growing up in a large city, IQ low but normal and drug consumption. However, with odds ratios around 2, each of these factors appears to increase the lifetime risk of the disease only slightly (13). Thus, the currently known risk factors, either alone or taken together, cannot be used for prediction and prevention without knowledge of the complete predispositional basis and the gene-gene and gene-environment interactions, which are probably numerous.

In view of this situation, it may be argued that the current efforts towards prediction and prevention are still premature and that further progress of etiological research is needed. However, a different perspective has emerged from the work of the centers for early recognition and prevention, established first in Melbourne, Australia and in Cologne, Germany in the mid 1990s, and later on in many other places around the world. This resulted from retrospective research of the early course of psychosis, in which the pathophysiologically active disturbances in brain development extend beyond early abnormalities in behavior into psychopathologically definable early risk and ultra high risk (UHR) symptoms, depending on the individual combination of stressors and resilience factors. First episode psychosis (FEP) research has shown that the outbreak of the disease is preceded in about 70% to nearly 100% of cases by an initial prodrome, which lasts for an average of five to six years. Even in highly devel-

oped health care systems, an average of one year thereafter elapses from the first manifestation of psychotic positive symptoms to the initiation of adequate treatment (14,15).

The period over which the FEP remains untreated (duration of untreated psychosis, DUP) correlates with: delayed and incomplete remission of the symptoms; necessity of more protracted treatment and greater risk of relapse; lower compliance, greater burden on the family, and a higher level of “expressed emotion”; increased risk of depression and suicide; greater impact on the individual’s employment or education; increased drug abuse and delinquent behavior; markedly increased costs of treatment (16).

These correlations have recently been confirmed by a meta-analysis (17), with coefficients ranging from 0.285 to 0.434 (95% CI). This does not only provide strong arguments in favor of treating the FEP as early as possible, but has also led to a systematic effort to decrease the incidence of psychosis through indicated prevention.

PREDICTION OF SCHIZOPHRENIA USING BASIC SYMPTOM CRITERIA

Two important studies concerning the early stage prior to the conversion to FEP have demonstrated that the earliest and most common symptoms, which generally dominate during the prodrome, are unspecific and cannot be distinguished from impairment in mood, drive, contact, and concentration of depressive episodes. These are the Age-Beginning-Course (ABC) study of schizophrenia, a retrospective study with optimized methods (14), and the Cologne Early Recognition (CER) Study, a long-term prospective study with an average follow-up period just below 10 years (18). These studies also found striking cognitive impairments in the form of self-expe-

rienced disturbances in thought, speech, and perception processes. This subgroup of so-called basic symptoms, which were found in more than a quarter of patients, had high specificity and a high positive predictive power, accompanied by only low rates of false positive predictions (19-21).

Basic symptoms were first operationalized in the Bonn Scale for the Assessment of Basic Symptoms (BSABS). Shorter versions of the scale for adults and for children and adolescents – the Schizophrenia Proneness Instrument, Adult version (SPI-A) and the Schizophrenia Proneness Instrument, Child and Youth version (SPI-CY) – were later developed from dimensional analyses (22-24). While the BSABS only allows an assessment of the current state, the SPI-A and the SPI-CY also allow severity ratings according to the maximum frequency of occurrence within the past 3 months.

In the CER study, 385 patients who were presumably in the prodromal phase of schizophrenia were followed up for an average of 9.6 (± 7.6) years past baseline. Twenty percent of the initial criterion-positive cases (1 of 66 basic symptoms) who agreed to be followed up developed schizophrenia after 12 months, a further 17% after 24 months, a further 13% after 36 months, and finally a total of 70% after an average of 4.5 years. Thus, only 30% did not convert to schizophrenia. The overall presence/absence of at least one basic symptom correctly predicted presence/absence of a subsequent transition to schizophrenia in 78.1% of cases. From further analyses, two partially overlapping basic symptom criteria for defining at risk mental states (ARMS) for psychosis, primarily schizophrenia, were developed (Table 1).

The first criterion, which consists of ten cognitive-perceptive basic symptoms and is abbreviated as COPER, was based on findings concerning the predictive accuracy of individual basic symptoms (18,25). The second was based on a methodological re-analysis of the same data set, in which

Table 1 Definitions of a mental state at risk for psychosis based on basic symptoms and their predictive accuracy in the Cologne Early Recognition (CER) study

Criterion	Predictive accuracy
<p><i>Cognitive-perceptive basic symptoms (COPER)</i> At least any 1 of the following 10 basic symptoms with a SPI-A/SPI-CY score of ≥ 3 within the last 3 months and first occurrence ≥ 12 months ago: thought interference; thought perseveration; thought pressure; thought blockages; disturbance of receptive speech; decreased ability to discriminate between ideas and perception, fantasy and true memories; unstable ideas of reference; derealization; visual perception disturbances (excluding blurred vision and hypersensitivity to light); acoustic perception disturbances (excluding hypersensitivity to sounds/noises)</p>	<p>sensitivity = .87 specificity = .54 positive predictive value = .65 negative predictive value = .82 positive likelihood ratio = 1.89 negative likelihood ratio = .24 odds ratio = 7.86 false positives = 23.1% false negatives = 6.3%</p>
<p><i>Cognitive disturbances (COGDIS)</i> At least any 2 of the following 9 basic symptoms with a SPI-A/SPI-CY score of ≥ 3 within the last 3 months: inability to divide attention; thought interference; thought pressure; thought blockages; disturbance of receptive speech; disturbance of expressive speech; unstable ideas of reference; disturbances of abstract thinking; captivation of attention by details of the visual field</p>	<p>sensitivity = .67 specificity = .83 positive predictive value = .79 negative predictive value = .72 positive likelihood ratio = 3.94 negative likelihood ratio = .40 odds ratio = 9.91 false positives = 8.8% false negatives = 16.3%</p>

SPI-A – Schizophrenia Proneness Instrument, Adult version; SPI-CY – Schizophrenia Proneness Instrument, Child and Youth version

a cluster of nine cognitive basic symptoms had repeatedly been selected as the most predictive. This cluster was called “cognitive disturbances” (COGDIS). In terms of general predictive accuracy, the two criteria slightly differed in the CER study, as COGDIS tended to be more conservative than COPER, i.e. to perform better in ruling in subsequent schizophrenia at the cost of performing worse in ruling it out. The transition rate throughout the average follow-up period of roughly 10 years was 65% for COPER and 79% for COGDIS, with the majority of transitions occurring within the first 3 years past baseline.

In a second prospective study (26), conducted with the SPI-A and with a systematic follow-up of 24 months, 38% of the initially included 146 at-risk subjects developed a frank psychosis, mainly schizophrenia, within 12.3 (± 10.4) months on average (1-48; median=9) according to COPER. Thus, the positive results of the CER study were confirmed. Again, COGDIS appeared to be more specific but less sensitive than COPER.

As a consequence of these findings, predictive basic symp-

toms have been established as a set of criteria for risk assessment in international research on the early recognition of psychosis. In particular, the German Research Network on Schizophrenia used these symptoms, together with a combined criterion of functional deterioration and biological risk, in defining an “early at-risk of psychosis state” (ERPS), thereby suggesting a clinical risk staging model (Figure 1).

PREDICTION OF SCHIZOPHRENIA USING ULTRA-HIGH RISK CRITERIA

The positive symptoms typical of schizophrenia – such as delusions, hallucinations or formal thought disorders – often first appear in an attenuated or transient form during the initial prodromal phase. These symptoms provide a valid prediction of conversion into FEP, particularly in the short term. Warning signs of this sort have been used as ultra-high risk (UHR) criteria (27,28). Notwithstanding their differences across studies, these criteria are generally composed of three

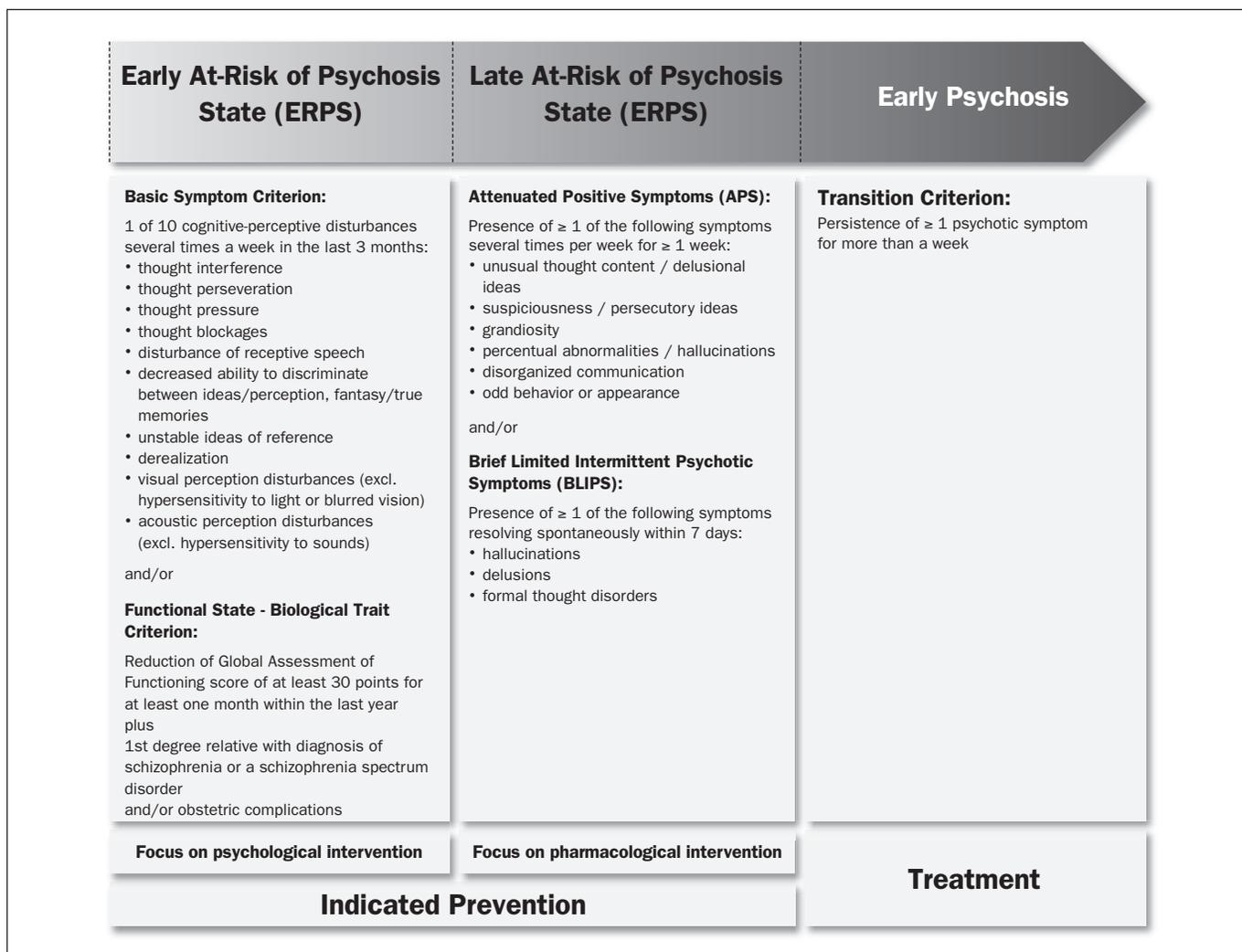


Figure 1 Early and late initial prodromal state: a clinical staging approach

Table 2 Prognostic accuracy of different predictors of psychosis

Study	At-risk criteria	Follow-up	Predictors	Sensitivity	Specificity	PPV	NPV	Pos. LR	Neg. LR
Klosterkötter et al (18); Schultze-Luttner et al (25)	BS	9.6±7.6 years	1/66 BS positive	0.98	0.59	0.70	0.96	2.4	0.03
			1/10 cognitive-perceptive BS (COPER)	0.87	0.54	0.65	0.82	1.9	0.2
			2/9 cognitive BS (COGDIS)	0.67	0.83	0.79	0.72	3.9	0.4
Yung et al (34)	UHR	6 months	UHR positive	0.92	0.62	0.10	0.99	2.4	0.1
			50≤GAF<50	0.69	0.62	0.10	0.97	1.8	0.5
Yung et al (35)	UHR	24 months	UHR positive	0.91	0.63	0.16	0.99	2.5	0.1
Woods et al (36)	UHR	30 months	UHR positive	0.89	0.60			2.2	0.2
Lencz et al (37)	APS	24.7±15.9 months	SIPS-positive syndrome scale ≥15	0.67	1.00	1.00	0.89	a/0	0.3
			highest items score (SIPS P.1.-P.5.) = 5	0.78	0.76	0.54	0.90	3.3	0.3
Mason et al (38)	UHR	>12 months, 26.3±9.2	schizotypal personality disorder unusual thought content/magical ideation, marked impairment in role functioning, acoustic hallucinations, anhedonia/asociality	0.76 0.84	0.76 0.86			3.2 6.0	0.3 0.2
Yung et al (39)	UHR	12 months	trait-state criterion positive plus APS positive	0.31	0.93	0.69	0.72	4.4	0.7
			duration of symptoms >5 years	0.08	1.00	1.00	0.69	a/0	0.9
			GAF <40	0.17	1.00	1.00	0.70	a/0	0.8
			SANS attention >2	0.14	1.00	1.00	0.89	a/0	0.9
			model of "≥1 predictor positive"	0.60	0.93	0.81	0.82	8.1	0.4
Cannon et al (40)	UHR	30 months	1. genetic risk and GAF reduction ≥10%,						
			2. unusual thought content (SIPS item P.1. >2),						
			3. paranoid ideation (SIPS item P.2. >2),						
			4. social functioning (<7),						
			5. any substance abuse						
all of the 5	0.08	0.98	0.79	0.72	4.0	0.9			
1, 2 and 3	0.34	0.89	0.74	0.74	3.1	0.7			
1, 2 and 4	0.50	0.90	0.81	0.81	3.0	0.8			
Ruhmann et al (41)	UHR COGDIS	18 months	SIPS positive score >16 bizarre thinking (SIPS item D.2.>2) sleep disturbances (SIPS item G.1. >2) schizotypal personality disorder (SIPS definition) GAF-M score, highest past year years of education	0.42	0.98	0.83	0.87	19.9	0.6

PPV – positive predictive value; NPV – negative predictive value; pos. LR – likelihood ratio when test result is positive; neg. LR – likelihood ratio when test result is negative; BS – basic symptoms; UHR – ultra high risk symptoms; GAF – Global Assessment of Functioning; APS – attenuated positive symptoms; SIPS - Structured Interview for Prodromal Syndromes; a/0 – division by zero; SANS – Scale for the Assessment of Negative Symptoms; GAF-M – Global Assessment of Functioning, modified version

alternative elements: attenuated positive symptoms (APS), brief limited intermittent psychotic symptoms (BLIPS), or a combination of one or more risk factors (always including genetic risk) and functional decline within a certain recent period.

For the ascertainment of the UHR criteria, the Melbourne group gradually developed a specific instrument, the Comprehensive Assessment of At Risk Mental States (CAARMS) (29). Based on the Australian definition of the UHR criteria, the Structured Interview for Prodromal Syndromes (SIPS), the Scale for Prodromal Syndromes (SOPS) and, subsequently, the Criteria of Prodromal Syndromes (COPS) were developed (30,31). Different UHR-related approaches to an early detection of FEP, particularly schizophrenia, were developed by the Hillside Recognition and Prevention (RAP) program in New York (32) and the Basel Früherkennung von Psychosen (FEPSY) study (33).

There have been at least 15 prediction studies using UHR criteria, some of which with large samples (34-41). The 12-month rates of transition into FEP published so far range between approximately 13% and 50%. A substantial variance is even observed with comparable observation periods in the same center (34,35). Yet, as the annual incidence for all forms of psychosis in the general population is only about 0.034% (42), even the lowest conversion rates still indicate a dramatic increase in the relative risk of illness, at least in the help-seeking samples of specialized centers. Table 2 depicts the predictive accuracy measures published so far, with the last five listed studies representing secondary predictor analyses of samples meeting at risk criteria. As a result, in the German Research Network on Schizophrenia, the UHR approach was combined with the basic symptom approach and applied in a slightly modified form for the definition of “late at-risk of psychosis state” (LRPS) (Figure 1). This clinical staging model, which suggests a syndromal sequence for the development of FEP progressing from unspecific prodromal symptoms to predictive basic symptoms, and then to APS, to BLIPS and to full-blown psychotic symptoms, was recently strongly supported (15).

PREVENTION OF SCHIZOPHRENIA WITH A DIFFERENTIATED PREVENTION STRATEGY

Universal or selective prevention measures target healthy population groups or clinically still healthy risk carriers, respectively (43). Indicated prevention, instead, targets individuals with basic symptoms and UHR symptoms. Even at the early stages when these individuals seek advice and help at the early recognition and prevention centers, they must be regarded as ill and in need of treatment. Furthermore, the impending deterioration of psychosocial performance in schizophrenia often already occurs in the initial prodromal phase, even prior to the conversion into FEP (14,15). These clinical and psychosocial impairments justify defining the interventions in EPRS and LPRS as indicated prevention,

pursuing the following three objectives: a) improvement in the current burden of prodromal symptoms; b) avoidance or perhaps delay in the development of psychosocial handicap; c) prevention of or at least delay or attenuation of psychosis.

Five international intervention studies have attempted to find out whether or to what extent these three objectives can be reached (44-51) (Table 3). The preventive measures used were either cognitive behavioral therapy (CBT), adapted to the requirements of the persons at risk, or atypical antipsychotics (risperidone, olanzapine, and amisulpride). These were randomized controlled studies, but there were problems with the blinding condition in the two CBT interventions. This and other methodological shortcomings currently limit conclusions and have encouraged the research groups working in this area to set up new, optimized intervention studies. For example, the protocol of the ongoing parallel group PREVENT study includes careful comparative analyses and superiority and inferiority tests of the psychological and pharmacological treatments (52).

A staging of risk, thereby implying a temporal dimension, was considered for the first time in the two intervention studies of the German Research Network on Schizophrenia. One of these studies covered ERPS and only offered CBT as a preventive measure (49,50). The other study was designed for LRPS and used only preventive treatment with amisulpride (51). When the symptom development in the initial prodromal state follows the sequence shown in Figure 1, it would be beneficial for scientific and especially ethical reasons to focus on psychological interventions in ERPS, which are well tolerated and highly accepted. As soon as the first attenuated or transient psychotic symptoms occur, it seems justifiable to apply well tolerated antipsychotics with few side effects. This differential prevention strategy is now pursued in all German early recognition centers and is also increasingly gaining support in other countries.

Another pharmacological option is aripiprazole, tested in a pilot study in UHR states (53). Its possible preventive effects are currently being analyzed in the PREVENT study. Antidepressants were used in a naturalistic, non-randomized observational study of an adolescent sample employing only the APS criterion for inclusion, but, for methodological reasons, this study does not allow any conclusion about differential preventive effects of these medications (54).

FUTURE TASKS

A critical evaluation of the achievements over the past 15 years through continuous efforts to enhance prediction and prevention of psychoses, particularly of schizophrenia, reveals quite impressive results. However, the results achieved thus far need to be evaluated in the light of the ambitious, initially mentioned objectives of modern predictive and preventive medicine. Once predictive basic symptoms and UHR symptoms have occurred, the underlying pathophysiological process might have already progressed. For such a complex

Table 3 Prospective, randomized, controlled prevention studies in persons with increased risk of psychosis

Study	Inclusion criteria: early risk and high risk criteria	Transition criterion	Sample (n)	Design	Experimental condition	Control condition	Catamnesis	Results
McGorry et al (44) Phillips et al (45)	APS and/or BLIPS and/or reduction in the level of social function and first degree relatives with schizophrenia or index person has diagnosis of schizotypal personality disorder	More than one week of consistent positive symptoms	59	Randomized controlled unblinded study	6 months individual CBT and risperidone	6 months supportive psychosocial intervention	12 months; 2nd follow-up: 46 months (mean)	Improvement in symptoms and social adjustment under both conditions; significant reduction in transition rate in experimental group after 6 months by intention-to-treat analysis and after 12 months by per-protocol analysis; difference not significant at 46 month follow-up
Morrison et al (46) Morrison et al (47)	APS and/or BLIPS and/or reduction in the level of social function and first degree relatives with schizophrenia or index person has diagnosis of schizotypal personality disorder	More than one week of consistent positive symptoms	58	Randomized controlled study	6 months individual CBT	6 months monitoring	12 months; 2nd follow-up: 36 months	Significant improvement in positive symptoms with CT; improvement in social adjustment in both conditions; significant reduction in the transition rate after 12 months; difference not significant at 36 month follow-up
McGlashan et al (48)	APS (modified) and/or BLIPS (modified) and/or reduction in the level of social function and first degree relatives with schizophrenia or index person has diagnosis of schizotypal personality disorder	4 weeks consistent positive symptoms, behavior disorganized or a danger to self or others	60	Randomized placebo-controlled double-blind study	12 months olanzapine, supportive psychoeducational individual and family intervention	12 months placebo, supportive psychoeducational individual and family intervention	24 months	12 months improvement in the positive, negative, and general psychopathology significantly greater in the olanzapine group than in the placebo group; statistical trend towards reduction in the transition rate after 12 months
Häfner et al (49) Bechdorf et al (50)	Basic symptoms predictive of psychosis and/or reduction in the level of social function with genetic and/or obstetric risk factors	APS*1 and/or BLIPS*2 and/or more than one week of consistent positive symptoms	128	Randomized controlled study	12 months individual CBT, cognitive training, psychoeducational family intervention	12 months supportive individual treatment	24 months	Significant improvement in prodromal symptoms and level of social function in the pre vs. post comparison; significant reduction in transition rate in experimental group after 12 months
Ruhrmann et al (51)	APS and/or BLIPS	More than one week of consistent positive symptoms	124	Randomized controlled study	24 months amisulpride, supportive psychoeducational individual and family intervention	24 months needs focused intervention	24 months	Significant improvement in prodromal symptoms and level of social function in pre vs. post comparison after 6 and 12 months; significant reduction in transition rate in experimental group after 6 and 12 months

APS – attenuated positive symptoms; BLIPS – brief limited intermittent psychotic symptoms; CBT – cognitive behavioral therapy; CT – cognitive therapy

disease with a long-term course and a pre-dispositional basis, this kind of risk identification and risk-oriented prevention may possibly come too late. A more substantial reduction in incidence could be reached with selective and universal prevention measures. Therefore, symptom-based prediction and prevention need to be further developed into the direction of selective prevention for symptom-free risk carriers. In the future, it is necessary to strive for: a) an improvement of risk enrichment with the inclusion of biological risk factors; b) a stronger individualization of the risk estimation by stratification; c) the inclusion of sub-psychotic mental states, as cross-sectionally defined by current at risk criteria, in the diagnostic systems; d) the application of prevention strategies more closely associated with the etiology of the disease.

Risk enrichment

If the initial prodromal phase persists for as much as 5 years, then most of the follow-up periods shown in Table 2 are not sufficient to acquire the true transition rates. A significant number of later converters may be classified as non-converters and, thereby, the predictive power of the risk syndromes may be systematically underestimated (12). Therefore, the first and most important future task is to carry out new, methodologically optimized large-scale studies with long follow-up periods spanning the full duration of the initial prodromal phase, as in the CER study (18).

The risk enrichment can also be advanced through the inclusion of biomarkers, following the example of recent research on the prediction of Alzheimer's dementia through the mild cognitive impairment (MCI) syndrome (55). This condition indicates a risk for Alzheimer's dementia with a conversion rate comparable to the risk syndrome for FEPS. If, however, the MCI patients simultaneously show certain imaging and biochemical markers, the predictive power increases significantly. Such risk enrichment may be possible for FEPS using brain morphological changes, but also impairments of processing speed and verbal memory, which are associated with the psychosis risk syndrome, and are more frequent and severe in those cases with a later transition to schizophrenia and other psychoses (12,56-60). Only new large-scale studies with sufficiently long observation periods could clarify whether the risk enrichment can be achieved by means of such biomarkers. The success of this strategy is dependent on the progress of research on biological and environmental risk factors and their interactions, as is currently attempted in the European Network of national schizophrenia networks studying Gene-Environment Interactions (EU-GEI) study (61).

Risk stratification

In other medical disciplines, such as oncology or pneumology, a well-established risk modeling procedure, which

does not result in a loss of sensitivity, is using prognostic indices (PI) for multivariate clinical staging by risk stratification. In the European Prediction of Psychosis (EPOS) study, this approach was introduced into psychosis prediction research for the first time (41). A clinical model was developed based on a Cox regression equation including six variables (SIPS positive score, SIPS bizarre thinking score, SIPS sleep disturbances score, SIPS schizotypal personality disorder, highest Global Assessment of Functioning score in the past year, and years of education). Based on the individual regression scores, a multivariate PI for further stratifying the risk of transition to psychosis into four risk classes was suggested, each delineating a significantly increased relative risk compared to the general population, increasing with each class.

This 4-class model was argued to significantly improve the prediction of psychosis by enabling a differentiation of the individual risk in terms of magnitude and time. Such a more individualized risk estimation or clinical staging of risk, if validated in future studies, could significantly advance the development of risk adapted inclusion criteria for future randomized preventive trials. In the first application of this approach in the EPOS, only clinical and demographic variables were considered. It remains to be explored whether a multi-level model including neurocognitive, neurobiological, sociobiographical or environmental variables would increase the predictive accuracy even further. In addition, future studies will have to examine whether such models can also be applied to the prediction of psychosis within different time frames.

Introduction of at risk mental states (ARMS) in diagnostic systems

The currently ongoing revision of the DSM has stimulated a debate about the inclusion of a risk syndrome for psychosis in order to facilitate prevention (62). Several researchers initially argued against this project and drew attention to the dangers that the application of ARMS as diagnostic criteria could imply. They emphasized that the high rate of false-positive predictions in specialist clinics (60-70%) would be expected to increase up to 90% in general outpatient clinics. This criticism is certainly justified and should receive attention prior to deciding whether to include the ARMS in the upcoming revisions of the diagnostic systems. The debate, however, almost exclusively focuses on the predictive validity of at risk criteria, thereby disregarding the main finding: persons meeting at risk criteria already suffer from multiple mental and functional disturbances, for which they seek help. Moreover, they exhibit various psychological and cognitive deficits along with morphological and functional cerebral changes. Thereby, the majority of help-seeking at risk persons fulfil DSM-IV general criteria for mental disorder (i.e., a clinically significant behavioral or psychological syndrome associated with disability and/or severe distress) and have to be considered as ill, i.e. as people with the need and right to be treated. Keeping these considerations in mind,

there are good reasons for the inclusion of a clinical profile in the diagnostic system as delineated by current at risk criteria, not as a prodromal risk syndrome for first psychosis, but as an independent disorder. Besides allowing access to standard medical care, the introduction of such an independent diagnosis would have the additional advantage of avoiding the stigmatization potentially caused by explicitly linking the current mental state to a threatening and negatively labeled outcome. Although an increased risk of psychosis would continue to be a characteristic of such a diagnosis, the psychological and medical focus would be shifted from an uncertain future outcome to psychopathology and needs. At this current state of knowledge, the DSM-5 criteria would be the right framework for the inclusion of this syndrome. A great impetus for the planning and implementation of a new generation of international and national studies would be triggered with this inclusion in DSM-5 and later on also in ICD-11.

More etiologically oriented prevention strategies

A new prevention approach is driven by the idea of neuroprotection (63,64) and studies indicating a progressive loss of gray matter volume before the onset of psychosis (56,58,60). Among the various substances with potential neuroprotective properties, the first results are available for high-dose omega-3 fatty acids, glycine and low-dose lithium. The 12-week transition rate was significantly lower in an omega-3 fatty acids-treated group of UHR adolescents than in a placebo group (65), and this effect was maintained at a 6-month follow-up. Glycine, an N-methyl-d-aspartate receptor coagonist, was evaluated in 10 patients in an open pilot trial, and a significant improvement in different psychopathological domains was reported (66). In an open proof-of-concept study, hippocampal T2 relaxation time was significantly reduced in an UHR group treated with low-dose lithium, as compared with a similar group receiving supportive standard treatment, suggesting a protection of hippocampal microstructure (58,67). This was the first study providing imaging data on neuroprotective effects in individuals at risk. The apparent preventive effect of omega-3 fatty acids is currently in the process of getting reviewed in the North-American, European, Australian Prodrome (NEURAPRO) large-sample study (68).

CONCLUSIONS

With the exception of Alzheimer's dementia, schizophrenia is the first mental disorder to which the prediction and prevention program of modern medicine has hitherto systematically been applied. The results are promising and justify the expectation that in the years to come it will be possible to provide preventive strategies tailored specifically to the individual risk of illness of each person seeking advice.

In order to attain a major reduction in incidence, symptom-oriented risk assessment has to be enriched by neurobiological and psychosocial risk factors, and indicated prevention has to be further developed towards selective prevention. This requires a new generation of large sample studies for prediction as well as prevention, with significantly longer observation periods. In these studies, promising combinations of risk indicators, selected to maximize predictive values, must be evaluated, psychological and pharmacological interventions need to be assessed on a long-term basis, more etiologically oriented prevention strategies have to be tested. In order to be able to plan and conduct such studies, it would certainly be helpful to include sub-psychotic mental states, as defined by the currently used risk symptoms, in the upcoming revision of the diagnostic systems.

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Intellectual developmental disorders: towards a new name, definition and framework for “mental retardation/intellectual disability” in ICD-11

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Although “intellectual disability” has widely replaced the term “mental retardation”, the debate as to whether this entity should be conceptualized as a health condition or as a disability has intensified as the revision of the World Health Organization (WHO)’s International Classification of Diseases (ICD) advances. Defining intellectual disability as a health condition is central to retaining it in ICD, with significant implications for health policy and access to health services. This paper presents the consensus reached to date by the WHO ICD Working Group on the Classification of Intellectual Disabilities. Literature reviews were conducted and a mixed qualitative approach was followed in a series of meetings to produce consensus-based recommendations combining prior expert knowledge and available evidence. The Working Group proposes replacing mental retardation with intellectual developmental disorders, defined as “a group of developmental conditions characterized by significant impairment of cognitive functions, which are associated with limitations of learning, adaptive behaviour and skills”. The Working Group further advises that intellectual developmental disorders be incorporated in the larger grouping (parent category) of neurodevelopmental disorders, that current subcategories based on clinical severity (i.e., mild, moderate, severe, profound) be continued, and that problem behaviours be removed from the core classification structure of intellectual developmental disorders and instead described as associated features.

Key words: Intellectual disability, mental retardation, intellectual developmental disorders, health terminology, classification, mental disorders, ICD, ICF

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The health condition currently defined as “mental retardation” (MR) is a cluster of syndromes and disorders characterized by low intelligence and associated limitations in adaptive behaviour. Examination of the conceptual basis and terminology related to MR is relevant at present because the World Health Organization (WHO) is in the process of revising the International Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) (1). This paper describes the rationale and process for replacing the ICD-10 conceptualization of MR with the concept of *intellectual developmental disorders* (IDD) in ICD-11.

IDD have a long history within the taxonomy of mental disorders (2). Their prevalence is around 1% in high income countries and 2% in low and middle income (LAMI) countries (3,4). They have a major impact on functioning and disability throughout the life course, and high comorbidity with other mental disorders (5). They are frequently misdiagnosed, are associated with poor access to health care services, and involve very high costs for the health care system and for society as a whole (6-10). In spite of these facts, IDD are largely disregarded in the mental health sector, where

specific training on IDD and specialized services are limited to a few high income, primarily Western, countries (11,12).

During the past 15 years, an intense debate has taken place on how to properly name, define and assess IDD (13). In summary, the term “intellectual disability” (ID) has widely replaced MR for policy, administrative and legislative purposes in many developed countries and in an increasing number of LAMI countries. However, the question as to whether IDD are a disability or a health condition remains a hotly debated one, with two co-existing approaches used as a basis for new conceptualizations of this entity. Based on a health condition perspective, MR is currently coded as a disorder in ICD (category F.70). At the same time, impairments in intellectual functions that are central components of IDD can be classified within WHO’s International Classification of Functioning, Disability and Health (ICF) (14), and therefore seen as a part of disability.

Based on a disability perspective, the American Association on Intellectual and Developmental Disabilities (AAIDD) has assembled a comprehensive definition, classification, and system of supports that focus mainly on functioning, adaptive

behaviour and support needs and are consistent with the conceptual model proposed by the ICF (15,16). According to AAIDD, ID is a disability characterized by “significant limitations *both* in intellectual functioning and in adaptive behaviour as expressed in conceptual, social, and practical adaptive skills. This disability originates before age 18” (16).

In contrast, the WPA Section on Psychiatry of Intellectual Disability considers IDD to be a health condition: “a syndromic grouping or meta-syndrome analogous to the construct of dementia, which is characterized by a deficit in cognitive functioning prior to the acquisition of skills through learning. The intensity of the deficit is such that it interferes in a significant way with individual normal functioning as expressed in limitations in activities and restriction in participation (disabilities)” (17).

The debate regarding these differing conceptualizations of IDD has gained momentum and importance in the context of the current revision of the two major classifications of mental disorders: the ICD-10 and the American Psychiatric Association (APA)’s Diagnostic and Statistical Manual of Mental Disorders (DSM) (18). An extreme position in this debate suggests that if IDD are defined solely as disabilities and not as a health condition, they should be deleted from the ICD and classified using only codes from the ICF. Regardless of whether there is conceptual validity to this position, it is the ICD – not the ICF – that is widely used by the 194 WHO member countries to define the responsibilities of governments to provide health care and other services to their citizens. ICD categories, including categories related to IDD, are used throughout the world to specify which people are eligible for what health care, educational and social services under what conditions. Therefore, removing IDD from the list of health conditions would have a major impact on the visibility of IDD, on national and global health statistics, on health policy, and on the services available to this vulnerable population.

Conversely, if IDD are considered solely as a health condition, then the term “disability” should not be used to refer to them. But this would be at odds with the position already adopted by many governments and international organizations. Such a solution might be judged as a reductionist, biomedical approach and rejected by many key international stakeholders, users and experts in the field. Additionally, there are major unresolved questions in the definition of IDD as a health condition, including in what part of a health classification IDD should be placed, the age cut-off for onset, and the nature of the association between cognitive impairments and behavioural skills.

Collective experience related to terminology and ontology in the IDD field may help to clarify the conceptualization of the disease and disability components in ICD-11 and ICF; that is, where the health condition component of IDD can be appropriately placed within a classification of diseases and disorders, and how their functional consequences can be conceptualized using a classification of functioning and disability (6). Such an approach may provide alternative solutions to similar problems related to other mental disorders

that may be associated with disability.

The work described in this article has been conducted in the context of the revision of the classification of mental and behavioural disorders within the ICD-10, led by the WHO Department of Mental Health and Substance Abuse, which has been described elsewhere (19,20). In the area of IDD, an important purpose of the ICD-11 will be to provide tools to enable more widespread, efficient, and accurate identification and prioritization of persons with IDD who need services. In most countries, service eligibility and treatment selection for persons with IDD are heavily influenced by diagnostic classification. Persons with IDD are more likely to receive the services they need if health workers in the settings where they are most likely to be seen have a diagnostic system that is reliable, valid, clinically useful and feasible. It is very unlikely that such front-line personnel will be psychiatrists and, in LAMI countries, they are unlikely to be specialist mental health professionals of any kind, and are often not physicians. These factors have strongly influenced the conceptualization of the tasks and workflow for the revision of the ICD-10, as well as the composition of ICD revision Working Groups, including the one on IDD. The revision process is also influenced by the newly created Content Model for the overall ICD-11, which determines the structure and nature of the information to be provided for each diagnostic category, integrating the category within much larger informational infrastructure (21).

A mixed qualitative approach was used by the Working Group on IDD to combine available evidence with prior expert knowledge (22). This approach was applied in three face-to-face meetings, seven teleconferences, and electronic exchanges to generate consensus on the proposals submitted to the ICD International Advisory Group. This paper focuses on the proposals agreed upon by the Working Group related to the parent or supra-ordinal category for IDD, the name of the entity, its definition, and its subtypes.

OUTCOME OF THE WORKING GROUP’S DISCUSSIONS

Placement in the classification

There was consensus among the Working Group on the need to relocate IDD in the larger grouping (supraordinal or parent category) of neurodevelopmental disorders. In ontological terminology, subcategories are called children categories, and the supraordinal category is called the parent category. This position recognizes IDD as a health condition, and not solely as a constellation of disabilities.

Terminology

The term “intellectual” was favoured because in most countries it is well understood and widely used, and is broadly acceptable in the context of clinical and policy ap-

plications. In parallel with current definitions of intelligence (23), it does not refer to a unitary characteristic but rather is an umbrella term that includes cognitive functioning, adaptive behaviour, and learning that is age-appropriate and meets the standards of culture-appropriate demands of daily life. Even though “cognitive” may be seen as a more precise term that more closely reflects underlying phenomena of IDD, it also has a broader meaning in psychology. The use of the term “cognitive” in connection with dementia and schizophrenia may also cause confusion.

General support was expressed for adopting the term “developmental”, in that it refers to a period of time during which the brain and its functions are developing. The term “developmental” implies a process and a lifespan perspective and emphasizes the dynamic nature of IDD.

During the discussion, three words emerged as possible descriptors of the entity in question: “impairment”, “difficulties”, “disorder”. The term “impairment” is specifically used in the ICF to refer to problems in body functions and body structures that may be associated with a wide variety of health conditions. The term “difficulties” was proposed to avoid medical connotations and because it is less likely to be rejected by consumers, family groups and care providers. It may imply that the person can overcome his/her problems with some help or support, but it may also be confusing because for many people these difficulties are long-standing and will not be overcome completely. The term “spectrum” was also discussed, but it was discarded due to its low taxonomical value within a categorical classification.

WHO’s Clinical Descriptions and Diagnostic Guidelines for ICD-10 Mental and Behavioural Disorders (24) define a “disorder” as “clinically recognizable set of symptoms or behaviour” that is usually associated with interference with personal functions or with distress. The term “disorder” was seen as having utility, because it places intellectual disability at the same level of other major disorders such as dementia or schizophrenia. The term implies that it is not just a question of intelligence, and it fits with the existence of multiple etiologies and comorbidities and with the variability of IDD.

Definition

It was agreed that the definition of IDD should include terms related to the developmental origin of the brain impairment, manifestations in cognitive functioning and adaptive deficits, aetiology, course and outcomes. The Working Group’s proposed definition and its main descriptors are shown in Table 1.

Subcategories

The Working Group reached a consensus to maintain the subcategories (children categories) corresponding to the four clinical severity levels of mild, moderate, severe and

Table 1 Definition and main descriptors of intellectual developmental disorders (IDD) agreed by the ICD Working Group

Definition

A group of developmental conditions characterized by significant impairment of cognitive functions, which are associated with limitations of learning, adaptive behaviour and skills.

Main descriptors

- IDD is characterized by a marked impairment of core cognitive functions necessary for the development of knowledge, reasoning, and symbolic representation of the level expected of one’s age peers, cultural and community environment. Nevertheless, very different patterns of cognitive impairments appear for particular conditions of IDD.
 - In general, persons with IDD have difficulties with verbal comprehension, perceptual reasoning, working memory and processing speed.
 - The cognitive impairment in persons with IDD is associated to difficulties in different domains of learning, including academic and practical knowledge.
 - Persons with IDD typically manifest difficulties in adaptive behaviour; that is, meeting the demands of daily life expected for one’s age peers, cultural, and community environment. These difficulties include limitations in relevant conceptual, social, and practical skills.
 - Persons with IDD often have difficulties in managing their behaviour, emotions, and interpersonal relationships, and maintaining motivation in the learning process.
 - IDD is a life span condition requiring consideration of developmental stages and life transitions.
-

profound IDD, in addition to the provisional categories of other and unspecified IDD.

A number of important organizations in the field have called for a discontinuation of children categories based solely on IQ. The AAIDD, for example, proposes a multidimensional system for classification and considers IQ ranges insufficient to be the sole determinant of cognitive functioning or clinical severity level (16). The Working Group argued that the determination of clinical severity levels for IDD should rely on a clinical description of the characteristics of each subcategory, and that the IQ score should be considered as one clinical descriptor among others also considered important in determining severity level.

The Working Group decided against discontinuing clinical severity levels, due to their current diagnostic and clinical utility (25). For example, increasing severity of IDD has been shown to be associated with lower levels of self-determination in choosing living arrangements, including where and with whom to live (26). Those with profound IDD are much more likely to live in a long-term care facility than those with mild IDD, and are less often able to determine their living arrangement. In addition, severity levels are already in wide use in many public health systems, determining the level of services and benefits provided. They may be helpful for communication between professionals in different disciplines, families, and users.

The subcategorization by clinical severity levels does not contradict the use of other approaches to subclassification, including multidimensional approaches aimed at connecting the IDD diagnosis to needed supports including intervention and planning (23). In the future, subcategorization based on clinical severity levels should be complemented by

subcategorization based on functional and personal characteristics and/or supports needed (ICF). A number of tools have been developed for classifying support needs and relevant characteristics of persons with IDD (27,28), but this field is still in its infancy and has not progressed to the point that such measures are available for worldwide use.

The subcategories of other and unspecified IDD will be maintained in the ICD-11, as they are standard components of the ICD-11 taxonomical system. However, they will be used as provisional diagnoses for specific age-defined populations. In children less than 4 years of age, there are well-known difficulties in diagnosing IDD or severity level due to the lack of reliable cognitive assessment tools and the temporal instability of measured cognitive impairments (29-31). For these reasons, it has been agreed that the provisional diagnosis of "unspecified IDD" should be used for all infants and children less than 4 years of age, where evidence exists of significant cognitive impairment. While a subset of these children will not go on to meet criteria for IDD, the ability to make this transitional diagnosis allows for the provision of early intervention services and clinical evaluation that are critical to improving developmental outcome.

The subcategory of "other IDD" is a provisional diagnosis to be used when IDD can be diagnosed, but where clinical severity level cannot be determined due to barriers in assessment, such as those presented by certain problem behaviours, psychiatric disorders, sensory or physical impairments. However, this provisional diagnosis is reserved for persons over the age of 4 years of age, so that the subcategories of unspecified and other IDD are mutually exclusive.

Problem behaviours

The Working Group agreed that problem behaviours, though very relevant to treatment and service usage, are not a core component of the linear structure of IDD as in ICD-10, and therefore they may be considered associated features rather than being subcategories or specifiers for IDD.

DISCUSSION

To the best of our knowledge, this is the widest international effort undertaken to date to reach a consensus on the name and definition of IDD. It has involved 30 experts from 13 countries, representing the different WHO regions, and experts from both high income and developing countries. This process has taken place in the context of an intense social and scientific debate on how to properly name and define IDD, which may have broad implications for users and families, and for eligibility and care provision in the future.

One of the major changes recommended by the Working Group is the integration of IDD with neurodevelopmental disorders. In ICD-9 (32), IDD were separated into a different large grouping from other neurodevelopmental disorders, an

action intended to provide greater visibility to these disorders and to underscore their common co-occurrence with other developmental disorders. Subsequently, the APA's DSM-III (33), which was multiaxial, excluded MR from Axis I, while analogous meta-syndromic categories more characteristic of adults (e.g., dementia) were retained as part of the main axis of mental disorders. Unfortunately, the separation of IDD diagnoses from other developmental disorders does not seem to have spurred the development of more specifically targeted services in most countries, as may be deduced from WHO's Global Atlas on Intellectual Disabilities (34). The incorporation of IDD in the large grouping of neurodevelopmental disorders will have significant implications for this supraordinal or parent category, and it may require a re-analysis of the hierarchy and the conceptual map of neurodevelopmental disorders to avoid double coding (e.g., in the case of Rett's and fragile X syndromes).

The recommended name and definition of IDD clearly identify them as a health condition. These recommendations are consistent with the 2008 position paper by the WPA Section on Psychiatry of Intellectual Disability (17), which recommended a polysemic-polynomial approach for complex entities such as IDD, allowing for the use of more than one name and meaning for different audiences and purposes so long as their relationship and semantic similarity is unambiguous and formally defined (35). It is important to have a clear description of the different meanings and uses of these terms in the scientific, social and policy arenas.

Disabilities should be seen as potential consequences of IDD health conditions. This is consistent with the approach promoted by the WHO within the Family of International Classifications, in which conceptually separate, though clinically overlapping, disease entities and functional impacts are coded using the ICD and the ICF. The position adopted by the Working Group on IDD may provide an example on how to formulate the hierarchy and the operationalization of the disease and disability components in ICD and ICF, which would also apply to other neurodevelopmental disorders (e.g., autism, specific developmental disorders), and more broadly to other mental disorders (e.g., dementia, schizophrenia).

The name and definition of IDD proposed by the Working Group do not conflict with the use of the terminology of ID, the functional definition approved by AAIDD, or a functional definition based on the ICF model. The proposed model preserves the distinction made in the WHO Family of International Classifications, and therefore in international health policy, between disease and disorder on the one hand, and the functional impacts of health conditions (i.e., disability) on the other (14).

In conclusion, the Working Group conceptualized IDD as a meta-syndromic health condition, parallel to other meta-syndromic conditions such as dementia, which may be related to a variety of specific etiologies. The Working Group endorses a polysemic-polynomial approach to the classification of IDD. This approach distinguishes between IDD (a

clinical meta-syndrome) and ID (the functioning/disability counterpart), which have different scientific, social and policy applications. The Working Group believes that this approach best supports the public health mission of WHO and the provision of appropriate services and opportunities to persons with IDD.

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Broadening the diagnosis of bipolar disorder: benefits vs. risks

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There is considerable debate over whether bipolar and related disorders that share common signs and symptoms, but are currently defined as distinct clinical entities in DSM-IV and ICD-10, may be better characterized as falling within a more broadly defined “bipolar spectrum”. With a spectrum view in mind, the possibility of broadening the diagnosis of bipolar disorder has been proposed. This paper discusses some of the rationale for an expanded diagnostic scheme from both clinical and research perspectives in light of potential drawbacks. The ultimate goal of broadening the diagnosis of bipolar disorder is to help identify a common etiopathogenesis for these conditions to better guide treatment. To help achieve this goal, bipolar researchers have increasingly expanded their patient populations to identify objective biological or endophenotypic markers that transcend phenomenological observation. Although this approach has and will likely continue to produce beneficial results, the upcoming DSM-IV and ICD-10 revisions will place increasing scrutiny on psychiatry’s diagnostic classification systems and pressure to re-evaluate our conceptions of bipolar disorder. However, until research findings can provide consistent and converging evidence as to the validity of a broader diagnostic conception, clinical expansion to a dimensional bipolar spectrum should be considered with caution.

Key words: Bipolar I disorder, bipolar II disorder, bipolar spectrum, depression, diagnosis, hypomania, mania

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Bipolar disorder is a dynamic illness characterized by dramatic changes in mood, energy, cognition, and behavior that fluctuate over time. There are no objective markers for bipolar disorder, so that identification relies on clinical assessment of these changing symptoms in order to place them within a diagnostic framework (e.g., DSM-IV or ICD-10) (1). However, many of the symptoms used to define bipolar disorder overlap with other psychiatric conditions. Consequently, identifying the edges of the bipolar diagnosis can be difficult. This difficulty is highlighted by variable prevalence rates observed in epidemiological studies. For example, the Epidemiological Catchment Area study reported one-year prevalence rates of bipolar I disorder of 0.9% and bipolar II disorder of 0.4%; however, when clinical significance criteria were applied, these rates dropped to 0.5% and 0.2%, respectively (2). Moreover, in this same study, the lifetime rate of subthreshold mania/hypomania exceeded 5% (3). Hirschfeld et al (4) reported that the population prevalence of bipolar I and II disorder combined exceeds 3% when appropriately sensitive instruments are used, but Zimmerman et al (5) suggested that

such instruments overdiagnose bipolar disorder by misattributing symptoms of other conditions.

The variability in rates of bipolar disorders in these studies occurs in part from difficulty distinguishing bipolar disorder from related illnesses. At the boundaries between diagnoses there are overlapping symptoms, such that subtle differences in only one or two DSM-IV or ICD-10 criteria determine whether a patient is diagnosed with bipolar disorder or with something else (e.g., unipolar depression). As reviewed by Phelps et al (1), there are no obvious “points of rarity” in the continuum of affective symptoms between bipolar and unipolar disorders, or with healthy subjects and other diagnoses. Because transitions between diagnostic conditions are stepwise rather than abrupt, some investigators advocate for a broader or “spectrum” approach to bipolar disorder (6,7). To some extent, this approach moves away from the categorical definitions of DSM-IV or ICD-10 toward identifying individual symptoms that suggest “bipolarity”. For example, in the pediatric realm, clinicians struggle with the potential “bipolarity” of attention-deficit/hyperactivity disorder (ADHD)

symptoms, temper tantrums, and severe mood dysregulation (8). In adults with depression, Akiskal (7) suggested a wide range of signs of bipolarity, including “ornamentation” with red clothes and creative achievement.

Before discussing the potential value of broadening the bipolar disorder diagnosis, it is useful to remind ourselves why we make diagnoses. People with bipolar disorder are identified from the general population in order to assign therapies that will alleviate their suffering (i.e., symptoms), ideally through evidence-based treatment guidelines developed from past studies of similar individuals (9,10). Diagnoses also identify individual cases to populate research efforts toward improving our understanding of the condition, ideally in order to identify an etiopathogenesis that will lead to better treatments. In the absence of treatment and research considerations, diagnostic debates can quickly degenerate into circular academic blustering of little value. With these thoughts in mind, we discuss the potential risks and benefits associated with broadening the diagnosis of bipolar disorder.

RISKS AND BENEFITS: TREATMENT

One reason to broaden the diagnosis of bipolar disorder is that patients who exhibit bipolar-like symptoms, but do not meet DSM-IV or ICD-10 criteria for bipolar I or II disorder, might benefit from treatment approaches used for managing bipolar illness. By expanding the diagnosis of bipolar disorder, applying bipolar treatment algorithms might improve the likelihood that these “spectrum” individuals will find an effective therapeutic regimen. Indirect support for this notion has come when “mood stabilizers”, that are thought to be relatively specific for bipolar disorder, have been found to be effective for other conditions. For example, lithium augmentation has been effective in major depressive disorder following partial antidepressant response (11), and carbamazepine improved outcomes in borderline personality disorder (12). One interpretation of these types of studies is that improvement occurred from a failure to recognize the underlying “bipolarity” of the depressed or borderline patients.

Indeed, a major impetus for broadening the bipolar diagnosis is recent research suggesting that hypomania is commonly missed in depressed patients, leading to misdiagnoses of major depressive disorder when bipolar II disorder would be more appropriate (e.g., 7). Many other depressed patients exhibit subthreshold mania or hypomania, i.e., symptoms of mania or hypomania that are too few to reach DSM-IV or ICD-10 criteria (1,3,6,7,13-19). These observations suggest that there may be a subgroup of people with major depressive disorder who exhibit “bipolarity”, e.g. symptoms and signs of mania, multiple recurrent affective episodes, or a family history of bipolar disorder, that suggest that the patients would be better considered “bipolar spectrum”. These subgroups of “major depressive” patients may be over-represented in treatment unresponsive samples (20-22), so that a broader bipolar framework might lead to improved treatment response.

In particular, one concern related to missing “bipolarity” in a depressed sub-

ject is the putative risk of antidepressants worsening the course of illness by increasing affective cycling or precipitating mania (23). However, considerable controversy rages about the level of this risk, with recent data from the large STEP-BD study suggesting that newer antidepressants do not impart these risks in bipolar I or II depression (24). Nonetheless, in STEP-BD, antidepressants appeared to be largely ineffective, supporting the notion that “bipolarity” in a depressed subject may decrease the likelihood of a standard antidepressant treatment response.

To directly determine whether “bipolarity” was associated with treatment resistance, Perlis et al (25) identified a bipolar spectrum (excluding bipolar I and II disorder) in 4041 major depressed patients that were part of the large STAR*D depression study. In STAR*D, all subjects received the same treatment algorithm designed for unipolar depression, and bipolar spectrum patients comprised 28% of the sample. However, the presence of a bipolar spectrum was not associated with any differences in outcome or treatment response in these depressed subjects, suggesting “bipolarity” in these depressed subjects did not impact treatment response. Further complicating this discussion are recent studies suggesting that patients with bipolar II disorder respond well to antidepressant monotherapy (26-28). To our knowledge, there are no studies demonstrating that depressed bipolar spectrum patients exhibit a better course and outcome when following bipolar rather than unipolar depression treatment guidelines.

Similar considerations arise along the borders of bipolar disorder with other conditions. For example, psychotic mania and an acute exacerbation of schizophrenia can be difficult to distinguish (29). The boundary with schizophrenia is further complicated by the presence of schizoaffective disorder, which itself is subcategorized into “depressive” and “bipolar” types. Schizoaffective disorder is a controversial classification that has been criticized as a “waste basket” for schizophrenic and psychotic mood disorder patients who do not fit neatly

into either of the major categories (30). Alternatively, other investigators suggest that schizoaffective patients have unique characteristics setting them apart from the other patient groups (30). Other than recent studies with paliperidone (31), there have been few specific controlled treatment trials for schizoaffective disorder. Treatment guidelines tend to combine interventions for mood and schizophrenic disorders (30,32), rather than develop specific approaches to schizoaffective disorder *per se*. A few studies have suggested that the newer, so-called atypical, antipsychotics may be more effective than conventional antipsychotics in schizoaffective disorder, consistent with “bipolarity” in this group (33,34). However, atypical antipsychotics in general appear to have similar efficacy in both bipolar and schizophrenic disorders (e.g., 35).

A number of other diagnoses have been suggested to potentially include bipolar spectrum patients, including borderline personality disorder (36,37), eating disorders (38,39), and ADHD (40). In these conditions, bipolar symptoms may occur, but whether these subjects with subthreshold bipolar disorder will respond more effectively to a bipolar treatment algorithm rather than the algorithm for their “primary” diagnosis is unknown. Complicating considerations in all of these instances, psychotropic medication effects are generally modest, and many of our interventions appear to be relatively nonspecific. For example, in treating large groups of people with well-defined bipolar I disorder mania, only about 50% respond to any given medication (41). Trial and error, sometimes for many years, is often required to find an effective intervention (41). Nonetheless, in a small study of “bipolar spectrum” youth who had bipolar parents, Duffy et al (42) found that lithium response was predicted by a history of lithium responsiveness in the family, suggesting that, even with the limitations of our current treatments, treatment response provides a useful metric to inform diagnostic discussions. However, lithium is unusual among psychotropic drugs for its relative specificity in the treatment of classic bipolar I

disorder. Most of the other psychotropic drugs are modestly but broadly effective across a wide range of conditions.

Indeed, the advent of lithium dramatically altered the psychiatric landscape. Lithium was specifically useful for patients with a traditional bipolar I course (i.e., mania alternating with depression), yet had little benefit in schizophrenia and unipolar depression (at least as monotherapy). The eventual approval of lithium in the US in 1970 led psychiatry to critically examine how bipolar disorder was distinguished from schizophrenia, leading to the US/UK cross-national studies and recognition that schizophrenia was over-diagnosed in the US at the expense of bipolar disorder (43). The presence of nonspecific treatments may contribute to diagnostic imprecision, as was the case for schizophrenia in the US prior to 1970. Faced with a number of new treatments (e.g., atypical antipsychotics) that appear to be relatively nonspecific across a wide range of psychiatric conditions, we need to be careful that treatment nonspecificity is not driving our diagnostic categories, as doing so may limit our ability to identify patients for more effective and specific treatments in the future (1,44).

A significant risk, then, of broadening the diagnosis of bipolar disorder is that the label will be overused, misclassifying patients who might benefit from alternative treatment approaches. For example, in a series of papers, Zimmerman et al (45-47) found that patients with borderline personality are frequently misdiagnosed with bipolar disorder, which might lead to excessive medication trials when specific therapies, for example dialectical behavioral therapy, would be more effective (48). The potential benefits of a broader treatment algorithm applied to “bipolar spectrum” patients must be balanced against the risks of exposing individuals to adverse medication effects from unnecessary drug trials. None of the compounds commonly used to treat major mental illness are without risks for adverse effects (41). From a treatment standpoint, then, the advantages of broadening the diagnosis of bipolar disorder should meaningfully advance how affected individuals are

therapeutically managed. More studies are needed like that of Perlis et al (25) to specifically test the treatment advantages of expanding diagnostic groups.

RISKS AND BENEFITS: RESEARCH

In addition to guiding therapeutic decisions, diagnostic considerations are critically important for defining patient subgroups for scientific inquiry into the etiopathogenesis of bipolar disorder. The primary benefit of expanding the diagnosis for research would be to improve our ability to identify objective markers that transcend phenomenological observation (49). Such markers would be specific to the broadly-defined bipolar diagnosis, but independent of mood symptoms and mood episodes, so could serve as treatment targets and to help predict clinical outcomes. Before these expectations can be met, however, there are still significant issues complicating inquiries into the etiopathogenesis of bipolar disorder at the level of basic science. For example, there are few animal models of mania, the defining mood state of bipolar disorder. It is difficult to produce manic-like symptoms in rodents, so only proxy behaviors can be examined (e.g., social behavior, motivation, and certain cognitive abilities). Additionally, there is no model of spontaneously alternating manic and depressive behaviors to date (50). Considering these knowledge gaps, the question remains: “Does expanding the diagnosis of bipolar disorder assist research efforts toward clarifying the etiopathogenesis of bipolar disorder to improve treatment assignment in the future?”

Genetic studies provide one foundation for addressing this question. There is compelling evidence that bipolar disorder is highly heritable. Concordance rates are estimated to be at least 67% in monozygotic twins (51), and family studies demonstrate a relative risk 8-10 times higher in first-degree relatives than in the general population (52). To date, however, twin and family studies have failed to identify consistent disease specific genetic underpinnings for bipolar disorder, and, instead, demonstrate

considerable genetic overlap with related conditions. For example, as reviewed in Barnett and Smoller (53), individuals at risk for bipolar disorder are also at increased risk for unipolar depression, schizophrenia, and schizoaffective disorder. Even in the context of a greater relative risk for developing bipolar disorder than these other conditions, much of the genetic risk for bipolar disorder is shared with spectrum conditions, which can be interpreted as research evidence for expanding the bipolar diagnosis.

Although genetic research, in large part, seems to support a bipolar spectrum view, due to the nonspecificity of findings to date for DSM-IV or ICD-10 categorizations, this may as likely be due to methodological inadequacies and “low signal” as to a true lack of disease specific findings. In comparing bipolar disorder and schizophrenia specifically, common linkage regions and candidate genes appear to support a spectrum view (54) but, as yet, results are not fully replicable and the make up of the spectrum itself is unsettled. Although the bipolar spectrum might be expected to involve mood dysregulation at its core, common genetic findings in bipolar disorder and schizophrenia may be primarily the result of commonalities in psychotic symptoms. It has been proposed, based on risk factor and clinical history considerations, that bipolar disorder may be better classified with schizophrenia in a psychotic cluster than with unipolar depression in an emotional cluster (55). Since the occurrence of mania is predominantly accompanied by psychotic symptoms (56), and in light of suggestions that psychosis provides a reliable phenotype for genetics research (57), psychotic symptoms might, then, provide as reasonable a basis for defining the bipolar spectrum as mood dysregulation. Until the make up of the bipolar spectrum receives support from converging lines of research, however, there is a risk of broadening the diagnosis prematurely. Moreover, there may also be a vicious cycle in which failure to isolate homogeneous subpopulations of bipolar disorder leads to “noisy” and nonspecific genetic finding; further broadening the diagnosis might worsen this situation.

Another reason for exercising caution in expanding the bipolar diagnosis is that clinical outcomes are difficult to predict, due to the interaction of various genetic and environmental factors. Although one model recently estimated that 22% of the genetic risk in bipolar disorder may be explained by six common gene variants (58), it is difficult to ascertain the disease specificity of such findings, and the relative importance of various genes is not easy to estimate. Different gene combinations and interactions can have an additive effect on behavior, resulting in variable phenotypic expression, which is particularly pronounced in complex behavioral disorders like bipolar disorder. Exactly how genes, experience, and their interaction influence etiopathogenesis, psychopathology, and outcome in bipolar disorder remains a complicated and speculative issue. Other overarching issues, such as why certain individuals are more or less “resilient” to genetic and psychosocial stressors that produce and propagate psychopathology, provide additional challenges for researchers (59).

Despite these challenges, the identification of cognitive markers has already begun to address the question of whether to broaden the bipolar diagnosis. A few investigators have recently compared, or reviewed, neurocognitive performance between bipolar I and related disorders (60-62). These studies provide direct tests of the bipolar spectrum hypothesis. The research to date has fairly consistently identified differences in the neurocognitive profiles of bipolar I and II individuals (61). Bipolar I patient groups appear to have widespread dysfunction of verbal learning and memory, attention and executive function, and a greater likelihood of clinically significant impairment relative to bipolar II groups, who have less functional impairment, primarily restricted to working memory and executive function (60). A similar study, this time comparing bipolar II depressed and unipolar depressed patients matched on depression severity, also showed distinct cognitive profiles, with the bipolar and unipolar groups showing relatively intact cognition and impaired executive function, respec-

tively (62). Each of these studies, then, supports the view that there may be biologically-based cognitive differences between bipolar II and related mood disorders, inconsistent with a bipolar spectrum hypothesis.

Similar to cognitive research, much of neuroimaging research also provides little support for the spectrum hypothesis. For example, in a positron emission tomography study, it was demonstrated that midbrain serotonin transporter binding was lower in medicated bipolar I relative to bipolar II participants, supporting the current DSM-IV dichotomy (63). In a voxel-based morphometry study, Ha et al (64) demonstrated that bipolar I and II participants both show gray matter deficits at the intersection of the ventral prefrontal and anterior limbic circuits relative to healthy comparison participants. However, the bipolar I group also had greater gray matter deficits than the bipolar II group in four other widely distributed brain regions, suggesting some degree of neuro-structural distinction between these two subgroups as well.

Taken together, then, genetic, cognitive and imaging research to date provides no real consensus regarding the appropriateness of broadening the bipolar diagnosis. Although the research findings from a given perspective may lean toward or away from the spectrum view on the whole, there are instances of support for the contrary view, and the current state of the art in instrumentation and methodology can shift the equilibrium substantially. Of course, if null effects between spectrum conditions are not as widely reported in the research literature, as is often the case, the range and validity of the bipolar spectrum could be underestimated. This possibility further highlights the need for well-designed studies testing the assumptions of the spectrum itself, rather than simple disorder specific comparison studies.

CONCLUSIONS

Broadening the diagnosis of bipolar disorder offers the potential to identify

patients who might respond to bipolar treatment algorithms, and who might not otherwise be successfully treated. Similarly, less categorical and more dimensional conceptions of bipolar illness might help identify genetic risks or new endophenotypes. However, with frequent diagnostic changes, it becomes difficult to complete studies to validate the new diagnostic systems. Broadening the bipolar diagnosis risks diluting samples to the point of such heterogeneity that neither basic nor clinical research can progress, limiting discovery and potentially exposing patients to unnecessary adverse medication effects. In fact, bipolar disorder as defined by DSM-IV and ICD-10 is likely comprised by a heterogeneous collection of underlying etiologies that are too complex to distinguish by clinical presentation alone. However, to date the empirical evidence is still too scant to say with conviction whether or not broadening the diagnosis of bipolar disorder will assist with etiologic discovery or improvements in treatment development.

Until research findings can provide better insight into the validity of a broader diagnostic conception of bipolar disorder, clinical expansion to a “spectrum” concept should be considered with caution (49,73). Prematurely broadening a diagnostic category, prior to substantial evidence that doing so enhances either treatment development or etiological research, runs the risk of eliminating any value of the diagnosis (44). Before advancing a new bipolar diagnostic schema, it would seem prudent first to develop an agreed upon operational approach (1) and then develop specific studies to compare the advantages of the new approach for treatment and discovery. Changing diagnoses simply to meet new theoretical constructs prevents adequate systematic testing of the new approach and risks losing many of the evidence-based advances we have seen in psychiatry in the past 50 years.

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Expanding the bipolar construct while preserving its diagnostic integrity: are we keeping the baby or the bathwater?

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Strakowski et al provide a thought-provoking discussion of the clinical and scientific merits, and shortcomings, of adopting a broadened nosologic construct of bipolar disorder, extending beyond the categorical limits of bipolar I and II disorder. Perhaps the most scientifically compelling argument for such a conceptualization involves the realization that bipolar disorder encompasses varied dimensions of psychopathology that entail more than mood disturbances, including cognitive dysfunction, chronobiological disruptions, psychosis, interpersonal conflict, and behavioral activation. Unlike Mendelian diseases, complex traits such as bipolar disorder – though robustly heritable – are believed to involve multiple genes that collectively exert small effects. In that sense, casting a wider phenotypic “net” could potentially enhance the yield for detecting signals that are true phenotypes, or more probably, non-obvious endophenotypes. Furthermore, variable expressivity of putative risk alleles can readily account for *form fruste* clinical presentations of affective illness that defy categorical distinction. On the other hand, efforts to discern links between suspected genotypes and presumptive disease entities suffer when phenotypes are poorly defined or unrefined.

The dilemma at hand fundamentally involves the limits with which descriptive psychopathology can be expected to shed light on biological disease states. Strakowski et al point out the arbitrary and incomplete nature of current diagnostic descriptors, but one must ask whether additional phenomenologic descriptors would be any less arbitrary. Clearly the features that now define bi-

polar I or II disorder fail to capture many variations of complex mood disorder; and similarly, the designation of unipolar depression alone often inadequately describes cases with poor treatment responses or levels of functional impairment that are not commensurate with the prognosis of uncomplicated major depression. Polarity is only one of many dimensions of mood disorder complexity, alongside psychosis, agitation, anxiety, acuity, chronicity, comorbidity, and melancholia. One wonders how broadened phenomenology would clarify *polarity* as a central organizing principle for mood disorder nosology.

One must equally consider the hazards of extracting symptoms from other known disorders and refitting them as bipolar equivalents – such as the impulsivity or affective instability of borderline personality disorder, the distractibility and hyperactivity of attention-deficit/hyperactivity disorder, or the autonomic hyperarousal and psychomotor acceleration of severe anxiety disorders – when doing so compromises the diagnostic integrity of other disorders. Without prior knowledge about disease etiology, phenomenologic expansion may lead researchers and clinicians toward altogether wrong conceptual frameworks. Imagine reformulating pulmonary emboli, costochondritis and peptic ulcer disease as collectively falling within the angina spectrum based solely on the presence of chest pain (and proposing lytic therapy for all such presentations); or deciding that pregnancy, anasarca, and obesity plausibly have common etiologies based on shared disturbances of abdominal girth. Since DSM-III, psychiatric nosology has made no pretense that descriptive diagnoses impart information about etiology. Until novel external validators of disease states are established, expanded phenomenology seems inescapably arbitrary.

From a practical standpoint, the great-

est clinical peril in prematurely broadening the bipolar construct likely concerns recommendations about best treatments for difficult mood disorders. Strakowski et al suggest that patients with “bipolar-like symptoms” might benefit from the same drugs used to treat bipolar I disorder, arguing that mood stabilizers “are thought to be relatively specific for bipolar disorder”. Yet, one might challenge the diagnostic specificity of virtually any psychotropic drug, and there is little basis for inferring diagnosis from clinical response elsewhere in medicine. Consider, for example, that successful diuresis with furosemide does not establish a cardiogenic versus peripheral etiology for edema; nor does an anti-inflammatory response to corticosteroids point to an autoimmune versus infectious etiology for joint pain. Moreover, as intriguing as the hypothesis may be that mood stabilizers could have value for complex forms of non-bipolar I or II “spectrum” disorders, it must be acknowledged that no controlled studies exist to determine the efficacy of mood stabilizing drugs for “expanded bipolar spectrum” patients.

Extrapolation about possible treatment outcomes from studies of mood stabilizers for treatment-resistant or highly recurrent unipolar depression is less than encouraging. For example, the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) comprised a study group with highly recurrent unipolar depression – a designation some authorities would construe as tantamount to Kraepelinian manic-depressive illness – yet adjunctive lithium yielded only a 15.9% response rate (1), despite earlier promising results with much smaller samples in highly recurrent unipolar depression (2). Similarly, despite encouraging preliminary open label data, three placebo-controlled studies have failed to demonstrate efficacy for adjunctive lamotrigine in treatment-resistant unipolar depression (3-5). No randomized stud-

ies exist with divalproex or carbamazepine for complex unipolar depression, although efficacy with either of these mood stabilizers is more robust for mania than depression in bipolar I disorder.

Strakowski et al preface their discussion of a possible expanded role for mood stabilizers by pointing out unresolved controversies regarding the safety and efficacy of antidepressants in bipolar depression. Strikingly, though, randomized trials indicate that antidepressant safety and efficacy appear more substantial in bipolar II than bipolar I disorders (6,7) – and perhaps even superior to lithium for relapse prevention – suggesting that “soft” spectrum bipolar disorders may in fact be the most hospitable niche for antidepressant use, in contrast to bipolar I disorder.

As hypotheses about an expanded bipolar spectrum await empirical study, several points merit consideration for future clinical and research efforts:

- There is a need to empirically determine inclusion and exclusion criteria for candidate entities within the bipolar “spectrum”. With no proposed exclusion criteria, risks for diagnostic incoherence run high.
- Endophenotypic approaches, particularly focusing on clinically unaffected first-degree relatives of bipolar I or II probands, may be especially useful to discern observable characteristics that reflect the expression of bipolar risk alleles, and help to parse true phenotypes from phenocopies.
- Meaningful clinical trials of mood stabilizers are needed for non-bipolar I or II spectrum disorders in order to base treatment recommendations on empirical observation and replace speculation and opinion with factual outcome data.

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Broadening the concept of bipolar disorder: what should be done in the face of uncertainty?

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Early in the course of treatment I am sometimes not sure if a currently depressed patient has bipolar disorder. This uncertainty occurs despite an extensive evaluation that includes the administration of a semi-structured interview, a review of prior records, and an interview with an informant. When diagnosis is based on the occurrence of symptom episodes in the past, as is the case with bipolar disorder in currently depressed patients, diagnostic clarity is sometimes elusive.

Similarly, I am not sure how the bipolar spectrum should be defined. This is despite conducting research in the area and keeping up with the literature.

What should be done in the face of uncertainty? With my patients I adopt a wait and see approach. That is, I closely monitor my patients' symptoms over time, looking for the emergence of hypomanic or, less frequently, manic episodes. Treatment for bipolar disorder follows when the diagnostic declaration is made.

In a like manner, changes to the nomenclature should follow a sober, conservative approach and only be made when replicated, empirical evidence has dem-

onstrated that the new method is superior to the old. As summarized by Strakowski et al, such empirical evidence is lacking with regards to an expansion of the boundaries of bipolar disorder. They therefore urged caution.

Wherever the boundaries of bipolar disorder are drawn, there will be some false positive as well as false negative diagnoses. The question is not whether there is diagnostic error, but rather which type of error predominates and how much will shifting the diagnostic threshold impact the number of each of these diagnostic errors. Also important to consider are the clinical consequences of each type of error, and which error is more difficult to undo after it has been made.

In support of the expansion of the diagnostic boundary for bipolar disorder, some studies have suggested that the duration of a hypomanic episode should be lowered to 1 or 2 days (1,2). However, I am not aware of any studies of the potential impact this change would have on diagnosis and outcome in clinical practice. With the existing diagnostic criteria, overdiagnosis (i.e., false positives) is already a problem (3). If the duration threshold is lowered, how many more patients will be overdiagnosed with bipolar disorder because episodes of affective instability characteristic of cluster B personality pathol-

ogy are incorrectly considered indicative of hypomania (4)? Of course, the question should also be asked: how frequently does a clinician currently underdiagnose "true" bipolar disorder because the observed, or recently occurring, hypomanic syndrome has not lasted long enough to qualify as a DSM-IV hypomanic episode? However, clinicians are not rigid in the application of the DSM-IV diagnostic thresholds (5); thus, patients with recurrent hypomanic episodes of presumably insufficient duration would nonetheless likely be diagnosed with bipolar disorder and treated accordingly.

Both false positive and false negative diagnoses are associated with adverse consequences. Unrecognized bipolar disorder is associated with underprescription of mood stabilizing medications, an increased risk of rapid cycling, and increased costs of care (6-8). Overdiagnosed bipolar disorder is associated with overtreatment with unneeded medications and consequent exposure to potential side effects and medical risk and the potential failure to offer more appropriate treatments. In trying to decide where to set the threshold for diagnosing bipolar disorder and minimize diagnostic errors of all types, it should be acknowledged that the consequence of a false positive diagnosis is likely to be more long-lasting than a false negative diagnosis. While diagnosis may be a dynamic, fluid process, that is reconsidered as additional clinical material becomes available, it is probably easier to add a diagnosis than to take one away. Thus, it is easier to change a patient's diagnosis from nonbipolar depression to bipolar disorder than from bipolar to nonbipolar depression. I suspect that a patient with a false positive diagnosis of bipolar disorder who is doing well on an antidepressant and a mood stabilizer is unlikely to have the mood stabilizer discontinued.

Let us consider the recently published 10-year prospective study of community residents which found that individuals with a subthreshold number of manic/hypomanic symptoms had an elevated rate of bipolar disorder in their families, elevated comorbidity rates, and an increased rate of converting to DSM-IV bipolar I or bipolar II disorder during the

follow-up interval (9). The authors interpreted the findings as support for broadening the concept of bipolar disorder. However, less than 15% of the subjects actually converted to bipolar I or bipolar II disorder. As noted by Strakowski et al, there are no studies establishing the efficacy of mood stabilizers in the treatment of subthreshold bipolar disorder. Thus, if the diagnostic boundary was expanded, many individuals who would never develop DSM-IV-defined bipolar disorder would be prescribed such medications in the absence of controlled research establishing their efficacy.

First and Frances (10) have cautioned the developers of DSM-5 against making changes in diagnostic criteria without sufficient consideration of the unforeseen consequences of such changes. DSM-IV symptom-based diagnoses represent a probabilistic estimate of a disease whose underlying pathophysiology we hope to one day understand. Shifting the diagnostic boundary downward will reduce the rate of underdiagnosis of true bipolar disorder at the cost of increasing the rate of overdiagnosing pseudobipolar disorder.

We are therefore left with several nodes of uncertainty. In the absence of valid biological diagnostic markers, the relative frequency of each type of phenomenology-based diagnostic error is uncertain. The efficacy of mood stabilizers in treating subthreshold bipolar disorder is uncertain. The impact of lowering the threshold to diagnose bipolar disorder on overdiagnosing bipolar in clinical practice is uncertain. From a public health perspective, the benefit of expanding the diagnostic boundary is uncertain. In the face of such uncertainty, a wait and see attitude is the most prudent

before redrawing bipolar disorder's diagnostic boundaries.

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Broadening bipolar diagnostic criteria: why not start with hypomania?

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Strakowski et al have done an outstanding job in discussing the benefits and risks of broadening the diagnostic criteria for bipolar disorder. They note that advantages are more accurate diagnosis

and more appropriate treatment of those with bipolar disorder, while disadvantages are overdiagnosis and exposure to ineffective medications with deleterious side effects of those without the illness, as well as impediment of scientific discovery. In support of broadened criteria, they cite evidence that bipolar I disorder is on a spectrum with major depressive disorder (MDD) via bipolar II disorder, and with schizophrenia via schizoaffective disorder. This includes response of antidepressant-resistant MDD to lithium; common genetic findings between bipolar disorder and MDD and between bipolar disorder and schizophrenia; and the response of all three conditions to second generation antipsychotics (SGAs). More evidence, however, is given against broadening bipolar diagnostic criteria, including recent findings from a large study by Perlis et al (1) that measures of bipolar spectrum disorder among patients with MDD did not predict antidepressant treatment response, and findings of neurocognitive and neuroimaging differences between patients with bipolar I and II disorder. They conclude that it is premature to advance a new bipolar diagnostic schema, arguing that extant nosologies are already likely compromised by a heterogeneous collection of etiologies.

A spectrum may be defined as a range of linked conditions such that there is not a unitary disorder but rather a syndrome composed of subgroups. That there are differences between bipolar I and bipolar II disorder, or between bipolar II disorder and MDD, does not argue against a spectrum construct, especially since the disorders are thought to represent complex genetic illnesses. Indeed, the first published cross-disorder genome wide association study of bipolar disorder, MDD, and schizophrenia has revealed a chromosomal region having effects specific to bipolar II disorder, as well as several chromosomal regions having pleiotropic effects influencing all three diagnostic classes (2). Such a finding lends support to the bipolar spectrum concept by inferring specific as well as shared genetic liabilities across the member disorders. A number of diagnostic criteria for a bipolar spectrum have been proposed

(3,4). Some of these models include forms that lack mania or hypomania but have other indicators of bipolarity, such as early onset of depression, highly recurrent depressive episodes, and/or family history of bipolar disorder. As noted by Strakowski et al, a large study of patients with MDD by Perlis et al (1) did not support such a broad construct when using antidepressant response as the validating variable.

Growing epidemiological and prospective data, however, indicate that subthreshold hypomanic symptoms are common and of nosological relevance, lending support to narrower bipolar spectrum models. Angst et al (5) found that nearly 40% of study participants in the National Comorbidity Survey Replication with MDD had a history of subthreshold hypomania, defined as the presence of at least 1 of the 2 screening questions for mania but failure to meet full diagnostic criteria for mania. According to these questions, hypomanic symptoms had to last several days or longer. Individuals with MDD and subthreshold hypomania had an earlier age of onset, more episodes of depression, and higher rates of comorbidity than those without hypomania, but lower levels of clinical severity than those with bipolar II disorder. That the differences among the three categories were graded could be taken as further support of an underlying spectrum. Fiedorowic et al (6) followed 550 individuals in the National Institute of Mental Health (NIMH) Collaborative Depression Study with MDD at intake for a mean of 17.5 years and up to 31 years. On survival analysis, 20% of the sample experienced hypomania or mania, and conversion to a bipolar diagnosis. Number of subthreshold hypomanic symptoms (3 of 5 was the optimal cut off) was associated with subsequent onset of hypomania or mania independent of other risk factors.

Studies of subthreshold hypomania might be important to the understanding of antidepressant-associated switch, about which much controversy exists, and other treatment questions. In a study of 176 bipolar patients participating in 10-week adjunctive antidepressant treatment trials, 46 experienced treatment-

emergent mania or hypomania (7). The only difference between the group that switched and the group that did not was a small but significantly higher Young Mania Rating Scale score (i.e., subthreshold hypomanic symptoms) before antidepressant exposure. As patients with bipolar II depression have been shown to be less likely to switch with antidepressants than those with bipolar I depression (8), there may be a spectrum of liability for the antidepressant-induced switch process that is highest for bipolar I disorder, lowest for MDD, and intermediate for bipolar II disorder. It may also be that antidepressants are more likely to trigger subthreshold hypomania than threshold hypomania or mania, and that in MDD inadequately responsive to an antidepressant, subthreshold hypomania (spontaneous or antidepressant-related) might predict better response to augmentation with lithium or a SGA rather than with a second antidepressant. These hypotheses can be empirically tested with operationally-defined diagnostic criteria for subthreshold hypomania and interviews to evaluate them (9).

In light of well-founded concerns about prematurely broadening bipolar diagnostic schema, provisional criteria for subthreshold hypomania could be provided for further study in DSM-5 or ICD-11 (e.g., in an appendix). Examples could be the DSM-IV or ICD-10 definitions of hypomania except for a symptom duration of 1-3 days, or definitions focusing on behavioral overactivity, but there are others (9). A definition of subthreshold hypomania, in turn, would allow identification of specific subtypes of bipolar disorder not otherwise specified (e.g., bipolar III disorder or MDD with subthreshold hypomania), provisional criteria for which could also be provided.

Identifying discrete disease entities along dimensions of continuous variation is an important goal of medical classification, and phenotypic refinement needs to advance hand-in-hand with findings in neuroscience, genetics, and treatment response (10). Subthreshold hypomanic symptoms are a public health problem, and identifying the border of hypomania with depression, other conditions characterized by hypomanic

symptoms (e.g., impulse control disorders), and mental health has emerged as an important public health need. Criteria sets for subthreshold hypomania provided for further study in the DSM-5 or ICD-11 could help further delineate the boundaries of hypomania, and thus the bipolar spectrum, in an empirical manner without prematurely broadening bipolar disorder diagnostic criteria.

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Problems in the current concepts and definitions of bipolar disorders

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One can only agree with the conclusion of Strakowski et al that future changes to the current definitions of bipolar disorders should be based on consistent and converging evidence of their validity; but this also applies to the existing definitions.

My remarks are complementary and focus mainly on DSM-IV mood disorders. Changes can be recommendable for several reasons: a) some current diagnostic criteria for bipolarity (mania/hypomania) may not base on clinical evidence and not be valid; b) the current diagnostic spectrum of major mood disorders may be considered invalid (in its over-diagnosis of major depressive disorders at the expense of bipolar disorder) or regarded as illogical (labeling unipolar mania/hypomania as bipolar disorder but unipolar depression as major depressive disorder); c) the current DSM-IV severity spectrum is insufficient in its coverage: more than 50% of patients treated professionally for depression do not meet formal criteria for DSM-IV mood disorders (1) but are allocated to the fuzzy category “not

otherwise specified”. ICD-10’s severity spectrum performs better in this respect and is much closer to nature.

The DSM-III introduced the term “mood disorders”, which suggests that mood changes are the only main symptoms, neglecting for instance increased energy/activity. The latter is frequently more clearly perceived and reported by hypomanic patients themselves than is irritability (often better observed by others). The Zurich Study and the Bridge Study demonstrated the validity of increased energy/activity as a gate question in addition to elevated or irritable mood.

Even more important is the finding that the exclusion criteria for manic and hypomanic episodes screen out patients who show all the typical bipolar characteristics (positive family history for mania, early onset, high recurrence, course progression, and high comorbidity with panic, generalized anxiety disorder, social phobia, obsessive-compulsive disorder, binge eating, substance use and borderline personality disorders). It has been shown that conversions from depression to hypomania under antidepressants are not a simple unwanted effect of the treatment (2) but a natural consequence of response. The draft DSM-5 has, to some extent, taken heed of these findings.

A third problem with the current DSM-IV concept is the 4-day duration criterion for hypomanic episodes; brief episodes are common and typical, especially in adolescents and between major episodes in adults. The 4-day criterion is not data based and is therefore questionable (3).

The spectrum from depression to mania has been only partially explored by representative epidemiological research, mainly because the interviews used assume that the DSM-IV concept is correct; this top-down approach excludes important information. A continuum of depressive and manic symptoms was shown by Cassano et al (4), who examined patients with major depressive disorders. Recent re-analyses of two large epidemiological studies have demonstrated that roughly 40% of subjects with major depressive disorders manifest subthreshold bipolar syndromes with the corresponding validity and comorbidity (5,6). This group of depressed subjects is at great risk of developing full-blown bipolar I and II disorders. There are as yet no treatment data on such patients; but, in contrast to the results from the STAR*D study reported by Strakowski et al, two multicentre studies from France and Poland demonstrated that treatment-resistant depression was highly correlated with bipolarity as assessed by the Hypomania Checklist-32 R (7,8).

An unsolved nosological problem is pure mania and hypomania, which seem

to differ from bipolar disorders as regards family history (negative for depression) and other important characteristics. There exist almost no data on this aspect (9).

The severity aspect of the two-dimensional spectrum concept (10) has long been *the* spectrum view, going back to the work of Klerman (11) and Akiskal (12). The current DSM-IV diagnostic classification is still incomplete in its coverage of treated patients. Minor and recurrent brief depression appear only as subjects for further study in the appendix. Cyclothymic disorders are included, but only as a more chronic condition. Acute recurrent and minor depression and minor bipolar disorders should be incorporated instead of being allocated to the ragbag “not otherwise specified”. Operational definitions would then allow precise diagnoses of most of the treated patients, providing clinical/epidemiological research with important data for future diagnostic developments.

On the other hand, tendencies to merge personality traits or disorders (borderline personality disorder) or temperaments (cyclothymic, hyperthymic, depressive) with bipolar and depressive diagnostic concepts need approaching with caution. These traits are very closely associated with bipolar disorders but should nonetheless be considered as a third spectrum dimension, not to be mixed with the severity or diagnostic spectra.

Diagnostic manuals are essential but will need constant improvement. To enable the collection of the necessary information for further data-based changes, the manuals should include (not just in an appendix) potential new categories and should encourage a patient-centred, bottom-up approach to examination and diagnosis. This would register first and foremost the patients' complaints without the restricting lenses of diagnostic concepts. The same, of course, applies to standardized epidemiological assessments. Important, here, is to make gate questions broader in order to avoid false negatives. Finally, causation is always multifactorial and, at our present stage of knowledge, to a certain extent arbitrary. Exclusion criteria based on causal attributions should, if possible, be avoided.

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Bipolar spectrum: just broadening or an integration between categories and dimensions?

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In their thoughtful paper, Strakowski et al review the extensive literature regarding the benefits and risks of broadening the boundaries of bipolar disorders. According to the authors, the adoption of a bipolar spectrum model, not adequately supported by research evidence, is premature.

While we underscore that DSM categories are rarely based on research evidence, we agree with the authors. We believe that keeping a more conservative approach, until new insights into underlying biological mechanisms allow a more rationale change of the borders among different diagnoses and among threshold and subthreshold symptoms, ensures that the existing categories maintain the current levels of diagnos-

tic reliability and acceptable levels of communication among clinicians and researchers.

Nevertheless, we need to acknowledge that the current diagnostic system does not adequately take into account the subthreshold phenomenology, which limits the possibility of considering its influence in the disease course. In a recent paper, the lifetime prevalence of subthreshold bipolarity in the general population has been estimated to be 1.4% (1).

Among the multiple borders of bipolar spectrum, three appear to have clinical relevance. The first is the widely accepted schizophrenia/bipolar I continuum. Electroconvulsive therapy, lithium and atypical antipsychotics have contributed to the progressive erosion of the schizophrenia borders, to the advantage of bipolar spectrum diagnoses. The continuum schizophrenia-schizoaf-fective-mixed-psychotic bipolar-unipolar

psychotic, initially supported by treatment response, found recent support from molecular genetics and imaging data. Indeed, the motor and cognitive disturbances, ranging from retardation to catatonic excitement, as well as the cognitive decay in chronic mania and the so-called negative symptoms, may represent a common ground between mood disorders and schizophrenia. In our opinion, the identification of subtypes may be facilitated by a clustering process rather than a simple comparison between two diagnoses. Such a process will need biomarkers that are more likely to be associated with psychopathological dimensions than with current diagnostic categories.

The second border is the bipolar/“unipolar” depression continuum, which is still the target of a remarkable research effort initiated by the pioneering work of H. S. Akiskal, who proposed different subtypes of bipolarity. Our data and clinical experience emphasize the relevance of subthreshold bipolarity, that consists of multiple dimensions spanning the entire bipolar/unipolar continuum. Most of these dimensions, such as psychomotor activation and retardation, suicidality, irritability, diurnal variation and need for sleep, can be measured by means of a traditional clinical evaluation, aided by questionnaires that assess the lifetime presence of typical, atypical, precursor and residual symptoms and signs. Such an approach may contribute to increasing the validity and the diagnostic accuracy while preserving the current criteria for bipolar II disorder.

In a large sample of patients with bipolar and unipolar disorder we demonstrated the ability of a “psychomotor activation” dimension to identify subgroups of subjects with a progressively higher likelihood of belonging to the bipolar category (2). Only 25 patients with unipolar depression out of 571 (4.4%) were misclassified by classification tree analysis as belonging to bipolar II disorder group.

Moreover, in a sample of 291 SCID-diagnosed unipolar patients (3), 9 patients (8 treated with selective serotonin reuptake inhibitors and one with interpersonal psychotherapy) developed an episode of mania or hypomania during

the course of the study. When we examined their pre-treatment factor scores on the lifetime MOODS questionnaire, we found that 8 out of 9 exceeded at least one of the thresholds on psychomotor activation, mixed instability or suicidality measured by this questionnaire.

A third border of the bipolar spectrum is subthreshold bipolarity which may be observed in a variety of disorders, including anxiety, eating and personality disorders. In these cases, mood dysregulation may be secondary as well as primary and genetically independent. This is similar to what we observe for medical illnesses. For instance, myocardial infarction, kidney failure and pulmonary edema can be progressive manifestations of a single disease or represent three relatively independent disorders. Therefore, it appears to be hazardous to include different categories such as anxiety or eating disorders in the bipolar spectrum, since they often stand in a relationship of comorbidity. Genetic research has moved through models with growing levels of complexity: from “one disorder-one gene” to “one disorder-multiple genes” and finally to a model envisioning a group of genes controlling one or more psychological or psychopathological trans-nosographic dimensions.

In conclusion, the clinical validity of a diagnosis should include the ability to predict evolution, establish prognosis and inform treatment choice. Such goals are better achieved when nosography is linked to biological mechanisms. Therefore, we agree with the need to retain the current categories until more insight into their etiology is achieved and until valid biological markers are identified and

can be utilized in clinical practice. This would avoid problems that result from rapid and continuous changes in diagnoses and classification.

However, it must be noted that the present categories do not consider the halo of subthreshold and atypicality that surrounds each of them. An integration of the categorical classification with a dimensional approach could improve the ability to measure bipolarity and predict the progression to bipolar disorder. Subthreshold bipolarity, though a strong predictor, does not necessarily warrant a change in diagnosis. Given our poor ability to predict which individuals with major depression will develop hypomania or mania, close longitudinal monitoring remains the best tool for an early diagnosis of patients whose major depressive disorder moves toward a bipolar diagnosis (4).

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Bipolar spectrum: has its time come?

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Strakowski et al carefully assess the risks versus benefits of broadening the diagnosis of bipolar disorder and con-

clude that “until research findings can provide better insight into the validity of a broader conception of bipolar disorder, clinical expansion to a ‘spectrum’ concept should be considered with caution”. They argue that such expansion should await evidence that the concept, and clear definition thereof, lead to improve-

ments in treatment development or in our understanding of etiopathogenesis. As the authors point out, one problem is that there are currently multiple definitions of “bipolar spectrum” and it is not clear that the risks and benefits associated with adopting one of these concepts are necessarily the same as adopting another of these concepts.

Retracing the recent history of psychiatric diagnosis may help us to understand why we find ourselves having this debate. As Hyman points out (1), roughly coincident with the advent of disorder-specific pharmacotherapies and psychotherapies, Western psychiatry moved from very vague disorder constructs to a focus on reliability. This focus provided a shared language that facilitated an explosion of controlled research on these new medications and psychotherapies which continues to this day; however, it also had the effect of reifying the categories. Those categories then became the basis for studies of genetics and other biomarkers such as the cognitive ones discussed by Strakowski et al, as well as those identified in various forms of neuroimaging. And, therein, lies the problem. In most cases, each of these study methods finds some evidence to suggest that the distinct categories are correct and some evidence for a bipolar spectrum, however defined. Thus, to some extent our very reliable categories can be considered to have been a barrier to understanding the etiology of mental disorders and to the development of new approaches to treating them.

The US National Institute of Mental Health (NIMH), in its Research Domain Criteria (RDoC) Project (2), is currently taking a completely different approach to this conundrum by looking at five domains believed to be relevant to mental disorders (*negative valence systems* including fear/extinction, stress/distress and aggression; *positive valence systems* including reward seeking and reward/habit learning; *cognitive systems* including attention, perceptions,

working memory, declarative memory, language behavior and cognitive [effortful] control; *systems for social processes* including imitation, theory of mind, social dominance, facial expression identification, attachment/separation feat and self-representation areas; and *arousal regulatory systems* including arousal and regulation and resting state activity) across seven increasingly broad units of analysis (genes, molecules, cells, circuits, physiology, behavior and self-reports). This approach is intended to be complementary to the diagnostic developments taking place in the DSM-5 and ICD-11.

The primary intention of the RDoC is to advance science, while the DSM and ICD must serve multiple purposes, including clinical decision-making, clinical record-keeping, regulatory decision-making and forensics. Thus, the NIMH approach may eventually provide a better way of understanding which aspects of “bipolarity”, however defined, are common across the “bipolar spectrum”, however defined. Working from the RDoC perspective, there would be nothing problematic about the fact that bipolar I disorder and bipolar disorder “not elsewhere classified” or NEC (the new term being proposed for what was formerly “not otherwise specified” or NOS) are similar with respect to the genes related to reward-seeking, but different with respect to the genes related to cognitive control. Concern about benefits and risks would not be relevant. Rather, the focus would be on understanding what combination of genes, coupled with what combination of life experiences, leads to the reward-seeking unmodulated by any sort of cognitive control that is characteristic of full-blown mania in one individual and to the modulated reward-seeking that is characteristic of mild hypomania in another individual.

There is little doubt that efforts to date to understand the genetic basis of major psychiatric disorders such as schizophrenia and bipolar disorder, despite their very high heritabilities, have

been hampered by our categorical diagnostic approaches (and, early on, by the naïve hope that we were dealing with Mendelian traits). An approach such as the one being proposed for the RDoC, which avoids the category vs. spectrum dichotomy, seems more likely to bear fruit in terms of understanding etiology. How it might relate to our understanding of treatment effects and to the development of improved treatments is, perhaps, less clear.

Having had the opportunity to treat patients with mood and anxiety disorders through most of the psychopharmacologic era and virtually all of the disorder-specific psychotherapy era, I have witnessed an evolution from more specific pharmacotherapies (e.g., tricyclic antidepressants and typical antipsychotics) to ones that seem to treat a broad range of conditions (e.g., atypical antipsychotics and the SSRIs/SNRIs). Likewise, psychotherapies originally developed for unipolar depression have now been adapted to the needs of those with anxiety disorders and bipolar disorders. It occurs to me that a better understanding of for whom our treatments work might be obtained by “dismantling” our current disorder groups and subgroups in the way the RDoC proposes and using the RDoC parameters in sophisticated analyses of treatment moderation and mediation. Once we have those answers, a final step could be figuring out how to define useful categories that represent combinations of the RDoC parameters. Then, broadening our constructs might not be as risky as it currently appears.

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Broadening bipolar disorder – by design or by accident?

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The discussion by Strakowski et al makes explicit a state of affairs that has not often been clearly articulated. That is, there is a tension between narrow and broad definitions of bipolar disorder in adults just as there is in children and adolescents. However, while the concept of a bipolar spectrum from cyclothymia to schizoaffective mania is well recognized, the real expansion of the bipolar disorder diagnosis may have been the unintended consequence of certain DSM decisions – not a trivial consideration given that we are on the cusp of a new DSM. In the following paragraphs, I submit some hypotheses.

First, the concept of an episode of mania was not defined well in the DSM-III. A distinct period was defined as “at least a week”, but no offset was required to delineate an episode, nor was there a requirement that the episode be different from one’s “usual self”. The DSM-III-R muddied the waters even further by eliminating duration criteria and just requiring “a distinct period”. As we see with much of the childhood bipolar disorders research, the onset of a manic episode is said to have begun in early childhood and has either never stopped (1,2) or has lasted for years. It is difficult to consider an episode as something that has characterized one’s entire life. On the other end of the duration spectrum, ultra-rapid cycles, and ultradian cycles, i.e. distinct periods that last minutes to hours, are very difficult to distinguish from mood lability and temper tantrums, certainly in children and probably adults, too. The DSM-5 committee appears to have recognized this misunderstanding and, at least according to the DSM-5 website, is proposing changes in “episode” definition.

Another DSM change that may have altered bipolar disorder prevalence is the elimination of “irritability” as a symptom of depression because mania was felt to

be a better home for that symptom. It is not surprising that the frequency of “mixed episodes” increased dramatically after DSM-III-R. In the DSM-III, the criterion for a major depressive episode was “dysphoric mood” which was characterized by, among other things, irritability. Childhood depression was initially studied with interviews that incorporated irritability in depression. For instance, the 1983 version of the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) stated “Some children will deny feeling ‘sad’ and only report being ‘bad’. If during a depressed period patient is also irritable this should be counted as dysphoric mood and rated as such” (3). When it came time to re-examine criteria, the DSM-IV child mood subcommittee and I (I was chair) insisted that irritability be kept in the definition of childhood depression, since there was no evidence to eliminate it. What has evolved in recent research suggests it was a wise decision. Irritability in a number of studies predicts a depressed and anxious outcome, not a bipolar outcome (4-6).

Another downstream result of DSM criteria is the assessment approach that has arisen to diagnose children and adults with mood disorders. Although interviews all do a decent job of assessing a review of systems, none of them does a very good job of ascertaining history (7). Some interviews obtain a time line but those data are not entered. It is, therefore, impossible to review anyone’s interview protocol and reconstruct the history of any given patient. We cannot tell whether the subject of the interview has “classic” or narrowly defined manic-depressive illness or more broadly diagnosed bipolar disorder. In child studies, furthermore, all sorts of other assessment issues occur that can broaden the diagnosis. The “OR” rule accepts as positive any informant’s symptom endorsement (parent OR child), so more children will have mania than if parent/child agreement is required. Changing the meanings of elation and grandiosity will get a different sample than if requiring adult definitions. Severe mood dysregulation was

designed to capture irritable, explosive youth with “broad phenotype” mania and contrast it with narrow phenotype (8). However, those who characterize children with mania as very irritable and explosive do not consider them to have the “broad phenotype”.

As consumers, we never know whether the sample being described in any given study is “narrowly” or “broadly” diagnosed. The implications of understanding study results are considerable. Findings on age of onset of bipolar disorder, a marker that may have genetic implications, differ depending on one’s conceptualization. Bipolar disorder traditionally has an age of onset in late adolescence and young adulthood (9). However, those findings are probably based on “classic” bipolar disorder. The STEP-BD data (10) report subjects with onsets in early childhood. Perhaps subjects in this large sample are “broadly diagnosed”, which is also one of the reasons they do so poorly in treatment. They may well be emotionally dysregulated people who “meet criteria” but do not have “classic” bipolar disorder. They are similarly impaired but should be identified as separate from the narrow phenotype.

As Strakowski et al point out, the research question of whether and when a broad vs. narrow concept of bipolar disorder has traction is important. The tragedy is that there is no way to resolve the question because of how we collect and how we report the data.

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The continuum of unipolar depression - bipolar II depression - bipolar I depression: different treatments indicated?

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Strakowski et al indicate that bipolar depression may need to be treated differently from unipolar depression because in bipolar depression antidepressants may be ineffective and may precipitate the risk of a switch to (hypo)mania (and induction of rapid cycling). While this could be a major argument to discriminate bipolar depression from unipolar depression, a critical appraisal of the available literature is indicated.

First, are antidepressants ineffective in bipolar depression? Compared to around 1,500 randomized controlled trials (RCTs) with antidepressants in unipolar depression, there are around 15 RCTs in bipolar depression and only four of them exceeded 50 patients per treatment arm. Therefore, the main conclusion is that, compared to unipolar depression, bipolar depression is heavily understudied (1). Nevertheless, in a meta-analysis, antidepressants as a group appeared to be effective (1). Of the four larger studies, two reported positive results. The first study found that the combination of fluoxetine and olanzapine was more effective than placebo plus olanzapine (2). The second study reported response rates of 50-60% when sertraline, bupropion or venlafaxine was added to an ongoing treatment with mood stabilizers (3). The limitation of this study was

the lack of a placebo arm. On the other hand, in a third study, paroxetine was not more effective than placebo, while two doses of quetiapine (300 and 600 mg/day) did separate from placebo (4). Finally, in the STEP-BD study, sertraline or bupropion as add-on to ongoing treatment with (among other medications) lithium or valproate was not found more effective than the addition of placebo (5). Although this is the largest study which investigated the efficacy of antidepressants in bipolar depression, it has major methodological limitations (e.g., patients were allowed to continue with another antidepressant during the first two weeks of the study; they could also use other drugs with an antidepressant effect, such as quetiapine, olanzapine and lamotrigine; 69% of the patients participated at the same time in a study comparing three different forms of psychotherapy with treatment as usual). It is clear that the conclusion that antidepressants are not effective cannot be drawn on the basis of this study. My overall conclusion is that, due to a lack of well designed RCTs, we can only state that it has not (yet) been proven that antidepressants are effective in bipolar depression.

Second, do antidepressants cause a switch into (hypo)mania and rapid cycling? In our meta-analysis (1), we did not find that in the acute treatment of bipolar depression antidepressants were more often associated with a switch into (hypo)mania than placebo. However, in all studies comparing different anti-

depressants, the treatment arms with a tricyclic (TCA) were associated with a greater risk of switch into (hypo)mania than the treatment arms with other antidepressants, suggesting that TCAs have a greater risk of switch. Concerning the risk associated with long-term antidepressant treatment, we argued that there is a scarcity of randomized studies, and that the available studies all suffer from various forms of bias (6). Nevertheless, we concluded that antidepressants, when combined with a mood stabilizer, seemingly do not induce a switch into hypomania or mania. Ghaemi et al (7) presented a meta-analysis of seven RCTs in which antidepressants were used for at least 6 months. Three of these RCTs (total n=50) compared the effects of antidepressants monotherapy with placebo; five (total n=246) compared antidepressants plus a mood stabilizer versus a mood stabilizer alone (or in combination with placebo); and three (total n=108) compared antidepressants alone with a mood stabilizer alone. In most of the studies the antidepressant was a TCA. When combining all RCTs, the antidepressants yielded a significant 27% lower risk of a depressive recurrence versus control treatment without an antidepressant, but also a significant 72% greater risk for a manic recurrence. However, in RCTs with an antidepressant alone versus placebo, the only significant result was fewer depressive recurrences with the antidepressant, while in RCTs with an antidepressant alone versus a mood stabilizer alone

(lithium), the only significant result was fewer manic recurrences with lithium. Therefore, my conclusion is that antidepressants do protect against depressive recurrences, while lithium does protect against manic recurrences. Whether antidepressants may accelerate episode frequency and/or cause other forms of destabilization in patients with bipolar disorder remains to be properly studied.

In conclusion, there is not enough evidence to conclude that bipolar depression needs to be treated differently from unipolar depression. Especially in bipolar II depression, antidepressants still have a role even in monotherapy, as also suggested by recent guidelines (8,9). Therefore, bipolar I depression and unipolar depression should be seen as the ends of a continuum, with arbitrary demarcations and bipolar II depression in between.

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At the edge of the bipolar spectrum: primacy of affective over psychotic symptoms or vice versa?

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Strakowski et al should be congratulated upon this very comprehensive and well balanced essay of pros and cons about a broadening of diagnostic criteria for bipolar disorder. They very well point out potential benefits for otherwise insufficiently treated patients, but also that, given our lack of a full understanding of the biological basis, such a broadening might be premature in treatment research.

So far, we still have a long way to go if we want to define groups of mental disorder by shared genetic underpinnings or biological markers, and thus we rely on phenomenology and derived categorizations when we conduct treatment research. And, in my opinion, these categorizations still need to be strict, reliable and largely unaltered over time, until we find better (and tested) definitions. With rising placebo response rates in randomized clinical trials and subsequent narrowing of drug-placebo differences, it becomes increasingly difficult to identify specific benefits of a drug, e.g. against core manic symptoms. Allowing, for example, patients into trials whose “mania” manifests itself just by agitation and irritability may give rise to large numbers of subjects with manifold features which are in fact related to substance use or personality. As a consequence, we would not expect a drug to differentiate from placebo unless it probably has a strong sedative component, but would we consider this as a true and specific antimanic agent?

Strakowski et al also make it quite clear that bipolar disorder has a huge overlap of symptoms and features with other major mental disorders. Besides the grey zone that does (or does not) divide bipolar disorder from other affective, or more generalized, emotional states, a fascinating question is the relationship of bipolar disorder and schizophrenia. As Strakowski et al point out, a future trend might be, “based on risk factor and clinical history considerations, that bipolar disorder may be better classified with schizophrenia in a psychotic cluster than with unipolar depression in an emotional cluster”. But, how valid is the clinical observation of psychotic symptoms to serve as a basis of categorical clustering, and are they not more likely subsidiary to emotional processes?

Looking back, for many decades bipolar disorder has been an orphan of psychiatry, whereas schizophrenia was considered the most important challenge. At the beginning of last century, it was still well accepted that all psychotic symptoms arise from mood dysregulation (1). In the post-Kraepelinian area, diagnostic habits continuously shifted towards schizophrenia, putting much more weight on psychotic than affective symptoms. Kraepelin's successor Schneider reports that the ratio of patients diagnosed with schizophrenia vs. cyclothymia at the Munich hospital between 1934 and 1936 was greater than 5:1, while in the same department 35 years earlier Kraepelin had stated that 10-15% of hospital admissions were suffering from manic-depressive illness (2). Whereas it was hard to neglect the obvious existence of (unipolar) depression,

bipolar disorder was almost cut down to clinical (and research) insignificance. This tendency of overdiagnosing schizophrenia at the expense of bipolar disorder continued well into the 1970s (3).

Now the pendulum seems to swing back the other way. Lake and Hurwitz (4) questioned the validity of the diagnosis of schizophrenia, postulating that a single disease, a mood disorder with a broad spectrum of severity, accounts for functional psychoses. Compared to schizophrenia, and despite all limitations, diagnostic criteria for bipolar disorder may still have a better validity (5). Schneiderian first-rank symptoms (FRS) are not exclusive to schizophrenia; they also occur in some bipolar patients (6), although they may be more frequent and more severe in patients with schizophrenia than bipolar disorder. Schizophrenia patients with FRS during the acute phase are more likely to have poorer long-term

outcome than those who do not have these symptoms. However, the same is true also for bipolar patients exhibiting FRS (7).

But what really matters in end is how we can improve our bipolar patient's life. Strakowski et al make it clear that the categorical vs. spectrum discussion is not a academic one in an ivory tower, but has clinical significance: "People with bipolar disorder are identified from the general population in order to assign therapies that will alleviate their suffering (i.e., symptoms), ideally through evidence-based treatment guidelines developed from past studies of similar individuals".

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A renovation of psychiatry is needed

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Strakowski et al carefully discuss the benefits and risks of broadening the diagnosis of bipolar disorder, from treatment and research perspectives. Their conclusion that it is premature to broaden the bipolar disorder diagnosis before the identification of an etiology common to bipolar spectrum disorders is quite reasonable.

It is theoretically apparent that patients currently receiving a diagnosis of "major depression" include those who will develop bipolar disorder in later life. However, those patients cannot be identified just by clinical interviews. Only after the neurobiological basis of bipolar disorder is discovered and an *in vivo* identification of such neurobiological signature becomes feasible, it will be possible to reliably diagnose potential bipolar disorder in depressive patients. If we make a bipolar spectrum disorder diag-

nosis based solely on clinical interview, false positive cannot be avoided. Some patients might benefit from a correct diagnosis of potential bipolar disorder, but others will be misdiagnosed and receive inadequate treatment.

Recently, family and genome wide association studies have shown that bipolar disorder and schizophrenia share some common genetic background. The risk of schizophrenia is increased in first-degree relatives of probands with bipolar disorder, and the risk of bipolar disorder is increased in first-degree relatives of probands with schizophrenia, with relative risks between 2.4 and 5.2 (1). In the study by the International Schizophrenia Consortium, the involvement of thousands of common alleles of very small effect was suggested in schizophrenia. It was shown that this polygenic component also contributes to the risk of bipolar disorder (2). This finding apparently supports the idea of a continuum between these two disorders. However, it should be noted that 7% of patients with schizophrenia were also diagnosed

as having bipolar disorder in the former study. Can we discriminate between "existence of common pathology between these two disorders" and "difficulty in differential diagnosis of these two disorders" using currently available research schemes? If we loosen the diagnostic boundary based on the interpretation that these two disorders share common pathology, future research will suffer from lack of adequate clinical validity. If we deconstruct psychosis and combine these two disorders, we will only return to the chaos before Kraepelin.

We psychiatrists have been trying to differentiate mental disorders based on clinical interviews since the era of Kraepelin. After an extensive effort, we realize now that our diagnostic criteria are not perfect. Because there was little progress in psychiatric diagnosis in the last century, refinement of DSM can make only modest improvement, if any. To further refine psychiatric diagnosis, the only way is to establish a new disease classification based on the neurobiological features of each mental disorder.

A recent study of 153 brains of non-demented elderly people reported that patients receiving a diagnosis of de-

pression during their life by interview showed more Lewy bodies in locus coeruleus. At the same time, neurofibrillary tangles were also more frequently seen in this region (3). Can we differentiate depression in the early stages of diffuse Lewy body or Alzheimer's disease from depression without neuropathology only by clinical interviews? We psychiatrists should be aware that we cannot identify "diseases" only by interviews. What we are doing now is just like trying to diagnose diabetes mellitus without measuring blood sugar.

Medicine is fundamentally based on pathology. Psychiatry should also be

based on pathology rather than psychology. When the concept of Alzheimer's disease was established more than 100 years ago, there were few staining methods, such as silver and Nissl staining. After one century, we have completely sequenced the human genome, and we can potentially stain tens of thousands of molecules in the brain by mRNA in situ hybridization or immunohistochemistry. All the technologies we need to refine psychiatry have already been established. What we should do is to study the neurobiological basis of mental disorders using updated technologies and give rise to the renovation in psychiatry.

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Self-experience in the early phases of schizophrenia: 5-year follow-up of the Copenhagen Prodromal Study

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Despite the avalanche of empirical data on prodromal/"at risk" conditions, the essential aspects of the vulnerability to the schizophrenia spectrum remain largely unaddressed. We report here the results of the Copenhagen Schizophrenia Prodromal Study, a prospective, observational study of first admission patients in putative state of beginning psychosis (N=151) with a follow-up length of 60 months. At follow-up, the rate of conversion to schizophrenia spectrum diagnosis was 37%, whereas the conversion rate from schizotypal disorder to schizophrenia was 25%. High levels of perplexity and self-disorders baseline scores yielded the best prediction of the subsequent development of schizophrenia spectrum disorders. Escalating transitions within the spectrum (i.e., from schizotypal disorder to schizophrenia) were not associated to any candidate psychopathological predictor.

Key words: Schizophrenia spectrum, schizotypal disorder, psychosis, diagnostic stability, prodrome, vulnerability, anomalous subjective experiences

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In most of the Western world, several projects are being implemented, focusing on the pre-onset identification and early treatment of schizophrenia and other psychoses, based on the assumption that untreated illness becomes more chronic, socially invalidating and treatment resistant (1-4). In this context, subtle (non-psychotic) qualitative anomalies of subjective experience (such as disorders of affect, perception, bodily experience, cognition, volition and action) have regained the status of potential precursors of schizophrenia, and specific subsets of these anomalies (e.g., at risk basic symptoms) have been proposed for the pragmatic purposes of early detection (5-9).

Our research programme, in continuity with the Copenhagen high-risk, adoption, and linkage studies (10-16), focuses on trait features characteristic of the typical core of schizophrenia (17-19). We have studied in particular some alterations of the very experience of the self (i.e., self-disturbances, SDs). These comprise an unstable sense of self-presence and first person perspective, a lack of basic sense of self-identity, disturbances of the tacit fluidity of the field of awareness, hyper-reflexivity, and perplexity, i.e. a pervasive difficulty in grasping the familiar and taken for granted meanings (19-21). SDs are not to be considered as contingent symptomatic constellations, but rather express enduring, profound trait-like distortions of subjectivity, articulating specific, non-psychotic modes of experience (i.e., changes in the qualitative, first-personal givenness of experience) (19,20).

Our first empirical report on SDs (9) was based on explorative interviews with 19 first admission patients with the diagnosis of a schizophrenia spectrum disorder, and was supported by a similar report from Norway (8). We wished to replicate these findings in a systematic prospective study of consecutive first-admitted patients. We aimed to assess anomalies of subjective experience (including SDs), and their longitudinal association with the schizophrenia spec-

trum disorders. Moreover, we aimed to explore the diagnostic stability of schizophrenia spectrum (over an observation period of 5 years) and identify potential clinical-psychopathological predictors for intra-spectrum diagnostic spiralling (schizotypal disorder transiting to schizophrenia) and towards-spectrum diagnostic spiralling (i.e., incident cases of schizophrenia spectrum, either schizotypal disorder or schizophrenia).

METHODS

The sample consisted of 155 first-admission patients with age <40 years consecutively referred to the University Psychiatric Center Hvidovre, during the period from September 1, 1998 to September 1, 2000. The psychiatric center serves a catchment area of approximately 130,000 inhabitants, residing in the City of Copenhagen.

Exclusion criteria comprised a diagnosis of melancholia, bipolar disorder or organic brain disorder, primary or clinically dominating substance abuse, involuntary or forensic patient status. Severely psychotic, aggressive patients were first interviewed after initial stabilization.

The patients participated upon a written informed consent. Four patients were ultimately excluded because they were diagnosed with organic psychiatric disorder, undetected at the inclusion, leaving a total of 151 subjects.

At baseline, the patients were assessed with a semi-structured interview comprising overall psychosocial and family history (including second informant information), psychopathological anamnesis and psychodiagnostic assessment with a phenomenological exploration of anomalous subjective experiences (22,23). These were explored with the Bonn Scale for the Assessment of Basic Symptoms (BSABS) (24), expanded with additional items concerning self-experience

(23). All interviews were performed by a consultant psychiatrist with extensive research interview experience, who was trained in the use of BSABS by the Huber-Klosterkötter group in Germany. On the basis of all information, an ICD-10 operational research diagnosis was allocated by the interviewer after case discussion with another senior clinician.

Five years later, the sample was located through a national personal register (25) and invited to participate upon a written consent. The reassessment, blind to the information gathered at the initial assessment, repeated all the baseline interview components (22,23). Briefly, those included the OPCRIT Checklist (26), the BSABS (24), the Positive and Negative Syndrome Scale (PANSS) (27), and the DSM-III-R Severity of Psychosocial Stressors Scale: Adults (28). Expressive features (e.g., affect modulation, contact-quality, gaze, stereotypies, mannerisms, disorganization, and disorder of language) were coded on the mental status items, developed and used in the Copenhagen High Risk Study (13) and the Copenhagen Linkage Study (29,30). The re-assessment interviewer was a consultant psychiatrist with research experience. She allocated an ICD-10 research diagnosis at a case conference with another senior psychiatric clinician, who reviewed the chart material and witnessed the patient interviews. Reassessment diagnoses were lifetime and based only on the follow-up interview and chart material.

During the follow-up period, the patients adhered to their individual treatments led by clinicians in charge. Thus, treatment modalities and their efficacy were not part of the study.

An interrater reliability assessment between the two interviewing psychiatrists, checking all study instruments, was performed and demonstrated excellent reliabilities. For example, in the section dealing with anomalies of subjective experience, out of 41 items targeting perplexity, self-disorders and perceptual disorders, 16 had a very good kappa (i.e., above 0.81), 20 a good kappa (i.e., between 0.61 and 0.80), four had a moderate kappa (i.e., between 0.41 and 0.60) and one (diplopia/oblique vision) a fair kappa.

The diagnoses were grouped into three major categories:

group 1 with schizophrenia/all non-affective, non-organic psychoses; group 2 with schizotypal disorder; and group 3, a miscellaneous category containing all other disorders outside the schizophrenia spectrum (e.g., panic disorder, major depression, obsessive-compulsive disorder).

We adopted a dimensional approach to characterize the psychopathological profile in terms of both major diagnostic symptoms (i.e. positive, negative, formal thought disorder, affective-anxious) and anomalous subjective experiences. These experiences were grouped in three *a priori* scales: perplexity, self-disorders, perceptual disorders. Briefly, “perplexity” addresses a sense of lacking immersion in the world, lack of spontaneous grasping of commonsensical meanings, puzzlement, and alienation; “self-disorders” maps anomalies of pre-reflective self-awareness, i.e., of the tacit sense of existing as a self-coinciding subject of experience and action; “perceptual disorders” encompasses a wide variety of non-psychotic perceptual (mostly visual-acoustic) aberrations.

SAS 9.1 version was used with both parametric and non-parametric and uni- and multivariate approaches. Diagnostic transitions were charted graphically. Predictors of diagnostic transitions of escalating severity (i.e., intra-spectrum from schizotypal disorder to schizophrenia, and towards-spectrum from other diagnosis to schizotypal disorder or schizophrenia) were weighted by binary logistic regression.

RESULTS

Baseline socio-demographic, clinical and psychopathological features of the sample are reported in Table 1. Whereas PANSS scores decreased linearly from schizophrenia to non-spectrum disorders (with schizotypal disorder in intermediate position), this was not the case for anomalous subjective experiences (schizophrenia and schizotypal disorder had comparable scores, which were significantly higher than those of non-spectrum disorders).

The full face-to-face reassessment interview was obtained

Table 1 Baseline profiles of the diagnostic subgroups: socio-demographic and psychopathological features

	Schizophrenia/ Psychoses (N=51)	Schizotypal disorder (N=50)	Other psychiatric disorder (N=50)	p
Age at inclusion (mean±SD)	25.3±5.0	24.6±4.4	26.2±4.6	0.183
Male/female	26/25	14/36	17/33	0.059
Age of illness onset (years, mean±SD)	20.9±6.3	17.5±5.2	18.7±6.0	0.028
Duration of illness (months, mean±SD)	54.6±59.2	84.4±60.9	90.8±77.7	0.008
Duration of untreated psychosis (months, mean±SD)	27.3±42.9	-	-	-
PANSS positive symptoms (mean±SD)	19.06±5.8	11.9±3.1	9.1±2.3	<0.0001
PANSS negative symptoms (mean±SD)	16.95±6.06	13.3±4.0	9.7±3.3	<0.0001
Formal thought disorders (mean±SD)	4.31±3.07	2.8±2.3	1.0±1.5	<0.0001
Anxiety and affective symptoms (mean±SD)	5.91±3.60	8.6±3.2	7.8±3.3	0.0003
Perplexity (mean±SD)	5.27±4.39	5.63±3.3	2.4±3.1	<0.0001
Self-disorders (mean±SD)	9.59±6.11	9.4±4.8	4.2±4.2	<0.0001
Perceptual disorders (mean±SD)	2.99±3.41	2.6±3.0	1.0±1.5	0.0008

PANSS – Positive and Negative Syndrome Scale

Statistical test: Kruskal-Wallis (non-parametric ANOVA) or X-square when appropriate

in 99 patients (64%). Four patients (3%) declined personal interview but accepted a telephone interview. Nineteen patients refused (12%) but could be followed-up and reassessed through the chart material over the entire 5 years period. Thus, of the initial sample of 151 patients, 121 (80%) could be rediagnosed. There were no differences in age, gender or education between the interviewed and non-interviewed groups. The groups did not differ with respect to the diagnosis at the initial assessment. However, the non-interviewed patients more often reported substance abuse at the initial assessment ($p=0.02$). For the personally re-interviewed patients, the mean and median follow-up periods were 1889 and 1811 days, respectively (approximately 5 years, range: 1334-2571 days).

Table 2 and Figure 1 show the diagnostic changes over the 5-year follow-up period. The overall kappa value of agreement for the three diagnostic groupings across the first and the follow-up assessments is 0.64, which reflects a rather pronounced stability.

Within group 1, five patients, initially diagnosed with acute non-affective psychosis, were rediagnosed with paranoid schizophrenia. Only three patients left the group 1: one, originally diagnosed with hebephrenic schizophrenia, was rediagnosed as suffering from a schizotypal disorder; another patient with acute non-affective psychosis was rediagnosed

with bipolar disorder; a third patient with schizophrenia was rediagnosed as suffering from a psychotic depression. Thus, of the 43 patients originally in group 1, 40 still remained there at the follow-up (93%).

Group 2 also manifested a relative stability of diagnosis. Ten schizotypal patients (25%) were rediagnosed with schizophrenia 5 years later, one with affective disorder (depression) and one with borderline personality disorder (hence only 5% exited from the schizophrenia spectrum).

From group 3, two patients (originally with mixed and borderline personality disorder) were rediagnosed with schizophrenia. Twelve additional patients (initially diagnosed with depression, $n=3$, or mixed, borderline or unspecified personality disorder, $n=9$) were rediagnosed with schizotypal disorder.

Schizotypal patients rediagnosed with schizophrenia were 25% of the original group. Logistic regression analysis contrasting these patients and the other 30 who did not change their diagnostic status revealed no significant influence of any baseline variable (i.e. age, sex, psychopathological dimensions, anomalous subjective experience, total number of individual schizotypal criteria).

In total, 14 incident cases with a schizophrenia spectrum disorder were diagnosed at the follow-up. Logistic regression analysis (comparing these 14 individuals with the individuals remaining in group 3) revealed that high baseline scores on self-disorders and perplexity predicted a subsequent evolution of the schizophrenia spectrum disorder (self-disorders: Fischer's exact $p=0.003$, $OR=12.00$; 95%CI 2.15-67.07; perplexity: Fischer's exact $p=0.02$, $OR=6.11$; 95%CI 1.34-27.96). The PANSS measures were not predictive and the transition was gender- and age unrelated (Table 3).

Table 2 Changes in lifetime diagnoses from inclusion to follow-up

	BASELINE			Total number
	Schizophrenia/ Psychoses	Schizotypal disorder	Other psychiatric illness	
Schizophrenia/ Psychoses	40	10	2	52
Schizotypal Disorder	1	28	12	41
Other psychiatric Illness	2	2	24	28
Total number	43	40	38	121
Drop-outs	8	10	12	30

FOLLOW-UP

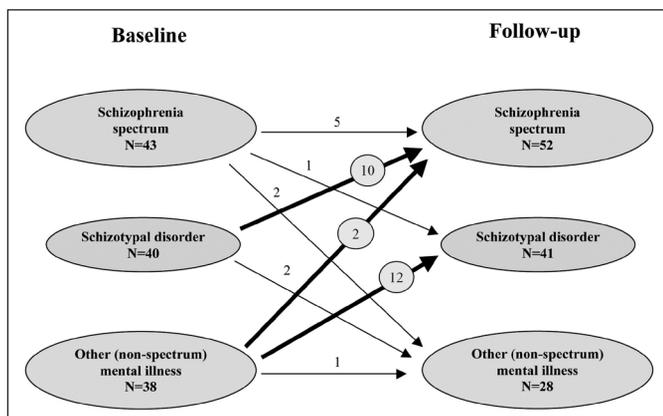


Figure 1 Diagnostic fluxes

DISCUSSION

The pragmatic diagnostic partition based on ICD-10 schizophrenia/non-affective psychosis, schizotypal disorder and other psychiatric illness revealed an overall high stability over 5 years ($kappa=.64$). The stability was higher for the diagnosis of schizophrenia (93%) than for schizotypal disorder (70%) and the diagnostically miscellaneous category "other psychiatric illness" (63%).

One fourth of the schizotypal patients were rediagnosed with schizophrenia at follow-up. However, none of the baseline socio-demographic or psychopathological variables (including the number and the frequency of individual schizotypal criteria) was predictive of this outcome. This suggests that these two spectrum phenotypes (schizotypal disorder and schizophrenia) are more dissimilar in degree than in kind. Concretely, schizotypal disorder appears to be a sub-psychotic condition, in many respects similar to schizophrenia. The ICD-10 category of schizotypal disorder seems to diagnose severely ill clinical cases that do not fully meet the criteria for schizophrenia. Those prospectively rediagnosed cases with schizophrenia appear to cross the border, at any

Table 3 Binary logistic regression with diagnostic transition to schizophrenia spectrum as follow-up outcome

	Spectrum				p	OR ^a	95%CI
	diagnostic conversion		No diagnostic conversion				
	High score (N)	Low score (N)	High score (N)	Low score (N)			
<i>Symptom dimensions</i>							
PANSS positive symptoms	8	6	13	11	1.00	1.13	0.30-4.26
PANSS negative symptoms	9	5	16	8	1.00	0.90	0.23-3.59
Formal thought disorder	8	6	10	14	0.50	1.87	0.49-7.08
Anxiety and affective symptoms	10	4	11	13	0.18	2.95	0.72-12.11
<i>Anomalous subjective experiences</i>							
Perplexity	11	3	9	15	0.02	6.11	1.34-27.96
Self-disorders	12	2	8	16	0.003	12.00	2.15-67.07
Perceptual disorders	8	6	8	16	0.19	2.67	0.69-10.36
	26-38 years (N)	19-25 years (N)	26-38 years (N)	19-25 years (N)		OR^b	
Age at inclusion	6	8	15	9	0.32	0.45	0.12-1.72
	Male (N)	Female (N)	Male (N)	Female (N)		OR^c	
Gender	5	9	8	16	1.00	0.90	0.23-3.59

Significant results in bold; p-value from Fischer's exact test for independence between changing/keeping diagnose and scoring high/low
OR^a – odds ratio if the scale score is high; OR^b – odds ratio if age is 26-28 years; OR^c – odds ratio if gender is female

moment of their clinical history, by a contingent intensification of this or that symptom (e.g., from constricted to flat affect; from privately experienced to publically accessible audible thoughts). Such considerations cohere with the recent findings of the NAPLS study, rediscovering (DSM-IV) schizotypal personality disorder as a possible “independent risk syndrome for psychosis” (31), and another Danish study (OPUS), which reported comparable diagnostic conversion rates from ICD-10 schizotypal disorder to schizophrenia (32).

Above one third of the subjects receiving a non-spectrum diagnosis at baseline were re-diagnosed within the schizophrenia spectrum five years later. On the contrary, only 5% of subjects originally allocated in the schizophrenia spectrum were re-diagnosed outside that category at the follow-up. With respect to the incident cases of schizophrenia spectrum, the comparison with the individuals remaining in the initial group indicated two clusters of anomalous subjective experiences that were predictive of the diagnostic transition: self-disorders and perplexity. None of the PANSS scores was associated with increased risk of transition. Overall, this indicates that self-disorders and perplexity capture rather essential features of the spectrum-proneness among clinical phenotypes. This is in line with converging evidences from other quantitative (16,33,34) and quali-quantitative (8,9,35) studies.

The results of the study must be viewed through some contextual limitations. The sample was based on referrals to a hospital-based inpatient unit. Hence the “caseness” (severity) threshold for referrals is probably higher than that associated to outpatient service admissions. Therefore, the sample features might be of limited generalizability to mental health systems with rich, easily accessible outpatient psychiatric services. Furthermore, we adopted diagnostic stability and transition within the ICD-10 categories as outcome variables. In particular, the incident cases of schizophrenia spectrum diagnosis (“transition to the schizophrenia spectrum”) constitutes a clinically and conceptually different construct than the “transition to psychosis” which is the ty-

pical outcome in prodromal/ultra-high-risk research (where psychosis threshold is conceived as a quantitatively defined severity cut-off point of positive psychotic symptoms) (36). Finally, the data collection is based on the two chronological nodes – baseline and five-year reassessment – and is therefore unsuitable to track a more fine-grained timing of the transitions related to relapse and possible readmission. In this respect, it must be emphasized that, whereas the baseline assessment was related to consecutive referrals and, therefore, coinciding with severe and acute psychopathological states, this was not the case for the reassessment 5 years apart, which is an arbitrary point in the natural history of the illness (37).

CONCLUSION

In conclusion, our results indicate that certain trait-like anomalous subjective experiences, particularly self-disorders and perplexity, could be important prognostic indicators for identifying (within newly admitted subjects) those with vulnerability traits of a schizophrenia spectrum disorder. Crucially, none of the canonical psychopathological dimensions that are usually considered as a core assessment standard of schizotropic symptomatology (e.g., positive, negative, disorganized symptoms) showed any predictive power. The results also indicate that about one fourth of the subpsychotic configurations of the schizophrenia spectrum intercepted by the ICD-10 diagnosis of schizotypal disorder are re-diagnosed with schizophrenia within five years. This suggests that the current ICD-10 definition of schizophrenia relies on symptoms and signs set at a very high level of severity (and chronicity). Consequently, in a clinical setting, the category of schizotypal disorder includes less symptomatic, subthreshold patients, who would have been considered by the ICD-8 as suffering from non-paranoid or beginning paranoid schizophrenia (38-40).

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A randomized controlled effectiveness trial of cognitive behavior therapy for post-traumatic stress disorder in terrorist-affected people in Thailand

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Although cognitive behaviour therapy (CBT) is the treatment of choice for post-traumatic stress disorder (PTSD), there is no evidence of its success with PTSD patients still under direct threat of terrorist attacks. This study reports the first randomized controlled trial of CBT for PTSD terrorist-affected people. Twenty-eight survivors of terrorist attacks in southern Thailand were randomized to 8 sessions of either CBT or treatment as usual (TAU). CBT was modified to accommodate the realistic threats facing patients. There were independent assessments conducted before, immediately after, and 3 months following treatment. Main outcome measures included symptoms of PTSD (PTSD Symptom Scale - Interview), depression (Beck Depression Inventory) and complicated grief (Inventory of Complicated Grief). CBT resulted in significantly greater reduction in symptoms, including PTSD, depression, and complicated grief, at follow-up than TAU. Relative to TAU, CBT had stronger effect sizes at follow-up for PTSD, depression, and complicated grief. More patients in the CBT condition (75%) achieved high end-state functioning than participants in the TAU (33%). This preliminary evidence suggests that PTSD, depression, and complicated grief can be effectively treated despite ongoing threats of terrorism. Further, it demonstrates that non-specialist mental health workers in a non-western setting can be efficiently trained in using CBT, and this training can translate into successful treatment gains in trauma-affected individuals.

Key words: Cognitive behaviour therapy, post-traumatic stress disorder, complicated grief, terrorism, culture

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Cognitive behaviour therapy (CBT) is the treatment of choice for post-traumatic stress disorder (PTSD) (1-3). However, there is little information concerning the application of CBT in contexts where terrorism continues to directly threaten people with PTSD. In the context of repeated terrorist attacks across the world in recent years, the utility of CBT for people affected by ongoing terrorism has attracted marked attention. There is evidence that CBT can be efficacious in treating terrorist-related PTSD (4), but this evidence is limited to post-terrorism environments in which treatment occurs in a context of relative safety. To date, no randomized controlled trials of CBT have been reported in the context of ongoing active terrorist attacks.

There are reasons to question how CBT will function in contexts of ongoing terrorist attacks. The two major components of CBT involve exposure therapy and cognitive restructuring. Exposure therapy involves having the patient confront reminders of the trauma, typically by focusing on memories of the trauma or remaining with situational reminders (5). This practice presumes that extinction learning occurs, in which initial fear conditioning is inhibited by learning that trauma reminders now signal safety rather than danger (6). This goal may be difficult to reach, however, when reminders may be occurring frequently and actually result in harm to self or others – as is the case in the context of active terrorism. CBT has been shown to be efficacious with patients who are suffering ongoing threat, such as those suffering domestic violence (7). Terrorism may represent a more pervasive threat, however, because it involves intentional attacks on a communal basis, and this may compli-

cate the capacity for extinction learning, because of the frequent occurrence of harmful events happening to people in one's immediate environment.

Cognitive restructuring is based on cognitive models which posit that PTSD patients catastrophize about their reactions to the trauma and the likelihood of further harm (8). Accordingly, cognitive restructuring teaches the patient not to appraise the traumatic event or its aftermath in an excessively negative manner. This task may be hindered when appraisals about future threat may be partially realistic because of the actual likelihood of future harm. For example, people who have been exposed to a terrorist attack in a region that is frequently bombed may report an appraisal that their world is dangerous and they can never feel safe; this appraisal may be largely justified because of the frequency of bombings. For this reason, recent commentaries have noted the need to tailor cognitive restructuring to explicitly acknowledge the possibility of actual threat and to determine the relative risk when using cognitive restructuring (9). This approach attempts to teach the patient to appraise the likelihood of risk in realistic terms, and also understand the benefits of accepting a certain level of risk (e.g., being able to leave one's house and complete daily duties).

Another critical omission in the literature is the absence of effectiveness studies that adapt evidence-based approaches to terrorist-affected settings in non-western environments. This study attempted an effectiveness evaluation by adapting CBT in a non-western country and using local health providers. We conducted a randomized controlled trial of terrorism survivors in southern Thailand, where over 3,000 people

have been killed since 2004. This terrorist activity has arisen from extremist Muslim separatists operating against the Thai government. Many terrorist activities in the three southern provinces of Thailand have targeted schools, health workers, and other non-combatant people. We compared CBT and treatment as usual (TAU), which involved generic counselling, to treat PTSD, depression, and complicated grief.

MATERIALS AND METHODS

The study based its sample sizes on a previous trial that compared exposure combined with cognitive restructuring against supportive counselling (10). Using these data on treatment completers at 6 month follow-up, we estimated that, with 50% power and two-sided alpha = .05, n=30 would be needed to detect an anticipated meaningful follow-up difference on PTSD severity.

Twenty eight people (27 female, 1 male) were identified by the Thai Department of Mental Health, who were seeking treatment through Yala Hospital in southern Thailand between May 2007 and February 2009 for PTSD after direct exposure to a terrorist attack. Inclusion criteria were that the patient had been directly exposed to a terrorist attack and had a primary diagnosis of PTSD based on DSM-IV criteria (11). Exclusion criteria included severe suicidal risk, psychosis, substance dependence, and aged less than 17 years or more than 70 years. No patients were excluded on these criteria. Patients were randomized according to a random numbers system administered by health officials in Bangkok (fully independent of counsellors and the study co-ordinator) to either CBT (n=16) or TAU (n=12) (see Figure 1). A family member was killed in the attacks in 24 cases (14 in CBT, 10 in TAU) and all these patients also suffered complicated grief (12). Recruitment to the study was terminated prematurely because at that stage of the study terrorist attacks increased and health workers were being targeted by the terrorists. Accordingly, the study was forced to terminate with a sample of 28 because of risks to health workers providing therapy. Participant flow during the study is presented in Figure 1.

PTSD diagnosis was determined by the PTSD Symptom Scale - Interview (PSS-I) (13). This semi-structured interview consists of 17 PTSD symptoms that are rated on a 0-3 scale combining frequency and severity in the past 2 weeks. It has very good inter-rater reliability for PTSD diagnosis ($r=.91$) and severity ($r=.97$) (13). Depression was assessed using the Beck Depression Inventory-II (14), which is a self-report measure with sound psychometric properties (14). Complicated grief was assessed using the Inventory of Complicated Grief (15); this self-report measure assesses the core symptoms of complicated grief, which involves persistent yearning for the deceased, emotional pain following the loss, bitterness, hopelessness, and loss of identity (12). All measures were translated into Thai and back-translated into English.

Following informed consent, patients in CBT were offered 8 weekly individual 60-min sessions that included education

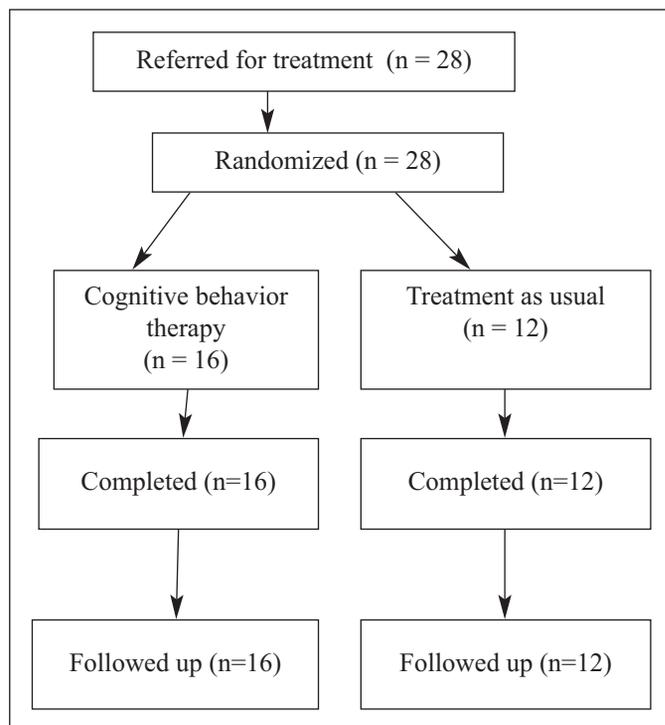


Figure 1 Patient participation in the study

about trauma, anxiety management techniques, repeated exposure to trauma memories, *in vivo* exposure to avoided situations, and cognitive restructuring to modify catastrophic appraisals about future harm. Therapy was conducted by Thai psychologists or psychiatric nurses who were trained to use the treatment manual in three 2-day workshops occurring over 12 months. Each workshop comprised didactic training, modelling, and role-plays to ensure that each therapist was competent in therapy skills. Therapists rehearsed clinical skills with patients during the four months after the first and the second workshop, and received supervision on treated cases during the second and third workshop. During the trial itself, therapists conducted treatment without formal supervision.

The first session of CBT comprised education about trauma reactions. The second session commenced progressive muscle relaxation training. Rather than relying exclusively on western methods of relaxation training (e.g., muscle relaxation and breathing control), relaxation also encouraged Thai meditation techniques. This practice was reviewed in each subsequent session. The second session commenced prolonged imaginal exposure to traumatic memories. Forty minutes of each session was devoted to participants reliving their trauma by focusing attention on their memories and engaging with their affective responses (16). In the second session, participants were also taught to create a hierarchy of feared situations. In session 3, *in vivo* exposure was commenced in which participants were instructed to remain in feared situations until anxiety reduced by 50%, commencing with the least feared situations, and then increasing exposure

to more feared situations. In session 3, cognitive restructuring was commenced. Participants were taught to identify unrealistic and catastrophic thoughts and to modify thoughts by Socratic questioning, probabilistic reasoning, and evidence-based thinking. Cognitive restructuring was modified to recognize the realistic threats of possible terrorist attacks. Specifically, treatment taught patients to evaluate the absolute risk of being harmed and to recognize the benefits of accepting a level of risk in order to permit normal functioning (e.g., attending the local market to buy the family food, despite the possibility that markets were targeted for bombings) (9). Each of these components were rehearsed in each session, and relapse prevention was conducted in the final session. TAU comprised the equivalent number of sessions of supportive counselling being provided by psychiatrists who were not trained in CBT.

At the completion of treatment sessions, therapists compiled checklists that itemized each of the therapy components. Therapists providing CBT indicated on their checklists that all patients in CBT received education, anxiety management, imaginal exposure, and cognitive restructuring. Three patients did not receive *in vivo* exposure. No patients in TAU received anxiety management, exposure, or cognitive restructuring. Assessments conducted at post-treatment and 3 months following treatment were conducted by independent personnel unaware of patients' treatment condition.

RESULTS

There were no differences between conditions in terms of age, gender, religion, number of therapy sessions, or pre-treatment psychopathology scores (see Table 1). There were no treatment drop-outs, and so analyses focus on all patients who were randomized into the study.

A multivariate analysis of covariance (MANCOVA) on post-treatment PSS, BDI-II, and ICG scores indicated a significant main effect: $F(3,21) = 7.02, p = 0.002, \eta^2 = .50$. Post-

Table 1 Characteristics of the participants in the trial

	CBT	Treatment as usual	Test	<i>p</i>
Age (years, mean ±SD)	42.3±6.3	43.9±11.9	$t(26) = 0.46$	0.65
Time since trauma (months, mean±SD)	13.1±6.6	15.2± 8.0	$t(26) = 0.76$	0.45
Number of sessions (mean±SD)	6.6±1.0	5.5±2.5	$t(26) = 1.65$	0.11
Gender				
Male	0	1	$\chi^2 = 1.38$	0.24
Female	16	11		
Marital status (%)				
Single/Widowed	87	83	$\chi^2 = 0.10$	0.76
Married	13	17		
Religion				
Buddhist	11	5	$\chi^2 = 2.05$	0.15
Muslim	5	7		
Employed (%)	93	75	$\chi^2 = 1.97$	0.16
Education (%)				
Less than high school	44	42	$\chi^2 = 0.01$	0.91
At least high school	56	58		

CBT – cognitive behaviour therapy

treatment ANCOVAs indicated that patients who received CBT scored lower on the PSS, BDI-II, and ICG than patients in the TAU condition (Table 2). The MANCOVA on follow-up symptom scores also indicated a significant main effect: $F(3,21) = .11, p = 0.02, \eta^2 = .37$; CBT resulted in lower PSS, BDI-II, and ICG scores than TAU.

Treatment effect sizes were calculated between treatment conditions at post-treatment and follow-up. We derived Cohen's *d* effect size by calculating the mean difference between assessments of each treatment condition and dividing this by the pooled standard deviation (17). We used Hedges *G* effect sizes to correct for variations due to small sample sizes (18). Between condition effect sizes (Table 2) indicated that CBT had large effects relative to TAU for PTSD, depression and complicated grief. Effect sizes for CBT prior to and at 3

Table 2 Psychopathology measures at pre-treatment, post-treatment and follow-up (mean±SD)

Measure	CBT (n= 16)	Treatment as usual (n= 12)	F (df = 25)	<i>p</i>	η^2	Between condition effect size
<i>Pre-treatment</i>						
PSS	26.8±10.0	22.7±12.4	0.95	0.34	0.03	-0.36 (95% CI: -0.40-1.11)
BDI-II	22.3±13.4	17.8±14.7	0.71	0.41	0.03	-0.31 (95% CI: -0.44-1.06)
ICG	24.3±10.2	24.2±10.1	1.32	0.26	0.05	0.01 (95% CI: -0.74-0.76)
<i>Post-treatment</i>						
PSS	4.1±8.0	12.3±8.4	13.49	0.001	0.35	0.96 (95% CI: 0.17-1.75)
BDI-II	3.2±8.7	11.3±11.3	10.12	0.004	0.29	0.81 (95% CI: 0.03-1.58)
ICG	10.7±5.8	15.2±9.5	14.52	0.001	0.37	0.58 (95% CI: -0.18-1.35)
<i>Follow-up</i>						
PSS	7.5±11.1	15.2±13.1	8.63	0.007	0.26	0.62 (95% CI: -0.14-1.39)
BDI-II	6.4±12.2	11.0±11.6	11.15	0.003	0.31	0.37 (95% CI: -0.38-1.13)
ICG	11.5±7.2	14.8±9.4	10.94	0.003	0.30	0.38 (95% CI: -0.37-1.38)

CBT – cognitive behavior therapy; PSS – PTSD Symptom Scale; BDI-II – Beck Depression Inventory, 2nd ed.; ICG – Inventory for Complicated Grief

months after treatment were 1.78 (95% CI: 0.96-2.60) for PSS, 1.22 (95% CI: 0.46-1.97) for BDI-II, and 1.41 (95% CI: 0.64-2.18) for ICG. Effect sizes for TAU were 0.57 (95% CI: 0.25-1.38) for PSS, 0.45 (95% CI: -0.36-1.26) for BDI-II, and 0.41 (95% CI: -0.39-1.22) for ICG.

We calculated high end-state adjustment as being below 19 on the Clinician-Administered PTSD Scale (CAPS) (combining frequency and intensity scores) as a measure of the absence of PTSD (19), and below 10 on the BDI-2 (20). More patients in the CBT condition (75%) achieved high end-state functioning than participants in the TAU (33%) condition: ($\chi^2 = 4.86, p < 0.05$).

We also calculated the number of patients needed to treat as 1 divided by the proportion responding to CBT as an estimate of the number of patients who would need to be given CBT for one of them to achieve a response outcome he would not have achieved with TAU. Efficacious treatments typically have a number needed to treat between 2 and 4 (21). The number needed to treat was 2.40.

DISCUSSION

This study represents the first demonstration of the efficacy of CBT to successfully treat PTSD in people who are living with significant threat from terrorist activity. Although the success of CBT has been demonstrated before in populations who live with potential threat, such as domestic violence (7), this study highlights that CBT can also be usefully applied in settings where very regular attacks are made upon communities in which the patient lives.

Several points emerge from this study. First, therapy was specifically adapted so that it accommodated the particular needs of people currently under terrorist threat. Participants in this study were regularly exposed to regional bombings and shootings during the course of therapy. Therapy emphasized the advantages of taking reasonable risks (i.e., attending local markets allows the individual to purchase required supplies for their children) and also the importance of evaluating the absolute risk of harm (i.e., low statistical probability of being at a specific market when a bomb explodes) (9). Despite the difficulties associated with this reasoning, patients appear to have recognized the utility in accepting some level of risk in order to maintain some level of functioning.

Second, the finding that there were no adverse effects or drop-outs extends previous reports that exposure therapy is not aversive (22,23). The finding that participants tolerated, and benefited from, exposure even in the context of ongoing terrorist attacks counters the notion that exposure may not be applicable in populations experiencing anxiety as a result of actual threat. Extinction learning presumes that the reminder of the trauma (conditioned stimulus) is a benign reminder that signals safety to the trauma survivor (6). It seems that even when the reminders are periodically associated with actual threat, exposure therapy achieved extinction learning.

Third, the therapists conducting this trial had fundamental

training in mental health and had no previous knowledge or experience with CBT. They were trained in these techniques in a 2-day workshop that involved didactic training and provision of a manual, followed by two separate 2-day workshops held four months apart. By rehearsing CBT with trauma survivors between training workshops, therapists were able to receive feedback and learn more refined skills. The success of their therapy confirms previous reports that brief training of CBT to lay counsellors can result in significant treatment outcomes in the trauma survivors they treat (4,24).

Fourth, this trial illustrates the capacity for CBT to be successfully implemented into a non-western culture in ways that build on the culture's strengths. Some commentators argue that western evidence-based therapy approaches may not be appropriate to non-western cultures (25). In the planning stage of the program, there was initial concern that exposure may not be acceptable to Thai therapists or trauma survivors, because eliciting distress in others and expressing distress is not encouraged in Thai culture; following explanation of the rationale for exposure, however, this strategy was implemented. Therapy also usefully encouraged Buddhist meditation in those participants who were skilled in this practice as an important adjunct to western relaxation methods. Further, Buddhist techniques of distancing oneself from one's thoughts (similar to mindfulness strategies in western psychotherapy (26)) were integrated into cognitive restructuring to reduce preoccupation with catastrophic thinking.

Fifth, CBT resulted in marked reductions in complicated grief reactions. Recent CBT trials including exposure-based therapy, often complemented with other strategies to reduce grieving (e.g., promoting positive memories of the deceased, goal setting) have been successful in reducing grief symptoms (27,28). The current trial adds to the evidence that treatment strategies applied to PTSD (exposure, cognitive restructuring) have benefits in reducing persistent grief, and suggests that similar change mechanisms may be involved in reduction of these symptoms.

We note that this study's conclusions are limited by the small sample size, lack of independent fidelity checks, and rather short-term follow-up. These limitations were unavoidable because of the dangerous context in which the trial was conducted and the limited resources available in southern Thailand. Nonetheless, this trial is the first demonstration that culturally adapted CBT is efficacious in reducing PTSD, depression, and grief reactions in the context of ongoing terrorist attacks.

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Mental health system in China: history, recent service reform and future challenges

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This paper summarizes the history of the development of Chinese mental health system; the current situation in the mental health field that China has to face in its effort to reform the system, including mental health burden, workforce and resources, as well as structural issues; the process of national mental health service reform, including how it was included into the national public health program, how it began as a training program and then became a treatment and intervention program, its unique training and capacity building model, and its outcomes and impacts; the barriers and challenges of the reform process; future suggestions for policy; and Chinese experiences as response to the international advocacy for the development of mental health.

Key words: Mental health system, China, history, service, reform, challenge

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The first officially documented management of the mentally ill in China was in the Tang Dynasty (618-907 AD), when homeless widows, orphans and the mentally ill were cared for in the Bei Tian Fang, a type of charity facility administered by monks (1). The first western style psychiatric hospital for the homeless mentally ill was established and funded in 1898 by an American missionary, John Kerr, in what is currently the Guangzhou Brain Hospital. In the next 50 years, psychiatric hospitals were built very slowly in a limited number of large cities. The number of psychiatrists gradually increased to 100, and the number of beds gradually amounted to 1,000.

After the founding of the People's Republic of China in 1949, psychiatric hospitals were gradually built in every province. The role of these early provincial hospitals was to maintain social security and stability. Following the first National Mental Health Meeting in 1958, community mental health work started in Beijing, Shanghai, Hunan, Sichuan and Jiangsu. Facilities were established in these areas to train professionals and to develop work plans for the prevention and treatment of psychoses, including early detection and treatment and relapse prevention (2).

Though community mental health programs almost ceased during the Cultural Revolution (1966-1976), work-rehabilitation centers for patients with psychoses and caring networks were organized by neighborhood committees (the lowest level of governmental facilities) in Shanghai (3), and a treatment model for 256 patients with schizophrenia and their families was developed in a suburb of Beijing (4).

In the 1980s, the health, civil affairs and public security sectors set up a three-tier network (at city, district/county

and street/town levels) for the prevention and treatment of psychoses. Successful experiences with treatment models, such as work-rehabilitation centers in urban communities in Shanghai and Shenyang, and family-based therapy in rural areas in Haidian District in Beijing and Yantai Shandong, were extended to other places (2).

With the economic reform, hospitals were encouraged, as part of the market economy, to make a profit. Financially dependent mental health rehabilitation facilities closed or were transformed into small-scale psychiatric hospitals. In Shanghai, before 1990, there was at least one community-level rehabilitation facility in each district or town. By June 2004, the numbers of these facilities had decreased by 62% (5).

By the late 1990s, some psychiatrists started to doubt the rationale for large hospital-based and profit-making models for mental health service delivery, and the Ministry of Health began to reconsider principles and approaches for mental health care. Through advocacy by the Ministry, senior ranked officials facilitated the establishment of a mental health plan.

In November 1999, a high-level mental health seminar was convened by ten Chinese Ministries and the World Health Organization (WHO) in Beijing. The meeting resulted in a declaration that all levels of government would improve their leadership for and support of mental health care, strengthen inter-sectoral collaboration and cooperation, establish a mental health strategy and action plan, facilitate the enactment of a national mental health law, and protect patients' rights (6).

The first National Mental Health Plan (2002-2010) was signed by the Ministries of Health, Public Security and Civil

Affairs, and China Disabled Persons' Federation (CDPF) in April 2002. It identified a series of detailed targets and indices to achieve the main goals of: a) establishing an effective system of mental health care led by the government with the participation and cooperation of other sectors; b) accelerating the process of mental health legislation development and implementation; c) improving the knowledge and raising the awareness of mental health among all citizens; d) strengthening mental health services to decrease burden and disability; and e) developing human resources for mental health services and enhancing the capacity of current psychiatric hospitals (7).

In August 2004, the Proposal on Further Strengthening Mental Health Work was approved by the Ministries of Health, Education, Public Security, Civil Affairs, Justice and Finance, and the CDPF. This proposal provides explicit instructions on interventions for psychological and behavioral problems for key population subgroups (including children and adolescents, women, the elderly and victims of disasters), treatment and rehabilitation of mental disorders, research on mental health and surveillance of mental disorders, and the protection of the rights of the mentally ill. The Proposal serves as the *de facto* Chinese national mental health policy.

The mental health service model proposed in the above two documents is led by psychiatric hospitals, supported by departments of psychiatry in general hospitals, community-based health facilities and rehabilitation centres.

THE MENTAL HEALTH SCENARIO IN CHINA

Mental health burden

In a large epidemiological study carried out in four provinces (Shandong, Zhejiang, Qinghai and Gansu) from 2001 to 2005, the adjusted 1-month prevalence of any mental disorder in people aged 18 years or older was 17.5% (95% CI 16.6-18.5), and that of psychotic disorders was 1.0% (95% CI 0.8-1.1) (8).

In health economic terms, the estimated total disability adjusted life years (DALYs) of ten psychiatric conditions, including unipolar depressive disorder, bipolar disorder, schizophrenia, alcohol use disorders, Alzheimer's and other dementias, drug use disorders, post-traumatic stress disorder, obsessive-compulsive disorder, panic disorder, and insomnia (primary), was 253,851,896 years in China in 2004 (9). This translates into a loss of gross domestic product (GDP) amounting to a country-wide total of CNY 2,681 billion, with schizophrenia and bipolar disorder accounting for CNY 532 billion.

The huge burden of mental disorders highlights the pressing need for improved mental health services. However, similar to most countries, the rate of treatment gap of those with mental disorders is unacceptably high in China, with 91.8% of all individuals with any diagnosis of men-

tal disorders never seeking help. For psychotic disorders, 27.6% never sought help and 12.0% saw non-mental health professionals only (8).

Mental health workforce and resources

The vast majority of mental health professionals in China are psychiatrists or psychiatric nurses, with few clinical psychologists and social workers, and no occupational therapists. Psychiatrists and licensed psychiatric nurses are accredited by the Ministry of Health, psychological counselors by the Ministry of Human Resources and Social Security, and psychotherapists by both Ministries.

In 2004, there were 16,103 licensed psychiatrists and psychiatric registrars (1.24/100,000 population) and 24,793 licensed psychiatric nurses (1.91/100,000 population) (9). Relative to the global average mental health workforce (i.e., 4.15 psychiatrists and 12.97 psychiatric nurses per 100,000 population respectively) (10), mental health human resources in China are quite limited. The shortage of skilled mental health professionals represents one of the most critical issues facing the Chinese mental health system currently.

In 2004, there were 557 psychiatric hospitals. Among them, 359 (64.5%) had 100 or more beds, and 44 (7.9%) had 500 or more beds. The total number of psychiatric beds was 129,314, i.e. 1.00/10,000 population (11), which is significantly lower than the global average of 4.36/10,000 psychiatric beds (10).

Structural issues

China does not organize its services in catchment areas. Specialist mental health services remain the predominant component of the system. China's community-based mental health system was largely eliminated with the introduction of the market economy. Therefore, mental health service provision has become primarily hospital-based. Patients can access tertiary psychiatric hospitals directly, bypassing the primary and secondary health care levels. This partly reflects the disproportionate concentration of health resources in large cities.

The funding model for the mental health system is complex, with hospital inpatient services provided by three ministries, Health, Civil Affairs and Public Security, while other facilities are administered under other ministries. According to the WHO, only 2.35% of the total health budget is spent on mental health and less than 15% of the population has health insurance that includes coverage of psychiatric disorders (10).

China is undergoing a rapid change, with an economic growth rate of 7.5-13.0% per annum in the last ten years (12). However, the growth in wealth has not been equitably distributed, resulting in an increasing gap between the rich and the poor. It is evident that those with the greatest

socio-economic disadvantage are often those with the highest mental health care needs (13).

NATIONAL MENTAL HEALTH SERVICE REFORM

Policy change and inclusion of mental health in the national public health program

In October 2003, supported by the Ministry of Health, an application process was initiated for specialized public health projects that would have investment from the Ministry of Finance. All relevant public health sectors were active in developing appropriate models with critical indicators and drafting proposals for funding.

Although several approaches and different models were considered, the mental health sector was yet to identify a suitable and practical model for China. A delegation led by Guihua Xu (Vice Director of China Centre for Disease Control) and three psychiatrists, Xin Yu, Hong Ma and Jin Liu from Peking University Institute of Mental Health, visited Melbourne, in order to build knowledge and understanding of the Victorian community mental health service system. The delegates and their Australian hosts also began to analyze the concept of community in China, and to investigate possible ways to integrate mental health care into secondary and tertiary facilities in the country. Complemented by other international exchanges with the USA, Norway, Thailand, Japan, UK and Germany, and guided by international benchmarks on mental health services by WHO and previous experiences in community mental health in China, a mental health sector model for reform emerged. The model has at its core a patient-centered approach that is community-based, seamless, function-oriented and multi-disciplinary.

Due to China's vast, multi-ethnic and diverse population, social harmony and stability is a well recognized concern for the Chinese government. The focus on psychoses, especially those associated with violent or socially disruptive behaviours, was considered as a critical step to engage government in mental health issues. Although community-based mental health services were the long-term goal, current lack of resources and capacity in community mental health and primary mental health, combined with the difficulty in attracting mental health professionals to work in the community, meant that a different, less ambitious and more targeted model needed to be followed initially. An integrated hospital and community treatment model for psychoses was suggested, and a pilot project that included monitoring, intervention, prevention and rehabilitation management of psychoses was proposed.

In September 2004, after competing with over fifty proposals and supported by a group of leading sociologists, economists and psychiatrists in China, the program for mental health service reform was the only non-communicable disease program included in China's national public health program. This event became a major historical milestone for

China: mental health became officially included into public health.

The mental health reform program formally received support from Ministry of Finance in December 2004, and was named the 686 Program after its initial funding of CNY 6.86 million. The National Centre for Mental Health of China located at Peking University Institute of Mental Health was authorized to be the implementing facility for this program by the Ministry of Health. The project was overseen by a national working group as well as an international advisory group with experts mainly from the University of Melbourne.

By early 2005, 60 demonstration sites were established, with one urban and one rural area in each of the 30 provinces of China, covering a population of 43 million. The priority in the first year was to build a capable mental health workforce through an extensive training program. A two-level training mode was adopted, first at the national level utilizing a train-the-trainer approach, and then with trained trainers delivering the programs at the provincial level. The contents of the training included guidance on project management, standardized treatment protocols, case management, information management, family education, and the training of police and neighborhood committees.

Treatment and intervention program

In 2006, the 686 Program incorporated an intervention component into the training program, which was then called the National Continuing Management and Intervention Program for Psychoses. The aim was to consolidate the reform through the key provisions of continuity of care, treatment accessibility, and equitable mental health care. Four types of psychoses were included: schizophrenia, bipolar disorder, delusional disorder, and schizoaffective disorder.

Patients screened for possible psychosis were referred from psychiatric hospitals or departments, the CDPF, community and village health centres, and neighborhood or village committees. These patients were subsequently examined by psychiatrists, and those who met diagnostic criteria for psychotic disorders were evaluated for their risk of violence based on a 0 to 5 score scale established by the national working group.

The patients at risk of violence received monthly follow-up and, if they were socio-economically disadvantaged, were provided with free medication, laboratory tests, and a subsidy for hospitalization. About 5% of patients who received free medications were treatment refractory and were therefore provided with second generation antipsychotics, mainly risperidone. In the event of any psychiatric emergencies or severe cases of medication side effects, the program provided free crisis management. Moreover, as some patients were physically restrained or chained at home, the program provided support for the unlocking and freeing of these patients, and hospitalization when necessary. After hospital-

ization, if patients lacked finances to pay for treatment, they were included in the free services mentioned above.

Training and capacity building

A key challenge for successful implementation of the 686 Program was the limited capacity of the workforce to deliver the program at the local level. To meet this enormous challenge, a tripartite training program was collaboratively developed in 2007 by the Peking University Institute of Mental Health, the University of Melbourne and the Chinese University of Hong Kong. The primary aim of the program was to train up multi-skilled case workers by: a) developing understanding of the key principles of community-based mental health care in general and basic case management; b) providing practical skills in developing individualized service plans to maximize integration and continuity of care; c) exploring culturally appropriate ways to build partnerships with the patient, families and community; d) building skills to work in multidisciplinary teams; and e) providing opportunities to share ideas and plan for implementation.

Encompassing best practice principles drawn from allied health disciplines (nursing, social work, occupational therapy, psychology), a basic set of knowledge and skills for case management was outlined (14). A key underpinning for the training program was to provide a rehabilitation focus in a community setting. Field site visits to a range of community mental health facilities (e.g., day hospitals, half way houses, training centres, mental health support programs) and supervision by the community mental health team members provided direct opportunity for such clinical experience.

Outcomes and impacts

The program needed to build broad partnerships that included different sectors and facilities into the mental health service system, including local government, health, civil affairs, public security, the CDPF and Women's Federation. In 2009, a total of 34,861 facilities participated in this program, including 44 provincial hospitals, 92 municipal hospitals, 168 district/county-level hospitals, 986 urban community health centers, 2,748 urban community health stations, 1,136 township clinics, 11,480 village clinics, 5,660 urban neighborhood committees and 12,547 village committees.

A multidisciplinary mental health team was also established. By the end of 2009, a total of 38,227 participants worked for the program. Among these, neighborhood/village committee staff, who were mainly responsible for helping finding the patients and leading community advocacy, accounted for 53.3%; case managers accounted for 25%; policemen, who mainly helped crisis intervention for violence, accounted for 7.1%; psychiatrists for 4.3%, psychiatric nurses for 3.9%, and officials/administrators at different levels for 3.4%.

Data from the police offices in 42 demonstration sites showed that the number of minor violent events declined from 531 in July-December 2005 to 140 in January-June 2006 (decrease of 73.6%), and that of major violent events declined from 223 to 72 (decrease of 66.7%).

By the end of 2009, 96.88 million general population in 112 cities were covered by this program. A total of 161,800 patients were registered; 42,400 patients received regular follow-up (the average longest one-way follow-up distance in demonstration sites was 75 km); 15,300 economically disadvantaged patients received free medication, 12,800 free crisis management interventions were provided, and 7,200 poor patients were given a subsidy for hospitalization; 340 previously restrained patients were freed.

In the first year of the 686 Program, a total of 602 training courses were conducted and nearly 30,000 people were trained, including psychiatrists, psychiatric nurses, community physicians, case managers, community workers, public security staff and family members.

To date, nearly 500 mental health professionals from 80 districts in China have participated in tripartite program training sessions. Ten groups of ten mental health professionals from mainland China have had practical training in Hong Kong and more than 100 hospital directors and heads of mental health departments have undertaken on-site study in Melbourne.

One of the most profound impacts of the program has been in the area of policy reform. This probably has the greatest influence on long-term sustainability. Along with the 686 Program, five vital national policies on mental health have been developed: the Guiding Compendium on Development of National Mental Health Work System (aimed to improve inter-ministerial coordination and reform mental health work system); the Government Work Report (for the first time in Chinese history, mental diseases were addressed in the annual report of the Central Government); the Short-term Strategy of Health System Reform (psychiatric hospitals were to be improved as part of public health service capacity building); the Opinions on Improving Gradual Equity of Basic Public Health Services (in which the management of psychoses was included as one of nine national basic public health service domains); and the Working Criteria on Management of Psychoses (in which responsibility of different sectors in the management of psychoses, and the relevant procedures, were clarified).

BARRIERS AND CHALLENGES TO THE REFORM PROCESS

A determined government is an essential element for achieving success in a short period of time in China. However, the magnitude and the complexity of the mental health problems as well as the changing situation are always threatening the achievement of mental health reform. All stakeholders of mental health services in China and readers of this article should be aware that, despite the significant

progress, mental health service system development and service delivery in China still face many difficulties. Some of the main problems are the following:

Disparity is huge in China. Although national policies are quite comprehensive and instructive, a wide disparity exists among provinces and cities in terms of social, economical, and developmental levels. In some rich and reform-driven coastal or eastern areas, the mental health service system is being quickly reformed within whole provinces or cities. However, in some under-developed western areas, the reform process is slowed down by poor understanding, and lack of resources and skills. In those areas, the existing national mental health policies become just “well-written documents”.

Resources are not properly allocated between the community and psychiatric hospitals. Though community mental health is strongly encouraged as part of the equalization of public health service, and national funding has been given to each province to cover registration and following up of the patients at community level, general physicians lack basic knowledge and skills for these tasks. In the next two or three years, CNY 15 billion will go to the construction of 550 psychiatric hospitals that are often located in less populous suburban areas, and the funding structure still remains primarily based on psychiatric hospital beds rather than care received from personnel and treatment programs. This will discourage hospitals to be involved in community services. In addition, social insurance policy only subsidizes the expenses of hospitalization, leading more patients to use unnecessary in-patient services.

Some important outcomes are unclear about psychoses. It is understandable that, from the social stability point of view, psychosis treatment and management is always the top priority of the government. However, due to the lack of relevant laws and regulations, involuntary admission is undertaken under the name of “caring about mentally ill”. Social mobilization and resources re-allocation do increase the treatment rate of patients with psychoses. However, whether duration of untreated psychosis is shortened, or patients’ functional levels are improved, are yet to be answered questions.

Psychiatry is being made less attractive. The focus on psychosis management makes psychiatry less attractive. Fewer medical graduates are willing to be trained as psychiatrists, and psychiatric hospitals continuously lose professionals with higher levels of education, training and expertise. The government, therefore, is considering to transform psychiatric facilities into “public health institutions” in which staff are regarded as “paracivil servants”. This may further discourage graduates from entry training in psychiatry.

Partnership with other sectors is unsatisfactory. Al-

though the responsibility of each relevant ministry or sector has been stated in various documents, inter-organizational cooperation and collaboration is still not fully or firmly established, with the health and mental health sectors working in isolation in many areas.

SUGGESTIONS FOR FUTURE POLICY

In a country with highly centralized government structures such as China, mental health development needs strong and continuous support from government at all levels. Without this support, the mental health sector will find it hard to fulfill the management of psychoses by itself. In addition, China needs to develop awareness of the importance of non-governmental organizations and their potential role in integrating various social resources and providing valuable supplementary services for mentally ill patients living in the community to enhance their recovery.

Community physicians in urban areas and village physicians in rural areas will require training in order to understand and develop individual care plans for four types of psychotic patients (similar to the 686 Program) at the primary care level, and to follow up stable patients at least four times per year.

Given the large number of patients with chronic mental disorders in China, community and home-based care for most patients needs to be encouraged and promoted. Family members should be supported to provide ongoing care in the community for their mentally ill relatives.

The limited amount of funding could only support the basic administration and transportation of staff in the national program, but the mental health facilities that employ these professionals have to make a profit in order to pay their salary. Mental health service fee for psychoses should be provided by the government as either salary of the service providers or insurance for the patients.

Government support and investment in clinical studies and health policy research are necessary to establish evidence-based treatment strategies and policy that are relevant in a Chinese context. Moreover, economic evaluations from the perspective of functional recovery and long-term outcomes and benefits for patients with mental disorders are needed to inform policies and reimbursement provided by the Social Security Department.

CHINESE EXPERIENCES AS RESPONSE TO INTERNATIONAL ADVOCACY

This reform program in China is consistent with policy recommendations issued in recent years by the WHO and supported by other international authorities. In 2001, the WHO recommended that countries develop community-based services for people with mental disorders (15). This recommendation has been recently strengthened by a call

for action to scale up services for people with mental disorders (16), the development of the Mental Health Gap Action Programme (mhGAP) (17), the activities of the WPA (18-20), and the guidelines published recently in *World Psychiatry* (21,22).

The work on the 686 Program and other developments in China are important steps in moving towards internationally agreed and accepted standards in mental health service provision. However, mental health services in China, as in many low- and middle-income countries (LAMIC), have a long way to go to meet the target of providing mental health care in the community.

Locally driven research provides relevant information to guide policy makers in the expansion of cost effective and culturally adapted health services (16). However, dissemination of this work to national and international audiences is hampered by the poor representation of publications from LAMIC in mainstream psychiatric journals (23,24). Recent work by WPA has demonstrated that, despite a significant level of scientific activity shown by China (as well as India, South Africa and South Korea), none of these countries, and indeed, no LAMIC in the African and Asian regions, is so far represented by a psychiatric journal in the main international databases (25,26). Internationally supported action to improve indexation of journals and research dissemination will aid the publication of data from this and similar projects. The WPA journal, *World Psychiatry*, and the recently indexed *Asia Pacific Psychiatry*, the journal of the Pacific Rim College of Psychiatrists, have the opportunity to bridge this gap.

CONCLUSIONS

Although China's mental health service reform has focused only on psychoses so far, the scale of the reform, and the sheer numbers of psychiatric patients involved, represent a massive and ambitious program, which has had to overcome huge challenges. The reform began earlier than the reform of general health care in China, and is consistent with the Chinese public health strategy and the framework for country directions according to the WHO mhGAP.

With continued political commitment, timely assessment of needs and matching resources, development of appropriate public health policies, delivery of effective interventions, strengthening of human capacity, efficient mobilization of financial resources, rigorous monitoring and evaluation, China will be in a favorable position to build and strengthen a national sustainable community mental health system and service for the benefit of the mental health of its population.

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Lessons learned in developing community mental health care in Europe

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This paper summarizes the findings for the European Region of the WPA Task Force on Steps, Obstacles and Mistakes to Avoid in the Implementation of Community Mental Health Care. The article presents a description of the region, an overview of mental health policies and legislation, a summary of relevant research in the region, a precis of community mental health services, a discussion of the key lessons learned, and some recommendations for the future.

Key words: Community mental health care, Europe, mental health in primary care, legislation and policies, research, human rights, treatment gap, human resources

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This paper is part of a series which describes the development of community mental health care in regions around the world (see 1). It is one of the products of the Task Force appointed by the WPA, as part of its Action Plan 2008-2011 (2,3), to produce a Guidance on Steps, Obstacles and Mistakes to Avoid in the Implementation of Community Mental Health Care. The purpose, methods and main findings of this Task Force have been previously published in this journal (4). In this article, we describe these issues in relation to the World Health Organization (WHO) European region.

The WHO European Region consists of 53 countries and over 886 million people (5). It includes the former EU-15 countries (the fifteen countries that have been part of the European Union (EU) since before 2004), the 12 countries that joined the EU from 2004 onwards, the 11 countries of the Commonwealth of Independent States (CIS) (which incorporates most of the former Soviet Union's member states), eight countries from South-Eastern Europe, and seven non-EU high income countries (see Table 1). Generally speaking, there is an economic divide across Europe, with most of the high income countries (n=30) amongst EU (especially EU-15) countries and other primarily Western countries, all of the low income (n=3) and lower-middle income countries (n=7) in the non-EU Eastern parts of the region (most of which are CIS countries), and many of the upper-middle income countries (n=13) in the post-2004 EU countries and South-Eastern Europe (6).

Mental health problems are common and have a huge economic and social impact across Europe, with at least 25% of people in the region experiencing a mental disorder over their lifetime (7). In 2004, neuropsychiatric disorders accounted for 19.1% of all disability-adjusted life-years (DALYs), and 39% of all first-ranked cause of years lived with disability (YLD) (8). Unipolar depression alone was the third leading cause of DALYs (after ischaemic heart disease and cerebrovascular disease), accounting for 5.6% of DALYs in the region (9). Suicide rates are also high across the region, with a prevalence rate of 14.01 per 100,000 population in 2007 (5), and

contributing 2% of total DALYs and 1.6% of all deaths in 2004 (8).

MENTAL HEALTH POLICIES AND LEGISLATION

Following various mental health treaties, action programmes and plans within the EU throughout the 1990s and early 2000s (9), a significant milestone in the development and reform of mental health policies across Europe was the Mental Health Declaration for Europe (10) and the Mental Health Action Plan for Europe (11) in 2005. Here all European health ministers acknowledged mental health as a priority area, recognized the need for evidence-based mental health policies, defined a broad scope for these policies, committed themselves to the development, implementation and reinforcement of such policies, and proposed twelve action areas and milestones to be implemented by 2010. This included a commitment to develop community-based mental health services, to downgrade large mental institutions, and to integrate mental health services into primary health care.

Most countries in Europe (around 83%) now have a mental health policy in place (see Table 1), with around 89% of the population in the region covered by 2005 (13). Similarly, almost all countries (over 95%) now have mental health legislation in place (see Table 1), with around 90% of the population covered by 2005 (13). Specific policies, strategies or plans for the development of community mental health services, as well as for the downgrading of large mental hospitals, and an integration of mental health into primary care, have now been developed in at least two thirds of European countries (see Table 1).

However, there are still large differences in policies between countries, and whilst in many countries policies have been updated in recent years to fit in with changing ideals of mental health service provision (with around half of the countries with mental health policies in place having either adopted new, or updated existing, policies since 2005), oth-

Table 1 Overview of mental health legislation, policies, services and psychiatrists in the European Region

	Mental health legislation and policies				Mental health in primary health care				Inpatient mental health services					
	Year of most recently approved mental health legislation	Year of most recent mental health policy	Policies, strategies or plans: development of community mental health services	Policies, strategies or plans: downsizing mental health in primary care hospitals	Policies, strategies or plans: mental health in primary care	Identification and referral to specialist common mental disorders in primary care	Diagnosis and/or treatment for common mental disorders in primary care	Identification and referral to specialist services for severe mental disorders in primary care	Diagnosis and/or treatment for severe mental disorders in primary care	Mental hospitals (inpatient services)	Community psychiatric inpatient units/ general hospitals	Number of psychiatric public hospital beds per 100,000 population	Percentage of psychiatric beds in facilities other than mental hospitals (approximate)	Number of psychiatrists per 100,000 population
<i>Former EU-15</i>														
Austria	after 2005	after 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	52	29%	15	
Belgium	after 2005	after 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	152	42%	23	
Denmark	after 2005	after 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	61	N/A	11	
Finland	after 2005	after 2005	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	72	99%	26	
France	after 2005	after 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	95	42%	22	
Germany	after 2005	after 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	75	40%	8.7	
Greece	1999	1999-2004	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	18	22%	15	
Ireland	after 2005	after 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	94	24%	7.3	
Italy	1978	after 2005	Yes	N/A	Yes	Yes	Yes	No	No	Yes	8	100%	9.8	
Luxembourg	2000	1999-2004	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	97	46%	12	
Netherlands	1999-2004	1999	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	114	18%	14.5	
Portugal	1999-2004	after 2005	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	27	37%	6.7	
Spain	after 2005	after 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	47	16%	6.1	
Sweden	2000	before 1998	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	54	93%	24	
UK	after 2005	after 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	23	39%	11	
<i>Other EU</i>														
Bulgaria	after 2005	after 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	64	56%	8.7	
Cyprus	1999-2004	after 2005	Yes	Yes	Yes	N/A	N/A	Yes	Yes	Yes	27	22%	6.5	
Czech Republic	after 2005	1999-2004	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	110	13%	13.7	
Estonia	after 2005	No policy	No	No	Yes	Yes	Yes	Yes	Yes	Yes	56	22%	13	
Hungary	1997	1999-2004	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	93	76%	13.7	
Latvia	after 2005	2004	Yes	No	Yes	Yes	No	No	Yes	Yes	148	7%	11.3	
Lithuania	after 2005	after 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	88	11%	18	
Malta	1981	1994	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	185	under 1%	4	
Poland	after 2005	after 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	65	25%	5.5	
Romania	2002	after 2005	Yes	No	Yes	Yes	Yes	No	Yes	Yes	75	28%	4.7	
Slovakia	after 2005	1999-2004	Yes	Yes	Yes	Yes	N/A	Yes	Yes	Yes	96	81%	9	
Slovenia	before 1998	1999-2004	No	No	Yes	N/A	Yes	Yes	Yes	Yes	85	15%	5.4	
<i>South-Eastern</i>														
Albania	1996	2003	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	24	25%	3	
Bosnia and Herzegovina	2000	after 2005	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	36	33%	1.8	
Croatia	1999-2004	after 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	93	20%	8	
Georgia	after 2005	No policy	No	No	No	Yes	No	No	Yes	No	29	0%	5.6	
Montenegro	after 2005	1999-2004	Yes	No	Yes	Yes	Yes	Yes	Yes	No	49	0%	6.4	
Serbia	Has legislation	after 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	95	N/A	12	
T.F.Y.R. of Macedonia	after 2005	after 2005	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	74	14%	9.5	
Turkey	1999-2004	after 2005	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	12	25%	1	

N/A: information not available
 Data are taken from World Health Organization's publications (5,12-16). Where data were conflicting between publications, the most recent source was used

Table 1 Overview of mental health legislation, policies, services and psychiatrists in the European Region (*continued*)

	Mental health legislation and policies					Mental health in primary health care					Inpatient mental health services				
	Year of most recently approved or updated mental health legislation	Year of most recent mental health policy	Policies, strategies or plans: development of community mental health services	Policies, strategies or plans: downsizing mental health in primary care hospitals	Policies, strategies or plans: mental health	Identification and referral to specialist services for common mental disorders in primary care	Diagnosis and/or treatment for severe mental disorders in primary care	Identification and referral to specialist services for severe mental disorders in primary care	Diagnosis and/or treatment for severe mental disorders in primary care	Mental hospitals (inpatient services)	Community psychiatric inpatient units/ general hospitals	Number of psychiatric public hospital beds per 100,000 population	Percentage of psychiatric beds in facilities other than mental hospitals (approximate)	Number of psychiatrists per 100,000 population	
<i>CIS</i>															
Armenia	2004	1994	N/A	N/A	N/A	N/A	N/A	N/A	No	Yes	45	under 1%	5.8		
Azerbaijan	2001	No policy	No	No	N/A	Yes	N/A	Yes	No	No	48	0%	5		
Belarus	1999	No policy	N/A	N/A	N/A	N/A	N/A	Yes	Yes	Yes	70	6%	10.1		
Kazakhstan	1997	N/A	N/A	N/A	N/A	N/A	N/A	No	Yes	Yes	63	9%	6		
Kyrgyzstan	1999	N/A	N/A	N/A	N/A	N/A	N/A	No	Yes	Yes	43	10%	3.4		
R. of Moldova	1998	No policy	Yes	Yes	Yes	Yes	Yes	No	No	No	63	0%	6		
Russian Federation	1999-2004	after 2005	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	112	12%	10.9		
Tajikistan	N/A	No policy	N/A	N/A	N/A	N/A	N/A	No	Yes	N/A	25	N/A	1.8		
Turkmenistan	1993	1995	N/A	N/A	N/A	N/A	N/A	No	Yes	Yes	33	9%	3		
Ukraine	2000	1988	N/A	N/A	N/A	N/A	N/A	No	Yes	Yes	94	3%	8.9		
Uzbekistan	2000	1999-2004	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	32	3%	4		
<i>Other</i>															
Andorra	No legislation	No policy	N/A	N/A	N/A	N/A	N/A	Yes	No	Yes	15	100%	10		
Iceland	1997	No policy	N/A	N/A	N/A	N/A	N/A	Yes	No	Yes	50	100%	25		
Israel	2000	after 2005	Yes	Yes	Yes	Yes	No	No	Yes	Yes	59	7%	8.8		
Monaco	1981	Has policy	N/A	N/A	N/A	N/A	N/A	Yes	No	Yes	173	100%	28.5		
Norway	after 2005	after 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	119	42%	16		
San Marino	Has legislation	No policy	N/A	N/A	N/A	N/A	N/A	Yes	No	Yes	38	100%	15		
Switzerland	1981	after 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	106	6%	30		

N/A: information not available

Data are taken from World Health Organization's publications (5,12-16). Where data were conflicting between publications, the most recent source was used

ers are out-of-date and in need of improvement (17). What is more, although around 40% of countries with mental health legislation in place have updated their legislation or adopted new legislation since 2005, around one quarter of countries still have legislation in place that is over 10 years old (see Table 1).

RESEARCH IN THE REGION

Research evidence from systematic reviews and randomized controlled trials (RCTs) evaluating community mental health services across the region is displayed in Tables 2 and 3. Overall, this evidence suggests that, in principle, community-based mental health care is effective. There is some evidence for the effectiveness of an integration of mental health into primary health services across different models of care, as well as for community mental health teams, assertive community treatment, intensive case management, crisis intervention, and supported employment. However, high-quality evaluative evidence for other mainstream or specialized community mental health services is inconsistent or missing. In fact, for most European countries, there is a dearth of high-quality research on community-based mental health services, with most RCTs in the region having been conducted in the UK (around 80%) and a few other high-income countries. Findings may therefore not be applicable to other countries. Moreover, results may be difficult to compare across studies due to a lack of clarity about the model of care (18,19), differences between control treatments (18), or an overlap of components of community-based treatment with standard treatment (and therefore differences in outcomes being reduced) (19). Further issues are that services assessed in studies are often not sustained (19), and that there is a lack of studies assessing cost-effectiveness of services.

Other than trials of effectiveness, there have been some observational and qualitative studies conducted in Europe (mostly in the UK). These have shown that home treatment is viewed positively by service providers (44), and that specific community mental health services, such as women's crisis houses, are highly valued by service users (45). Some of the processes that may be important to the effectiveness and sustainability of community mental health services have also been identified in this way, including staff satisfaction (47), views on interdisciplinary working (46-51), and involvement of service user views (52-60).

OVERVIEW OF MENTAL HEALTH SERVICES

Generally, a wide range of community mental health services exists within Europe, with at least some available in every country. However, whilst a few countries lead the way in the successful implementation of community-based mental health services according to an evidence-based "balanced care model" that integrates elements of community and hos-

pital services (4,61-65), in many others access to community-based services is still very limited and may commonly consist of small pilot projects (12).

Broadly speaking, consistent with economic differences across the region, the division is mostly between the Eastern and Western countries of Europe. In the EU-15 countries and other predominantly Western high income countries, following a move towards human rights, social inclusion and empowerment over the last few decades, a large array of multidisciplinary community-based services may be available to people with mental health problems, with most patients being treated outside of mental institutions (5). In line with the "balanced care model" approach, the mental hospitals that do exist in these countries are often relatively small, close to communities (12), and usually located in acute wards in general hospitals, with hospital stays reduced as far as possible (9,61).

In the low or lower-middle income non-EU countries of Eastern Europe, in particular the CIS countries, access to community-based care tends to be far more limited. Large mental health institutions are commonly still the mainstay of the mental health care system (5), and community mental health services are often restricted to polyclinics or dispensaries attached to a psychiatric office. Where any additional community-based services exist, these are often implemented by non-governmental organizations (NGOs) or international agencies. The range and quality of mental health services in the post-2004 EU countries and other middle income countries tend to lie somewhere between those of the EU-15 and CIS countries. However, the boundaries of this divide are blurry, and no two countries in the region have the exact same mental health system in place.

Inpatient services

In general, the number of psychiatric beds has been decreasing steadily across Europe and mental hospitals are increasingly being closed down (7). However, in some countries this process has been much slower than in others (9,17). Although inpatient services in mental hospitals still exist in almost all European countries (the exceptions are Italy, Iceland, Andorra, Monaco and San Marino), the number of psychiatric beds and the balance between beds in mental institutions and inpatient community-based facilities varies greatly between countries (see Table 1). Whilst in some countries the small number of inpatient beds is due to the substantial progress that has been made in replacing mental hospitals with community-based care (the UK and Italy for example), in others (such as Albania and Turkey) the small number of beds reflects a lack in funding and a deficit in service provision for mental health overall. Other countries, primarily EU-15 countries such as Belgium, France, Germany, and the Netherlands, have a combination of large numbers of inpatient beds and community services (12). However, in most European countries (in particular those in Eastern parts) institutional care still outweighs community care

Table 2 Overview of systematic reviews evaluating community mental health services in the European Region

Authors	Service evaluated	N. studies included	Main outcomes
Burns et al (18)	Community care (range of services) compared to admission	91	Benefits in terms of days hospitalized (regardless of service type) Inconclusive in terms of cost-effectiveness
Wright et al (19)	Community care (components of care related to effectiveness)	55	Regular home visiting and taking responsibility for both health and social care associated with reduced hospitalization (regardless of service type)
Harkness and Bower (20)	On-site mental health workers in primary health care (replacement model) compared to off-site mental health services	42	Small and inconsistent reduction in number of consultations with primary care providers, psychotropic prescribing, prescribing costs and rates of referral No effects on prescribing or referrals in the wider patient population Cost-benefits unclear
Gilbody et al (21)	Collaborative care compared to usual care	34	No significant predictor of antidepressant use Key predictors of depression symptom outcomes were systematic identification of patients, professional background of staff and specialist supervision
Malone et al (22)	Community mental health teams compared to non-team standard care (delivered as community, outpatient or hospital treatment)	3	Reduction in hospital admissions and number of deaths by suicide Promoted greater acceptance of treatment
Marshall et al (23)	Case management compared to standard community care	10	Increased number of patients remaining in contact with services Greater proportion of patients hospitalized No significant benefits on psychiatric or social variables Cost-effectiveness inconclusive
Marshall and Lockwood (24)	Assertive community treatment compared to standard community care, hospital-based rehabilitation, or case management	20	Improves outcome and patient satisfaction Reduces costs of hospital care for high users of in-patient care
Burns et al (25)	Intensive case management compared to standard care for people with serious mental disorders	29	Small but statistically significant reduction in days spent in hospital overall, but large variation between studies Largest effects when patients had high hospital use at baseline, and the more closely treatment adhered to principles of assertive community treatment Setting of trial did not have effect
Marshall and Lockwood (26)	Early intervention for psychosis	7	Evidence of poor quality overall and studies not comparable due to different intervention approaches taken
Irving et al (27)	Crisis intervention and resolution teams (delivered as part of an on-going home treatment package)	5	Reduction in admissions May be less expensive than standard care, but more data is needed to confirm this
Macpherson et al (28)	Community-based residential care (24-hour staffed) compared to standard hospital care	1	Patients more likely to use social facilities and spent more time in socially constructive facilities (such as self-care, eating with group) Study was small and of poor quality
Marshall et al (29)	Acute day hospital care compared to inpatient care	9	At least one fifth of patients admitted to inpatient care could be cared for in an acute day hospital More rapid improvement in mental state, but not social functioning Less expensive

by far, with around two thirds of all psychiatric beds across the region still located in mental hospitals (7).

Mental health in primary health care

Whilst all countries in the European Region increasingly have mental health services integrated into primary health care (see Table 1), the extent of this varies widely. In many

countries the primary health care system for mental health is still inadequate (12), and even in high income countries the provision of mental health services within primary care has often been found to be less than optimal (66). Mental health training for primary care staff is only available in around two thirds of countries (12), and is often insufficient, which frequently results in mental health problems not being recognized or treatment methods being unknown (7,9).

Table 3 Overview of randomized controlled trials (RCTs) evaluating community mental health services in the European Region

Authors	Service evaluated	Country, N. subjects	Main outcomes
Richards et al (30)	Collaborative care compared to usual care	UK, 114	Reduction in symptoms for depressive patients
Killaspy et al (31,32) McCrone et al (33)	Assertive community treatment compared to usual care from a community mental health team	UK, 251	No difference in the need for in-patient care, clinical or social outcomes More contact with patients involved, but no difference in costs Increased client satisfaction and engagement with services
Morrison et al (34)	Early intervention in patients with prodromal symptoms (cognitive behaviour therapy compared to monitoring only)	UK, 60	No difference in leaving the study early or transition to psychosis
Agius et al (35)	Assertive early intervention compared to standard community mental health team	UK, 125	Range of benefits over three years, but study not fully randomized and patients were unusually engaged with services (so results should be treated with caution)
Petersen et al (36) Bertelsen et al (37)	Intensive early intervention compared to standard treatment in patients with first episode schizophrenia	Denmark, 547	Improved clinical outcome at two years, but effects not sustained at 5-year follow-up Differences in the proportion of patients living in supported housing and days in hospital in favour of early intervention at 5-year follow-up
Johnson et al (38) Cotton et al (39)	Crisis resolution team (24-hour short-term care) compared to standard care in patients who were experiencing a crisis severe enough to be eligible for admission	UK, 260	Reduction in admissions Patients most likely to be admitted to hospital were those who were uncooperative with initial assessment, were at risk of self-neglect, had history of compulsory admission, were assessed outside usual office hours and/or were assessed in hospital casualty departments Increased patient satisfaction
Priebe et al (40)	Acute day hospital care compared to conventional wards	UK, 260	Greater improvement in psychopathology at discharge, but not at follow-up Higher patient treatment satisfaction at discharge and after 3 months, but not after 12 months More expensive
Burns et al (41,42) Catty et al (43)	Vocational rehabilitation services (supported employment) compared to other high-quality vocational services	UK, Germany, Italy, Switzerland, Netherlands, Bulgaria; 312	Competitive employment obtained more often, jobs kept longer and more hours worked More unwell people helped into work Working associated with better clinical and social outcomes at 18 months Patients with previous work history, fewer met social needs and better relationships with their vocational workers were more likely to obtain employment and work for longer

Note: Where there has been a systematic review published of a particular service, only those RCTs are displayed which were conducted after the review

Community mental health services

Although there is a definite trend towards an increase in community-based mental health services and a decrease in institutional care (12), the pace and scale at which this is occurring, as well as the quality of services, varies widely throughout the region (7,17). For instance, at least 85% of countries now report having mental health day care, but in some countries such services tend to be attached to long-term mental hospitals or may be very limited in number, while in others there may be a variety of day care services available in a selection of community settings (12). Furthermore, access to such services may be very limited within countries, especially in the Eastern parts of the region (12). Variables such as location,

age, gender, ethnicity, employment status, type of diagnosis, educational background or socioeconomic status may determine whether care, and what type of care, is received (7,9, 12,67,68). One example of this is that more services tend to be available in urban areas compared to rural settings.

LESSONS LEARNED AND RECOMMENDATIONS

We present here an overview of the lessons learned in the implementation of community mental health services across Europe, as well as recommendations for the region in the future. Specific steps on how to facilitate and implement these can be found in the WPA Guidance (4).

Treatment gap

Clinical experience and research evidence have shown that the implementation of community mental health services according to a “balanced care model” is possible and desirable (4,61-65). However, there is still a gap between population need and actual service provision across Europe, both between and within countries (67,68). To reduce the gap between the Eastern and Western parts of Europe and to scale up services across the region, the focus should be on the development of community-based services in the low and middle income countries, whilst sustaining and improving services in high income settings. Furthermore, equal access for all needs to be ensured *within* countries, that is across different regions and subgroups of the population (9,12). Changes in service provision should be carefully planned to ensure gradual, balanced and sustainable reform, which takes into account local conditions and resources, as well as the cultural context (61,64).

One important factor in making services accessible to whole populations is the continued integration of mental health services into primary health care, and an improvement in the quality of care within these systems. This may be facilitated by ensuring that there are sufficient numbers of primary care staff, regulating training, organizing adequate and ongoing supervision of primary care staff by mental health professionals, addressing staff attitudes, and by developing and managing coordinated support networks with specialized community mental health services and other relevant sectors (such as social welfare, health, housing and employment, as well as NGOs and the private sector) (7).

Human rights, stigma and social inclusion

The lack of adequate community mental health services in some parts of Europe may lead to the social isolation of people with mental health problems, or even a violation of their human rights through neglect and abuse (12). Even in high income countries (where community services tend to be more established), people with mental health problems may still be subject to stigma, prejudice and discrimination (7). National programmes and plans should therefore be implemented to ensure that the human rights of people with mental disorders are upheld, their social inclusion and full integration into society (including in the workplace) is encouraged, and stigma and discrimination are reduced. These may include public mental health promotion, advocacy and awareness-raising programmes, both for the general population (for instance through media campaigns) as well as for health staff and personnel in the other relevant sectors mentioned above (7,9-12). Furthermore, care services should be monitored and reviewed regularly to ensure that human rights standards are upheld (12). Importantly, the views of service users, their families and carers (as well as any other stakeholders) should be included in the planning and implementation of policies, and in service

development, monitoring and provision (7,9,12,61,64). Currently, service user involvement is highest amongst EU-15 and other EU countries, but is only in the early stages of development in most Eastern European countries (12).

Legislation, policies, plans and programmes

One of the first steps in ensuring fair access to services for all is the formulation of carefully planned mental health legislation and policies that take into account a wide range of stakeholders' views (9). Even though there has been much progress in recent years, several countries in the European Region still do not have adequate mental health legislation and policies in place. Comprehensive new national policies and legislation (including mental health promotion, prevention and advocacy) should be developed where these are absent, and older existing mental health policies and legislation should be updated. This needs to consist of a commitment not just by health ministries, but also by the other sectors already mentioned which may be relevant to mental health care (7,9). To address challenges in the implementation of these policies and to reduce the gap between mental health policy and practice, in particular in some of the Eastern and South-Eastern countries of the region (12), detailed, feasible (though ambitious), sustainable and highly practical implementation plans and programmes should be developed.

Resources (financial and human)

A common challenge in implementing mental health policies is the lack of adequate funding mechanisms for mental health, in particular in much of Eastern Europe (17). Related to this is a shortage of human resources. Mental health staff numbers have increased in several EU countries (9), but most of the mental health workforce in Europe is concentrated in a few high income countries, and human resources for mental health are still lacking in many other parts of the region (12). For example, whilst some of the high income countries such as Belgium, Finland and Iceland have over 20 psychiatrists per 100,000 population, other countries such as Turkey or Tajikistan have less than 2 (see Table 1). This shortage typically results in mental institutions being retained and staff being assigned to mental institutions (7), which in turn leads to community mental health facilities being hugely understaffed (17). Moreover, mental health workers are often underskilled due to insufficient resources for training (7,12).

Since community mental health care overall has been shown to be cost-neutral compared to institutional care (61,62,64,65), one solution in optimizing the use of available resources is to gradually shift financial and human resources from large mental institutions to community services (9,61, 62,64,65). This requires a changing of staff roles, responsibilities and expertise, for instance through mental health workforce strategies (12), as well as new ongoing mental health

training programmes and an inclusion of mental health into general health care education programmes (7,9, 12,61,64). Staff anxieties and uncertainties due to changing roles and service structures should also be addressed (61,64), and working conditions and pathways for career development should be improved to reduce staff turnover (7).

Research evidence

An evidence base is vital to determine the effectiveness of community mental health services. However, this is still lacking for most countries in the European Region, in particular outside the UK and other high income (primarily EU-15) countries. High-quality and well-defined evaluative research is needed across countries to strengthen the evidence base for clinical outcomes and cost-effectiveness of community mental health services, as well as the relative effectiveness and efficiency of policies and programmes (12). To avoid duplicating information unnecessarily, this should include standardizing data collection systems and indicators across the region (for instance through the publishing of data collection guidelines) (7,9,12), and forming a consensus on definitions of service components (12). This, together with adequate dissemination systems, may enable evidence-based comparisons of services and programmes to be made, which may in turn inform policies (7,9,12) and allow for a more informed allocation of limited resources (7).

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The heterogeneity of “major depression”

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The concept of major depression, in both the ICD and the DSM, has been a flagship for mental health in general medical settings. It is the principal mental disorder emphasized to general practitioners and hospital doctors, and it has been used by governments to raise awareness of mental health issues in the population at large and in the medical community (1-3). It has encouraged the development of specialized forms of psychotherapy for depression, it has allowed the formation of community groups to propagate accurate information about depression, and has led to the development of computer programmes to assist self-treatment using the principles of cognitive-behavioural therapy (4,5). These are substantial achievements, but they come at a price. This is the belief that “major depression” is a homogeneous entity, and indeed that it is usually a “major” disorder.

The DSM diagnosis of major depression is made when a patient has any 5 out of 9 symptoms, several of which are opposites. Thus, a patient who has psychomotor retardation, hypersomnia and gaining weight is scored as having identical symptoms as another who is agitated, sleeping badly and has weight loss. This causes real problems with research designs: for example, Lux and Kendler (6) had to group these opposite symptoms together. Even so, it was possible for them to distinguish between “cognitive” and “neurovegetative” symptoms, and show that these have different relationships to a larger set of potential validators. They concluded that their results “challenge our understanding of major depression as a homogeneous categorical entity”. Others have been able to separate the various depressive symptoms, and to compare the relative efficiency of each symptom to making the diagnosis (7). Jang et al (8) factor analysed a larger set of depressive symptom scales, and found that they could identify 14 different subscales, which had rather low intercorrelations, and very different heritabilities.

Given these findings, to declare that all those satisfying the DSM criteria for the diagnosis of major depression are suffering from the same disorder seems like magical thinking. We know that many milder cases remit without specific treatment, suggesting that they are indeed homeostatic responses to life stress (9). Depression may be a toxic reaction to drugs or may result from endocrine disorders such as myxoedema or Cushing's syndrome. The depressed phase of bipolar illness may be difficult or impossible to distinguish from unipolar depression. Melancholic, atypical and psychotic forms of depression are yet other variants. Agitated depression needs to be distinguished from retarded depression when choosing the most suitable antidepressant. But even with these exclusions, there are five other forms of ma-

major depression that require a range of different responses from the clinician.

The first form is depression presenting with somatic symptoms (10). Many patients with this condition may be resistant to accepting that they are depressed. They benefit from special additional measures that explain how emotional arousal and depression can cause their somatic symptoms. Such measures have been developed for many years, and have recently been elaborated (11).

The second form is depression with panic attacks. While treatment of depression is the first priority in these patients, it is also important to give them advice on what to do during a panic attack, as it may take a little time before improvement in their depression stops further attacks. They need advice about not immediately leaving the environment in which the panic attack is taking place, explanations about catastrophizing thoughts and advice on helpful “self-talk”. They need to remind themselves that they have had such attacks before, and they will pass off if they calm down and remember the reassuring thoughts that run counter to the content of their thoughts during an attack. Such advice makes the attacks easier to deal with, and less likely to become still worse.

The third form is depression in people with obsessional traits. People with these traits in their usual personality often develop quite severe obsessional behaviour and depressive ruminations during a depression. These symptoms may be experienced as the leading symptoms, but can be thought of as epiphenomena of their depressive illness. It is helpful to take the patient through thought-stopping techniques, distraction techniques and response prevention.

The fourth form is depression accompanying known physical illnesses. These depressions are particularly poorly recognized by generalists, who typically confine themselves to the treatments for the physical illness (12). Diagnosis of these depressions is complicated by the fact that four of the “diagnostic features” of depression (fatigue, poor sleep, poor appetite and weight loss) may well be caused by the physical illness. This may generate confusion, since no clear threshold for the number of symptoms needed for a diagnosis seems to exist if such symptoms are to be discounted. However, if there is a positive reply to either of the usual two screening questions for depression, it is only necessary to ask three additional questions dealing with poor concentration, ideas of worthlessness and thoughts of death. A total of three or more from this list of five symptoms allows depression to be diagnosed with high sensitivity and specificity, when assessed against the full list of criteria (13,14). Successful treatment of the depression is associated with a low-

er mortality and better collaboration with the necessary physical treatments. The special task of the physician is to reach agreement with the patient that he/she is indeed depressed, and to explain the effects that this is having on the quality of the patient's life, the severity of any pains that are experienced, and the disability associated with the physical illness. The range of treatments that are effective in depression among the physically healthy are all effective in these patients, and the only special measure required of the clinician is to guard against harmful interactions between antidepressants and drugs used for the physical illness.

The fifth form is pseudo-demented depression. In older people, depression may present as an apparent dementia, but the presenting symptoms turn out to be due to inattention and impaired concentration, while symptoms of depression are undoubtedly present and may be elicited by direct enquiry. The special task here is to reassure both patient and carer that the memory problems are not due to cerebral disease, and are likely to improve a great deal with treatment of the depression.

Official classifications of mental disorders often deal with the above heterogeneity by invoking the idea that an individual patient has simultaneously developed more than one "co-morbid" disorders. Many depressions are likely to be accompanied by anxious symptoms, so these disorders should more properly be described as "anxious depressions". The concept of "co-morbid generalized anxiety disorder and major depression" does not describe most cases of anxious depression, since for this concept the anxious symptoms should have lasted 6 months, while the depressive symptoms need only have lasted 2 weeks. It is therefore describing a depressive reaction grafted on to a chronically anxious person, and is thus a more restrictive concept than anxious depression.

However, anxious symptoms are by no means the only symptoms that often occur with depression, as most patients presenting to generalists will present with the various combinations described above. The concept of "co-morbidity" has not led to the development of special recommendations for the management of the very different ways in which a depressive illness presents in different people. Instead, while there are recommended treatments for each separate mental disorder, the implication has been that these treatments are just added together for each co-morbid disorder. Symptoms arising as epiphenomena of depression do not necessarily need the same range of interventions as when similar symptoms are occurring in a non-depressed person, but they do need some help. It is also worth remembering that telling a person that he/she has multiple mental disorders is both stigmatizing and somewhat depressing.

It may be questioned whether it is worth making these distinctions between the various subtypes of depressive illness, since once a remission has occurred all these ancillary symptoms are likely to have remitted anyway. The justification is partly due to the need to provide different advice for the ancillary symptoms while the episode lasts, as well as the

possibility that remission might occur more quickly if additional advice is provided for the patient during the episode.

The five subtypes listed above have been chosen because they each have particular features that attract different clinical approaches to the problem posed by the depression. Rather than making multiple diagnoses, it seems preferable to have regard to the principal manifestations of the patient's present problems, and to respond appropriately to them.

If we develop depressive symptoms, we may develop other symptoms, dependent upon any vulnerability factors in early life, on our personality structure, and on stressful features in our present social environment. It is profoundly mistaken to assume that the various common symptom patterns described are rigidly demarcated, and that a classification exists in which the various syndromes are "mutually exclusive and jointly exhaustive".

The clinician must aim to give useful advice to the particular patient seen, without foisting an arcane system of multiple diagnostic labels onto him/her.

At present major depression has become a monolith, with the assumption that the diagnosis can be made merely on the number of depressive symptoms present, with an associated disability. It may be politically important to utter such simplifications to doctors in general medical setting, but it is a convenient fiction.

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Partnerships for better mental health worldwide: WPA recommendations on best practices in working with service users and family carers

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WPA President M. Maj established the Task Force on Best Practice in Working with Service Users and Carers in 2008, chaired by H. Herrman. The Task Force had the remit to create recommendations for the international mental health community on how to develop successful partnership working. The work began with a review of literature on service user and carer involvement and partnership. This set out a range of considerations for good practice, including choice of appropriate terminology, clarifying the partnership process and identifying and reducing barriers to partnership working. Based on the literature review and on the shared knowledge in the Task Force, a set of ten recommendations for good practice was developed. These recommendations were the basis for a worldwide consultation of stakeholders with expertise as service users, families and carers, and the WPA Board and Council. The results showed a strong consensus across the international mental health community on the ten recommendations, with the strongest agreement coming from service users and carers. This general consensus gives a basis for Task Force plans to seek support for activities to promote shared work worldwide to identify best practice examples and create a resource to assist others to begin successful collaboration.

Key words: Service users, family carers, mental health, partnerships, best practices

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During the last years, several countries (including USA, UK, Ireland, Australia, New Zealand, and Canada) have embraced recovery-orientation as a guiding principle of their mental health policy (1). Key to this development is a partnership approach between mental health experts and users of mental health services and their families and friends.

Service users and their families have an important role in advocacy in order to enhance the reputation of mental health expertise and services as well as that of people with a lived experience of mental ill health. In recent years, service users and carers have been involved positively in a range of activities including advocacy for support for research, care and social inclusion, and self-help projects. The WPA has cooperated on several levels with different user and carer organizations, as with triologic symposia at congresses and affiliated memberships, with encouraging results. Efforts in several countries to change community attitudes and improve mental health care in partnership have produced resolutions and guidelines, but their wide use and the structural changes they call for are yet to be achieved (2).

The founders of WPA included among its aims an important role as a voice for the dignity and human rights of patients and families (3). Subsequently, the WPA has developed ethical guidelines for psychiatric practice, including the Madrid Declaration (4), which sets out standards for respecting patients, treating them as partners in the therapeutic process, and safeguarding human dignity and legal rights.

WPA TASK FORCE ON BEST PRACTICE IN WORKING WITH SERVICE USERS AND CARERS

In 2008, a Task Force on Best Practice in Working with Service Users and Carers was established by WPA President M. Maj under the leadership of H. Herrman to support the WPA Action Plan for the years 2008 to 2011 (5) and one of its goals: "To support international and national programmes aiming to protect the human rights of persons with mental disorders; to promote the meaningful involvement of these persons in the planning and implementation of mental health services; to encourage the development of a person-centred practice in psychiatry and medicine; and to promote equity in the access to mental health services for persons of different age, gender, race/ethnicity, religion and socioeconomic status".

The WPA invited service users and family carers to join the Task Force, recognizing their essential contribution to improving mental health in any country. The Task Force had a remit to prepare recommendations for the international mental health community on best practices in working with service users and carers.

The Task Force defined the primary need to develop a unified approach to advocacy for mental health and human rights at country and international levels. Adequate support for mental health services and improvement of mental health in any population require a united voice. Achieving this will need support for the capacity of each group to work effec-

tively in partnership. As service users and family carers typically lack the power to interact equally with professionals and government decision makers, assistance in developing this power is mutually important for them and for the WPA and the wider international mental health community (2).

LITERATURE REVIEW ON SERVICE USER AND CARER INVOLVEMENT

A literature review on service user and carer involvement in improving mental health was carried out. The brief was to identify and summarize existing research and guidelines relating to collaboration between mental health professionals and service user/family/carer stakeholders in the areas of policy, practice, research, evaluation, training, education, fighting stigma and discrimination, and joint lobbying for resources to support good practice in research, care, rehabilitation and social inclusion. The literature review methods included: searching databases, and making links with service user and carer organizations, and with national and international mental health bodies and other entities that involve and promote the rights of people with disabilities. The results of the review are set out in the following paragraphs in terms of the key themes found in the literature.

Terminology

Terminology is an important aspect of working in partnership, as it enables clarity about who should be involved, how those people and groups see themselves and their respective roles, and the forms and levels of involvement, and where and how it happens (6,7).

Terminology for each stakeholder group can be controversial even among the group concerned, for instance, whether people want to be called “consumers”, “service users”, “patients”, “clients” or “survivors” differs from one person and group to another, as well as causing controversy among the other groups. Similarly, people who are involved as family members may want to be called “carers” or “caregivers” or simply “family” or “friends” (8).

Partnership is defined as a collaborative relationship between users, carers and clinicians. Forms of partnership can range from information giving to service user- or family/carer-run services, and include various types of collaboration (9,10). The forms and levels, from informing to power-sharing and leadership by families and service users, must be a key aspect of guidelines, as clarity about what is on offer or available is an essential aspect of setting out the terms for partnership (11).

Sites for partnership include personal care at the basic level (12), all the way through local, regional, national and international sites where involvement can happen. Each site can have its own levels (13,14). For instance, at the site of the person, someone can be informed of his/her choices, sup-

ported to make choices, or given the resources to buy his/her own services. At the national site, people can be informed of decisions made, consulted at an early stage via surveys, invited as members onto national committees, or given funding to develop their own national programmes.

Other criteria for partnership include the type of service, or the diagnostic group, when partnership is focused on particular aspects of psychiatric work, for instance on developing new community services for people diagnosed with personality disorders (15).

Clarifying the partnership process

This begins with setting goals, and proceeds through all the actions to specify how the work will proceed, how to monitor and evaluate the work and use what has been learned to inform future work. The review identified a range of work in which service users and families have been involved, including training and education, advocacy, research and evaluation, planning, management, and service provision (16-18). Clarity on the aims, objectives, processes, outcome measurement and learning from doing are relevant to each of these and help assure success and longevity (7).

Barriers to partnership

The review showed that the same barriers to partnership emerge repeatedly in the literature (19,20), while actions and systems that support involvement are also becoming clear.

Partnership can be hindered by lack of clarity on the issue of representativeness or accountability (21). Lack of commitment by service providers, planners and professional staff is often shown in “tokenism” – i.e., low numbers involved, poor support in terms of funding and access to resources, or lack of support and training for the stakeholders (9). Everyone needs training in how to work together.

Another typical barrier relates to policy and strategy. Organizations need a clear policy about partnership, and staff should be aware of existing policies and how to implement them.

Differing objectives among stakeholders can create barriers to successful partnership working (22,23), and the literature review showed a range of objectives each group may bring with them to the process. Service users and patients may be concerned with basic facilities and treatments, human rights and choices, while families also seek better care for the person cared for, plus the right to be more involved in care, and more help for themselves. Staff concerns can range from concern about what is expected of them and how to add involvement to their other duties, to overall service improvement and meeting targets. Managers may be concerned with costs and government objectives. Commissioners have to balance public concerns with choice and rights, and governments want to deal with issues of concern to the electorate.

Good practice that supports partnership

The review identified several aspects of good practice in involvement of service users and families, including the following: involvement from the outset in new ventures and in changing existing services; awareness of cultural issues that relate to different groups within the population; addressing stigma and discrimination among public and staff; clarity and honesty about what is possible, what is expected, what is not possible; ensure that involvement is not tainted with coercion, control or manipulation; ensure there is a genuine willingness to instigate change; a range of involvement methods and opportunities to suit needs and abilities; accessibility issues addressed (practical and financial); giving more control of involvement budgets to service user/carer groups; support and supervision available and regular for persons involved; support and finance to enable representativeness and accountability to wider groups; capacity building for service users/families/public; staff training in involvement good practice; involvement championed and supported from the highest levels downward; support for staff to do involvement work; clear involvement policies that are “owned” and understood by all stakeholders; monitoring and evaluation of involvement and dissemination of results; involvement being valued and being seen to be valued by service providers and planners.

Examples of involvement that work

The literature review identified examples of successful partnerships. Service users and carers are involved in training mental health workers in the UK (17). Service users are involved in monitoring of services or developing outcome measures in some countries (24,25). In many countries, service users and carers sit on committees to plan and manage services (26), though family involvement on committees is less frequent (27). Consumer consultants are successfully employed in Australia (20,28). Trialogue (regular discussion meetings outside work environments between stakeholders) is another method that has been found effective in Germany and Austria (29,30). Guidelines for partnership working have been developed in some countries (11,31,32).

TASK FORCE CONSULTATION PROCESS

The first meeting of the Task Force was held in Vienna in March 2010. Before the meeting, members were asked to rate and comment on the relevance and importance of the themes drawn from the literature. The Task Force drew on the literature survey and this thematic analysis, as well as best practice examples in their own countries and personal experiences of mental health systems and practice. The meeting set an example of partnership and cooperation, bringing together a range of stakeholders. One person took part from India through a Skype connection. Over two days, the group

brought together a range of knowledge and ideas, debated the issues, and drew shared conclusions that were set out in the first version of the ten recommendations.

Consultation methods

Two methods of consultation were developed. The first was an online survey of service users and carers and the WPA Board and Council members. In the second, the Task Force sought to consult ordinary people who are service users and carers. C. Underhill and S. Raja, special advisers to the Task Force from BasicNeeds, offered this organisation’s experience of grassroots consultation to reach people with personal experience of mental illness in Kenya, Laos and Sri Lanka. The consultation was designed to enable people in remote areas and those who could not read to be consulted. B. Davar coordinated a series of micro-consultations with organizations and one individual expert in four cities in India.

The Task Force also consulted the WPA Committee on Ethics and invited the Chair and an additional member, who is also an officer of the World Association of Psychosocial Rehabilitation, to attend the Task Force as special advisers to consider amendments to the WPA’s Declaration of Madrid.

Online survey

Individual experts were contacted by e-mail and invited to complete a short electronic questionnaire. For the survey of service users and carers, a consultation list was drawn up. Some people included were leaders in non-governmental organizations (NGOs) working in the mental health field. Other organizations and individuals were identified from the literature review. Each of the Task Force members had a contribution to make in terms of individuals, groups and networks that could participate in the consultation. Expert stakeholders were sought in every country where the Task Force group members had contacts, which included most of the world’s continents. Since there were no resources for translation, participants had to be English-speaking. The decision was taken to consult individual experts, as consulting members of organizations could take too long. However, one organization, the European Federation of Associations of Families of People with Mental Illness (EUFAMI), was able to consult its membership.

Each of the ten recommendations was the subject of a question. Respondents were asked to rate agreement with the recommendation, and were also given space for an optional comment. The eleventh question was an open invitation to list additional topics.

The survey was circulated in June and July 2010 and responses returned in August. Among the 151 service users and carers who were invited to participate, 126 responded. There were 24 responses from 30 members of the WPA Board and Council.

The results were presented and discussed at the second meeting of the Task Force at the WPA International Congress in Beijing in September 2010.

Consultations in four low-income countries

A series of consultations with users and carers participating in BasicNeeds' field programmes was held in three countries. A total of 1197 users and carers participated: 32 in Lao PDR, 62 in Sri Lanka and 1103 in Kenya. Most came from rural low-income families. In Kenya, consultations were also held with existing national organizations of service users, namely the Schizophrenia Foundation of Kenya, and The Users and Survivors of Psychiatry, where participants were drawn from urban middle and upper class families. In Sri Lanka and Kenya, discussion topic guides were developed based on the recommendations selected for use in the consultations. In Lao PDR, a discussion instrument was developed which had six questions, as prompts to facilitate the discussions at the consultations.

In a similar time period, consultations with five organizations and one individual expert were carried out in four cities in India (Pune, Bangalore, Delhi and Chennai).

RESULTS OF SURVEYS AND CONSULTATIONS

In the following paragraphs, we report the outcome of the survey concerning each of the ten recommendations drafted in March 2010.

Respecting human rights is the basis of successful partnerships for mental health

Service user and carer respondents generally agreed that rights are the basis for partnerships. However, there were differing opinions about the application of human rights. Some argued that, even if physical restraint is needed, attitudes and behaviour should be respectful of the person. Others argued that coercion is almost always experienced as disrespectful, and were concerned that enactments of human rights legislation in some countries explicitly exclude people with a psychiatric diagnosis from some provisions. Some argued that human rights have to be set aside when someone is in a psychotic state.

Respondents from the WPA Board and Council similarly agreed that human rights are a basis for practice, but some argued that respect was more important than generalized rights. Some stated that health and treatment are rights, and this could necessitate treatment against someone's will when psychotic.

Legislation, policy and clinical practice relevant to the lives and care of people with mental disorders need to be developed in collaboration with users and carers

Service user and carer respondents agreed that collaboration is needed; otherwise legislation, policy and clinical practice will be based on a one-sided agenda led by government and service providers. Since mental health is a contested area, service users need to ensure the service they receive is respectful of persons as citizens. There were concerns that power differentials between patients and service providers can make genuine collaboration difficult.

Respondents from the WPA Board and Council agreed there should be more progress towards genuine collaboration, but raised concerns about who would be consulted, to ensure genuine representation of those who suffer most serious mental illness and their families, and local needs and cultures.

The international mental health community should promote and support the development of users' organizations and carers' organizations

Service user and carer respondents called for greater recognition of the contribution of peer support and service users' movements in supporting well-being and improving service provision. There were concerns that there should be strong, independent organizations to express the voices of service users and carers both separately and collaboratively where possible, without pitting them against each other.

Respondents from the WPA Board and Council agreed that support for service users and carers' organizations is important, with some reservations about which organizations would be supported and their aims and objectives, and that respect for different local cultures and values is important.

Improving the mental health of the community should be a fundamental condition for formulating policies to support economic and social development. This requires participation of all sectors of the community

Service user and carer respondents felt that mental health is a central aspect of health and called for a move beyond a focus solely on medical understandings of mental health, towards working also in ways that support the well-being of communities and healthier environments. However, reservations included the fact that some people might not want to participate, and also that community psychiatry could be misused to widen compliance with psychiatric medication without a broader focus on well-being.

Respondents from the WPA Board and Council agreed generally that there is greater need to lobby governments and try to educate the population about mental health, and that mental health cannot exist where basic needs for water, san-

itation, food and housing are absent. However, concern was expressed that money spent on wider mental health promotion would not necessarily help people living with mental illnesses.

International and local professional organizations, including WPA through its programs and member societies, should seek the involvement of consumers and carers in their own activities

Service user and carer respondents agreed inclusion is an important principle and there should be funding to ensure enough people could participate to make a real difference. Reservations included the fact that involvement might only be lip service and not make a real difference to service choices offered. There was concern raised that service users and carers should not be seen as interchangeable, and that groups invited to be involved should be independent of funding from the pharmaceutical industry.

Respondents from the WPA Board and Council agreed that professional organizations should be proactive in opening their ranks to non-governmental organizations and service users' and families' organizations.

The best clinical care of any person in acute or rehabilitation situations is done in collaboration between the user, the carers and the clinicians

Service user and carer respondents agreed that involvement needs to be meaningful, not just tokenistic. They argued that people need to contribute to discussions around their own care and health, and to be able to take responsibility for their own recovery. There was concern about who makes the decision about treatment, and about possible conflicts of interest between service users and family members. Family members were concerned they are often left out. Some service users questioned whether collaboration was possible when acute treatment can be forcibly administered.

The BasicNeeds consultation found that service users and carers see access to treatment and sensitive engagement with service providers as important to keep up their motivation for treatment. Carers felt they need support to deal with crises such as suicidal behaviour. They see collaboration between service users, carers and clinicians as important and much needed. They want to ensure clinicians understand that there is more to patients than their illness.

Service user participants in the micro-consultations in India generally commented on their wish for greater involvement in their own treatment, to be listened to by doctors, and to receive explanations for treatments. They ask for treatment that takes into account people's creativity and spirituality, and want to be offered alternatives to medication or medicines with fewer side effects. Family members in India expressed concern that people with mental illness receive

worse services than other health groups. Doctors are held in high respect, but this gives their words great power and they should take care about the effect of their words. Family members also want more multi-dimensional diagnoses and interdisciplinary teams.

Respondents from the WPA Board and Council agreed that collaboration is important but that this might not always require all three members of the dialogue, and may at times engage others such as community elders in traditional societies.

Education, research and quality improvement in mental health care require collaboration between users, carers and clinicians

All groups of respondents agreed with this principle. Service user and carer respondents noted its importance given new ideas and paradigms such as recovery and community care which are changing treatment and care in some countries. Some wanted service users to lead the way to enable new understandings of mental health topics from their perspectives. Family members also argued for a stronger role based on their contribution to care. There was a suggestion that traditional healers could also be involved.

The path to recovery of mental health should include attention to economic and social inclusion (e.g., in areas such as the provision of appropriate education, housing, employment and legal and family support)

Service user and carer respondents generally agreed that recovery should go beyond symptom control, and include improvement in the quality of people's lives. Concerns included worries that there is now too much emphasis on employment, which may not be appropriate for everyone. Also it was pointed out that people might need to recover from the side effects of drugs and electroconvulsive therapy used in treatment.

The BasicNeeds consultation found that users and carers want education and work opportunities as these are important factors, which can enable people to manage their illness and to contribute to their family and gain social acceptance. Recovery includes being able to participate in religious and community activities.

Family members in India wanted more community support, in touch with local cultures, and taking in environmental factors.

Respondents from the WPA Board and Council generally agreed that social and economic determinants of mental health are important. However, some said there is a need to get the balance right between medical psychiatric treatment and the provision of education and housing, and some expressed a concern that there is a current movement to ignore the biological causes of severe mental illnesses and understand these illnesses as "diseases of society".

WPA Member Societies and other professional groups should collaborate with users' organizations, carers' organizations and other community organizations to lobby governments for political will and action for better funding of services, community education and fighting stigma

Service user and carer respondents generally agreed that this is important, and that fighting stigma and discrimination is essential. However, there were concerns that there are economic and power differentials, as well as differences of perspective between the groups that might make this collaboration difficult. There were reservations about anti-stigma work, which has been seen as unhelpful when led by governments or funded by the pharmaceutical industry. Anti-discrimination, especially in rights and employment, is preferred as a concept for which to struggle.

The BasicNeeds consultation found that service users and carers feel it is important to educate and sensitize their communities as well as local administrators about mental health and the needs of affected families, and about shortages of psychotropic medicines and availability of skilled personnel.

Enhancing user and carer empowerment includes the development of self-help groups, participation in service planning and management boards, employment of people with mental health disabilities in mental health service provision, user-run community centres and psychosocial clubhouses, speakers bureaux and local anti stigma programs

Service user and care respondents carers basically agreed with this, but also suggested that in some cases it meant moving beyond services and diagnosis to mainstream living. Carers said that they could also be employed in mental health service provision. However, in developing countries there is a long way to go to realize these aspirations. One person drew attention to the new United Nations convention giving equal rights to disabled people, and argued that this is a new agenda beyond empowerment.

Respondents from the WPA Board and Council agreed with some reservations, including a concern that employment of people with mental health disabilities in mental health service provision could lead to further stigmatization rather than empowerment.

TASK FORCE RESULTS AND ACHIEVEMENTS

At the second meeting of the Task Force in Beijing, the draft recommendations were discussed in the light of the consultation findings. Minor revisions were made. The new version was subsequently accepted by the WPA Executive Committee and posted on the WPA website (Table 1).

In consultation with the Task Force, the WPA Committee on Ethics drafted a paragraph based on six of the recommen-

Table 1 Recommendations for the international mental health community on best practices in working with service users and carers

Based on the understanding that recovery from mental illness includes attention to social and economic inclusion as well as adequate access to a balanced system of hospital and community mental health care, the World Psychiatric Association (WPA) recommends to the international mental health community the following approach for collaborative work between mental health practitioners**, service users** and family/carers**

WPA recommends that:

1. Respecting human rights is the basis of successful partnerships for mental health.
2. Legislation, policy and clinical practice relevant to the lives and care of people with mental disorders need to be developed in collaboration between mental health practitioners, service users, and carers.
3. The international mental health community should promote and support the development of service users' organizations and carers' organizations.
4. Improving mental health is essential for economic and social development. This requires participation of all sectors of the community.
5. International and local professional organizations, including WPA through its programs and member societies, are expected to seek meaningful involvement of service users and carers in their own activities where appropriate.
6. The best mental health care of any person in acute or rehabilitation situations is done in collaboration between mental health practitioners, service users, and carers. Working in this way generally benefits from special skills and training.
7. Education, research and quality improvement in mental health care requires collaboration between mental health practitioners, service users and carers.
8. The recovery process in mental health includes economic and social inclusion, as well as medical care. Examples of economic and social inclusion are access to: education and training, housing, employment, advocacy and family support.
9. WPA member societies and other professional groups should collaborate with service users' organizations, carers' organizations and other community organizations to lobby governments for political will and action for better mental health services, community education and fighting stigma and discrimination.
10. Enhancing user and carer empowerment should be sought through a range of different approaches and ideas, for example: the development of self-help groups; participation in service planning and management boards; employment of people with mental health disabilities as service providers and inclusive local anti-stigma-anti discrimination programs.

* These recommendations are intended for the international mental health community. Each country needs specific guidelines to apply these recommendations.

** "Mental health practitioners" include psychiatrists and other mental health service providers.

The term "service users" refers here to the people receiving or who have received mental health services. Other terms in common use are clients, patients, consumers, ex-patients and survivors. No one of these terms is current in all settings and countries, and different groups of practitioners and people with mental disorders have traditionally used different terms. Their historical, cultural and personal meaning carry considerable significance (for example, patient implies to some people the passive receipt of health care), but this is beyond the scope of these recommendations.

The term "carers" refers to family members and other people who are living with, or informally looking after, people with mental health problems. This differentiates these people from professional carers meaning employed mental health personnel.

dations that is proposed as an additional paragraph for the Declaration of Madrid. It will be presented to the WPA General Assembly in 2011 for endorsement.

CONCLUSIONS

The consultations produced strong consensus across diverse groups in the international mental health community on the ten basic recommendations. This is a notable result in itself. It is not surprising that considerable differences are found in individual and group opinions on the prominence of topics such as access to treatment and the right to decide. These differences correspond among others to the fact that mental health situations vary dramatically across countries and cultures and sometimes to a difference in agendas between service users and family members even with considerable overlap. The recommendations can encourage interest groups in each country or locality to work together in areas of consensus and continue (through dialogue and other means) to discuss the contentious topics.

This process is strengthened by the accompanying work of the WPA Committee on Ethics, a process that is likely to lead to WPA embedding the essence of these recommendations in the Declaration of Madrid, the ethical guidelines for psychiatric practice.

The Task Force did not include members from a number of important countries and regions, including China and Latin America. Furthermore, in the time and with the resources available, the survey was carried out only in English. This was partly mitigated by the grassroots consultations. In future projects, it will be important to develop this aspect of the work, and to involve all world regions.

The Task Force plans to seek support for a series of activities that will promote these movements in countries worldwide. Collecting a series of best practice examples of collaboration, addressing each of the recommendations, is a useful next step. This becomes a demonstration of the value of collaboration, and also a resource to assist others to begin successful collaboration. The Task Force will also encourage the development of country projects that provide further examples and stimulate others to follow. An example may be the development of a workshop in a low-income country to create a network between users, carers, professionals and government, including leaders of organizations. Specific efforts to enhance the dialogue in various settings would also be valuable as evidenced by recent experience in Beijing. The WPA could also consider a global project to investigate pathways for psychiatrists engaging with service users and carers and implementing the guidelines. At the international level, it will be important for professional bodies to consider how to promote the involvement of service users and carers in major congresses and events.

Proposals are being developed for some of these ideas that will ideally result in projects in low- and high-income countries designed to test selected recommendations and create

new networks to encourage partnership and collaboration between stakeholder groups. Working with one or two countries in a more concerted way to create guidelines based on the recommendations and evaluating these experiences is a feasible and desirable way to continue the work initiated in this project.

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The most vulnerable travelers: patients with mental disorders

Severe mental illness occurring abroad is a difficult situation for patients, their families, and the local medical community. Patients with mental problems are stigmatized due to both their mental illness and the fact that they are foreigners in an unfamiliar country (1). The appropriate treatment is often delayed, while patients are often dealt with in a manner that violates their human rights. Repatriation, which is associated with a better outcome of the mental disorder (2), is often delayed due to the lack of international protocols for the transportation and treatment of mentally ill travelers.

Acute travel-induced psychotic attacks are a well-known phenomenon in travelers without a previous history of psychosis. Young adults may experience their first psychiatric episode abroad (3). Elderly people are also susceptible to these attacks (4). Patients with a pre-existing mental illness almost never seek for pre-travel advice, so the prevention of any acute exacerbation is difficult. Specialists in travel medicine usually have little experience with these issues as they usually focus on infectious diseases.

There is research evidence that 11.3% of travelers experience some kind of psychiatric problem, with 2.5% suffering from severe psychosis and 1.2% requiring more than two months of therapy at home (5,6). The acute psychotic attacks represent about one fifth of travel-related psychiatric problems. Psycho-organic problems during leisure activities are as high as 5% (7). In a French sample, 15–20% of repatriations were due to psychiatric illness. These problems were predominant in long-term travelers, migrants or expatriates.

According to international standards, public transportation should not be used for acute psychotic patients, unless stabilized on medication and accompanied by a knowledgeable companion (8). Most travel insurance policies exclude treatment and repatriation costs incurred due to acute mental illness.

Modifying the approach to this issue by police, airport security, and insurance companies represents a challenge for psychiatrists. We believe that a clear set of guidelines, similar

to those recently published by the WPA on other mental health issues (1,9–11), could help in detecting and managing the traveler with mental disorders abroad. An appropriate preparation of people with mental disorders who have to travel and the application of a protocol for repatriation when needed should decrease the reluctance of insurance companies to cover these patients.

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Training and practice of psychotherapy in Europe: results of a survey

Although psychotherapy has traditionally been an essential part of psychiatric training and practice, its role within psychiatry has become less evident in recent years. There have even been some doubts as to whether psychotherapy will remain in the armamentarium of future psychiatrists (1). Several differences have been reported among European countries concerning both training and practice of psychotherapy (2). However, few studies have explored residents' and early career psychiatrists' views and perspectives about their psychotherapy training experience and use of psychotherapy in clinical practice.

The WPA, within its Action Plan 2008-2011, established an Early Career Psychiatrists Council (ECPC), with the aim to "promote the professional development of early career psychiatrists worldwide" (3). One of the goals of the ECPC Action Plan was to run a survey on training and practice of psychotherapy in European countries (4,5).

This survey has been conducted online with the ECPC members in the countries of Europe I Zone (Northern, Southern and Western Europe). Respondents have been invited to complete a questionnaire on the basis of their own experience and collecting the opinions of their peers. Twelve out of the 13 ECPC members (representing Austria, Belgium, Cyprus, Estonia, France, Germany, Italy, Spain, Switzerland, Sweden, Turkey and the UK) returned the questionnaires.

The 16-item questionnaire explored the following aspects: a) quality of psychotherapy training (supervision, type of psychotherapy training available, barriers in accessing training); b) organizational aspects of psychotherapy training (compulsoriness, payment and assessment); c) satisfaction with training in psychotherapy; d) self-confidence in the use of psychotherapy.

Training in psychotherapy is mandatory in all countries considered in the survey except Belgium and France. Psychotherapy training is available in the public school of medicine only in four countries (Germany, Spain, Switzerland, UK). In most of the countries, in order to receive psychotherapy training, residents have to pay additional fees.

Training in psychodynamic and cognitive-behavioral therapies is available in almost all countries, whereas training in systemic psychotherapy is provided in 6 countries, training in interpersonal, supportive and psychoeducational techniques in 4 countries, and training in dialectical-behavioural psychotherapy in 3 countries. The requested number of patients to be treated by the residents during the training ranges from none (Estonia) to more than 15 (Turkey). A dedicated supervisor for training in psychotherapy is not available in 5 countries out of 12, while in Austria, Cyprus and Switzerland supervision has to be self-financed.

Psychotherapy competencies are evaluated differently: a logbook or a workplace-based assessment is used in 3 coun-

tries, a written or oral examination is required in 4 countries. In the remaining countries there is not a clear guidance regarding trainees' evaluation.

The main barriers in accessing training in psychotherapy are difficulties to get time away from other duties, lack of supervisors, and lack of funding. Although a personal psychotherapy is mandatory in 9 countries, most European early career psychiatrists have to pay themselves for it.

Despite this heterogeneity, most European early career psychiatrists (70%) are satisfied with the training they receive in psychotherapy and 80% of them feel confident to use psychotherapies.

We hope this information can contribute to promote a process of harmonization of psychotherapy training within the European Union.

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Young psychiatrists' meetings in Eastern Europe – Networking for the development of psychiatric training, education and service

Although it is heartening that training activities in Europe have been evaluated (1), and robust standards set (2,3), discrepancies still exist between Eastern and Western Europe (4). Undoubtedly, some of this relates to economic factors, though this is only part of the story. In some Eastern European countries, formal psychiatry residency programmes are shorter than a year, and trainees acquire most of their knowledge through courses outwith their training programme (3). Furthermore, national trainee organizations do not exist in every country, but even if they do, low membership numbers may impede any progress. It is also crucial to integrate trainees' organizations into educational and specialists' organizations to feedback concerns and implement change.

Technical problems like lack of Internet access may make trainee interaction difficult. One possible solution is the inception of pan-European trainee meetings, and promoting trainees' contributions to curriculum development in their own countries (5). Sweden has for several years had a specific interest in Eastern European psychiatry, evidenced by projects funded by the Swedish Eastern Europe Committee (SEEC). Until recently, however, few projects have involved trainees or young psychiatrists (YPs).

Through a SEEC initiative, a pilot meeting discussing needs of YPs in Eastern Europe took place in Kaliningrad in May 2009. YPs from Belarus, Lithuania, Russia and Sweden agreed to organize meetings to promote networking and the exchange of experiences, facilitating YP education. Using existing networks such as the European Federation of Psychiatric Trainees (EFPT) and the WPA Early Career Psychiatrists Council (6), an organizing committee was created, and a grant from the Swedish International Development Cooperation Agency (SIDA) facilitated the inaugural meeting. Entitled "Ways to exchange knowledge and experiences of Young Psychiatrists", the conference took place in May 2010, involving YPs from the Baltic states, Belarus, Greece, Poland, Russia, Scandinavia and the UK.

The contents of the conference included clinical topics, in addition to research and health care development issues. There were lectures, workshops, case and poster presentations, with Russian translation. A visit to local psychiatric institutions was arranged by the local organizing committee. The cultural diversity of participants was exemplified by a quote from one of the delegates, when giving feedback, "we look at the same but we see different things". The evaluation

of the conference showed workshops were identified as the most popular aspect, probably due to the possibility to discuss and exchange points of view. On a 5-point Likert scale (1 very poor to 5 excellent), 33 (100%) people described their general impression from the conference as "excellent" or "very good". More than twenty topics for future meetings were suggested, including skills for YPs (education, leadership and working within teams).

Latvian colleagues kindly offered to organize the 2011 meeting in Riga, from 6 to 8 April 2011. Thanks to financial support from WPA and SIDA, about 90 delegates from 15 Eastern and Western European countries will be participating.

It is rewarding that YPs have been able to organize these meetings and we hope it will lead to continuous collaborations, facilitating future conferences as well as personal international contacts.

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The new impact factor of *World Psychiatry* is 5.562

The impact factor of *World Psychiatry*, which was 3.896 in 2009 and 4.375 in 2010, has now become 5.562.

The journal ranks now 9 out of 126 psychiatric journals and is no. 4 (preceded only by the *American Journal of Psychiatry*, the *Archives of General Psychiatry* and the *British Journal of Psychiatry*) among journals of general psychiatry.

The papers which received the highest number of citations during the period considered in the calculation of the new impact factor are the Special Articles by De Hert et al (1) on the metabolic syndrome in people with schizophrenia, by Zisook and Shear (2) on grief and bereavement, by Corrigan et al (3) on self-stigma, by Alarcón (4) on culture and psychiatric diagnosis, by Alexopoulos and Kelly (5) on geriatric depression, and by Krueger and Bezdjian (6) on dimensional concepts in psychiatry; the intro-

ductory papers by Ustun and Kennedy (7) and McGorry et al (8) for the Forums on the role of functional impairment in psychiatric diagnosis and on early intervention in psychosis; and the editorials by Maj on physical health care in persons with severe mental illness (9) and on the WPA Action Plan (10).

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The 15th World Congress of Psychiatry and the WPA General Assembly

The 15th World Congress of Psychiatry, held in Buenos Aires, Argentina, from 18 to 22 September 2011, has been the most attended meeting in the history of the WPA and the most attended psychiatric meeting ever held outside North America, with 14,013 participants.

The theme of the Congress was "World Psychiatry 2011: Our Heritage and Our Future". The aim was to provide an overview of those achievements which have stood the test of time and of the most promising trends in the various areas of psychiatry.

The scientific programme, whose quality was unanimously appreciated,

consisted of 24 Keynote Lectures, 15 Core Symposia, 94 Regular Symposia, 17 Workshops, 58 WPA Section Symposia or Workshops, 14 WPA Zonal Symposia or Workshops, 28 Oral Communication Sessions, 5 Poster Sessions, and 92 Sessions in the Spanish/Portuguese Track.

In the Opening Session of the Congress, Prof. Mario Maj reported on the implementation of the WPA Action Plan 2008-2011 and introduced the lecture of the recipient of the Jean Delay Prize 2011, Prof. Kenneth Kendler.

The WPA General Assembly was held on September 21. The Assembly approved unanimously the admission of the Mental Health Association of Cam-

bodia among the WPA Member Societies. These Societies are now 135: 28 in the Americas, 62 in Europe, 23 in Africa and the Middle East, and 22 in Asia and the Australasia.

The Assembly also approved the admission of a new Scientific Section, dealing with Evolutionary Psychiatry. The WPA Scientific Sections are now 66.

Resulting from the elections held during the General Assembly, Dinesh Bhugra is the new President-Elect of the WPA, Edgard Belfort the new Secretary for Education, Michelle Riba the new Secretary for Publications, and Afzal Javed the new Secretary for Sections.

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