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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 134, spanning 112 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 65 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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WPA-WHO collaborative activities 2009-2011

Mario Maj

President, World Psychiatric Association

The WPA has recently finalized with the World Health Organization (WHO) a Work Plan for the triennium 2009-2011, covering five items: a) the revision of the chapter on mental and behavioural disorders of the ICD-10; b) collaboration in the Mental Health Gap Action Programme (mhGAP); c) partnership on mental health care in emergencies; d) collaboration in the area of substance abuse; e) partnership on involvement of users and carers. I will focus here on the first three of these items.

WHO-WPA collaboration in the revision of the ICD-10

The process of revision of the ICD-10 is ongoing, and WPA Member Societies and Scientific Sections are going to be formally involved in this process.

One of the aspects of this involvement will be the participation of WPA Member Societies in one or more surveys and field trials aiming to provide a cross-cultural perspective on the following issues: a) what is a mental disorder; mental disorders vs. homeostatic responses to adverse life events (e.g., how to differentiate between normal grief, complicated grief and major depression, or between normal vs. pathological responses to trauma); b) the stigmatizing potential of psychiatric nomenclature (several terms we use in international classifications sound odd or even offensive in some languages, and we have only partial information on this matter at the moment); c) the utility of national vs. international classifications, and the need for national adaptations of diagnostic systems (several countries and regions still have their own classifications or use adaptations of international classifications: what are the main reasons why these national classifications or adaptations may be needed?); d) the use of current diagnostic systems; the main barriers to their use (we have only partial information about the use of the ICD-10 in the various contexts in the different countries, and about the main reasons why the system is not adopted); e) the relevance of specific ICD-10 categories or criteria to various cultures (e.g., of the category of post-traumatic stress disorder, or of current criteria for the identification of the various degrees of severity of a depressive episode); f) the relevance and applicability of proposed new diagnostic approaches, categories or criteria in various cultural contexts (e.g., of prototypes, dimensions or rating scales incorporated in the system; or of the inclusion of a cognitive impairment criterion in the diagnosis of schizophrenia); g) the conceptual equivalence of syndromes and symptoms across cultures (e.g., is the meaning of the term "depression" the same across cultures?); h) the assessment of "severity", "impairment" and "distress" (how this assessment should be made and what should be its place in the diagnostic system); i) the applicability of diagnostic categories or criteria by non-psychiatrists in specific settings (especially in low-income countries); j) gender and age issues (what modifications are needed in the system in order to make it more sensitive to gender and age differences in the various cultures?) (1-11).

WHO-WPA collaboration in the mhGAP

The WPA is committed to provide assistance to the WHO in the preparation of the mhGAP intervention packages and to support the WHO in the country implementation of the programme.

Along the first line, we have conducted a survey on the availability and feasibility of evidence-based interventions for priority mental disorders in the various countries and regions of the world, with the participation of WPA Zonal Representatives and Member Societies. The results of this survey will be used for a paper to be published in the *Lancet*.

Along the second line, we have started an effort to strengthen human resources in some countries in which the resource gap is large, but the WPA Member Society is active and there is an interest of the government to collaborate. The first country in which this effort is ongoing is Nigeria. WPA ongoing activities in this country include: a) a train-the-trainers programme focusing on the integration of mental health into primary care and targeting nurses and clinical officers working in community health centers (a first workshop, targeting the six south-western and the two Yoruba-speaking north-central states of Nigeria, took place in Ibadan last January, and is being followed now by a phase of supervision of the participants, in collaboration with the government); b) a programme of continuing education of psychiatrists (a CME event on improving psychosocial functioning in people with severe mental illness, led by T. Burns, will take place next October); c) a programme aimed to foster leadership and professional skills in young psychiatrists (the WPA will co-sponsor a workshop in Abuja, led by N. Sartorius); d) a plan to reinforce partnership with health authorities in the country (we are organizing with the AFRO office of the WHO an event with the participation of the Minister of Health and other relevant health authorities); e) an effort to better understand and address the issue of psychiatric brain drain (12-14).

WHO-WPA partnership on mental health care in emergencies

The WHO-WPA partnership on mental health care in emergencies includes two components.

The first is represented by train-the-trainers activities on prevention and management of mental health consequences of disasters and conflicts. A WPA-WHO workshop took place at the WHO headquarters in Geneva in July, with 20 participants selected from 124 applicants. This will be followed by a workshop in Dhaka, Bangladesh in January 2010. Our aim is to create a group of well-trained, highly qualified psychiatrists who will become themselves trainers for other psychiatrists in their regions, and will represent a resource for the WPA, the WHO and other relevant United Nations agencies when a new major emergency occurs.

The second component of the partnership is the coordination of intervention of psychiatrists when a major emergency occurs in a country or region in which external help is needed. We already implemented this coordination recently on the occasion of the Gaza emergency. The collaboration has two elements, a short-term and a medium-term one. The short-term element is the recruitment of psychiatrists who are able to speak the local language, are well trained and are willing to serve in the area of the emergency. The medium-term element consists in a partnership with relevant governments and Member Societies aimed to strengthen the national/regional mental health system. In fact, one of the lessons we have learnt from the experience of the past is that disasters are indeed very unfortunate events, but they also represent an opportunity for strengthening local mental health services, because they mobilize resources and call the attention of policy makers on mental health issues.

Conclusion

These are some of the activities that the WPA is implementing in collaboration with the WHO, having in mind two objectives: to help as much as possible some countries in need, and to enhance the image and increase the political influence of our discipline and profession in the international health arena.

A continuing update on the WPA-WHO collaboration can be found on the WPA website (www.wpanet.org).

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Culture, cultural factors and psychiatric diagnosis: review and projections

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This paper aims to provide conceptual justifications for the inclusion of culture and cultural factors in psychiatric diagnosis, and logistic suggestions as to the content and use of this approach. A discussion of the scope and limitations of current diagnostic practice, criticisms from different quarters, and the role and relevance of culture in the diagnostic encounter, precede the examination of advantages and disadvantages of the approach. The cultural content of psychiatric diagnosis should include the main, well-recognized cultural variables, adequate family data, explanatory models, and strengths and weaknesses of every individual patient. The practical aspects include the acceptance of "cultural discordances" as a component of an updated definition of mental disorder, and the use of a refurbished cultural formulation. Clinical "telescoping" strategies to obtain relevant cultural data during the diagnostic interview, and areas of future research (including field trials on the cultural formulation and on "culture bound syndromes"), are outlined.

Key words: Culture, psychiatric diagnosis, cultural formulation

(World Psychiatry 2009:8:131-139)

Diagnosis is probably the dominant topic of discussion and debate in the psychiatric field today. The announcement of the publication of new editions of the two best known classifications, the DSM-V and the ICD-11, for 2012 and 2014 respectively, has generated a predictable, at times heated exchange of opinions, suggestions, criticisms, and research initiatives. A variety of activities (conferences, meetings, symposia) across the world, and joint declarations of harmonious work at the international level, have kept a momentum that, most likely, will not cease until long after the actual publications.

It is expected that the new nomenclatures will incorporate significant changes in structure, diagnostic modalities, clinical evaluation approaches, definition and scope of disorders, and measurements of severity and level of functioning. Contributions from neurosciences and social sciences, clinical and epidemiological research, and a public health perspective will hopefully be included at realistic levels. Last but not least, national government agencies, insurance companies, the pharmaceutical industry, and worldwide medical and professional organizations as well as the public at large are keeping a close eye on the whole process (1-3).

The cultural perspective on psychiatric diagnosis has experienced uneven levels of reception and actual implementation (4), in spite of uniform pronouncements from the leading bodies of organized psychiatry and mental health across the world, professing respect and due consideration of cultural factors in the elaboration of previous, current, and future nomenclatures.

Assuming the sincerity of such statements, this article will attempt an objective examination of why, what, how and when should culture be an integral part of diagnosis in psychiatry. After a brief review of general basic concepts of diagnosis, the paper will focus on history, evolution and current status of the two main classification systems in today's psychiatry. An examination of basic concepts of culture and cultural factors in psychiatric diagnosis will, then, be followed by specific recommendations regarding a reasonable integration of cultural issues into the diagnostic enterprise.

DIAGNOSIS IN PSYCHIATRY: A BRIEF REVIEW

Understood as the processing of complex information regarding symptoms, behaviors, emotional correlates and eventual neurobiological substrates by means of history-taking and actual observation of psychopathological events, psychiatric diagnosis aims at reaching a comprehensive perspective of the patient's experience, so that the most appropriate treatment can be offered, and result in clinical improvement, more efficient personal functioning, and a more comfortable quality of life for the patient and his/her family.

Modern perspectives make diagnosis, in addition to all of the above, an essential component of epidemiological surveys, an important item in the elucidation of risk and protective factors for the clinical entity under study, a tool in the ascertainment of roles of families and communities, and the basis for policy-making and delivery of services to individuals and the general population (5). One could safely assume that the modern view of diagnosis would actively incorporate cultural elements in the structure, conduction and desired outcomes of the diagnostic process (6,7).

With all its imperfections and deficiencies, diagnosis is an essential step in the psychiatric encounter, perhaps more relevant than in any other field of medicine. It is mostly based on pure clinical components, i.e. the anamnestic dialogue between patient and psychiatrist, assessment of deeply subjective emotional states, and exploration of interpersonal issues and experiences (8). Diagnosis in psychiatry does not have the option of laboratory tests or the categorical (pathognomonic) ascription of symptoms or "biomarkers" utilized in medical or surgical specialties. It responds rather well to the characterization of a "work in progress".

DSM and ICD: history and evolution

The first edition of DSM was published in 1952. It was primarily a listing of clinical entities with a strong ideological twist, an almost paradoxical mix of psychoanalytic terminology and Mayerian "psychobiological" conceptualizations. Adolf Mayer, a Switzerland-born pathologist who came and work first in Chicago, had elaborated a pioneering integrative effort at defining mental illness. His influence in American psychiatry, as the first chair of the psychiatric department at Johns Hopkins Hospital in Baltimore between 1912 and 1960, was powerful, both as a symbol of the openness of a still young nation to the contributions from an immigrant scientist, and the permeability of American medicine and psychiatry to innovative ideas (9). Mayer considered mental illnesses as "reactions" to a variety of psychobiological factors and, like Freud did with the "unconscious" phenomena, conferred them a categorical, irrefutable etiological nature.

This approach persisted in the second edition of DSM (1968), regardless of the elimination of the term "reaction". The acceptance of an assumed or pre-established etiology, not even the consideration of a mediating pathogenic chain in response to still unknown etiological factors, presided the theoretical background of these classifications.

DSM-III came to light in 1980. Many within and outside psychiatry consider it a "revolution" in the nosology of mental disorders. It was, indeed, a drastic change in the approach to diagnosis, breaking away from psychoanalytic jargon and weak "psychobiological" concepts, adopting a phenomenological/descriptive/categorical approach (Jaspersian and Kraepelinian for the most part), seeking and using documented research findings, enumerating more precise criteria, and assigning coded quantifications. Before and after its publication, DSM-III generated abundant numbers of books, articles, and new research that, while supportive, emphasized reliability at the expense of a non-demonstrable validity (10).

The worldwide acceptance of DSM-III made it the *de facto* classification of mental disorders in practically all countries, as demonstrated by the translation of the manual into more than 30 languages. This happened in spite of a practically total omission of cultural factors, other than a few timid phrases here and there, or casebooks attempting to demonstrate the manual's applicability to cases from different areas of the world (11). This approach persisted in the DSM-III-R, published in 1987, that included broader criteria for some conditions but, most importantly, multiplied even further the total number of diagnostic entities.

The success of DSM-III and DSM-III-R brought diagnosis to the forefront of world psychiatry. There is no question about the new relevance that a well-based diagnosis acquired for research work, teaching activities, and actual treatment approaches. Lawyers, administrators, insurance companies, bureaucrats and politicians paid more attention to diagnoses and their implications. Reliability was not all that was needed, but was good enough for an acceptable diagnosis.

Some may say that DSM-IV represented a modest improvement in terms of recognition and acceptance of a cultural perspective. A distinguished group of cultural psychiatrists (clinicians and researchers) and social scientists submitted a series of suggestions and recommendations to the DSM-IV Task Force. Unfortunately, these contributions were drastically trimmed down, and resulted in just three additions: a mention of "cultural", together with "age" and "gender" considerations, as part of the text in some (not all) groups of disorders; the inclusion of a cultural formulation in Appendix I (next to last) of the manual; and the listing of an (incomplete) glossary of "culture-bound syndromes". The meagerness of DSM-IV's cultural content may have been just one of the reasons why medical schools, residency training programs, and practitioners in general have not paid to these concepts, and specifically to the cultural formulation, the same attention that was given, at the peak of the psychoanalytic influence on psychiatric practice in the US, to the then-called "psychodynamic formulation".

The fate of the cultural aspects of psychiatric diagnosis in the ICD is, in turn, ambiguous, if not nebulous. The nature of the World Health Organization (WHO) as an entity serving all the countries in the world (which, in turn, are officially committed to follow its rules, norms and recommendations), and its primary concern with the public health impact of all diseases, makes the consideration of culture in diagnosis a more likely occurrence, even if the deliberations may also have to pay attention to issues beyond nosology. Accordingly, one could think that the mention of cultural variants in some entities, the inclusion of "culture-bound syndromes", specific recommendations about interviewing styles and approaches, explanations of criteria and other aspects of the process would have a more focused presentation. Such has not always been the case, however, throughout decades and several versions of ICD, in spite of the scholarly and courageous examination of these issues made by Stengel, at WHO's request, fifty years ago (12), and several more recent publications (13,14).

Criticisms of psychiatric diagnosis

Representatives from different segments of the public and professional world have criticized the form and content of the current nomenclatures. This is, indeed, a reflection of the enormous importance that psychiatric diagnosis has in many quarters. Historically, psychoanalysts were the first in lamenting the disappearance, in DSM-III and subsequent editions, of many concepts and ideas precious to them. Their criticisms evolved around the omission of unconscious (or psychodynamic) phenomena as diagnostic criteria components, the deletion of some clinical or diagnostic terms, and the subjection to precise guidelines for interview, assessment and conclusions, instead of the lax "free-association" approach of the Freudian school (15).

Interestingly, phenomenologists also criticized DSM-III

and its successors, in spite of the adoption of clear descriptive approaches in the new system. These critics pointed out that the manual had more or less "manipulated" the classic phenomenology, depriving it from its rich philosophical content, in the interest of a more pragmatic use of old terms, and choice of new ones (16). Similarly, neuroscientists and basic researchers objected to what they considered lack of recognition of basic science contributions to some diagnoses, particularly in the area known as "neuropsychiatry", that included age-related or genetically-based symptom sets (17,18). Last but not least, social and cultural psychiatrists have consistently denounced the undeclared ethnocentrism (Caucasian-oriented) of DSM and its "benign neglect" towards specific issues. This will be more elaborated below.

Society at large has not been indifferent to the debates about this topic. Lay organizations, while recognizing the need for psychiatric nomenclatures, tend to see them, at times, as potentially threatening or unduly instruments of control, intrusiveness, and oppression. The extremist views of the Church of Scientology about psychiatry are known (19). In the corporative world, insurance companies balk at the scope of clinical entities and their management; until recently, they plainly refused to provide any kind of coverage for mental disorders diagnosed and managed in inpatient or outpatient settings in the US. On its side, the pharmaceutical industry has welcomed the growing number of diagnosable conditions, has pushed for more clinical indications for existing compounds (including the proliferation of off-label use suggestions), and has favored – without acknowledging it – the use of "polypharmacy", which is, in any practical sense, a gross denial or rejection of formal diagnostic systems.

Two other players contribute to what some have called the "subculture" of psychiatric diagnosis debates: the legal profession and the media. Some legal firms and individual attorneys misinterpret or abuse the insanity issues derived from the hint of any diagnosis, to justify law violations of all kinds; in turn, they may criticize diagnoses as imprecise or "cruel", according to the particular features of the case. And, as background drummer or, at times, conductor of this truly cultural upheaval, the media sensationalize psychiatry-related incidents, criticize diagnostic errors or neglect, blame treatment failures, or exaggerate disagreements within the profession, in order to maintain sellable topics alive.

Current status of psychiatric diagnosis

From a strictly clinical and scientific vantage point, the current state of diagnosis in psychiatry can respond better to the label "in transition". The last 15 years have witnessed significant advances in epidemiological research, neuroscientific inquiries, and clinical management of many mental disorders. At the same time, the experience with the use of the existing diagnostic systems has led to well founded observations, both favorable and critical, as well as suggestions for improvement. For instance, it is clear that, while improving the levels of reliability and communication in general, descriptive diagnostic criteria reflect a lack of consistent information about the etiology and pathophysiology of mental disorders, which is partly due to the absence of reliable "biological markers". Furthermore, these criteria are a mix of behavioral features (some of them not necessarily "pathological") and true symptoms. This may lead, in part, to high levels of comorbidity (and its inherent imprecision, clouded by complicated family aggregations of psychopathologies) or to excessive numbers of "not otherwise specified" diagnoses (20).

There are unclear relationships between validity, severity, disability and desirable quantitative aspects of diagnoses (21). In turn, this quantitative component cannot be captured by the multi-axial approach. The "cross cutting points", or transition from normality to psychopathology, are not clearly established, making the clinical course of any condition pre-determined if not artificial (22). The "required" number of criteria for a given diagnosis generates heterogeneity even among patients who end up with the same label. The differential diagnosis can become, then, difficult and confusing. The reification of diagnostic criteria invites rigidity and opaqueness in a diagnostic exercise that must be active and lucid. Limited or biased research may emphasize the most frequently studied symptoms, not necessarily the most relevant or decisive in the clinical presentation, generating significant variations in epidemiological studies, among others. Subtypes and "subthreshold" diagnoses are subjective, unstable, arbitrary and, ultimately, non-empirical (23). Closer to the cultural perspective, age, gender and developmental variants are essentially ignored.

CULTURE AND CULTURAL FACTORS IN PSYCHIATRIC DIAGNOSIS

Culture is defined as a set of behavioral norms, meanings, and values or reference points utilized by members of a particular society to construct their unique view of the world, and ascertain their identity. It includes a number of variables such as language, traditions, values, religious beliefs, moral thoughts and practices, gender and sexual orientation, and socio-economic status (24). Keeping pace with the times, this definition has also incorporated elements such as financial philosophies, and the ever-changing realities imposed by technological advances. The range of possible interactions between culture and its components with clinical phenomena in general, and psychiatric diagnosis in particular, is broad and multifaceted. The latter certainly requires familiarity with the growing discipline of cultural psychiatry.

Cultural psychiatry deals with the description, definition, assessment, and management of all psychiatric conditions, inasmuch as they reflect and are subjected to the patterning influence of cultural factors. It uses concepts and instruments from the social and biological sciences, to advance a full understanding of psychopathological events and their management by patients, families, professionals and the

community at large (25,26). The boundaries of this discipline are better delineated by defining what cultural psychiatry is not. It cannot be restricted to being a psychiatric subspecialty, because culture impregnates every clinical and non-clinical event in any and all diseases. It is not a new name for other disciplines (in fact, cultural psychiatry is the result of a historical evolution of areas called in the past comparative psychiatry, cross- or trans-cultural psychiatry, social psychiatry and others, avoiding precisely the "rehashing" of old ideas). Cultural psychiatry is not an anti-biological psychiatry, simply because it recognizes the difference between etiology (probably biological) and pathogenesis (probably psycho-socio-cultural) of mental phenomena, and accepts contributions of neurosciences as both reinforcing and clarifying factors in normality and pathology. In the same context, cultural psychiatry is neither a political ploy nor a mere piece of rhetoric (27,28).

Closer to its dealings with diagnosis, cultural psychiatry should not be considered only a psychiatry of ethnic minorities or of exotic lands, because that would deny the impact of cultural factors in the everyday life of majority populations in any country or continent, or reduce them to existing only in places far from urban centers, developed countries or, more precisely, Western nations. While it is true that, due to clinical convenience, the presentation and discussion of cultural issues in health, disease, diagnosis and treatment may utilize examples of ethnic minorities, immigrants, refugees, or the so-called "special populations" (children, adolescents, the elderly, women, homosexuals, or members of cults and religious sects, all of them considered "minorities"), it would be a great mistake to assume that culture exists only in and for these groups. Actually, the recognition of cultural components in psychiatric diagnosis *for all* would be a great step forward in correcting this erroneous view. It goes without saying that cultural psychiatry is not the same as international psychiatry, nor it is limited to race, gender and ethnicity as its leading indicators.

The patient's cultural background and identity must be thoroughly understood by the clinician, and its impact duly recognized and evaluated. Involving a crucial set of factors, culture plays several roles in the diagnostic process (29). Cultural factors may have a powerful pathogenic impact as triggers of psychopathology (e.g., the role of violence in television shows in the development of violent behavior among probably predisposed children or adolescents (30)). They can also contribute to higher or lower levels of severity of psychiatric symptoms (e.g., delayed help-seeking response to the appearance of acute psychotic symptoms in a family member). They can be agents in the expression of clinical symptoms, reflecting the dominant themes of the historical period in which the illness occurs. They are certainly decisive elements in treatment.

How is culture being used in current psychiatric diagnostic practice? The short answer is, very poorly. Declarations on the importance of cultural factors in diagnosis are not scarce, to be sure. But the use of the cultural formulation is limited, culture in clinical assessments is reduced to mentions of race, ethnicity, language or migrant status at the most, and in most training programs, cultural psychiatry didactics covers a few hours, most frequently during the senior year or in elective periods, when its impact may be minimized by the residents' forthcoming expectations or plans. Even in programs where these requirements are intended to be met, the demands of a growing body of knowledge relegates cultural psychiatry to marginal consideration. In practical terms, the message is condescending: "yes, cultural factors are important in psychiatric diagnosis, so check about race and ethnicity of your patients; if you have language difficulties, call an interpreter (if there is any available), be respectful, and move quickly to your next case".

The transactions between teachers and trainees, or between clinicians and patients, do not always have such a hasty, or cynic-sounding flavor. The staff of busy hospital units, outpatient clinics, emergency rooms, or private practice offices do their best to cover intense demands of time and professional skills. Those that find ways to provide decent cultural information, and gather solid cultural data, learn to recognize what is cultural in the clinical area generally called "environment". If and when this is done, the diagnosis will then be truly comprehensive, individualized and, for all these reasons, will also possess the humanistic seal that must always be at the core of any clinical interaction in medicine and, more particularly, in psychiatry.

Unfortunately, these advantages meet disadvantages resulting from the criticisms discussed above (31). Culture is said to be too broad a concept, too complex in content, and too heterogeneous in nature (the hundreds, even thousands of cultural and subcultural groups, languages and dialects all over the world are frequently cited as proof) to be covered by relatively simple clinical interactions (32). Literature contributions dealing with culture in clinical practice and diagnosis are mostly descriptive, narrative, and/or colored by sociological, anthropological or even ecological viewpoints (33), therefore labeled and dismissed as "soft science" by clinicians and scientists. Many authors insist that cultural factors are important *only* for treatment and management issues, perhaps preventive measures, but not for diagnosis *per se*. Finally, the disadvantages are rounded up by logistic difficulties in the instrumentation of cultural diagnostic inquiries: their proponents do not seem to agree on the content of such inquiries, there are not too many well proven tools, and even if they are, their use is time-consuming and complicated (21,32,33).

The so-called "culture-bound syndromes" deserve special comments. These are clinical pictures said to be uniquely related to specific cultural characteristics of the human groups in which they occur; as such, their etiological, pathogenic and clinical manifestations do not correspond to the conventional entities included in mostly Western-based nomenclatures. Culture-bound syndromes have, indeed, a venerable history enriched by contributions of notable clinicians and researchers in the last four or five decades (34,35). A

partial list of culture-bound syndromes was included in the Appendix I of DSM-IV, but it did not do justice to the extensive literature on the topic. Practically every region of the world has a set of culture-bound syndromes, yet it has to be said that, at times, the descriptions are quite similar, and at others, too generic or vague to be appropriately characterized. The basic question about culture-bound syndromes dwells on yet another dilemma: are they nosologically autonomous entities, or do they have enough similarities with existing clinical conditions currently listed in DSM or ICD?

WHAT SHOULD BE CULTURAL IN A MODERN PSYCHIATRIC DIAGNOSIS?

The purpose of including cultural elements in the diagnosis is neither to homogenize diagnostic procedures to the point of vague generalizations, nor to accentuate heterogeneity in the name of an ill-conceived thoroughness. The cultural components of modern psychiatric diagnosis cover a variety of areas. The following is a list of the main aspects about which information must be gathered in the process of a well-structured clinical interview.

Cultural variables

They should be recognized and duly described, thus setting the stage for more comprehensive information. Specifics about language (and how it is mastered), religion and spirituality (with possible mention of main rules, as understood and described by the patient and family members), gender and sexual orientation, traditions and beliefs (those that, together with ethnicity, confer a sense of personal and group identity), migration history and level of acculturation (when necessary and applicable) would conform the minimal set of variables to be covered in the initial phase of a clinical evaluation (24).

Family data

Information about family, being in itself another cultural variable, appears to be sufficiently important as to deserve a special focus. Family history, structure and life provide data about what are called "micro-cultural" or "micro-environmental" segments in the patient's story. Areas such as raising modalities, roles and/or hierarchies, value-infusing activities, eating habits, and social interactions (e.g., community celebrations) must be inquired about, as part of the whole assessment process. Last but not least in this section, help-seeking patterns, while not being strictly a diagnostic component, represent a useful context-revealing factor reflecting a great deal of family mentality about interactions with the outside world in general, and the health professions in particular (36).

Pathogenic and pathoplastic factors

The environment (or "macro-environment", to be more precise) is an almost inexhaustible source of both benign (or preventive) and harmful factors in the development of any clinical condition. For the purposes of a culturally-based diagnosis, the identification of environmental pathogenic factors is essential. Such factors include family life (deserving a special focus, as done above), but also estimates of the impact of broader agencies such as media, socio-political structures, rules and values of public behavior, church affiliation, schedules, rituals, schooling norms, and the like.

Pathoplastic factors refer to the uniqueness of symptom expression. The clinician should be prepared to recognize that the description of the symptoms by patient and relatives, the words and terms used, and the context in which the clinical story evolves (in short, the "narrative" component of the professional-patient transactions) respond to the particular moment in time when they are occurring. Environment shapes the form (not only the substance) of the symptoms: a delusion is a firm, unchangeable (in many cases, unusual and bizarre) belief identified in the psychopathological assessment of any patient, now and ever since clinical psychiatry became an established discipline; the delusion's content (of prominent cultural facture), however, will be different in a 21st century patient growing up in an urban, technologically-dominated world from that of a patient from 200 years ago, living in a predominantly rural, much less complicated environment. The distinction between the appearance of the symptom, its verbal description, and the patient's surrounding reality continues to be the key element of this part of the evaluation.

Explanatory models

A critical component in any cultural framing of psychiatric diagnosis, explanatory models offer the idiosyncratic perspective of patient and relatives about the origin (cultural etiology?) of the symptoms, why they occur, and how the process of "getting ill" has evolved (cultural pathogenesis?). The exploration could expand into why has the particular patient become the "target" of such symptoms, and what should be done to overcome them (37). The cultural stamp of these explanations should not be underestimated, as the information is valuable and relevant for both the diagnosis itself, and for aspects of the eventual multidisciplinary (multi-conceptual or multi-dimensional) management process.

Patient's strengths and weaknesses

The mental status examination part of a clinical history includes now a section outlining the individual patient's strengths and weaknesses as reported by him/her and/or by

family members. The cultural nature of this piece of information is undeniable: being the product of self-observation, it reflects issues of self-image and subsequent self-esteem, interaction styles, social disposition and skills, level of performance, even subtly disguised yearnings for change, or clear therapeutic targets (38). Furthermore, strengths and weaknesses (the latter considered barriers against treatment approaches) configure what is known as "coping styles" of the patient *vis-à-vis* the adverse events originating, leading to, or aggravating the pathological symptoms.

PRACTICAL ASPECTS OF THE INTEGRATION OF CULTURAL FACTORS IN PSYCHIATRIC DIAGNOSIS

The logistics of the process to incorporate cultural factors in both ICD and DSM is not simple. It has several steps or components that entail conceptual integration, ideological coherence, pragmatic vision, and even political commitment. It includes the incorporation of culture in the definition of mental disorder, a review and improvement of the cultural formulation, and specific steps in the processes of interview, instrumentation, clinical documentation, and needed research.

Definition of mental disorder

A first step should be the unequivocal recognition that cultural discordances play as important a role in the definition of mental disorder as maladaptive behaviors and subsequent functional inadequacy. It is not enough to limit this recognition to bland phrases such as "in contrast with accepted cultural norms of the individual's community or society of origin". The definition of mental disorder, or mental illness/disease, should be explicit about such discordances (i.e., against rules of coexistence, respect or solidarity in the culture of origin), enumerating them succinctly but comprehensively. That the definition of mental disorder will be in one of the opening pages of the new manuals seems to be generally accepted; that it should include a cultural component remains to be seen. It would certainly be a clear demonstration that the leaderships of WHO, American Psychiatric Association, World Psychiatric Association and other organizations involved in the effort really intend to materialize a long-expected feature for the process' final product (39,40).

Cultural formulation

The cultural formulation, as outlined in DSM-IV-TR, is a valuable tool that, however, has not been systematically tested. Its content includes most, but not all, the concepts discussed in this article. It has the advantage of being already a known instrument, usable by both mental health specialists and non-specialists, enhancing the value of ethnography as a clinical data-gathering method, covering the patient-owned perspective, and including data on the patient's identity, explanatory models, psychosocial environment and functioning, relationship with the diagnostician, and an overall cultural assessment for diagnosis and care (41). It provides a better understanding of symptoms, therefore increasing the accuracy of conventional clinical assessments.

As disadvantages of the current cultural formulation, imprecision and subsequent heterogeneity of the narrative data are mentioned. In an era of quantitative approaches to the clinical assessment of individual and groups of patients, and use of "evidence-based" documentation, some authors have suggested devising a scale to convey more objectively the qualitative nature of the cultural formulation's information. This is certainly a doable project. Be that as it may, there is consensus about the fact that the cultural formulation must be considered a formally sanctioned tool for use in clinical evaluations leading to a more comprehensive diagnosis (42).

Cultural axis? Cultural dimension?

A short-lived initiative fostered the idea of adding a cultural axis to the five included since DSM-III. Its proponents remarked the "visibility" that cultural issues would reach by being incorporated in one exclusive axis. However, it soon became clear that it would be enormously laborious and ineffective to pretend an inclusion of all that is cultural about the mentally ill person's experience in just one axis. Moreover, it would go against the universalistic nature of cultural assessments, and create a pseudo-independence that would further even more the isolation of culture as a diagnostic factor. Rather, the critics opined, culture should be at the forefront of all clinical interactions leading to a diagnosis, and preside the overall assessment of all patients, with specification of its impact on symptoms, syndromes and the whole illness experience (4).

The discussion about a cultural "dimension" is more current, given the debate about categorical vs. dimensional approaches in psychiatric diagnosis in general (43). It is true that culture implies (and plays) a greater role from a dimensional perspective, with factors (facets? traits?) that are also impacted by external realities such as poverty, unemployment, legal and political circumstances, "isms" of all kinds. Yet, the dimensionalization of culture could also create isolation and eventual neglect, its implementation would be time-consuming, and the information thus obtained would be fragmented. Once again, the reasonable response to this call should be a renewed effort to make the cultural evaluation a fluid component of the clinical interview, with easy-to-use instruments, and cohesive, encompassing views and procedures.

Clinical interview procedures

With a clear perspective on relevant cultural variables in mind, etiopathogenic factors and explanatory models to be inquired about in the course of the conventional clinical interview, a simple but informative scoring scale, and the cultural formulation's components handy, the clinician will be in a good position to integrate these factors in his/her routine work. This sense of alertness, however, is critical in that it would allow an early detection of what can be "cultural" in the patient's story (e.g., the ubiquitous topic of somatization (44)). If such content is mild, it will remain in the clinical documentation as a specific reminder that, later on, can be relevant or useful. If the clinician's intuition (or "suspicion") is moderate or even strong, he/she could use a sort of "telescoping" method that allows him/her going from broad to narrow (more precise, in this case) estimates, using now the tools at hand, to make either perception similarly clear. As telescoping requires not only "zooming", but also a variety of lenses with increasingly finer views and adjustment possibilities, this "clinical telescoping" *vis-à-vis* the assessment of cultural diagnostic factors can make use of new approaches, including questions to relatives, friends, neighbors, coworkers or acquaintances, or additional clinical instruments to ascertain true "cultural discordances" in the story being gathered (45,46). There may be a point in which referral to or assistance by an experienced colleague in this area is necessary.

This process can go on to the identification of, for instance, a "culture-bound syndrome" (35,47) or of a well defined culture-related aspect of a conventional clinical entity, e.g., consideration and assessment of concept, severity, and explanation of suicidal risk in a given patient (48). All this will be duly documented in the final clinical history. Obviously, this effort may ultimately lead to a more inclusive diagnosis, and an expected comprehensive set of treatment recommendations. Contrariwise, the exercise may end with a rational ruling out of cultural etiopathogenesis, while maintaining value as part of the general management recommendations, e.g. strengthening of family ties, group therapy, or spiritual counseling. The clinician will, again, make this clear in the medical record.

SUGGESTED FUTURE RESEARCH

The next few years offer a significant opportunity for research on culture and psychiatric diagnosis (32,33). There may be a better disposed set of funding sources as the need to fulfill old promises reaches compelling levels. The field remains substantially unexplored, in spite of culture's ubiquitous presence in all areas of research on psychiatric diagnosis. The American Psychiatric Association's launching volume on a research agenda for DSM-V (49) recognized the role of culture in practically all its chapters. Neuroscientists commented on the pervasiveness of ethnic and cultural issues in the interpretation of most genetic studies, and their influence on vulnerability and resilience, coping styles, cognitive responses to stress, and the nature of social support. The presence of ethnocultural components in endophenotypic manifestations of psychiatric conditions, and the realities of pharmacological epidemiology, ethnopsychopharmacological and pharmacogenomics findings (50), are now undeniable. It was also said that the new nomenclature should include clear delineation of core criteria, and recognition of cultural and cross-cultural variants in symptom definition, and behavioral and symptomatic manifestations.

Similarly, the work group on developmental issues elaborated on the topics of meaning and context and their effects on the expression of particular behaviors, and on the risks for psychopathology throughout the different developmental phases. The need to provide explanations about social, cultural and neurophysiological mechanisms at play in the impact of adaptive and maladaptive personality traits was also emphasized. The pertinent chapter pointed out typological and behavioral differences among cultures, and commented on the uneven results of well-known measurement instruments in different ethnic groups. Cultural psychiatry research must pay attention to the "desirability factor" in diagnostic processes, a prelude to the vast field on stigma and its diagnostic impact, as well as the ethnocultural and linguistic biases in mental health evaluations (51,52). The areas of cultural epidemiology (a potentially rich mix of anthropological and descriptive epidemiological variables), and comparative studies (urban vs. rural, DSM-ICD, international, and interhemispheric) are equally relevant (53,54).

Similarities and differences between ethnicity and identity, religiosity and spirituality are topics of worthy connections with psychiatric diagnosis in a variety of cultural settings (55). The connections between biology and culture in psychopathology may have a powerful repercussion in diagnostic factors such as resilience, response to traumatic events, violence, treatment susceptibility, and creativity among others (56,57). Cultural factors in specific diagnoses such as chronic pain, phobias, dissociative and eating disorders, as well as personality disorders, are prominent, yet not totally dissected (58). The same applies to the assessment of culture in the perception of severity of symptoms (by patients and clinicians), functional disturbances, and the all-encompassing area of quality of life (59). The consideration of studies about dimensionalization of cultural factors could set the stage for future diagnostic and nosological systems (43).

In the field of culture-bound syndromes, potential research items are abundant and in high need of implementation. The first and foremost area of inquiry has to do with their validity as clinical entities to be considered on their own, or be included as part of the existing groups of disorders, i.e. *"ataque de nervios"* being a form of panic disorder, *"amok"* a violently acute psychotic episode, *"susto"* a dissociative disorder, or *"koro"* a variant of obsessive-compulsive disorder (47, 60). In turn, how much is cultural in well established "Western" disorders such as anorexia nervosa or

pathological gambling? (61-63). Needless to say, the intense debates about this could only be solved by means of well conceived comparative research projects.

Prominently closer to current developments in psychiatric nosology, field research on the cultural formulation could test validity, feasibility (utility) and reliability of the tool. Gender- and racially/ethnically diverse samples would be required in order to include the much sought-after cultural variability in symptom presentation, and clarify the issues of under- or over-diagnosis of some entities in different ethnic groups (42,43). Input of the "cultural reference group", impact of factors such as sector of care, or the practitioner's personal and professional cultural background, must be adequate subjects of research. Applying the cultural formulation to and comparing it between different, comorbid or difficult-to-differentiate disorders, would make it more rigorous and reliable (60). Finally, the cultural formulation can and should be administered and tested in a variety of clinical settings, i.e., general medicine, primary care, and psychiatry clinics, as well as specialty medicine and psychiatry units.

CONCLUSIONS

The universality vs. distinctiveness dilemma implicit in the elaboration of diagnostic and classification systems across history has an emblematic angle in the debate about incorporation of culture and cultural factors in the forthcoming editions of DSM and ICD. The internationalization of the health and mental health fields due to globalization, nourished, in turn, by seemingly unstoppable migrations, has led to the acceptance and practical concerns of diversity in clinical settings around the world. While generally accepted, this effort is not free of difficulties in many areas: conceptual, methodological, clinical, financial, administrative, and political. Nevertheless, a historical opportunity for the materialization of old promises is now present, and must be decisively grabbed by all individuals, groups and organizations involved.

The trajectory of today's two main nosological systems has made clear that culture, as an etiopathogenic and pathoplastic factor, and as a contributing component of severity, has a significant impact on psychiatric diagnosis. But, such impact goes even beyond: every clinician needs to know about, and assess pertinent cultural variables, family data, explanatory models, strengths and weaknesses of individual patients and their communities of origin. Cultural psychiatry, as a young but robust discipline, helps in the systematization of these pieces of knowledge, thanks to its growing connections with both neurobiological and social sciences.

Together with an explicit declaration of a cultural referent ("cultural discordances") in a new definition of mental disorder, the use and refinement of, and additional field research on tools such as DSM-IV-TR's cultural formulation are needed for a new and pragmatic clinical interview, that should include an exploration of cultural factors in both history-taking and diagnosis-building phases. This article has elaborated on the theoretical/conceptual and logistic/pragmatic components of the effort.

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Research advances in geriatric depression

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Technical advances have facilitated the exploration of factors related to geriatric depression and have helped generate novel biological and psychosocial treatment approaches. This review summarizes the main advancements in epidemiology, clinical presentation and course, genetics, and other areas of biological research. Treatment interventions outlined in this paper include electroconvulsive therapy, repetitive transcranial magnetic stimulation, magnetic seizure therapy, vagus nerve stimulation, deep brain stimulation, depression prophylaxis, multidisciplinary approaches to depression treatment, and psychotherapy. Forms of psychotherapy for geriatric depression summarized include interpersonal psychotherapy, supportive psychotherapy, cognitive-behavioral therapy, problem-solving therapy, and ecosystem-focused therapy. Neuroimaging techniques based on magnetic resonance imaging are discussed briefly, including volumetric brain studies, diffusion tensor imaging, fractional anisotropy, fiber tractography, magnetization transfer imaging, and blood-oxygenation-level-dependent functional magnetic resonance imaging. Finally, treatment effectiveness is addressed in a discussion of new models to improve access to and quality of care offered in the community.

Key words: Geriatric depression, late-life depression, late-onset depression, vascular depression, post-stroke depression, cardiovascular disease, cerebrovascular disease, magnetic resonance imaging, treatment

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Depression is a leading cause of disability worldwide (1). It results in more years lived with disability (YLDs) than any other disease, and ranks fourth in terms of disability-adjusted life years (DALYs). Additionally, depression is associated with a greater decline in overall health due to multiple illnesses than angina, arthritis, asthma, and diabetes. Geriatric depression in particular not only causes suffering and involves suicide risk; it also increases medical comorbidity and disability among elderly individuals.

Although depression may be less common in old than in young adults, as younger birth cohorts mature and the elderly population grows in size, an unprecedented number of elderly depressed people will need psychiatric attention. Although the biological causes of depression remain unknown, clinical and biological observations provide the rationale for studying new psychosocial and somatic treatments, or existing treatments applied to new indications.

EPIDEMIOLOGY

Studies of community-residing older adults show a decline in the overall prevalence of depression compared with middle-aged adults (2). However, medically ill, disabled older adults have a high prevalence of depression. In particular, 10-12% of medical inpatients and 12-14% of nursing home residents have major depression, and larger numbers experience less severe depressive syndromes.

A large number of older adults develop depression for the first time in their lives, often in the context of increased medical disease burden or neurologic stigmata. It has been suggested that late-onset depression may include a group of patients with neurologic disorders that are not clinically evident when the depression first appears (3). Although some studies have not supported this view, most have shown that late-onset depression relative to early-onset depression is associated with higher medical morbidity and mortality (4,5), greater disability (6), and more neuropsychological (7,8) and neuroradiological abnormalities (9-11).

Cerebrovascular disease frequently occurs 2 to 3 years prior to hospital admission for severe depression (12,13). Depression is common after stroke (14-19), affecting more than 30% of stroke survivors (20). Heart disease (21,22) and broadly defined cerebrovascular disease are prevalent in elderly patients with depression, with an increase in relative risk of up to 4.5-fold (23,24). The relationship between vascular diseases and depression is likely bidirectional, as pre-existing vascular disease predicts the onset of depression and pre-existing depression predicts the onset of cardiovascular disease and stroke (24).

CLINICAL MANIFESTATIONS

Late-life depression frequently differs from early-life depression in its clinical characteristics, particularly if it is late in onset or accompanied by signs of executive dysfunction or vascular disease. Late-life depression is often associated with executive dysfunction (25-29), a neuropsychological expression of frontal system impairment, with a clinical presentation of depression resembling medial frontal lobe syndromes (25). Depression affects cognitive function in all age groups, but the executive tasks of response inhibition and sustained effort are more frequently impaired in geriatric depression (30). Executive dysfunction generally subsides as depression improves, but tends to persist after remission of depression (31-36). When depressed elderly patients have executive dysfunction, they are more likely to have reduced interest in activities, more profound psychomotor retardation (25), and poor and unstable response to antidepressants (35,37-39).

The clinical presentation of late-onset geriatric depression with comorbid vascular disease is similar to that of geriatric depression with executive dysfunction. Compared to elderly patients with early-onset depression and no vascular risk factors, patients with late-onset major depression and vascular risk factors have shown greater impairment in frontal functions, poorer insight, more psychomotor retardation, less agitation and guilt, and more disability (40,41). A comparison of magnetic resonance imaging (MRI)-defined vascular and non-vascular depression showed that the vascular group had significantly greater age, age of onset, anhedonia, and disability, but less psychosis. Despite some negative findings (42-44), much past and recent evidence indicates that vascular depression predicts poorer response to antidepressants (10,38,43,45-49).

GENETIC STUDIES

Family history of depression is less common in patients with late-onset depression than in elderly patients with early-onset recurrent depression (50,51); and less common in "vascular depression" than in non-vascular depression (52,53). In a recent, large Swedish twin-pair study, history of early-onset depression in one member of a twin pair was associated with high lifetime risk of depression in the other member. In contrast, late-onset depression was associated with high cotwin risk of vascular disease (54).

Finding genes predisposing to depression has been a formidable task. Depression has polygenic inheritance, thus making it difficult to identify the contribution of individual genes. To overcome this obstacle, research increasingly focuses on genes related to specific behavioral or biological functions (endophenotypes) related to depression.

Genetic studies of the serotonin transporter exemplify this work. The serotonin transporter is the site of action for serotonin reuptake inhibitors (SSRIs). A polymorphism of the serotonin transporter gene promoter region (5-HTTLPR) involves a 44-base pair insertion (L allele) or deletion (S allele). The S allele has been shown to reduce gene expression, thus reducing serotonin reuptake (55).

In addition to studies relating the S allele to risk for depression (56-58), a number of studies have found an association between the S allele and increased risk of vascular disease.

Elevated blood cholesterol and triglycerides, heart disease, and myocardial infarction have been more common among S allele carriers than L allele homozygotes (59); and after acute myocardial infarction, depressive symptoms and negative cardiac outcomes including cardiac death were more common in S-carriers than L-homozygotes (60). In one of our own recent late-life depression studies, we found that, compared with L-homozygotes, S-carriers had microstructural white matter abnormalities (lower fractional anisotropy, to be explained below) in frontolimbic brain regions as well as a lower remission rate of depression (61).

OTHER BIOLOGICAL FINDINGS

Neuroradiological and histopathological studies have found associations among depression, executive dysfunction, and brain abnormalities, most notably those affecting the structural integrity of frontostriatal circuits, which include subcortical regions. Executive dysfunction and depression are hypothesized to be related to fronto-striato-limbic network abnormalities (3). Five such frontostriatal circuits have been described (62,63). Glutamate, enkephalins, and gamma-aminobutyric acid (GABA) are important neurotransmitters in these circuits, with acetylcholine and dopamine serving a modulating role. Because these circuits appear to mediate positive affect-guided anticipation, damage to them, resulting in failure to anticipate incentives, is hypothesized to be a mechanism leading to depression (40).

Macroscopic and microscopic changes to brain regions have been associated with mood disorders in histopathological and neuroimaging studies. In post-mortem studies of depressed patients, glia reduction has been observed in the subgenual prelimbic anterior cingulate gyrus (64). Bipolar and unipolar depression studies have reported neuron abnormalities in the dorsolateral prefrontal cortex (65). Radiological studies have shown low orbitofrontal (66,67), anterior cingulate (68), and hippocampal volumes (69,70) in depressed elderly patients compared to healthy elderly controls, while reports of amygdala volumes have differed (71). Studies of white matter integrity in normal aging have shown a greater tendency for decline in prefrontal white matter with advancing age compared with other areas of the brain (72). Prefrontal white matter microstructural abnormalities have correlated with poorer performance on tasks of executive function, and have been hypothesized to reflect a disconnection state that can increase the risk of geriatric depression (73).

Depression has been associated with cerebral infarcts, even when no obvious neurological symptoms are present. In a Dutch study, such "silent" infarcts occurred five times more frequently than cerebral infarcts with peripheral neurologic signs (74). In a large US study, 28% of elderly subjects with no previous history of transient ischemic attack or stroke had evidence of previous infarcts. Eighty-one percent of these had lacunes only, and as a group they showed more cognitive dysfunction than those without any brain infarcts (75). In a Japanese study of 63 patients with late-onset depression, 59 (94%) had silent cerebral infarcts (76). Finally, in a study of infarcts in the thalamus and basal ganglia, such lesions were found in 14 of 35 depressed elderly patients without neurologic history, but in only 1 of 22 normal elderly volunteers (77).

Depression has been also associated with white matter abnormalities, including white matter hyperintensities (WMHs; areas of increased intensity on T2-weighted MR images) or microstructural abnormalities demonstrated as reduced fractional anisotropy in diffusion tensor imaging. WMHs have been more common in depressed older patients than healthy older adults (10,67,77-81), especially in frontal

and temporal regions (82). A post-mortem study has shown that deep WMHs of depressed elderly patients are more likely to be ischemic in nature than deep WMHs of elderly controls (83). WMHs are associated with cerebrovascular disease (84), cardiac disease (85), smoking (86), hypertension (53,84,86), reduced cerebral blood flow (85), executive dysfunction (73,87,88), and disability (52,89).

Based on these findings, the "vascular depression" hypothesis has been proposed, which postulates that cerebrovascular disease predisposes, precipitates, and perpetuates a late-life depression syndrome (3). Vascular disease might lead to depression through damage to specific brain circuits or less directly through inflammation. Proinflammatory cytokines, such as interleukins 1 and 6 (IL1 and IL6) and tissue necrosis factor alpha (TNF-α), are released after damage of the vascular endothelium (90). A post-mortem study found elevated levels of intercellular adhesion molecule-1 (ICAM-1), a marker of ischemia-induced inflammation, in the dorsolateral prefrontal cortex of depressed subjects compared with controls (91). The incidence of depression after treatment with the inflammatory cytokine interferon-alpha (IFN-α) ranges from 30 to 50% (92); and depression has been associated with increases in chemokines, cellular adhesion molecules, acute phase proteins, and proinflammatory cytokines (93,94). Given that proinflammatory cytokines have been associated with atherosclerosis and cardiovascular disease (90), it seems possible that inflammation predisposes to both depression and vascular disease simultaneously; or that inflammation might be involved in a vicious cycle of depression leading to inflammation, which leads to vascular disease, which leads to more inflammation and increased risk for depression.

Beyond inflammation, other factors may set forward a vicious cycle perpetuating depression and worsening vascular disease. These include sedentary lifestyle, overeating, diabetes, smoking, nonadherence with medical recommendations, hypertension, hyperhomocysteinemia, nervous system activation, hypothalamic-pituitary-adrenocortical axis activation and other physiological stress responses, cardiac rhythm disturbances, and hypercoagulability (90,94,95). The relationship between depression and hypercoagulability may in turn be mediated by physical inactivity, smoking, or increased platelet activity (96). Therefore, even in cases where vascular disease predisposes to depression, once depression sets in, a vicious cycle may occur that worsens both vascular disease and depression.

The "vascular depression" hypothesis has served as the conceptual background for further subclassification of geriatric depression. One group of investigators further described a "vascular depression" subtype, subcortical ischemic depression (SID), and defined it as major depression with MRI evidence of subcortical lesions. Unlike most psychiatric disorders, which are described in purely phenomenological terms, subcortical ischemic depression involves a measurable biological abnormality. The association of late-life depression with executive dysfunction led another group of investigators to describe the depression-executive dysfunction syndrome (DED). Although many patients with DED also meet criteria for SID or other "vascular depression syndromes", DED's focus on a functional abnormality rather than an anatomical one extends it beyond the vascular depression concept.

ADVANCES IN LATE-LIFE DEPRESSION TREATMENT

Advances in late-life depression research include novel or improved treatments, personalization of treatments according to depression type or characteristics of the individual, and strategies to improve access to and delivery of care. The reader is referred elsewhere for guidelines to treatment of geriatric depression (30,40,97). Here we focus on new developments and trends.

Biological studies of treatment response

Brain research is facilitated by a variety of MRI-based neuroimaging techniques (98,99). Many of these can be performed together in a single MRI scanning session. T1-weighted MRI images allow comparison of brain structure sizes in volumetric brain studies, in addition to classic lesion studies. Brain WMHs can be studied with T2-weighted images, while newer methods allow an examination of white matter tract integrity.

Diffusion tensor imaging (DTI) indicates the direction of water diffusion. Fiber tractography uses DTI information to map out putative white matter fiber tracts. Fractional anisotropy (FA) is a DTI measure of the tendency of water to move in a single direction. Low FA can be a sign of compromised white matter integrity. Another method that reflects white matter integrity, but from a different perspective, is magnetization transfer imaging (MTI), which indicates the amount of water bound to macromolecules such as myelin.

Blood-oxygenation-level-dependent functional magnetic resonance imaging (BOLD fMRI) involves collection of a series of brain images over time, typically 2 seconds apart, so that changes in blood flow reflecting activity throughout the brain can be monitored over time. If a task is performed by the subject in the scanner, usually the goal of the experiment is to identify regions of the brain that are activated in response to the experimental paradigm.

Some techniques allow for analysis of the fMRI data even in the absence of a known experimental paradigm, such as is the case in resting-state experiments, where subjects are not given any task except to "rest" without sleeping. Seed-based methods map out brain regions, whose activity time course is highly correlated with a chosen point or region in the brain. Independent component analysis (ICA) performs a linear decomposition of the fMRI data, treating the data as if it were the sum of numerous components that are spatial maps of brain regions in perfect synchrony with each other. ICA essentially considers the fMRI data to be a symphony of differ-

ent melodies from different constellations of brain regions and then picks out the melodies being played. In task-driven experiments, ICA has produced results comparable to those derived with *a priori* knowledge of the experimental time course (100-102).

Some findings employing these techniques have predicted poor treatment response of late-life depression. For example, WMHs in frontal regions were associated with poor response to pharmacotherapy (46) and severity of subcortical gray matter hyperintensities predicted poor response to electroconvulsive therapy (ECT) (45). Lower fractional anisotropy, mainly in frontolimbic areas, predicted poor antidepressant drug response in geriatric depression (103-105).

In adult fMRI studies, lower relative activation of the rostral anterior cingulate cortex (ACC) at baseline in response to negative vs. neutral stimuli was associated with poor response to venlafaxine (106); while decrease in activation (in response to sad faces) of the rostral ACC over the course of treatment with fluoxetine predicted depressive symptom improvement (107).

Novel or improved treatments

Electroconvulsive therapy

ECT remains the most effective treatment for depression. The response and remission rates for untreated late-life depression are up to 90% and 70%, respectively, and for medication-treatment-resistant depression 70% and 50% (108). Some ECT studies have reported higher rates of response and remission for late-life depression than early-life depression (109,110), but this may be due to a tendency to treat elderly depressed patients with ECT before exhausting all other common treatment options.

Much ECT research has focused on minimizing cognitive side effects, such as post-ECT disorientation, anterograde amnesia, and retrograde amnesia. Most cognitive effects are temporary, and scores on cognitive tests generally improve after ECT (due to improvement in depression) (111). However, for some individuals amnesia for events in the days, weeks, months, and in some cases years before ECT does not resolve and can be a distressing side effect.

Varying ECT parameters such as treatment frequency, placement of the electrodes, stimulus energy, and stimulus waveform generally results in a tradeoff between efficacy and cognitive side effects, but some important exceptions to this rule exist. In many studies, greater and faster response at the cost of increased cognitive side effects was obtained by choosing higher treatment frequency, bilateral (BL, bifronto-temporal) rather than right unilateral (RUL) electrode placement, and higher stimulus energy (111).

Some of the best recent research results have been obtained with high-dose RUL ECT. High-dose, brief pulse, RUL ECT resulted in milder cognitive side effects yet equivalent efficacy compared with BL ECT, and greater efficacy compared with lower doses of RUL ECT (112,113). More recently, the effect of ultra-brief pulse width (0.3 ms) combined with either high-dose RUL ECT (6 times seizure threshold) or BL ECT (2.5 time seizure threshold) was compared to traditional brief pulse (1.5 ms) width. The greatest remission rate occurred in patients receiving ultra-brief pulse RUL ECT (73%), and the lowest remission rate in those receiving ultra-brief pulse BL ECT (35%), while traditional pulse width BL ECT (65%) and RUL ECT (59%) had intermediate remission rates.

The ultra-brief RUL group also had less severe cognitive side effects than the other three groups (114). Finally, the efficacy of ultra-brief pulse, high-dose, RUL ECT (6 times seizure threshold) was recently found equivalent to that for ultra-brief pulse, bifrontal ECT (1.5 time seizure threshold), but response for RUL ECT required significantly fewer treatments (7.76 vs. 10.08) (115).

Repetitive transcranial magnetic stimulation

In October 2008, the US Food and Drug Administration (FDA) approved repetitive transcranial magnetic stimulation (rTMS) for treatment of depression resistant to one prior antidepressant medication trial (116). TMS induces flow of electricity at the surface of the brain through powerful, rapidly changing magnetic field pulses. "Repetitive" indicates that more than one pulse is administered. Because the magnetic field strength with conventional coils drops off dramatically with distance from the coil, the effect is much more localized than with ECT.

Unlike ECT, the goal with rTMS is to stimulate *without* causing a seizure, which eliminates treatment risks involved with seizure and general anesthesia. Neuropsychological and imaging studies have shown that, depending upon the frequency of rTMS pulses applied, rTMS has the capacity to increase (high-frequency pulses, > 1 Hz) or decrease (≤1 Hz) the level of activity in brain circuits at the surface of the brain, which returns to normal within hours (117). For treatment of depression, high-frequency rTMS is usually applied to the (left) dorsolateral prefrontal cortex in an attempt to normalize the low level of activity often found there in depressed patients (118).

Evidence from a recent double-blind, randomized, placebo-controlled trial (N=92) indicates that rTMS may be helpful in the treatment of vascular depression (119). The placebo was a sham coil designed to mimic the skin sensations and noise of rTMS without penetrating into the brain. The rates of response and remission for older patients (age ≥50, mean age 64) with clinically defined (subcortical stroke and/or presence of at least 3 cardiovascular risk factors) medication-treatment-resistant vascular depression were significantly higher for patients treated with a total cumulative dose of 18,000 pulses rTMS (response 39%, remission 27%) than with a sham coil (response 7%, remission 4%).

Magnetic seizure therapy

Magnetic seizure therapy (MST) is the application of high-intensity rTMS to induce a seizure. The main difference between MST and ECT is that MST imparts electrical energy to a limited area on the surface of the brain, while ECT causes electricity to flow throughout the brain as governed by Ohm's law. This difference might prove advantageous in terms of treatment efficacy or side effects.

Since the first treatment in Bern, Switzerland in May 2000 (120,121), MST's safety, efficacy, and side effect profile has been explored in small trials. Early MST studies demonstrated a significant antidepressant effect, but this effect was less robust than that of ECT (122), perhaps due to limitations in the maximum energy imparted by the MST device (average 1.3 times seizure threshold) (123). Human testing with a more powerful device began in 2006. With this device, time to recovery of orientation in 11 depressed patients was significantly less (7 minutes after treatment) than for ECT (22 minutes) in the same patients (123).

Vagus nerve stimulation

Vagus nerve stimulation (VNS) typically involves stimulation of the left cervical vagus nerve, with a pacemaker-like device placed in the left chest wall. In animal and human studies, VNS increases cerebrospinal fluid concentrations of neurotransmitters relevant to depression, and alters functional activity of brain regions including orbital frontal cortex, cingulate, thalamus, hypothalamus, insula, and hippocampus (124).

VNS was first used for drug-resistant epilepsy. Studies showed that mood in VNS also improved independently of epilepsy treatment response (125,126), prompting further studies of VNS for treatment-resistant depression. In a 10-week, randomized, controlled trial in drug-resistant depressed patients, the primary outcome measure did not differ significantly between VNS (15%) and sham treatment (10%) (124). Further, it was not clear to what extent the blinding procedure was successful, as VNS even at low intensities causes some subjects to experience physical sensations. However, in the 12-month open continuation phase of the study, where subjects also received treatment as usual (TAU, including medications and/or ECT), treatment response was significantly greater for VNS + TAU (27%) than for TAU alone (13%) (127). VNS for treatment-resistant depression was approved in the European Union in 2001 and by the FDA in 2005 (128).

Deep brain stimulation

Deep brain stimulation (DBS) involves electrically stimulating the brain through fine, deeply implanted electrodes. The electrodes typically are attached to a subdermal pacemaker-like device that delivers a continuous train of repeated, very brief, small voltage pulses.

DBS was first used in 1997 for the treatment of Parkinson's disease (129). Chronic stimulation of portions of the basal ganglia with DBS produced improvements in patients' motor function similar to those previously achieved with ablation, leading researchers to speculate that DBS produces a reversible "lesion" through transient electrical inactivation (130). Because a decrease in subgenual anterior cingulate cortex (sACC, also called subcallosal cingulate gyrus) activity levels is often associated with depression treatment response, the sACC became the target for the first reported (in 2005) application of DBS for treatment-resistant depression (131). A "striking and sustained remission" was reported in four of six patients, with several patients reporting an almost immediate remission of "painful emptiness" and "void" when the stimulation was turned on. Since then, of 20 depressed patients treated with sACC DBS, response (60%) and remission (35%) rates have been excellent for treatment-resistant (including ECT) depression (132). Post-operative side effects included headache (4 cases), craniotomy site infection (4 cases), and seizure (1 case), but no patient experienced permanent deficits.

The reasons for the good efficacy results are unclear. Some recent mechanistic findings indicate that, although DBS inhibits activity in neuron somata near (<2 mm) the stimulating electrode, DBS stimulates axons, causing activation of efferent nuclei (133). Also, in a more recent study of three persons with extremely resistant forms of depression (one was a 66-year-old woman), DBS to the nucleus accumbens resulted in significant reductions in depressive symptom scores within one week (134). Since increased nucleus accumbens activity has been associated with expectations of and experiences of rewards, it seems unlikely that the improvements in depression were due to inhibition of this nucleus. Results were also encouraging for another study (N=15) involving DBS to the ventral capsule/ventral striatum (VC/VS), with 53% response and 40% remission of treatment-resistant depression. The motivation for applying DBS to the VC/VS was the observation of improved mood in severe obsessive-compulsive disorder patients given this treatment (135).

Psychotherapy

Forms of psychotherapy reported efficacious in the cognitively intact elderly depressed include interpersonal psychotherapy (ITP) (136), problem-solving therapy (PST) (137), supportive psychotherapy (138), and cognitive-behavioral therapy (CBT) (139,140).

ITP's focus on loss, grief, and role transitions makes it highly suitable for the elderly depressed population, in whom these themes are common. PST's structured planning and problem-solving approach should stimulate activity in the dorsolateral prefrontal cortex, a goal of some biological

treatments. PST appears effective and well-suited for patients with depression and executive dysfunction (141).

Recently, development of behavioral approaches has begun, based on the concept that depression introduces new problems and at the same time reduces patients' ability to solve them. As a consequence, depressed older patients experience their environment as difficult to negotiate and stressful, which serves as a trigger perpetuating their symptoms. For this reason, novel treatments have been developed aiming to improve patient adaptation and reduce the experience of adversity. Improving depressed patients' problem-solving skills is part of several such therapies. However, depressed patients with significant cognitive impairment or physical disabilities may be unable to improve their coping skills with problem-solving techniques. For this reason, we have developed "ecosystem focused therapy" (EFT), a treatment that focuses on the "ecosystem" (patient + environment + family member/caregiver) of which the patient is a part (142). EFT imparts to the patient skills maximizing his/her remaining functions; modifies the patient's physical environment; and engages family members/caregivers in helping the patient bring to bear his/her skills. EFT uses problem-solving therapy as its framework along with tools and instructions that can be used by patients and caregivers to make the environment conducive to adaptation. Enabling patients to *assimilate* new skills and changing patients' environments, including caregivers, to *accommodate* to the patients' states, offers patients a good chance at adaptation, increases their sense of mastery, and may reduce depression.

Depression prophylaxis

Depression prophylaxis is considered in cases where risk of depression is exceptionally high, such as during the early stages after antidepressant treatment remission or in patients who have had multiple severe episodes of depression (40).

The high rate of depression after stroke has prompted some researchers to explore various forms of post-stroke depression prophylaxis. Prophylactic treatment with escitalopram or problem-solving therapy after stroke resulted in significantly lower rates of depression compared with placebo (143). A large Finnish study compared post-stroke depression rates in districts implementing usual care (mainly physiotherapy and speech therapy) with rates in districts adding an active rehabilitation program. The active rehabilitation group had significantly lower rates of depression (41% vs. 54% at 3 months post-stroke, and 42% vs. 55% after 1 year) (144).

Multidisciplinary approaches to depression treatment

Medical illness increases the risk of depression (95) and depression increases the risk of medical illness. The frequently bidirectional relationship between somatic illness and depression necessitates attention to both somatic and psychiatric issues, in order to break potentially vicious cycles of psychiatric illness predisposing to somatic illness, and vice versa. Non-psychiatric health care practitioners need to incorporate diagnosis and treatment of depression into their routine practice, while psychiatrists to a greater degree need to address somatic issues. Increased collaboration among health care practitioners is likely to improve health care on all levels.

For example, among chronic obstructive pulmonary disease (COPD) patients with depression, both somatic and psychiatric treatment approaches appear to impact both conditions. Depressive symptoms improved after a brief, multidisciplinary inpatient COPD rehabilitation treatment (145). In a study of depressed patients with COPD, physical symptoms, function, and mood improved after treatment with antidepressant medication (146).

Patients with chronic pain and depression are also likely to benefit from a multi-disciplinary approach. Moderate to severe pain is associated with increased rates of depression and poorer depression outcomes; and depression in pain patients is associated with more pain complaints and greater impairment. An estimated 65% of depressed patients have pain and 52% of patients in pain clinics or inpatient pain programs are depressed (147). Underassessment of pain is a major barrier to adequate pain treatment (148); asking depressed patients about pain symptoms and pain treatment can greatly facilitate proper care. Antidepressant medications that increase norepinephrine in synapses, such as tricyclic antidepressants, venlafaxine, and duloxetine, generally help diminish the experience of pain directly, in addition to their antidepressant effects (149).

Finally, the observed bidirectional relationship between depression and vascular disease means that somatic health care practitioners need to assess for depression for the same reasons they routinely assess for hypertension and hypercholesterolemia. Likewise, psychiatrists should consider cardiovascular health in their patient assessments. Such an assessment in psychiatry is particularly important because many psychotropic medications can potentially influence cardiovascular health. For example, by decreasing platelet activity, SSRIs may reduce the risk of heart attacks (150), and also increase bleeding risks in patients taking aspirin.

Psychotropic medications that increase weight, cholesterol levels, or risk of diabetes may also increase risk of atherosclerosis and cardiovascular disease, so many psychiatrists routinely monitor weight and blood pressure; and some prescribe medications such as metformin prophylactically when risk of obesity and diabetes is involved with psychiatric medication treatment (151).

Patients' concern about weight gain can interfere with treatment, so it is often helpful to choose medications that cause as little weight gain as possible. The medications bupropion (antidepressant) (152) and lamotrigine (mood stabilizer) (153) are generally not associated with weight gain. Among antipsychotic medications, weight tends not to increase much with aripiprazole and ziprasidone (154).

Care access and delivery

The greatest limitation in treatment of late-life depression concerns treatment access and delivery rather than treatment efficacy. In primary care settings, where most depressed older patients are treated, the diagnosis of depression is often missed. Further, correct diagnosis of depression often does not lead to treatment, and treatment is often inadequate. In one study, only 11% of depressed high utilizers of primary care treatment were found to receive adequate antidepressant treatment (155).

Studies such as PROSPECT (156,157) and IMPACT (158,159) have shown that collaborative care offered at the primary care setting has superior outcomes to usual care. However, inadequate third-party reimbursements restrict collaborative care to large providers, e.g. health maintenance organizations, which serve a minority of the US population. To overcome this barrier, we proposed a depression care management model (C-DCM) relying on collaboration of primary care physicians with trained social workers employed by community-based, public and nonprofit mental health clinics (142).

While widely available in the US, mental health clinics are rarely connected to primary care practices and underutilized by depressed elders. To utilize this resource, we proposed a collaborative care model, designed to satisfy four conditions. First, it should meet the clinical needs of depressed elders. Second, it should include organizational changes that would enable primary care practices and mental health clinics to work together effectively. Third, collaborative care should be modified in a way that can be used by trained social workers and brings to bear their special skills. Fourth, it should include procedures reimbursed by existing insurance codes so that it adds no cost to primary care physicians or mental health clinics.

CONCLUSIONS

Although the causes of depression remain unknown, recent advances have facilitated the exploration of factors related to depression and its many manifestations. Contrasting various forms of depression in late life with depression in early life has provided insight into mechanisms that might increase the risk of depression. This research has provided observations that have led to new hypotheses on the causes of depression, which in turn have generated new therapeutic advances in biological and psychosocial approaches to the treatment of late-life depression. Finally, research in care access and delivery has provided new models to improve the effectiveness of late-life depression treatment in the community.

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Salient components of a comprehensive service for eating disorders

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Eating disorders are challenging and difficult to treat, because of the necessity of a multidisciplinary treatment team for effective outcomes and the high mortality rate of anorexia nervosa. An adequate initial assessment and evaluation requires a psychiatric assessment, a medical history and medical examination, a social history and an interview of family members or collateral informants. A comprehensive eating disorder treatment team includes a psychiatrist coordinating the treatment and appropriate medical physician specialists, nutritionists, and psychotherapists. An adequate outpatient eating disorder clinic needs to provide individual psychotherapy with cognitive behavioral techniques specific for anorexia nervosa and bulimia nervosa, family therapy, pharmacological treatment and the resources to obtain appropriate laboratory tests. Eating disorder patients requiring inpatient care are best treated in a specialized eating disorder inpatient unit. A cognitive behavioral framework is most useful for the overall unit milieu. Medical management and nutritional rehabilitation are the primary goals for inpatient treatment. Various group therapies can cover common core eating disorder psychopathology problems and dialectical behavior therapy groups can be useful for managing emotional dysregulation. Residential, partial hospitalization and day treatment programs are useful for transitioning patients from an inpatient program or for patients needing some monitoring. In these programs, at least one structured meal is advisable as well as nutritional counseling, group therapy or individual counseling sessions. Group therapies usually address issues such as social skills training, social anxiety, body image distortion or maturity fears. Unfortunately there is s paucity of evidence based randomized control trials to recommend the salient components for a comprehensive service for eating disorders. Experienced eating disorder clinicians have come to the conclusion that a multidisciplinary team approach provides the most effective treatment.

Key words: Eating disorders, comprehensive treatment, outpatient, inpatient

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In the past decade, eating disorders have received a fair amount of dramatic attention in the public media. However, the true incidence and prevalence of these disorders have been difficult to ascertain for several reasons.

Most studies of incidence and prevalence of eating disorders have been conducted on limited populations and in various different countries. Many persons with eating disorders are reluctant to admit to their disorder and thus it is likely that a large number of persons with these problems go undiagnosed and untreated. Eating disorders may be transient or recurrent and thus point prevalence rates may not fully reflect the extent of eating disorder pathology in the population. Many persons suffering from eating disorders do not meet full criteria for anorexia nervosa or bulimia nervosa and thus fall into a less well-defined category of eating disorders not otherwise specified. Carefully defining this area in epidemiological studies is a problem.

A study of patients recruited from primary care practices in England showed that the prevalence of anorexia nervosa was 20.2 cases for 100,000 population (0.02% of the total population). The prevalence among female patients aged 15-29 years was 115.4 cases per 100,000 population (0.1%) (1). Another more recent study in the United States showed that the lifetime prevalence of anorexia nervosa was 0.6% (2). In a community sample in which a structured interview was used, the prevalence rate for bulimia nervosa was 1% (3).

With a standardized mortality rate of 23.14 (4), eating disorders have the highest mortality rate of any psychiatric disorder. Mortality can be due to suicide, medical complications of malnutrition or complicating comorbid medical disorders.

Anorexia nervosa is one of the most difficult psychiatric disorders to treat. There are few controlled treatment trials for this disorder for several reasons: a) the disorder is relatively rare, so it is difficult to obtain an adequate sample size in any one center; b) patients with anorexia nervosa have a strong resistance to treatment and c) medical complications often require withdrawal from treatment protocols.

The resistance to treatment compliance often present in anorexia nervosa patients may be due to the fact that this disorder serves a strong positive function in the patient's life, providing an escape from aversive developmental issues or distressing life events. The disorder becomes highly reinforcing and the prospect of relinquishing the anorectic behavior pattern is terrifying to the patient. Another possibility is the egosyntonic nature of the disorder, which is demonstrated by the patient's denial and refusal to except the seriousness of the medical consequences of the disorder. Thus, difficulties incur in recruiting sufficient numbers for treatment trials, in inducing compliance with treatments and in retaining patients to the completion of treatment. In a recent study of 122 randomized cases, the overall dropout rate of anorexia nervosa patients was 46% (5).

Involuntary admission may be necessary to manage a life-threatening emergency or a serious medical deterioration when the patient is unwilling to cooper-

ate in treatment. Nasal gastric tube feeding may be necessary for involuntary feeding. Follow-up studies have shown that involuntary admission and feeding do not have a detrimental influence on outcome (6).

Professional training for the diagnosis and treatment of eating disorders is best obtained in a well-established eating disorder program that provides outpatient, day program and inpatient treatment facilities for these disorders, with a multidisciplinary team of professionals including psychiatrists, primary care physicians, nutritionists, psychologists, as well as family therapists who may be psychologists or specifically trained social workers. The components for an ideal treatment and training center for eating disorders are summarized in this paper.

DIAGNOSTIC AND EVALUATION CLINIC

The initial assessment and evaluation of an eating disorder patient usually occurs in the context of an outpatient clinic. The assessment must take into account several unique features. First, eating disorder patients are often reluctant to give a complete informative history. Therefore the participation of family members or other collateral informants is desired and necessary in the case of adolescents and younger patients. Second, the evaluation must be comprehensive: a psychiatric assessment, a medical history and examination, and social history. Third, the assessment usually requires several hours.

Interview information necessary for the diagnosis of an eating disorder according to the DSM-IV (7) is summarized in Table 1. Most eating disorder patients have other common comorbid behaviors and psychiatric diagnoses: these need to be investigated and are listed in Table 2. The common abnormalities found on physical examination and laboratory findings are listed in Tables 3 and 4.

Table 1 Interview information for diagnosis of anorexia nervosa and bulimia nervosa

Weight history
Greatest weight patient has achieved, age at that time
Least weight (after weight loss) the patient has achieved, age at that time
Present weight
Eating behavior
Changes in eating pattern with family (e.g., eating alone)
Dieting behavior – what does patient eat and when?
Bingeing episode? Describe
Purging behavior
Self-induced vomiting
Laxative abuse
Diuretic abuse
Enemas
Preoccupations and rituals concerning food and weight
Frequency of patient weighing herself
Mirror gazing, comments about being fat
Collecting recipes, increased interest in cooking and baking
Constant calorie counting and concern of fat content of foods
Fear of being unable to stop eating
Peculiar eating rituals
Activity
Jogging – how far and for how long
Bike riding – how far and for how long
Exercising – what type and how long
General over-activity at home (paces, never sits)
Menstrual history
Age onset of menses
Date of last menstrual period
Regularity of cycles

Table 2 Interview information on common comorbid behaviors and psychiatric diagnoses

Depression
Sleep disturbance
Irritability and difficulty concentrating
Crying spells
Suicidal thoughts
Impulsive behavior
Drug abuse
Alcohol abuse
Suicide attempts
Self-mutilation, cutting on body
Anxiety symptoms
Obsessive–compulsive behaviors
Social phobia
Generalized anxiety and fearfulness
Panic attacks
Personality disorders
Pattern of instability in interpersonal relationships, self-image, affect
Pattern of social inhibition, feelings of inadequacy, hypersensitivity to negative evaluation
Pattern of dependent, submissive behavior with difficulty separating from parents
Preoccupation with orderliness, perfectionism and control

Assessing the family

Evidence should be obtained of eating disorders and other psychiatric disorders, alcoholism, substance use disorders and obesity in the first-degree relatives and extended family members who are involved with the patient. Inquiry should be made into a family history of physical or sexual abuse, family communication styles and family structural patterns.

It is important to identify family stressors that may aggravate the eating disorder and to determine the family's attitude towards the patient; for example, are they resentful and critical, burned out, or devoted and encouraging. This information is helpful for the clinician to determine the extent of the family's involvement in the treatment plan.

Table 3 Physical examination abnormalities in eating disorders

Physical symptoms	Cause
Dry, cracking skin	Dehydration, loss of subcutaneous fat
Lanugo hair	Starvation
Calluses on dorsum of hand	Self-induced vomiting with hand friction against teeth
Perioral dermatitis	Vomiting
Enlarged parotid glands (chipmunk face)	Vomiting
Teeth enamel erosion and caries	Vomiting
Periodontitis	Vomiting
Bradycardia	Starvation
Hypotension	Starvation and fluid depletion
Arrhythmias	Hypokalemia from purging

Table 4 Laboratory abnormalities in eating disorders

Laboratory findings	Cause
Complete blood count	
Leukopenia with a relative lymphocytosis	Starvation
Anemia	Starvation
Serum and plasma	
Hypokalemia	Purging, diuretic abuse
Hypochloremic metabolic alkalosis	Purging
Hyperamylasemia	Purging
Hypercholesterolemia	Starvation
Hypercarotinemia	Ingestion of high-carotene foods
Electrocardiogram	
Q-T and T-wave changes	Hypokalemia, cardiomyopathy from ipecac
Photon absorptiometry	
Reduced bone density	Starvation

A multidimensional treatment team

A comprehensive eating disorder treatment team means a collaborative team of specialists. It is recommended the psychiatrist assume the coordinating or leadership role within the team and program. For the management of acute and ongoing medical and dental complications, other physician specialists and dentists may need to be consulted.

The initial complete physical examination is usually conducted by a primary care physician. A nutrition specialist is helpful for nutritional rehabilitation counseling and giving advice for adequate and appropriate nutritional intake. Psychotherapy may be conducted by the psychiatrist or a psychologist and family therapy by a psychiatrist, psychologist or specifically trained social worker (8).

OUTPATIENT EATING DISORDER CLINIC

An outpatient eating disorder clinic should have available a comprehensive treatment team consisting of psychiatrists, psychologists, nutritionists, primary care physicians and social workers. Eating disorder patients admitted to outpatient treatment should be in a medically stable condition. This means that their weight should be above 75% of a normal weight for age, height and bone structure, with normal serum electrolytes, normal electrocardiogram and no evidence of suicidal ideation or incapacitating behaviors that result in non-functioning at work, school or family responsibilities.

Because the eating disorders require treatment of a variety of conditions, including psychological and medical, with needs of psychotherapy, pharmacological treatment and medical treatment, is it is advisable that a psychiatrist be in charge of the treatment plan for the individual eating disorder patient.

Eating disorder clinics should be able to provide individual psychotherapy, including cognitive behavioral therapy specifically designed for eating disorders, interpersonal therapy and dialectical behavior therapy. Pharmacotherapy may be needed for treatment of depression, anxiety disorders and extreme agitation. Family therapy must be available for all adolescents with eating disorders. Nutritional counseling and education is a useful component to all treatment plans for eating disorders.

A comprehensive assessment is necessary for organizing a treatment plan for the individual eating disorder patient. There will always be patients for whom evidence based treatments will not be effective and other innovative approaches may be needed. With a treatment team of experienced psychotherapists, psychopharmacologists, nutritionists and physicians, the possibilities of putting together creative and effective treatment plans are likely to be higher.

Anorexia nervosa

Evidence-based trials are particularly scarce for this disorder, due to unwillingness of the patients to participate in the trials and high dropout rate. For outpatient individual psychotherapy in adults with anorexia nervosa, the NICE guidelines (9) recommend a cognitive behavioral therapy. This type of therapy has been described in detail by Pike et al (10) and Kleifield et al (11).

The most robust evidence-based trials for anorexia nervosa are those of family therapy with adolescents. Eisler et al (12) and Lock et al (13) have shown that a cognitive behavioral style family therapy is effective for these adolescents (14).

It is recommended in most medical guidelines that medication be only considered as an adjunct treatment for anorexia nervosa. Randomized controlled trials have indicated that cyproheptadine (14) in large doses of up to 24 mg per day may marginally facilitate weight gain and decrease depression. There is also a suggestion that fluoxetine (15) may in some cases help prevent relapse. A more recent study showed olanzapine to be effective in facilitating weight gain and reducing anxiety and obsessive thoughts in anorexia nervosa patients (16).

Bulimia nervosa

A large number of randomized controlled trials have shown cognitive be-

havioral therapy to be a most effective treatment for bulimia nervosa. Many studies are summarized in a review article by Shapiro et al (17). These studies often give a detailed description of their technique or references to the manuals they used.

Evidence for a medication treatment for bulimia nervosa is not as strong as that of cognitive behavioral therapy. Numerous randomized medication trials indicate that all serotonin reuptake inhibitors are effective in reducing binge-purge behavior (17). Selective serotonin reuptake inhibitors (SSRIs) are preferred medications, because they have fewer side effects than the other medications that have been shown to also reduce binge-purge behavior.

Evidence for the effectiveness of self help is weak and for other interventions either weak or non-existent in the treatment of bulimia nervosa.

Binge eating disorder

The few randomized controlled psychotherapy trials for binge eating disorder (BED) indicate that cognitive behavioral therapy is the treatment of choice (18).

Medication trials for BED indicate that serotonin reuptake inhibitors are moderately effective in reducing binge frequency and illness severity (19,20). Randomized controlled trials with topirimate (21) and sibutramine (22) have also shown a moderate effect for reducing bingeing behavior in BED.

INPATIENT TREATMENT OF EATING DISORDERS

The majority of eating disorder patients requiring inpatient hospitalization have anorexia nervosa. The most frequent and compelling reasons for hospitalization of an anorexia nervosa patient are the medical indications listed in Table 5. Comorbid psychiatric conditions may also require the patient to be hospitalized and are listed in Table 6.

Ward milieu

A cognitive behavioral framework is useful for the overall ward milieu. Exposure and response prevention techniques can be used to prevent patients from purging and exercising. Group therapy can be used for interpersonal conflicts, psychoeducation about nutrition, medical complications and relapse prevention, assertiveness training, self control strategies, maturing and autonomy issues, and limit setting problems. In the group format the patients can discuss their symptoms and have an increased awareness of symptom triggers and coping strategies.

Physical structure of an inpatient unit

An ideal eating disorder inpatient unit will have an adequate dining room space, so that patients can be directly monitored during meals. Day room areas must also plan for onsite monitoring of patients by nursing staff. Some programs have employed closed circuit television monitoring to reduce surreptitious exercise. The latter requires informed consent and permission of the patients. Bathrooms on this unit need to be locked, to prevent engaging in purging behaviors. One novel program has utilized electronic key-controlled flush switch on toilets so that patients may

Table 5 Common medical indications for inpatient hospitalization for anorexia nervosa

- Generally, weight <75% of individually estimated healthy body weight or acute weight decline with food refusal
- For adults:
  Heart rate <40 beats per minute (bpm)
  Blood pressure <90/60 mmHg or orthostatic hypotension (with an increase in pulse of >20 bpm or a drop in blood pressure of >10-20 mmHg/min from lying to standing)
- For children:
  Heart rate <50 bpm
  Orthostatic changes of >20 bpm
  Blood pressure <80/50 mmHg
- Blood glucose levels <60 mg/dL, potassium <3 mEq/L
- Electrolyte imbalance (hypo- or hypernatremia, hypophosphatemia, hypomagnesemia, hypokalemia)
- Body temperature <97.0 ºF, dehydration
- Hepatic, renal, or cardiovascular organ compromise requiring acute treatment

Table 6 Comorbid psychiatric conditions for inpatient eating disorder admission

Suicidality
A specific plan with high lethality or intent: suicide attempt, psychotic depression.

Motivation
Very poor motivation: patients may be preoccupied with intrusive repetitive thoughts that cause severe impairment of function; patients may be very uncooperative in treatment and need a highly structured setting to initiate an effective treatment.

Purging behavior (including laxatives and diuretics)
These patients are unable to control multiple daily episodes of purging that are severe, persistent and disabling despite appropriate trials of outpatient care. They need supervision during and after all meals and in bathrooms.

Substance abuse disorder
These patients may require a combined withdrawal treatment plan in addition to nutritional rehabilitation in an inpatient unit.

Environmental stress
Significant environmental psychosocial stressors with inadequate social support may facilitate an impairment of function, and removal from this environment may be beneficial to the patient. An example is severe family conflict or absence of a family so the patient's is unable to receive a structured environment at home or the patient may live alone without a support system.

have privacy in the bathroom but must wait for a nurse to check the content of the toilet before it is flushed.

Medical management and nutritional rehabilitation

Medical management involves weight restoration, nutritional rehabilitation, rehydration and correction of serum electrolytes. This requires daily monitoring of weight and urine output, and frequent assessment of electrolytes. Physicians experienced in the medical management of severely emaciated anorexia nervosa patients are necessary for adequate care. The total number of calories in emaciated patients should begin with an intake of 30-40 kcal/kg/day and can be increased gradually if there is no evidence of peripheral edema or heart failure.

Liquid formulas are an advantage because they contain the necessary amount of vitamins and minerals and can be given in small amounts such as 6 equal feedings throughout the day. A randomly controlled study actually showed that this approach in early hospitalization was more effective than requiring the patient to eat food (23). At this stage of treatment, serum hypophosphatemia may develop during refeeding, requiring phosphate supplements.

Bed rest may be necessary with escorted assisted walks and special observation for the development of bedsores. Medications known to prolong QT_c intervals should be avoided. Occasionally, electrolyte abnormalities may have to be corrected by intravenous solutions.

As patients improve, they should receive nutritional counseling with devising meal plans to practice after they are discharged from the hospital.

Ideal discharge criteria from the inpatient setting are presented in Table 7.

Table 7 Ideal discharge criteria for eating disorder patients from an inpatient setting

- Attainment of ideal body weight
- Medical stability (a normal electrocardiogram and serum electrolytes)
- No suicide risks
- Ability to maintain ideal body weight and normal nutritional intake during passes outside the structured environment
- Ability to select foods in family style serving
- No binge eating, purging or over exercising for at least 1 week
- No incapacitating impairment from comorbid conditions
- Family educated about the eating disorder and prepared to assist the patient during outpatient recovery
- Identification of an outpatient treatment team and placement of appropriate referrals

Patients who are bingeing and purging and within a normal weight range usually require only a short hospitalization for stabilization. They often have comorbid diagnoses of borderline personality disorder or substance and alcohol abuse. Addiction withdrawal is usually better accomplished on a specialized unit, with transfer to the eating disorder unit at a later date. Dialectical behavior therapy groups can be useful for managing emotional dysregulation in borderline bingeing and purging patients. There is evidence that patients who are discharged from an inpatient setting with a body mass index of 19 or greater are less likely to relapse (24).

RESIDENTIAL, PARTIAL HOSPITALIZATION AND DAY TREATMENT PROGRAMS FOR EATING DISORDERS

Treatment programs with a variety of different titles have developed for patients transitioning from an inpatient program who are too incapacitated for outpatient treatment. These programs also apply to patients who have been outpatients and become more severely impaired, but not to a degree requiring inpatient hospitalization. A multifaceted program with a cognitive behavioral focus on symptom change is recommended. Such programs have reported weight gain in anorexia nervosa patients and improvements in eating disorder attitude and depressive symptoms (25-27). Programs of varying intensity have been described, but no randomized controlled trials have been conducted.

At least one structured meal is advisable in these programs, and nutritional counseling and meal planning can occur in the context of group therapy or in specific individual counseling sessions. Multiple group therapies addressing issues such as social skills training, social anxiety, body image distortion, or maturity fears are effective ways of continuing themes developed during inpatient treatment.

These intermediate treatment settings need to have physicians available for medical monitoring, nutritionists for nutritional counseling, psychotherapists for both individual and group therapy and psychopharmacologists for those patients who need medication.

There are no studies to provide evidence-based criteria for discharge in these intermediate programs. Generally it is advisable that patients be above 90% of a normal weight and have demonstrated improved functional behavior with a significant decrease of their core eating disorder symptoms. Evidence of intent to continue cognitive behavioral skills learned to reduce the core eating disorder behaviors is also a valuable criterion for transitioning a patient to outpatient treatment alone.

CONCLUSIONS

There is a paucity of evidence based randomized controlled trials to recommend the salient components of a comprehensive service for eating disorders. Established and experienced clinical eating disorder treatment centers have come to the conclusion that a multidisciplinary team approach provides the most effective treatment service for patients with these disorders.

A comprehensive service would include a diagnostic and evaluation clinic, an outpatient clinic, an inpatient service and a day program with a residential treatment component. A psychiatrist should be the captain of this multidisciplinary team, which includes psychotherapists, psychopharmacologists, nutritionists, and family therapists. Mental health support and coverage will deter-

mine the specifics of these salient features in the individual countries.

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Diagnosis, provision and service organization

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K. Halmi has shared her vision of the elements that need to be included in any "comprehensive" service response to the needs of people with clinical eating disorders. And few clinicians in the field would wish to argue with her about most of what she has set out.

Some card-carrying nit-pickers such as myself could find things about which to quibble. For instance, the figure of 23 which she quotes for the standardized mortality is rather an outlier on the high side (1,2). Indeed, it is probably for this reason that it gets quoted frequently when the case is being made that eating disorders need to be taken seriously. I have so used it myself.

Others in critical mode might question her proposal that multi-disciplinary teams should always have the psychiatrist as their "captain". As a medic myself this seems entirely reasonable and in tune with my view of how things should be, although an irritating part of my mind insists upon coming up with examples of good services that are led – either managerially or clinically or both – by non-medically qualified clinicians. And what about the nurses? They are not on Halmi's list. Yet, where I work they are the biggest professional group, both obviously in the inpatient unit but also less obviously in the outpatient teams, where with appropriate further training and support they make assessments and deliver psychological treatments. But to spend much time on such matters would be to miss the point. So, I shall flag up and comment mainly upon two issues. Each is touched upon but arguably neither receives sufficient emphasis in Halmi's text.

The first issue is that of diagnosis and its implications. Of course, this is mentioned in the text, but often the terms eating disorder and anorexia nervosa seem to be used almost interchangeably. Most of the statements about what is required sit well with a discussion of anorexia nervosa, but less so with other types of eating disorders. Thus, the emphasis on multi-disciplinary teams, including psychiatrists, psychologists, nutritionists, physicians and so on, is appropriate for the management of the most seriously ill and risky patients. These challenging cases will be in the main people with a diagnosis of anorexia nervosa, but even within that diagnostic category they will be a minority. Most eating disorders can be assessed and treated adequately by an appropriately trained clinician working within an outpatient service or in office practice. This majority – my guess is that it would be of the order of 90% or more of presenting cases – includes many people with anorexia nervosa and the great majority of those with bulimia nervosa and the various forms of eating disorders not otherwise specified, including binge eating disorder. Such a clinician would need to be aware of physical risk and should know how to seek relevant expertise when complication or uncertainty arises. But the requirement of a full multi-disciplinary team confronting all patients is neither necessary nor practical.

There are ways in which the current diagnostic classification of the eating disorders is unsatisfactory and in many respects the "transdiagnostic" view has merit (3). However, no one denies the practical relevance of very low weight and the associated complications. A comprehensive service needs to include a centre or team that can cope with the most difficult and risky cases. Inpatient treatment should be among the available interventions. However, this small part of clinical services for eating disorders need not predominate and arguably has been overemphasized in the past. What is often missing is the availability of suitably supported, competent and confident therapists/case managers who are able take on the majority of people with eating disorders.

The other issue that is not emphasized in Halmi's text is that of service organization. How are the various elements of a comprehensive service to relate to each other? To a degree this will vary with the economic and political framework within which services are delivered. This can be a touchy subject and clinical guidelines often avoid it (4,5). Taxation funded state provision, such as the National Health Service in the UK, tends to have problems, but so do insurance based systems. Furthermore, there is some convergence with the growth of massive comprehensive health systems in the latter and attempts to inject ideas of a "market" and "choice" in the former. Third parties of whatever kind are increasingly influential. There is a need for clinicians to consider how much provision of what kind is reasonable for a population. We need to address such issues and come up with clinically relevant answers if we are not to be buffeted or unduly constrained by those with a more distant and mainly financial perspective. Of course, for the patient what matters is the ready availability of good quality services which are coherent and manage transitions for instance between child and adult or between outpatient and inpatient provision with a minimum of fuss and disruption. Patient and carer organizations should be important allies in these matters.

The exercise of defining the components of a comprehensive service for people with eating disorders is important and K. Halmi and indeed *World Psychiatry* are to be congratulated on confronting this issue. The question is complicated but enriched by adding the issue of how these components may best be put together in practice. Undoubtedly there are more ways than one.

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Planning an eating disorder service on the basis of epidemiological data

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K. Halmi presents the salient components of a comprehensive service for eating disorders. In planning such a service, health policy makers need to understand the prevalence of eating disorders in the catchment area to be served. The size of an eating disorder service is not only dependent on the size of the catchment area, but also on the demographic characteristics of its population.

Because eating disorders occur mainly among young females, it is important to know the proportion of this high risk group in the total population served. But characteristics of the catchment area itself are also important, such as the degree of urbanization. For example, in the Netherlands, the incidence of bulimia nervosa was found to be five times higher in cities than in rural areas (1).

Also, most epidemiological data on eating disorders are derived from studies in Western countries, especially from Western Europe, because of the availability of comprehensive health registration systems and population statistics. With eating disorders, one has to be especially careful about applying the results from studies in Western countries for planning health care facilities in non-Western countries. In a comprehensive study on the Caribbean island of Curaçao, the incidence of eating disorders among the minority mixed-race and white population was similar to the incidence in the United States and Western Europe, while no cases were found among the majority black population (2).

In a meta-analysis providing one-year prevalence rates per 100,000 young females in the Netherlands at different levels of care (3), we reported that the rates for anorexia nervosa were 370 in the community, 160 at the primary care level, and 127 at the level of outpatient and inpatient mental health services. The corresponding rates for bulimia nervosa were 1,500, 170 and 87. These data confirm that only a minority of eating disorder patients in the community enters the mental health care system. This is particularly true for bulimia nervosa. These low rates of persons with eating disorders in care is likely to be the result of patient delay, due to denial or shame, and doctor delay, due to inadequate detection of these severe disorders.

In a community study of Finnish twins (4), the lifetime prevalence of DSM-IV bulimia nervosa was 2.3%, but few of these women were identified by the health care system. The lifetime prevalence of DSM-IV anorexia nervosa was 2.2% and as high as 4.2% for broadly defined anorexia nervosa (5). Only half of the anorexia nervosa cases ascertained in this study had been detected in the health care system, though most of them had suffered from anorexia nervosa for several years. Another remarkable finding was that the lifetime prevalence of anorexia nervosa in young males in the Finnish community was 0.24%, also much higher than previously thought (6).

Studies in the Netherlands and Sweden provide circumstantial evidence that early detection of anorexia nervosa is of major importance for a favorable outcome (7,8). Anorexia nervosa is still characterized by high lifetime mortality from both natural and unnatural causes (9). However, mortality among female patients with anorexia nervosa in hospital care in Sweden has decreased dramatically, which is probably related to the introduction of specialized care units (10).

Eating disorder treatment programs are traditionally developed for patients with anorexia or bulimia nervosa. However, nowadays the majority of cases suffering from an eating disorder can only be classified in the DSM-IV category of eating disorders not otherwise specified (EDNOS). These include partial syndromes of anorexia or bulimia nervosa as well as binge eating disorder, a proposed new category in DSM-IV for research purposes (11). In a community study of eating disorders in Portugal, three quarters of young females with an eating disorder were classified as EDNOS (12). Even in outpatient settings, EDNOS cases account for an average of 60% of all cases (13). Although these patients are characterized by similar core cognitive psychopathology, they represent the least studied group of patients with eating disorders.

Setting up an eating disorder service requires knowledge of its catchment area and of the epidemiology of eating disorders in general. But it is perhaps even more important to realize that most persons with eating disorders never come into treatment. In planning health services for persons with eating disorders, it is essential to take into account this enormous hidden morbidity of the disorders among the population and to develop methods to address it.

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A comprehensive treatment service must include developmental, systemic and collaborative components

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In the absence of a strong evidence base for treatment of eating disorders, it is inevitable that there will be disagreement about what is the most appropriate treatment service. Much of K. Halmi's overview of what constitutes such a service is helpful and uncontroversial. In this commentary, I will focus on what I believe to have been neglected, insufficiently acknowledged or out of keeping with contemporary views or practice.

The first omission is that of a developmental focus. The peak age of onset of eating disorders is between 14 and 18, a time of considerable physical and psychological maturation. Increasingly prepubertal children are developing these disorders. The potential for physical decompensation is far greater in childhood and adolescence than in adults. Particular attention needs to be paid to bone growth, both linear and density, and to reproductive organ status, all of which are threatened by inadequate nutrition. Body mass index (BMI) per se is unhelpful, as it needs to be monitored according to age, using BMI centiles for age (1). Stipulating a specific BMI for under 18s, upon which decisions are made, is misleading.

From a psychological perspective, developmental issues pay a vital part in the pathogenesis and maintenance of eating disorders and subsequently need to be central to assessment and treatment. Linked to this is the importance of a systemic perspective. Children and adolescents live with their families, attend school and are intensely involved with their peer group. The family history is far less important than parental management of the illness and the parents should *always* be included in both the treatment planning and its delivery. Indeed, family-based approaches to treatment for adolescent anorexia nervosa have a good evidence base and are central to the National Institute for Clinical Excellence (NICE) guidelines for its management (2).

The multi-disciplinary team is, as Halmi suggests, an essential part of any treatment programme. However, Halmi makes no mention of nurses, who are central to the treatment on in-patient units and are often involved in day-care, out-patient clinics and home-based treatments. Her description of the ward milieu and physical structure of an in-patient unit emphasises "compliance", with monitoring, controlling and restricting patient activities. Patient autonomy, privacy, comfort or rights receive virtually no attention. And there is no mention of some essential components of treatment, be that on an in- or out-patient basis: a) building a therapeutic alliance; b) skilled communication; c) empathic exploration of the patient's anxieties, concerns and cognitions; d) enhancing motivation – the unmotivated patient is far more likely to drop out of treatment (3).

Halmi suggests that a cognitive behavioural approach within an in-patient unit is best. However, while there is good evidence for the value of cognitive behavioural therapy for bulimia nervosa, there is no evidence that it is of any value for patients with anorexia nervosa who are of low weight, i.e. the vast majority of patients admitted to hospital with an eating disorder.

Turning to medical management, I disagree with Halmi's suggestion that in-patients should be weighed daily. Such an excessive preoccupation with weight mirrors that of our patients and simply reinforces it (1). In any event, weight is not a valid indicator of physical well-being, for numerous reasons: a) weight varies by as much as 1.5 kg within any 24 hour period; b) the process of weighing is totally unreliable, given the fallibility of scales; c) weight can be easily falsified and many patients will do so to escape from a coercive treatment regimen; in contrast, some children and adolescents will avoid weight gain to ensure they are not discharged home to an abusive environment; d) what constitutes

a satisfactory BMI for one person may be too high or too low for others, given the enormous variation in healthy BMI across the population.

Weight/BMI should be but one measure of physical well-being and its unreliability acknowledged and allowed for. Weight might be measured on a regular basis, but it should never be the sole determinant of management decisions, and most certainly daily weighing should be avoided. If there is considerable anxiety about a patient's physical state, then vital signs and electrolyte status will provide far more valid and useful information.

Halmi makes no reference to the exciting advances in our understanding of the neuroscience of eating disorders and their clinical applicability (4-6). A primary neurobiological basis for eating disorders is almost certain, given the neurotransmitter disturbances (7,8), the consistent and persisting abnormalities in very specific domains of neuropsychological functioning (9-13), and the specific, localized and persisting abnormalities on neuroimaging (5,14,15). The clinical implications are profound, pointing to the need for treatments targeted at the underlying neurobiological substrate. The use of cognitive remediation therapy is producing some impressive results, even in those with very long-standing illness, with symptomatic improvement in both symptoms and cognitive deficits (11,16).

Finally, Halmi makes no mention of the importance of including high dependency and secure facilities for those whose eating disorders require far more intensive nursing than usual or whose behaviour is life threatening. The availability of step-down facilities, from secure/high dependency units, via specialized in-patient units and day care, to out-patient clinics and domiciliary care would make for a far more comprehensive service.

A truly comprehensive service would need to have a full range of specialists, including nurses and therapists trained in motivational enhancement therapy and cognitive remediation therapy. The service would need to be clearly subdivided into two sections, one for children and adolescents, with an emphasis on developmental and systemic issues, and the other for adults. The ethos of this comprehensive service needs to be grounded, not in compliance, coercion and monitoring, but in the therapeutic alliance.

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Psychiatrists, milieu and glue

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K. Halmi states unequivocally in her thorough appraisal that the psychiatrist should be "captain of the multidisciplinary team", and correctly so, as only the psychiatrist would be expected to be suitably equipped for this role. It is, however, becoming difficult to interest psychiatrists or even physicians in taking this on, whilst other health professionals are being attracted in increasing numbers by better health insurance rebates, evidence based treatments and even prescribing rights. Thus, Halmi's ideal might become progressively less achievable, unless the reasons why suitably qualified medical practitioners avoid eating disorders can be understood and addressed.

In every component of a comprehensive eating disorders treatment program, the need for regular multidisciplinary team meetings cannot be stressed too greatly. These represent a forum in which team cohesion can be facilitated, treatment goals formulated, progress gauged, ongoing iterative knowledge of each patient developed and roles for team members clarified with support and direction for the challenges presented. Patients and carers should also have a voice. When treatment outcomes are disappointing, which they not infrequently are, psychiatrists, team members and

the program might become a repository for the anger and disenchantment of patients, families and carers. Not only can this result in complaints, non-payment of accounts and disputes about services rendered, but it can become a source of great angst, demoralisation and a major disincentive for the perfectionistic clinician. This burden needs to be shared, but ultimately treaters, particularly the psychiatrist who leads the team, will benefit from their own supervision, support and often therapy.

Milieu is an important element of all components of the program. It serves a "holding" function, which is most easily defined in the inpatient situation but still operates in day programs and outpatient clinics. In the first two, it includes the nursing staff, their unconditional respect and their availability for identification and modelling (1). When patients are attending an outpatient clinic, contact with administrative staff and the physical surrounds serve to keep them in treatment whilst they begin to manage their lives outside. Milieu in full or partial hospital programs also includes meal support and supervision. In our own inpatient program, much to our surprise, this was rated most highly by patients, who told us that this, in particular, was what they could not get at home (2). One would hope that, as the patient moves through the components of the program, which should include work with his or her immediate support system, this would no longer be the case.

The "Maudsley method" of empowering parents of anorexic children and younger adolescents is a way of providing a more appropriate milieu for these patients – when it works. Not all parents are equal to the task, and it can be a major imposition for siblings. Nevertheless, ample research seems to support its efficacy, even if it would be expected to become less developmentally appropriate from the mid teens (3). The "New Maudsley method" (4) is based on the increasingly realistic premise that older patients might take considerably longer to recover, if indeed they do, and the cost to their families can be considerable. A skills-based manual uses animal metaphors to describe desirable and undesirable parent or carer behaviours, which can equally apply to health professionals working in a multidisciplinary treatment setting. Parents and carers must be helped not only to take care of themselves, but to collaborate with the patient's effort towards recovery.

It would seem that less ill eating disorder patients, i.e. those requiring less behavioural containment, can recover with a variety of therapeutic approaches and treatment settings. The contingent of older chronic anorexia nervosa patients, however, seems to be growing apace and presents an increasing challenge. Thus far, pharmacological and endocrinological treatments have had relatively little impact, contributing to the lack of increase in recovery rates in the last two decades (5). Furthermore, the outlook seems to be worse with the greater number of failed inpatient admissions, but longer admissions have been shown to reduce metabolic factors in self-perpetuation of weight loss (6). These are the patients who often present clinicians with dilemmas around involuntary treatment and for how long this is still worthwhile (7). Patients with anorexia nervosa rarely request palliative care, yet we are often in a position where we might feel that this is all we can offer and what we offer is far from ideal.

The "glue" that holds the salient components of treatment together is often the general practitioner or primary care physician, whose role in eating disorders includes establishing engagement, early recognition and intervention. The latter might begin with referral to a specialist dietitian and/or psychologist, but is likely to eventually include referral to a component of a multidisciplinary program, then monitoring and support after the inpatient phase. The primary care physician or general practitioner often has the unenviable task of persuading patients and their parents, partners or carers that they need to return to or persevere with one component of the program.

Communication with personnel from the multidisciplinary program is absolutely essential, and patients' general practitioners and primary care physicians must receive adequate information, support and education for working with a supremely challenging group of patients and their families.

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Services for eating disorders: how comprehensive is comprehensive?

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The theme of my commentary will be "how comprehensive is comprehensive?". I will add a number of points that are not mentioned by K. Halmi that I think are important to developing a comprehensive service, and highlight a number of areas that are mentioned. These include: a) the emergence of new concepts in the nomenclature of eating disorders; b) the need to separate children and younger adolescents from adults and

older adolescents in treatment facilities; c) the role of prior trauma and its link to psychiatric comorbidity; d) the importance of the Maudsley family based treatment approach for the treatment of children and adolescents, and e) the role of complementary treatments.

Approximately one-half of patients treated in eating disorder clinics do not meet full criteria for either anorexia nervosa, bulimia nervosa or binge eating disorder, and are best diagnosed with eating disorder not otherwise specified according to DSM-IV. There has been some work aimed at more specifically delineating this large subgroup. One myth that exists is that patients with eating disorder not otherwise specified are less severely ill than patients with full syndromes, but this is not necessarily true. Consider someone who vomits several times a day but does not binge eat, in contrast to someone who binges and purges twice a week. The term "purging disorder" has been coined to describe such individuals who purge but don't binge, and they have been found to be just as impaired and to have similar medical morbidity, psychiatric comorbidity and course of illness as patients with bulimia nervosa (1,2). Brewerton et al reported that the lifetime prevalence of any purging to lose weight was 12.6% in a large representative sample of women in the United States (3). This group had significantly higher lifetime histories of major depression, substance abuse, post-traumatic stress disorder (PTSD) and victimization experiences, as well as higher body mass index and number of comorbid psychiatric disorders.

One of the issues that Halmi does not address is how to manage the treatment of eating disorder patients of different ages. Most experts in the field recommend age-appropriate services and consider it optimal to separate children and younger adolescents from adults and older adolescents during treatment in inpatient, residential, partial hospital and day treatment facilities (4). It is important to protect children and adolescents from being exposed to older patients, who may inadvertently "teach" children new maladaptive behaviors, and who often have very serious "adult" issues to process, such as working through traumatic life experiences.

It is now well established that eating disorder patients with bulimic symptomatology have significantly higher rates of criminal victimization experiences and resulting PTSD or partial PTSD, which in turn mediates higher rates of comorbidity (5-7). Such patients can be quite challenging and are overrepresented in inpatient settings. This necessitates that comprehensive eating disorder services are well prepared to assess and treat severely traumatized individuals and all trauma-related disorders (5).

Halmi notes that "the most robust evidence-based trials for anorexia nervosa are those of family therapy with adolescents", and this very important finding deserves further elaboration. The first major study that reported the efficacy of family therapy for anorexia nervosa indicated its usefulness in weight recovered patients upon discharge from the Maudsley hospital (8). After one year of treatment, family therapy was found to be more effective than individual therapy in patients whose illness was not chronic and had begun prior to age 19 years. In addition, a more provisional finding was the greater value of individual supportive therapy in older, more chronic patients. These results were confirmed at 5-year follow-up (9). Since then other studies have successfully applied the Maudsley model of family based treatment in underweight children and adolescents with anorexia nervosa (10).

Some comprehensive programs have incorporated specific complementary and spiritually oriented treatments into their armamentarium, such as massage therapy, yoga, meditation and 12-step groups. In one study of patients with anorexia nervosa, massage therapy significantly reduced measures of body dissatisfaction as well as plasma cortisol levels (11). In bulimia nervosa, those who received massage reported less depression and anxiety and had significantly improved scores on several subscales of the Eating Disorders Inventory (12). Other complementary treatments, such as yoga, can be an effective method for increasing self-awareness, personal reflection and body satisfaction, as well as reducing anxiety (13,14). Principles of mindfulness meditation are an integral part of dialectical behavior therapy, an empirically validated treatment for bulimia nervosa, binge eating disorder and borderline personality disorder (15-17). Some models have incorporated 12-step programs, such as Overeaters Anonymous, which has been shown to be helpful in eating disorder patients (18). Mounting evidence suggests that spirituality is an important but underestimated factor in the long-term process of full recovery from an eating disorder (19-23), and comprehensive treatment programs would do well to honor these findings.

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The eating disorders milieu

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K. Halmi offers a comprehensive and stimulating review of the salient components of service for eating disorders. In addition to those components, and in line with acknowledging the impact of the intense counter-transference reactions evoked when treating eating disorders on treatment outcome, a supervision system is a most crucial part of such services.

In a sample of 225 Canadian psychiatry residents, for example, 28% reported that they had encountered negative attitudes of fellow students, nursing staff, physicians, or other health professionals towards patients with eating disorders (1). In a sample of 90 therapists, 31% indicated that they did not want to treat patients with eating disorders (2). These reactions arise from multiple sources, including the therapists' and patients' histories and personal attributes, and the activation of intrapsychic and interpersonal processes such as identification, rejection, competition, testing, projective identification, splitting, or parallel processes (3).

Working with clients with eating disorders produces all the effects frequently associated with treatment providers' burnout, including the loss of drive and motivation, and the appearance of mental, physical, and emotional exhaustion. Moreover, health care professionals reported changes in eating habits, body image, and appearance as well as heightened awareness of food and physical health when working with patients with eating disorders (4, 5).

All therapists struggle at times with emotional responses that can be either creative or destructive for themselves or their clients. Thus, a sensitive arena of supervision, where the therapists receive "good enough parenting" to heal their "wounds" and the supervisors possess a broad range of skills and personal qualities to venture into uncomfortable places with their supervisees, is crucial (6).

Moreover, a conspicuous role of the therapeutic milieu is to act as a holding environment in which staff members can be encouraged to use counter-transferential feelings as a channel for moving inward to uncover the underpinnings of their own feelings. The therapeutic milieu should become an environment that provides highly reinforcing opportunities for new patterns of thinking, feeling, and acting, as well as for the expression and examination of old patterns and motivations (4). Intervention within the milieu must interrupt the vicious cycle of malevolent transformation wherein the perceived need for tenderness in relation to the patient automatically evokes foresight of anxiety or pain on the therapist's side. Through the appropriate interpretation of attitudes and behaviors with their transferential and counter-transferential underpinnings, milieu staff can create an environment that keeps negative phenomena in check and offers healthier alternatives for the expression of intense, yet valid, feeling states (7).

K. Halmi states that "a psychiatrist should be the captain of this multidisciplinary team". When it comes to outpatient services, it may be argued that, although "eating disorders require treatment of a variety of conditions", the management of such cases is a field where those with the most appropriate management skills are the most adequate answer for the captain position.

The management of eating disorders service requires coping with accumulating demands and emotional overload faced by patients, families and staff members. Thus, the captain should have, apart from clinical skills, excellent interpersonal and relationship skills, an ability to negotiate and discuss management plans with responsible clinicians, the ability to liaise with community agencies and work with them in a co-operative manner, and to use supervision, peer reviews and debriefing procedures for both clinical matters and staff issues.

These skills are acquired mainly via intuition and experience rather than via a specific professional education. Nevertheless, the psychiatrist plays a crucial role in the provision of psychiatric assessment and pharmacotherapy, and serves as a consultant to the therapists as well as to patients.

The current status quo in eating disor-

ders services is that many are directed by professionals who are not psychiatrists. In Israel, three out of the five community-based centers for the management of eating disorders are directed by social workers or other health-care providers, and their services are well established and flourishing.

Cawley (8), discussing psychiatrist training in the 21st century, argued: "Who should lead and who should follow? Nobody can win this sort of context. Matters of responsibility and accountability are complicated, but can surely be resolved if the members of the team recognize its collective purpose and strength, and remain aware of how feeble their efforts become if they are not integrated."

It is beyond the scope of this commentary to discuss the issue of psychotherapy for eating disorders. Nevertheless, I believe that eating disorders patients, especially those with difficulties in self-regulation and verbal communication, may benefit more when projective tools are used. Frequently the ability of our patients to profit from verbal psychotherapy is limited, due to deficit in reflective function, the acting-out nature of symptoms and because the patients may be trapped in the concreteness of body symbolism (9).

Moreover, many patients use rationalization and some do a lot of talking – distracting from the real conflict. Art therapies, biofeedback therapy and other non-verbal therapies may be superior, mainly in the first steps of therapy, to deal with the distress and internalize self-regulation more than simple cognitive-behavioral therapy.

In conclusion, in order to avoid the "revolving-door" when treating eating disorders in an outpatient clinic, the melody may be more important than the words themselves. How clinicians react and how they approach the illness and the clients (patients and their families) is the most precious component of the program. The challenge is to keep a tight rein on the eating disorder and nurture the patient.

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Therapeutic approach to eating disorders: the biological background

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There is a great deal of uncertainty about response of eating disorders to treatment. This is in part due to the fact that not only their etiologic and pathogenetic bases, but also their classification, prevalence, course, comorbidities and prognosis are continually undergoing new appraisal and definition. Eating disorders are the expression of both psychological and physical pathologies, and each of these components has prevailed from time to time and from study to study, orienting toward different diagnoses and supporting different treatments.

Today, the psychological component is considered the core of eating disorders, while the physical component is regarded as just the consequence of the aberrant eating behaviours. However, this is to some extent questionable, since some physical impairments are involved in the development of certain psychopathological aspects, contributing to their maintenance, prognosis and response to treatments.

Genetic, biological, temperamental and family-social factors have been in turn considered as primary causes for the development of eating disorders, but they are probably effective only when they act all together as a concurrence of causes (1-4). This raises some intriguing questions about treatment of eating disorders: which etiopathogenetic factors must we confront in our treatments? Which should we address as first? Or should we confront all of them simultaneously? Unfortunately, at the moment we have no definitive answer to these questions.

K. Halmi describes what can be considered today the optimal approach to the treatment of eating disorders. Why are the results of this approach not predictable and not always satisfactory? One reason could be that we do not know exactly what brain biological impairments are present in patients with eating disorders during the symptomatic phases of their disease, after recovery or when the disorder becomes chronic. Central neurotransmitter alterations have been reported in small groups of patients, with decreased serotonin, noradrenaline and brain-derived neurotrophic factor and increased neuropeptide Y and endocannabinoid production in anorexia nervosa and, in some cases, bulimia nervosa patients (5-7). As for dopamine, data are discordant, revealing either hypo- or hypersecretion of the amine in anorexia nervosa, and hypo- or normosecretion in bulimia nervosa (8,9). However, all these changes reflect mean values of study groups. We do not know whether these alterations occur in every patient or are limited to some of them, being responsible for the prognosis of eating disorders or for some aspects of psychopathology which char-

acterize subgroups of patients. At the moment, we do not have enough data to settle this issue, but the possible biochemical variability from patient to patient or from time to time during the course of the disease may be one reason for the relatively inconsistent and unpredictable responses to treatments (10).

Moreover, some of the neurotransmitter alterations are still present long after the recovery of eating disorders, possibly being responsible for relapses and chronicity. Increased 5-HT2A receptors in anorexia and bulimia nervosa, and reduced 5-HT1A receptors as well as increased D2/D3 receptors binding in anorexia nervosa have been observed in specific brain areas one year after recovery, and it has been suggested that a central serotonin and/or dopamine hyperactivity could represent a biological trait of vulnerability to eating disorders, needing correction to prevent relapses and/or recurrences (11-13). At present, no specific psychopharmacological trial has been conducted to verify this hypothesis.

As Halmi outlines in a recent editorial (14), "it is unlikely that predictably effective treatment for anorexia nervosa (and, we believe, also for other eating disorders) will be available until we decipher the reinforcing neurobiological mechanisms sustaining the disorder".

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Mindfulness in the management of eating disorders

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K. Halmi provides an excellent summary of recent advances in the treatment of eating disorders. There are no doubts concerning the usefulness of structured units for people with anorexia nervosa and cognitive behavioral therapy (CBT) for bulimia nervosa.

Structured clinical units require a multi-disciplinary (multi-dimensional) team including nurses, dietitians and psychologists, as well as social and family therapists. However, these experienced staff can be recruited only in environments where the standing of our specialty is high. Even in university hospitals, it happens frequently that nursing staff are moved periodically to other departments, so that it may be difficult to retain well trained nurses. Further, most psychiatric units are general, and to set up a specialized unit or sub-unit may not be easy. On the other hand, an intensive outpatient program or residential treatment cannot be replaced by a structured unit: all of them should be part of a comprehensive service.

CBT for patients who show bingeing/purging behavior within a normal weight range has become the standard. However, there are many non-responders and premature drop-outs. Most chronic eating disorder patients have already experienced the failure of CBT throughout their long history of illness, and do not improve through short-term motivational interviewing. Transdiagnostic therapy and enhanced CBT have shown promise (1), but it remains to be documented that they are more effective than routine CBT in ordinary clinical conditions.

Eating disorders arise as a way of patients trying to escape from difficulties they may have. On facing these life-threatening disorders, we must be mindful (2,3), honest, and be aware of our limitations. Structured units and enhanced CBT aim to rapidly change behaviors or patterns of thought, but chronic patients are usually extremely inflexible, and change is slow. Psychological "Judo" in motivational interviewing focuses on the patients' "moment of inertia" to change rather than confronting their relentless pursuit of thinness.

In Asia, the relationship between mother and daughter is closer than in Western countries. Even though similar percentages of eating disorder patients are impulsive (4), most patients have family support. Family support is

a double-edged sword (risks of over-involvement and being manipulated), but there is the possibility that the family be truly of help.

Treating eating disorders is always challenging. However, using a heavy-handed approach will make the patients more rigid.

We, psychiatrists dealing with eating disorder patients, should not treat aggressively, but rather share our understanding of patients' painful experiences and hope of recovery. It is important to develop a small-scale system that just one psychiatrist is able to run, even though it may be difficult in several contexts.

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Management of eating disorders: optimal vs. minimum treatment

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As K. Halmi points out, anorexia nervosa is *the* mental disorder of young people with the highest mortality rate. While Harris and Barrowclough's mortality rates for anorexia nervosa, reported in 1997 (1), are still correct, the data they presented for bulimia nervosa and binge eating disorder were based on too few cases. According to more recent larger case series, the mortality rate (raw percentages) in treated cases of bulimia nervosa is 2.04%, and that in binge eating disorder is 2.94%, whereas the mortality rate of anorexia nervosa is 7.7% over 12 years (2-4). Factors contributing to these high mortality rates, especially in anorexia nervosa, are denial of illness, secrecy of symptoms, and resistance to treatment, which still represent a challenge to successfully design and implement comprehensive services for eating disorders.

K. Halmi correctly emphasizes that there is a poverty of evidence-based randomized controlled trials on the basis of which we can recommend the salient components of a comprehensive service for eating disorders. A stepped care approach has been advocated, which would mean that each patient gets the *minimum* treatment needed. From the point of view of a close relative or friend, however, one would instead advocate for *optimal* treatment conditions. In the advocacy of stepped care approaches, it has at times been forgotten that the more intense a treatment is at the start, the less likely the course of illness will be chronic. Follow-up studies conducted by child and adolescent psychiatrists who treated anorexic patients at a younger age show that early and intensively treated cases have a much better prognosis than cases treated by psychiatrists in adult eating disorders services (5). Psychiatrists in adult services frequently treat cases which have become chronic, having not received or having refused appropriate treatment in time.

In the various countries of the world, there are significant differences in medical and psychotherapeutic services for eating disorders. Some countries highly restrict inpatient services. In many countries a large proportion of the population has no (adequate) health insurance. Frequently the amount of money which insurance companies or governments spend on health services for eating disorders is insufficient, especially as compared with disorders for which advocacy is more active, such as diabetes, cancer and hypertension. In many countries, eating disorders are considered tangential to the field of psychiatry and are not in its mainstream.

Nevertheless, over the past decades, the number and quality of services for eating disorders have improved in industrialized countries, and the relevance and importance of these disorders and their treatment has been more and more accepted by lay people and professionals. Specialized comprehensive services for eating disordered patients have been built up, which usually offer treatments focusing on the eating disorder itself (maturity fears, body image distortions, anxiety related to eating and gain weight), nutritional counseling, social skills training. Frequently they also offer specialized treatments focusing on comorbid conditions such as borderline personality disorder (dialectic behavior therapy), depression, social anxiety and phobias. Networking with general practitioners and self-help groups is often well developed. The possible use of specialized computer programs is currently being evaluated as part of a comprehensive service for eating disorders.

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Continuum of depressive and manic mixed states in patients with bipolar disorder: quantitative measurement and clinical features

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Bipolar mixed states combine depressive and manic features, presenting diagnostic and treatment challenges and reflecting a severe form of the illness. DSM-IV criteria for a mixed state require combined depressive and manic syndromes, but a range of mixed states has been described clinically. A unified definition of mixed states would be valuable in understanding their diagnosis, mechanism and treatment implications. We investigated the manner in which depressive and manic features combine to produce a continuum of mixed states. In 88 subjects with bipolar disorder (DSM-IV), we evaluated symptoms and clinical characteristics, and compared depression-based, mania-based, and other published definitions of mixed states. We developed an index of the extent to which symptoms were mixed (Mixed State Index, MSI) and characterized its relationship to clinical state. Predominately manic and depressive mixed states using criteria from recent literature, as well as Kraepelinian mixed states, had similar symptoms and MSI scores. Anxiety correlated significantly with depression scores in manic subjects and with mania scores in depressed subjects. Discriminant function analysis associated mixed states with symptoms of hyperactivity and negative cognitions, but not subjective depressive or elevated mood. High MSI scores were associated with severe course of illness. For depressive or manic episodes, characteristics of mixed states emerged with two symptoms of the opposite polarity. This was a cross-sectional study. Mixed states appear to be a continuum. An index of the degree to which depressive and manic symptoms combine appears useful in identifying and characterizing mixed states. We propose a depressive or manic episode with three or more symptoms of the opposite polarity as a parsimonious definition of a mixed state.

Key words: Bipolar disorder, depression, mania, mixed states

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Depressive and manic features can combine during the same episode of bipolar disorder. Patients who are susceptible to mixed states may differ in clinical, illness-course, and treatment response characteristics from those who are not susceptible (1-4). The definition of mixed states and its relationship to depressive and manic syndromes has been elusive. Kraepelin posited six mixed states based on combinations of depressive or manic affect, thought and behavior, resulting in mixed states that could be construed as predominately depressive or manic (5). Subsequent formulations focused on mixed mania, consisting of depressive symptoms during manic episodes (3,6). DSM-IV, for example, requires combined syndromal depression and mania for a mixed state and considers these states to be a form of mania (7).

The mixed mania formulation is problematic. First, clinical reality appears less restrictive than this definition. For example, only two depressive symptoms, not a full mixed state, can alter treatment response during mania (8). Second, there is increasing evidence that depressive mixed states, where manic symptoms occur during a predominately depressive episode, are clinically important and may be at least as prevalent as mixed mania (9). As with predominately manic states, depressive episodes require only two or three manic symptoms to have significant differences in course of illness and clinical characteristics (10,11). In addition to the combination of depressive and manic symptoms, anxiety appears to be a prominent aspect of mixed states (12). Mixed states that are predominately depressive or predominately manic may share clinical characteristics that are relevant to course of illness and response to treatment (13).

We have reported that, during bipolar depressive episodes, increases in severity of the course of illness, impulsivity, and complications like head trauma, substance abuse and attempted suicide emerged with modest levels of manic symptoms (11). If even mild manic symptoms were present, depressive episodes differed substantially from those without manic symptoms in the course of illness and clinical history. Characteristics of patients with mixed manias or mixed depressions suggest that mixed states are symptomatically continuous with depressive and manic states, but have characteristics related to a more severe course of illness. Susceptibility to mixed states may accordingly be a trait characteristic of a subset of patients with severe bipolar disorder (4,14-16). For example, patients with mixed episodes early in the course of illness had a higher prevalence of severe suicide attempts compared to other patients with bipolar disorder (17,18).

Here, we report the manner in which combinations of depressive and manic symptoms produce a continuum of mixed states. The main hypotheses of the study were that: a) clinical correlates of mixed states would be related to severity of manic symptoms in depressed subjects and depressed symptoms in manic subjects; b) the extent to which episodes were mixed could be measured quantitatively and independently of specific depressive or manic symptoms; and c) specific depressive or manic symptoms, related to activation, would be associated with mixed states.

METHODS

Subjects

Subjects were outpatients meeting DSM-IV criteria for bipolar I or II disorder (7). Before they participated in the study, it was thoroughly discussed with them and written informed consent was obtained. The study was reviewed and approved by the Committee for the Protection of Human Subjects, the Institutional Review Board of the University of Texas Houston Health Science Center. Subjects were recruited to cover a range of symptoms and represented euthymic (n=19, mean age 36.0±12.3 years), DSM-IV manic (n=23, age 32.2±9.7 years), DSM-IV depressive (n=28, age 38.2±9.5 years), and mixed states (defined as meeting symptomatic DSM-IV criteria for both depressive and manic states) (n=18, age 36.6±6.0 years). Age did not differ across subject groups ($F(3,84) = 1.4$, $p=0.25$).

Subjects were receiving one or more treatments, including lithium (n=7), anticonvulsants (n=44; predominately valproate and/or lamotrigine), atypical antipsychotics (n=15), or antidepressants (n=31). Seventeen subjects were receiving no psychopharmacological treatments, 30 were receiving one drug class, 26 were receiving two classes, and 5 were receiving three or more classes. Number of drugs was not related to episode type (X^2 (9 df) = 5.3, $p=0.8$). Subjects were studied when specific treatments had not changed, and doses not changed by over 20%, over the previous seven days. Participation in the study had no influence on treatment decisions.

Diagnostic, behavior, and symptom measures

Diagnoses were rendered using the Structured Clinical Interview for DSM-IV (SCID) (19) and confirmed in diagnostic consensus meetings. Symptoms of depression, mania, anxiety, and psychosis were measured using the Change Version of the Schedule for Affective Disorders and Schizophrenia (SADS-C), which was designed to measure these symptom domains concomitantly (20). As discussed in previous work, scores were reduced by one unit so that symptoms were scored as zero if absent, rather than one (8). Personnel were trained, using standard video training materials, in the SCID and SADS-C. DSM-IV mixed states were defined as subjects meeting full symptomatic criteria for manic and major depressive episodes. Symptoms were scored as present if they had a score of at least 2 on the modified SADS-C (mild but definitely present; equivalent to 3 on the original instrument).

For the purposes of identifying subjects in putative depressive or manic mixed states, we excluded SADS-C rating scale items that might, in a circular way, be related to the nominal opposite polarity. Depression item scores used included subjective depression, worry, self-reproach/guilt, negative evaluation of self, hopelessness, suicidal ideation or behavior, anhedonia, fatigue, and psychomotor retardation. Items possibly related to mania, including sleep disturbance, agitation, subjective or objective anger, or irritability, were excluded. Mania item scores included elevated mood, decreased need for sleep, increased energy, manifest anger, goal-directed activity, grandiosity, visible hyperactivity, accelerated speech, racing thoughts, and poor judgment. Anxiety and psychosis factor scores were not used in identifying subjects in mixed states but were compared in mixed vs. non-mixed subjects.

Subjects were defined as euthymic if they did not meet DSM-IV criteria for current depressive or manic episodes and had not had a depressive, hypomanic, or manic episode for at least three months. "Depressed" or "manic" subjects were those who met criteria for a depressive or manic episode, regardless of associated symptoms of the other polarity; subjects whose opposite polarity symptoms were less than relevant threshold criteria are referred to as "non-mixed". A predominately depressed mixed state, DM3, was defined as meeting criteria for a depressive episode and having three or more manic symptoms, corresponding to Benazzi's MX3 (9). A predominately manic state was defined, based on our data on treatment response, as a manic episode with at least three depressive symptoms, which will be referred to here as MD3 (8). Because of the lack of definitive data on duration of specific SADS-C symptoms, one cannot be certain which of these subjects met DSM-IV criteria for a mixed state.

Data analysis

Distributions were checked for normality; if they departed from normal, appropriate non-parametric methods were used. Statistical analyses used standard regression and analysis of variance procedures, or their non-parametric analogs, as described in the text. For correlations of variables whose distributions were not normal, Kendall tau was used, because it was shown to balance power and control of type 1 error more effectively than Pearson or Spearman correlation coefficients (21). Significance of differences between standard correlation coefficients was determined using the Fisher r-z transformation (22).

The extent to which an episode was mixed was estimated using the product of z-transformed depression and mania scores. This is referred to as the Mixed State Index (MSI). The MSI is high if both depression and mania scores are high, but low if either is low (even if the other is high). Z-transformation was used to reduce bias from any difference in numerical values between depression and mania scores (depression scores ranged from 0 to 36, mean 15.3±9.4; mania scores ranged from 0 to 37, mean 10.8±8.6). The absolute value of the minimum z-transformed depression or mania score for all subjects was added to the z-transformed score for each subject so all scores would be non-negative numbers.

Table 1 Symptom severity in predominately depressive or manic mixed states

SADS-C score	Manic (n)		Depressive (n)	
	Non-mixed (n=17)	MD3 (n=24)	Non-mixed (n=27)	DM3 (n=19)
Mania	18.8 ± 7.0	17.4 ± 6.9	4.1 ± 2.5	17.5 ± 7.7*
Depression	8.1 ± 4.7	20.8 ± 7.4**	23.9 ± 5.1	23.7 ± 7.3
Anxiety	7.4 ± 4.0	11.2 ± 3.8***	9.7 ± 3.9	12.0 ± 3.8****
Psychosis	2.2 ± 2.2	3.3 ± 2.5	2.7 ± 1.9	3.6 ± 2.5

SADS-C – Schedule for Affective Disorders and Schizophrenia: Change Version; MD3 – mania with at least three depressive symptoms; DM3 – depression with at least three manic symptoms
Significance of difference by Student's t test: *t(df=44) = 8.4, $p<10^{-6}$; **t(df=39)=6.2, $p<10^{-6}$; ***t(df=39)=3.0, p=0.005; ****t(df=44)=2.0, p=0.058

RESULTS

Mixed mania and mixed depression

DSM-IV defines a mixed state as meeting full criteria for a manic and a major depressive episode, for at least one week. Descriptions of mixed states in the literature, however, include predominant depression with subsyndromal mania (9) and predominant mania with subsyndromal depression (8). Table 1 compares psychiatric symptoms in subjects experiencing a depressive episode with three or more manic symptoms (DM3) (9) and subjects experiencing manic episodes with at least three depressive symptoms (MD3) (8). Anxiety scores correlated positively with mania scores in depressed subjects (r=0.427, n=46, p=0.003) and with depression scores in manic subjects r=0.671, n=41, p=0.001). Mixed states defined as predominately depressive or manic were essentially identical in symptom severity.

Subjects with DM3 or MD3, considered separately, did not differ from corresponding non-mixed depressed or manic subjects with respect to gender (Fisher exact test = 0.52 and 0.23, respectively). However, subjects with either DM3 or MD3 had a greater proportion of women than depressed or manic subjects not in a mixed state (women: 7 non-mixed and 15 mixed; men: 26 non-mixed and 17 mixed; Fisher exact test = 0.028). This confirms earlier reports that patients in broadly defined mixed states are more likely to be women (3,23).

There have been many alternative definitions of mixed states. We investigated two Kraepelinian mixed states (5) that can be considered as varieties of mixed depression (24): depression with flight of ideas (subjects having depressive episodes who also had definite flight of ideas/racing thoughts on SADS-C) and excited depression (depressive episode with hyperactivity on SADS-C). These subjects were essentially identical, in severity of depression, mania, anxiety, and psychosis to the DM3 or MD3 subjects in Table 3. Next, we investigated subjects with at least three depressive symptoms and at least three independent mania symptoms, without the requirement for meeting a full depressive or hypomanic/manic episode. These subjects (n=32) also did not differ in clinical characteristics from those described in Table 2 (data available on request).

Table 2 Mixed State Index (MSI) score and clinical state

	Group (n)	MSI (mean ± SD)
Euthymic (n=19)		0.58 ± 0.53
Depressed	Non-mixed (n=27)	1.53 ± 0.88
	DM3 (n=19)	6.84 ± 4.36
Manic	Non-mixed (n=17)	2.27 ± 1.57
	MD3 (n=24)	6.15 ± 4.10
Mixed (DSM-IV) (n=17)		6.83 ± 4.55

MD3 – mania with at least three depressive symptoms; DM3 – depression with at least three manic symptoms

A Mixed State Index: clinical correlates

The extent to which an episode is mixed can potentially be expressed as the extent to which both depression and mania are present. As defined in Methods, we used the product of z-transformed depression and mania scores as an index of how strongly mixed an episode was (Mixed State Index or MSI). Table 2 compares MSI in subjects experiencing euthymic, depressed, manic, and depression- or mania-based mixed states. MSI was similarly elevated in predominately depressive or manic mixed states. Across all subjects, MSI correlated positively with anxiety (Kendall tau = 0.27, p=0.001) and psychosis (Kendall tau = 0.24, p=0.004).

Figure 1 shows relationships between MSI scores and complications of bipolar disorder. Indices of severe illness, like early onset and suicide attempt, were associated with high MSI scores. Subjects with histories of a substance or alcohol use disorder, however, did not differ from those who had not met criteria for a substance-related disorder.

Depressive and manic symptoms associated with mixed states

In order to determine which specific depressive or manic symptoms were more likely to be associated with being in a mixed state, we conducted a discriminant function analysis using the depression and mania items in the SADS, and a broad classification of mixed states combining MD3 and DM3. After an initial analysis using all SADS depressive and

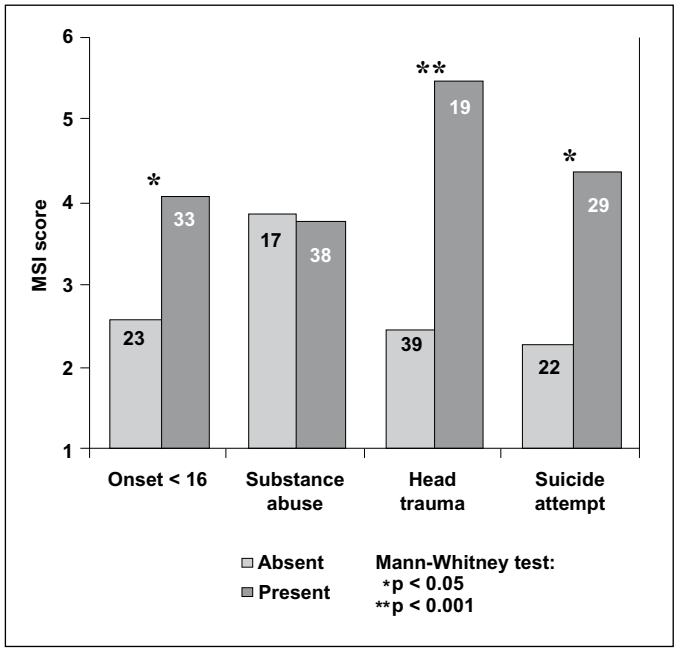

Figure 1 Mixed State Index score and clinical characteristics

manic symptoms, we repeated the analysis using only those symptoms with F>1 to remove from the model. Symptoms in the final group were worry, negative evaluation of self, suicidal ideation or behavior, anhedonia, psychomotor retardation, decreased need for sleep, increased energy, grandiosity, visible hyperactivity, accelerated speech, and racing thoughts. The resultant analysis had Wilks' lambda of 0.38 and overall $F(11,57) = 8.56$ ($p<10^{-4}$). The model classified 90% of cases correctly (86.5% of non-mixed and 93.7% of mixed). Depressive symptoms contributing to the model were worry ($F(1,57)$ to remove = 7.4, p=0.009) and negative evaluation of self (F = 3.74, p=0.05). Manic symptoms were increased energy (F = 5.6, p=0.02), visible hyperactivity (F = 21.9, $p<10^{-4}$), and racing thoughts (F = 5.9, p=0.018).

Thresholds for emergence of "mixed" features

Table 3 summarizes the numbers of depressive or manic symptoms at which differences between mixed and non-mixed episodes become statistically significant. Manic or depressive episodes with two or three symptoms from the opposite polarity differed significantly from those with fewer or no mixed symptoms in terms of symptoms (anxiety and MSI score) and course of illness (history of early onset or suicide attempt).

DISCUSSION

In these subjects with bipolar disorder, a range of predominately depressive or manic mixed state definitions appeared clinically similar, consistent with Kraepelin's suggestion that a greater underlying severity or affective instability drives the emergence of combined symptoms (5). Both depression and mania scores correlated with severity of anxiety in subjects with episodes of the opposite polarity. This underscores previous reports that anxiety is an important component of mixed states (25) and is associated with severe affective symptoms (26). The results suggest that there is a continuum of mixed states.

Dimensional nature of mixed states

The extent to which depressive and manic symptoms combine may be more salient than whether an episode meets DSM-IV criteria for a mixed state, or even whether the combination is predominately depressive or manic. Susceptibility to this combination may be a dimensional characteristic that is associated with greater severity, in terms of duration or treatment resistance of episodes and course of illness. In manic episodes, characteristics like lithium resistance and unstable course of illness emerge at relatively low severity of concomitant depressive symptoms, not requiring full syndromal depression (8). Similar characteristics emerge at relatively low severity of manic symptoms during depressive episodes (11). Even in subjects who have never had free-standing episodes meeting DSM-IV criteria for mania or hypomania, the presence of two or three manic symptoms during a depressive episode confers clinical characteristics resembling bipolar disorder with mixed states rather than unipolar disorder (27). Therefore, we combined depressive and

Table 3 Thresholds for clinical differences between mixed and non-mixed episodes

Number of mixed symptoms	Manic episode				Depressive episode			
	Anxiety	MSI	Suicide attempt	Early onset	Anxiety	MSI	Suicide attempt	Early onset
≥ 1	0.09	0.1	0.35	0.63	**0.003**	**0.001**	0.17	0.49
≥ 2	**0.007**	**0.0007**	0.09	0.18			0.07	0.2
≥ 3			**0.04**	**0.05**			**0.05**	**0.05**

MSI – Mixed State Index

The Table shows probability of t-tests (Anxiety or MSI scores) or Fisher exact test values (history of suicide attempt, onset of illness before age 16) as a function of the number of depressive symptoms in manic episodes or the number of manic symptoms in depressive episodes. Mixed symptoms are the number of depressive symptoms in manic subjects or the number of manic symptoms in depressed subjects

manic symptom scores to form a mixed state index (MSI), using a straightforward combination that would emphasize an interaction between depressive and manic symptoms.

Characteristics of mixed states: specific and nonspecific

Kraepelin described six mixed states, consisting of combinations of depressed or manic affect, thought, and action (5). More recent formulations have focused on mixed mania, corresponding to Kraepelin's depressive or anxious mania (25,28), or mixed depression, corresponding to at least two of Kraepelin's mixed states (24). Multivariate analyses have yielded varying numbers of predominately manic (28,29) or predominately depressive (28,30) mixed states. These states represent permutations of depressive and manic symptoms, whose apparent boundaries depend on the variables and assumptions used in the analyses (31,32).

Mixed mania and mixed depression both have poor response to treatment (33-35), increased risk for suicidal behavior (18,36-38), unstable or severe course of illness (29), and relationship to head trauma or other neurological problems (39,40). Further, mixed states appear not to occur randomly, but tend to recur true to type in susceptible individuals (15,16,41). These properties suggest that susceptibility to mixed states may be related to one or more of: a) pre-existing characteristics (1), possibly genetic (2), that influence course of illness and treatment response; b) consequences of having experienced many episodes (42,43); or c) effects of complications of bipolar disorder like substance abuse or head trauma (39).

Any explanation of susceptibility to mixed states must account for the fact that their symptomatic characteristics vary widely, yet the many symptomatic permutations of mixed states share the clinical and illness-course characteristics described above (13). Clinical characteristics of mixed episodes may result from the interaction between this susceptibility and the unknown factors that determine whether a given episode will be depressive or manic. A parsimonious model could require two characteristics, one related to course of illness, and one to characteristics of individual episodes. The course of bipolar disorder varies widely, but can be described as consisting of two basic types, an "episodic-stable" course and an inherently unstable course that may confer susceptibility to mixed states (1,2,34). In terms of individual episodes, some patients appear to have mostly manic, and others mostly depressive, episodes (44). Mixed states could be predominately depressed or manic, depending on individual characteristics, but would be similar in their relationships to course of illness and to treatment responsiveness.

Subjects who had at least three symptoms of both depression and mania, regardless of whether they met DSM-IV criteria for depressive or manic episodes, resembled subjects in predominately manic or depressed mixed states with respect to severity of psychosis or anxiety. Therefore, one could argue that at least three independent symptoms of depression and of mania define a mixed episode, without the requirement of DSM-IV criteria for depression or mania, and that these episodes are clinically similar or identical to conventionally defined mixed episodes, and may require the same vigorous treatment. This possibility should be investigated further in a larger group of subjects who do not meet full criteria for depressive or manic episodes. Mixed episodes with subsyndromal depressive and manic symptoms may contribute to the poor outcome associated with emergence of subsyndromal symptoms (45).

The data in Figure 1 and Table 3 confirm reports that mixed states are associated with severe course of illness, and suggest that this relationship persists regardless of dominant polarity of the mixed state. The absence of any relationship between mixed features and history of substance-related disorder shown in Figure 1, however, is not consistent with this. However, in interpreting this finding, it is important that the rate of substance use disorder was so high throughout the entire study population (about 70%) that this characteristic may not have been useful in delineating subtypes of illness.

Depressive or manic symptoms and mixed states

Mixed states can be defined equally well using criteria based on symptom rating scale scores or numbers of symptoms present (30). It is of clinical interest, however, to know which depressive or manic symptoms are most likely to be associated with a mixed state. Our data showed that the symptoms distinguishing mixed from non-mixed affective episodes were not primarily mood symptoms but were related to activity (increased energy, visible hyperactivity, racing thoughts) in the case of manic symptoms, and negative cognitions (worry and negative evaluation of self) in the case of depressive symptoms. Which specific symptoms distinguish mixed and non-mixed episodes will depend on the content of the diagnostic or rating measures used. Our data suggest that mixed states are characterized by the combination of negative cognition and hyperactivity, a potentially dangerous combination (36,46).

Specificity of depressive and manic symptom ratings

As noted by Suppes et al (23) in their study of mixed hypomania and reviewed earlier by McElroy et al (3), rating scale items for depressive and manic states may overlap. The SADS-C is designed to minimize this overlap, as it is intended for the simultaneous measurement of depression, mania, anxiety, and psychosis, in contrast to the use of separate individual scales for these entities (20). Items are scored with instructions designed to take clinical context into account. For example, sleep disturbance (which did not figure in the current results) is scored as part of the depression factor unless it is characterized by decreased need for sleep. Agitation is only scored as a depression item if depressive mood or

anhedonia is also present. Nevertheless, we excluded items related to agitation, irritability and anger from depression scores in the identification of predominately manic mixed episodes. The fact that overlap was minimized is confirmed by the lack of correlation between depression and mania scores across all subjects ($r=-0.085$, $n=88$, $p > 0.4$).

Limitations

This was a cross-sectional study, focusing on presence of symptoms at a given time rather than their duration or order of occurrence. The number of subjects limited ability to investigate possible contributing factors reliably. Treatment was not standardized.

CONCLUSIONS

Combined depression and mania, regardless of which predominates, is associated with increased psychosis and anxiety during the current episode, compared with episodes of depression or mania alone. A continuum of mixed states and a metric of susceptibility to these states may describe their characteristics better than a more syndrome-driven categorical model. It will be important to determine the neurobiological mechanisms and clinical course of illness underlying susceptibility to mixed states.

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Factors predicting drop-out in community mental health centres

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This study aimed to identify treatment, therapist and patient factors associated with dropping out of treatment in four outpatient mental health services. The experimental group comprised all 789 individuals who attended for the first time the mental health services during one year and dropped out of treatment in the same year or during the two following ones. The control group consisted of the same number of individuals, chosen at random from patients who, in the same year, attended for the first time the services and did not subsequently drop out of treatment. The overall drop-out rate was 33.2%. According to logistic regression analysis, the predictive factors of dropping out were: being treated in a particular centre, the involvement of more than one therapist in treatment, having no previous history of psychiatric disorders, being young and being male.

Key words: Drop-out, community mental health care, use of psychiatric services

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Estimated drop-out rates in outpatient psychiatric services vary considerably, ranging from 20 to 60% (1-9). This variation can be attributed to discrepancies in the way dropping out is defined (10), differences in sample composition, the setting in which the phenomenon is analysed and the study design. The drop-out rate is highest at initial appointments (11); therefore studies that include the first stages of treatment find higher drop-outs rates (12).

Younger patients are more likely to drop out of any kind of treatment (3,5,13-15). Living alone (3,6,16,17), being divorced, unmarried or widowed (3,17), a low socioeconomic status (2,3,5), being unemployed or having a job that is low on the social scale (18), and having a low level of education (14) are also associated with a higher drop-out rate.

The nature of the outpatient clinical setting and a lower level of patient satisfaction have also been identified as predictive factors for dropping out (16,19,20).

Concerning the factors related to patient's illness, a positive association has been found between dropping out and a higher degree of severity of the symptoms (1,12). There are some data supporting the notion that a diagnosis of schizophrenia increases the likelihood of dropping out (3,21,22), as well as data contradicting this notion (6,8,16). Low rates of adherence to treatment have been reported among patients with personality disorders and post-traumatic stress disorder (3), and higher levels of adherence to outpatient therapy among those with depressive disorders (3,23).

A previous history of psychiatric treatment has been associated with a lower drop-out rate (6,12). Adherence to outpatient treatment seems to improve when both pharmacological treatment and psychotherapy are prescribed, as opposed to the prescription of just one form of treatment (5,24). There are no specific studies on the influence of therapists' characteristics on drop-out rate in outpatient services.

The aim of this study was to analyse the factors associated with dropping out of contact with outpatient services. In particular, we explored the influence of patients' socio-demographic features, clinical diagnosis, type of treatment received and characteristics of therapists.

METHODS

The study was carried out in the public outpatient psychiatric services of one of Madrid health care areas, corresponding to two health care districts, namely Centro and Latina. Together, they have a population of 350,000 inhabitants with quite comparable socio-demographic characteristics. The studied catchment area has four mental health centres which are integrated in a network of services. All the professionals work with the same model of care, range of services and functional hierarchy. Each centre is staffed by psychiatrists, clinical psychologists, nurses, social workers and auxiliary personnel. For the purpose of this study, the four centres were identified as A, B, C and D. The patients selected for the study were attended to by a total of 22 psychiatrists and clinical psychologists.

The Register of Mental Health Cases of the Community of Madrid is the information system of Madrid outpatient services. It is a cumulative register containing a record of all the care-related dealings with patients of all mental health centres since 1987, including information on socio-demographic characteristics, ICD-9 diagnoses, the type of treatment received and the professional responsible for it. The register also contains data related to admissions to and discharges from hospitals. The register contains all the diagnoses received by each patient over the course of an episode of illness.

We carried out a non-matched retrospective case-control study based on administrative records, covering one year in the above-mentioned four mental health services. The experimental group included all the individuals over the age of 18 who, during the index year, were seen for the first time in

one of the four mental health centres and, after attending two initial appointments, agreed on a psychiatric treatment from which they dropped out in the same year or in the two following years. Specific exclusion criteria were: attending just one appointment; non-attending a pre-arranged appointment, in spite of a later contact with the mental health care centre, and age under 18.

For the purposes of this study, dropping out was defined as the unilateral interruption of treatment by the patient, without a further contact with the service in the following six months. Having been discharged on medical grounds, having died or having moved to a different health area were not considered as drop-outs.

The control group consisted of patients chosen at random from all those who, in the same period of time, were seen for the first time in the above-mentioned centres and who, after attending two initial appointments, were prescribed psychiatric treatment and duly complied to it. Due compliance was defined as continuous contact with the centre according to the agreements with the therapist.

The socio-demographic variables considered in the study were: age, sex, marital status, living arrangements (alone, with partner or children, with biological family, with other relatives, in sheltered accommodation), level of education (no education, primary studies, secondary studies, university studies), occupation, occupational status (active, unemployed, pensioner, student, domestic tasks). The level of education variable includes four categories referring to the highest level achieved as part of studies that can be accredited in accordance with Spanish legislation.

The type of care and treatment variables considered in the study were: the mental health care centre attended, the treatment received (pharmacological treatment, individual psychotherapy, group psychotherapy, combined pharmacological and psychotherapeutic treatment, other types), number of sessions attended during current episode (less than 5, from 5 to 9, more than 9), practitioner responsible for treatment (each practitioner was identified by a number from 1 to 22), number of practitioners responsible for the case during the period covered by the study (one practitioner, more than one practitioner).

The clinical variables considered in the study were: primary diagnosis (according to the ICD-9), number of diagnoses recorded, previous psychiatric treatment (outpatient treatment, hospital treatment, both). To simplify the analysis of the data, eight categories were considered for the primary diagnosis: organic psychotic disorders (290-294), neurotic disorders (300), alcohol and drug abuse and/or dependence (303-305), adjustment disorders (308, 309), schizophrenia and paranoid states (295, 297, 298.3, 298.4), affective disorders (296, 298.0, 311), personality and behaviour disorders (301, 312), and eating disorders (307.1, 307.5).

The therapist variables considered in the study were profession (psychiatrist or psychologist), sex, age, years of experience in the centre, type of contract (permanent staff, stand-in staff or temporary staff), years of professional experience in public health care system.

The data concerning the patients, the treatment they received and the type of care involved were obtained from the Register of Mental Health Cases of the Community of Madrid. To guarantee the reliability of the data obtained, the details of 75% of the sample were checked against the corresponding original medical records. There were no significant discrepancies between the two sources of information. The data concerning practitioners were obtained by an ad-hoc questionnaire. All the practitioners responsible for the subjects included in the sample compiled the questionnaire.

In the statistical analysis, dropping out of treatment was the dependent variable, and the above mentioned socio-demographic, type of care and treatment, clinical and therapist features were the independent variables. With all the study's variables being taken as qualitative, both descriptive statistics and cross tabs were produced. The cross tabs were used to obtain the Fisher exact statistic, the window value and the 95% confidence interval. Additionally, a logistic regression model was adjusted in steps in order to evaluate the association of the variables for which a bivariate analysis gave a $p<0.05$. The IT package used to carry out the entire statistical analysis was the version 11.0 of SPSS (Statistical Package for Social Sciences) for Windows.

RESULTS

The results of the comparative bivariate analysis of the socio-demographic characteristics of the patients who dropped out of treatment and those who did not are shown in Table 1. There were significant differences in terms of age, level of education, marital status, living arrangements, occupation and occupational status. The proportion of patients who dropped out was higher among the 18-32 age group and lower among the over 60 age group. Patients with university studies and those without studies had the lowest tendency to drop out of treatment. The drop-out rate was significantly higher among people who were unmarried, and in those who lived alone or with their biological family. Patients with lower skilled jobs were more likely to drop out of treatment. Additionally, there were higher drop-out rates among patients who were unemployed or students than among those who were in active employment, carried out domestic tasks or had retired.

The results of the comparative bivariate analysis between the two groups based on the clinical and care-related variables are shown in Table 2. Patients with eating disorders and those with a primary diagnosis of abuse of alcohol or other drugs had the highest drop-out rates, followed by those with personality disorders. The drop-out rate was substantially lower among subjects who had previously received psychiatric treatment as outpatients or in hospital. The drop-out rate was lower among patients who received pharmacological treatment in comparison to those whose only treatment was group or individual psychotherapy. Significant

Table 1 Socio-demographic characteristics of drop-outs and controls

Variables (%)	Drop-outs (n=789)	Controls (n=789)	p
Age			
18-32 years	57.7	42.3	
33-43 years	50.5	49.5	.009
44-60 years	49.4	50.1	
Over 60 years	45.6	54.4	
Gender			
Male	51.9	48.1	.256
Educational level			
No studies	37.1	62.9	
Elementary studies	51.6	48.4	.030
Secondary studies	53.2	46.8	
University studies	46.8	53.2	
Marital status			
Married	46.2	53.8	.015
Single, divorced, separated, widowed	52.6	47.4	
Living arrangements			
Alone	54.3	45.7	
With partner and/or children	45.4	54.6	
With father, mother or both	56.0	44.0	.002
With relatives other than the parents	57.3	42.7	
In an institution	30.0	70.0	
Occupation			
Professional, technical personnel, executive and manager	41.6	58.4	
Staff of administrative services	41.9	58.1	
Commercial and sales	58.3	41.7	.027
Tourism, security, construction and transportation	55.0	45.0	
Armed forces and not well-specified occupations	52.1	47.9	
Occupational status			
Employed	52.0	48.0	
Unemployed	57.4	42.6	
Retired or on pension	43.8	56.2	.046
Student	55.0	45.0	
Housewife	41.4	58.6	

Table 2 Clinical and mental health care variables in drop-outs and controls

Variables (%)	Drop-outs (n=789)	Controls (n=789)	p
Diagnoses			
Organic psychoses	40.0	60.0	
Neurosis	49.0	51.0	
Alcohol and drug abuse and/or dependence	61.7	38.3	
Adjustment disorder	43.7	56.3	.023
Schizophrenia and other psychoses	50.0	50.0	
Affective psychoses	50.7	49.3	
Personality disorders	55.3	44.7	
Eating disorders	66.7	33.3	
Previous psychiatric treatment			
Outpatient or hospital treatment	44.5	55.5	.000
No treatment	56.0	43.9	
Type of treatment			
Pharmacological treatment only	44.7	55.3	
Individual psychotherapy only	54.5	45.4	
Group psychotherapy only	63.5	36.5	.003
Pharmacological treatment + individual psychotherapy	50.4	49.6	
Other modalities	59.6	40.4	
Sessions			
Less than 4	44.7	55.3	
4 to 9	57.7	42.3	.000
More than 9	49.0	51.0	
Mental health centres			
Centre A	46.9	53.1	
Centre B	53.9	46.1	.008
Centre C	57.9	42.1	
Centre D	46.1	53.9	
Number of practitioners involved			
Only one therapist	46.5	53.5	
More than one therapist	59.4	40.6	.000

Table 3 Characteristics of the therapist in drop-outs and controls

Variables (%)	Drop-outs (n=789)	Controls (n=789)	p
Profession			
Psychologist	46.6	53.4	.160
Psychiatrist	51.2	48.8	
Gender			
Male	51.1	48.9	.344
Age			
46 year old or less	46.0	54.0	.008
More than 46 year old	54.9	45.1	
Years in the current job			
Less than 10 years	52.3	47.7	.552
10 years or more	50.4	49.6	
Type of contract			
Permanent staff	47.9	52.1	.001
Stand-in or temporary staff	58.3	41.7	
Years of experience			
Less than 16 year	50.4	49.6	.561
16 years or more	52.2	47.8	

differences were found with regard to the mental health care centres where patients were treated. The drop-out rate was lower among those from centres A and D.

The comparative bivariate analysis of the variables related to therapists is shown in Table 3. The drop-out rate was significantly higher among patients attended to by more than one practitioner over the course of their therapy. Patients treated by practitioners employed on a stand-in or temporary basis had a greater tendency to drop out than those treated by permanent staff. No difference was noted between patients treated by a psychiatrist and those treated by a clinical psychologist. The drop-out rate corresponding to individual therapists ranged from 0% to 66.7%, thus involving significant differences and a high level of variability.

The overall drop-out rate for the geographical area studied was 33.2%. It ranged from 28.9% in centre A to 51.4% in centre C.

The logistic regression model shown in Table 4 includes the possible predictive factors for patients dropping out of treatment at the centres studied. The model originally included all the variables for which there were significant differences in the comparison between the experimental and the control

Table 4 Logistic regression: factors predicting drop-out

Variables	p	OR	95% CI
Age (18-32 years vs. other age groups)	.013	1.446	(1.080 - 1.938)
Gender (male vs. female)	.016	1.429	(1.068 - 1.911)
Living arrangements (alone vs. other situations)	.009	1.818	(1.163 - 2.843)
Previous treatment (yes vs. no)	.002	1.504	(1.156 - 1.957)
Centre of care (C vs. other centres)	.030	1.710	(1.053 - 2.776)
Number of practitioners involved (one vs. more than one)	.000	2.045	(1.569 - 2.666)

group. In the end, the variables retained in the logistic regression equation were age (the 18-32 age group compared to the over-32 age group), sex (female compared to male), living arrangements (living alone compared to any other living arrangements), previous history of psychiatric care (no vs. yes), the centre providing care (centre C compared to any of the other three) and the number of practitioners involved in the process (involvement of more than one psychiatrist or psychologist in addition to the main practitioner responsible for treatment). The regression equation established on the basis of the variables in question has a predictive value concerning dropping out of treatment of 69.1%.

DISCUSSION

The outpatient care drop-out rate for patients receiving treatment for the first time during a year was 33.2% over the three-year period and ranged between 28.9 and 51.4% in the four mental health centres. This figure is within the average of previous studies, where the rates varied between 16 and 60% (1,5,7,8,13,25-27). However, it is difficult to compare the global drop-out figures, due to differences in study methodologies and in the health care systems. Our drop-out rate is lower than that found in α study by Percudani et al (7), carried out in Italy, in an area with a health care system similar to ours: the difference might be partly explained by the fact that we excluded patients who only attended the first appointment. On the other extreme, our figure is higher than that of Edlund et al (5), who used a much more conservative drop-out criterion and also included patients treated in different treatment settings. Two other studies similar to ours have been undertaken in Spain. They both included first visits and had higher drop-out rates: 42% (28) and 67% (29).

We found an interesting difference in the drop-out figures between the mental health centres. Patients treated in centre C had a 1.7 times higher risk of dropping out than the other three centres in the area. This fact, added to the difference observed in patient drop-out depending on the therapist responsible for their treatment (between 0 and 67%) leads us to conclude that the influence of a particular practitioner, as well as the centre's working methods, may be important factors. In the four centres, the organization of care was similar and there were no social differences between the relevant populations.

Our bivariate analysis showed that therapists under 46 years old and with stable employment in the service were associated with a lower drop-out rate, whereas there were no differences between patients treated by a psychiatrist or a psychologist, or by those with more or less professional experience. The logistic analysis found no specific professional characteristics which could be considered as factors predicting drop-out. In Hong Kong, Pang et al (27) reported that patients treated by permanent practitioners have a lower drop-out rate than those treated by temporary staff members.

We found that the fact of being attended to by more than one practitioner during the observation period, whether simultaneously or sequentially, was a factor increasing the drop-out rate. We were not able to find any previous studies focusing on the influence of therapist discontinuity on the drop-out phenomenon.

Male gender, being young and living alone were found to be risk factors for drop-out, in line with the majority of previous studies (3,5,8,13-15,28).

In our study, the clinical diagnosis does not appear as a drop-out risk factor in the logistic analysis. However, four European studies (6-8,16) reported that patients with a diagnosis of schizophrenia and other psychoses were more likely to continue their treatment than patients with neurotic and personality disorders. A diagnosis of schizophrenia was found to greatly increase the chance of continuing treatment in the study by Rossi et al (8). However, a study carried out in the US (15) reported that schizophrenia patients had higher drop-out rates than those with other illnesses. These differences may be explained by the differing models of psychiatric care in the various study locations.

The type of treatment received did not appear to be a predicting factor in the logistic regression analysis, while, in the bivariate analysis, patients receiving pharmacological treatment, alone or in combination with individual psychotherapy, had a lower tendency to drop out than those who only received group or individual psychotherapy. This finding is consistent with some previous studies (28,30).

Patients without a previous history of psychiatric treatment had a greater tendency to drop out than those who had been previously treated, whether as outpatients or admitted hospital patients. We lack sufficient data to be able to interpret this fact, although it is in line with other studies (6,12,31).

As our study was based on a register of cases, it was not possible to determine whether the subjects had genuinely dropped out of psychiatric treatment or had continued their therapy in the private sector or through primary healthcare services. The conclusions therefore only apply to non-compliance to the service and not to psychiatric treatment in general.

The sample included patients who attended at least two appointments, therefore excluding those who dropped out after just one appointment. Despite the limitation it entails, this selection criterion was established to guarantee that only patients prescribed treatment in the centres were included in

the sample, thus ruling out one-off consultations and cases immediately referred to primary healthcare services.

Finally, our findings cannot be generalized to settings with different models of care or types of services.

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Somatic and cognitive domains of depression in an underserved region of Ecuador: some cultural considerations

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Not enough research efforts on depression have been carried out up to now in Latin America. The knowledge that has resulted from research activities in the United States or Europe offers limited generalizability to other regions of the world, including Latin America. In the Andean highlands of Ecuador, we found very high rates of moderate and severe depressive symptoms, a finding that must be interpreted within its cultural context. Somatic manifestations of depression predominated over cognitive manifestations, and higher education level was protective against depression. These findings call for an appreciation of culturally-specific manifestations of depression and the social factors that influence them. These factors must be further studied in order to give them the deserved priority, allocate resources appropriately, and formulate innovative psychosocial interventions.

Key words: Depression, Latin America, cultural factors, somatization

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Although depression has been studied in numerous countries around the world (1-3), the majority of research efforts in this area have been conducted in the Western world, particularly in the United States (4,5). According to the 2007 World Health Organization Report, the contribution of psychiatric and neurological conditions to the burden of illness in Latin America more than doubled between 1990 and 2002, from an estimated 8.8% of disability-adjusted life years (DALYs) in 1990 to 22.2% in 2002 (6).

Despite its Iberian cultural influence, you clearly see in Latin America the presence of a new "identity". In this context, many psychiatric disorders tend to be expressed differently than is usually perceived in the Western world. For instance, in Latin America it is frequently observed that depression is manifested somatically through symptoms such as headaches, gastrointestinal disturbances, or complaints of "nervios" (meaning "nerves" in Spanish), rather than psychological symptoms such as sadness or guilt (7). Along those lines, clinical data suggests that women suffering from depression have a higher prevalence of somatic manifestations than men (8-10).

We carried out a study in an underserved region of the Andean highlands of Ecuador, aiming to better understand the somatic and cognitive domains of self-reported depressive symptoms, and to identify gender differences in these symptoms.

The Spanish version of the Beck Depression Inventory II (BDI-II, 11), a 21-item self-reported scale of depressive symptoms which has been validated in numerous Latin American countries, was administered to 167 patients (71 males and 96 females) in 7 small parishes along the southern Andes of the Zamora-Chinchipe province of Ecuador. A group of psychologists from the United States, Central and South America, and the Caribbean conducted multiple rounds of translation and back translation in order to reduce cultural bias (12). Institutional review board approval was obtained from the New York University School of Medicine to conduct this study.

Subjects were recruited from mobile medical clinics run by volunteer physicians and nurses. Literate individuals completed the self-report questionnaire on their own, while illiterate individuals had the questions read to them by a native Spanish speaker staff who worked at the clinic.

Nine subjects did not answer more than 20% of the BDI-II questions and, therefore, were excluded from the final analysis. The remaining subjects' ages ranged from 15 to 76 years, with an overall group mean of 33.8 ± 13.1 years.

Twenty-five percent of subjects had none or minimal depression (BDI-II <14) and 15% of subjects had mild depression (BDI-II 14-19). The remaining 60% of subjects had BDI-II scores that qualified them to have either moderate depression (28%) or severe depression (32%). Crying (55%) and past failure (41%) were reported by the greatest number of depressed respondents. Women self-reported higher levels of sleep disturbance ($t=2.77$, $df=146$, $p=0.006$) and fatigue ($t=2.09$, $df=154$, $p=0.038$) than men. Females exhibited more depressive symptoms and somatic symptoms than males, but the difference was not significant ($t=1.67$, $df=156$, $p=0.098$ and $t=1.98$, $df=154$, $p=0.058$, respectively). The mean item score on the somatic items was significantly higher than the mean item score on the cognitive items (1.25 ± 0.63 versus 0.78 ± 0.56, $t=12.42$, $df=148$, $p=0.001$).

On a logistic regression analysis, education level proved to be the only significant predictor of BDI-II depression. Additionally, a higher education level was associated with decreased symptom severity.

The Ecuadorian perspective of depression and mental illness must be taken into account to ensure a culturally-appropriate interpretation of our results. The Saraguro Indians of Ecuador identify a culturally-relevant psychiatric illness they term "nervios", which produces symptoms very similar to those seen in depression in the Western world (13). "Nervios" is a powerful idiom of distress used by Hispanics/Latinos from a variety of Caribbean, Central and South American countries to express concerns about physical distress, emotional states, and life changes (14). "Nervios" is not necessarily pathological but is seen as a natural consequence of the human condition.

The Saraguro Indians recognize that "nervios" exists on a spectrum. The symptoms of the illness have the potential to be so severe as to be pathological or even fatal in some individuals (15). Such cases may be characterized by an extreme lack of concern for personal hygiene, by significant disturbances of appetite or sleep, or by severe anhedonia. Those cases that involve suicidal thinking or non-epileptic seizure activity are recognized to be the most serious manifestations of "nervios" and are, therefore, considered to be pathological.

The high prevalence of self-reported depressive symptoms in our study may be partly attributable to the Saraguro's acceptance of "nervios" as a normal, non-pathological response to everyday stressors, thereby legitimatizing the experience and rendering it free of the stigma associated with mental illness (16,17). There is no incentive to medicalize the symptoms of "nervios" in this part of the world, where mental health services are virtually non-existent, antidepressants are available only at a hospital hundreds of miles away and occasionally at mobile medical clinics, and the primary mental health provider is a priest responsible for the care of several hundreds of people in the nearby provinces.

The differing gender manifestations found in our study may be reflective of different coping styles between males and females, with men often resorting to alcohol use as a means of warding off the more overt symptoms of "nervios" seen in women. In the Western world, where a cognitive and/or affective presentation of depression is the norm, beliefs about the tendency to somatize typically apply to historically disadvantaged groups, such as women and ethnic/racial minorities. Since cultural norms are socially constructed, we wonder if rather than asking why Latinos somatize, we can instead ask why Westerners "psychologize", or express distress in cognitive or affective terms (18).

Education is commonly seen as a proxy for socioeconomic status and has been shown to positively influence employment, work, earnings, and income (19). However, occupational grade, another common proxy for socioeconomic status, was not protective against depressive symptoms in our study. Education and occupation may be related in a different manner in the Ecuadorian population than in the population of industrialized nations. One explanation for these findings is that, unlike one's occupation, which produces external benefits like monetary profits and tangible achievements, the benefits of education (personal empowerment) are only internal (20). Moreover, in close-knit rural communal societies, high socioeconomic status comes at a price. In the Ecuadorian highlands, for instance, individuals in more prestigious and profitable professions are susceptible to greater effects of "nervios", due to the responsibilities placed on them by their community-oriented family and society (21). Those with certain occupations may even have an added incentive to purposefully exhibit symptoms of "nervios" as a means of having their responsibilities absolved temporarily.

In our study, no significant relationship was identified between age and depressive symptoms. The Saraguro Indians believe that everyone, regardless of age and gender, is susceptible to experiencing "nervios". Exceptions to the rule are children who are intentionally shielded from stressors of adult life, such as social expectations and work responsibilities, and are thus presumed not to experience "nervios". In the Ecuadorian community, increased age is associated with perceived greater wisdom and life experience; subsequently, elders in this community are treated with the greatest respect and esteem by all community members. As such, the emotional losses that the Ecuadorian elderly experience with increased age appear to be compensated by the commensurate increase of social self-worth, secondary to having a higher status within the community.

Although our study adds to the cross-cultural understanding of depressive symptoms, prospective studies are needed to elucidate causal relationships between these symptoms and psychosocial factors, as well as to enhance cross-cultural understanding of depression. Additional research efforts are needed to cross-culturally validate existing measures, as well as to validate the nature of the disorders themselves. In resource-poor settings with minimal mental health care access, an appreciation of culturally-specific manifestations of depression and the social factors that influence them is also needed, in order to improve advocacy efforts, ensure better detection of depression in the public at large, formulate innovative psychosocial interventions, and secure the allocation of resources commensurate with mental health needs.

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International guide to prescribing psychotropic medication for the management of problem behaviours in adults with intellectual disabilities

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Psychotropic medications are used regularly to manage problem behaviours among people with intellectual disabilities. This causes concern because often these medications are used out of their licensed indications in this context. The WPA Section on Psychiatry of Intellectual Disability has recently developed an evidence and consensus-based international guide for practitioners for the use of psychotropic medications for problem behaviours among adults with intellectual disabilities. This guide advises on assessment of behaviours, producing a formulation, initiation of treatment, assessment of outcome and adverse effects, follow-up arrangements, and possibility of discontinuation of treatment.

Key words: Intellectual disabilities, problem behaviours, psychotropic medications, international guide

(World Psychiatry 2009;8:181-186)

Intellectual disability (ID) or mental retardation or learning disability is a lifelong condition included in the group of mental disorders in all the international classification systems. It is a syndrome grouping (meta-syndrome) including a heterogeneous range of clinical conditions characterized by a deficit in cognitive functioning prior to the acquisition of skills through learning (1). Over 30% of people with ID have a comorbid psychiatric disorder, which often has its onset in childhood and persists through adolescence and adulthood (2,3).

In spite of this evidence, ID and related conditions are still considered a marginal area of psychiatry. In many countries there is little or no training provision on ID during undergraduate medical training or psychiatric specialization. The World Health Organization (WHO) has recently highlighted the unmet care needs of persons with ID (4). Psychiatrists are the first health professionals in contact with this population group and there is a global gap in training and guidelines on mental health issues related to ID.

Within the ID field, the assessment, differential diagnosis and treatment of problem behaviours (PBs) deserve special attention. The rate of PBs in people with ID is high (5) and their presentation is determined by many complex factors. The pathogenic contribution of organic conditions, psychiatric disorders, environmental influences, or a combination of these has to be carefully established for every single case.

The prevalence of PBs in people with ID seems to be sufficiently high (5,6) to constitute a major concern in this population. Depending on the definition and methodology, rates have been reported to vary from 5.7 to 17% (7-10). Using the Diagnostic Criteria for Psychiatric Disorders for Use with Adults with Learning Disabilities (DC-LD) (11), Cooper et al (12,13) recently found the point prevalence of aggression and self-injurious behaviour to be 9.8% and 4.9%, respectively, among adults (16 years and over) with ID in a community setting.

It has been reported that 20-45% of people with ID are receiving psychotropic medication and 14-30% are receiving psychotropic medication to manage PBs such as aggression or self-injurious behaviours (14,15) in the absence of a diagnosed psychiatric disorder. Examples of psychotropic medications used for adults with ID are antipsychotics, antidepressants, anti-anxiety drugs (benzodiazepines, buspirone, beta-blockers), mood stabilizers (lithium, anticonvulsants), psychostimulants, and opioid antagonists. Spreat et al (16) reported that as many as two thirds of psychotropic medications prescribed to people with ID are antipsychotics.

Studies suggest that PBs are not only prevalent but also persistent in people with ID (17-19). Totsika et al (20) found that serious physical attacks, self-injury and stereotypy were the most likely types of PBs to persist over time. It is therefore suggested that it may be necessary to start interventions as early as possible to prevent the behaviours from becoming more serious and to reduce the number of emergent behaviours. It has been pointed out that many of the behaviours that emerge are a direct consequence of limitations in people's ability to communicate effectively (21-25). Replacing "learned behaviour" at an early age with more acceptable forms of communication may therefore not only reduce the number of emerging behaviours, but also reduce the severity of the behaviours that do occur.

The rate of prescription of psychotropic medications for the management of PBs is a source of concern, due to the scarce evidence concerning their effectiveness and adverse events and their impact on quality of life in people with ID

(14,26-29). Many adults with ID receive multiple psychotropic medications and in high dose.

THE INTERNATIONAL GUIDE

Framework and development

The international guide is an adaptation from the recently developed guide on the subject (30) in the UK. The UK guide followed the NICE guideline development procedure. This includes a systematic review of evidence and a broad consensus based on the available evidence on good practice. A very extensive stakeholder consultation was carried out before finalizing the recommendations.

The international guide reflects the available knowledge and the perspectives of experts practicing in psychiatry of ID in different parts of the world. A PB is defined here as a "socially unacceptable behaviour that causes distress, harm or disadvantage to the persons themselves or to other people, and usually requires some intervention" (30). The guide neither supports nor refutes the use of psychotropic medications in this context, but provides clinicians and carers of adults with ID worldwide with good practice advice despite the lack of adequate good quality evidence on this subject. The main recommendations contained in the guide are summarized in the following sections.

Assessment and formulation

The primary aim of management of PBs in people with ID should be not to treat the behaviour per se but to identify and address the underlying cause of the behaviour. However, it is not always possible to find a cause for the PB. When a cause cannot be found, the management strategy should be to minimise the impact of the behaviour on the person, the environment around her/him and other people.

There may be many reasons for PBs, including physical or mental health problems. Many factors, internal (e.g., negative childhood experiences, maladaptive coping strategies) or external to the person (e.g., an under-stimulating or over-stimulating environment), may contribute to PBs. Sometimes behaviour may be used as a means of communication. For example, persons with severe ID who cannot speak or use a sign language may scream because they are in pain and they cannot communicate this message in any other way. Sometimes persons with ID may use behaviour to communicate their likes and dislikes.

Therefore, a thorough assessment of the causes of behaviour and their consequences, along with a formulation, is an absolute prerequisite in managing any PB. A comprehensive assessment may require input from several disciplines and from families and carers. It should cover personal, psychological, social, environmental, medical and psychiatric issues. A multi-axial/multilayered diagnostic formulation, such as that suggested in the DC-LD (11) and the Diagnostic Manual – Intellectual Disability (DM-ID) (31), may be useful in this context. A formulation should be made even in the absence of a medical or psychiatric diagnosis.

As a general rule, the formulation should consist of the following:

- A list of the target PB(s) to be managed.
- A clear description of the PB, including frequency and severity.
- An assessment of causes giving rise to the PB.
- A record of reactions to and outcomes of the behaviour.
- An evaluation of predisposing, precipitating and perpetuating risk factors.
- Consideration of all management options and their outcome.
- The rationale for the proposed management option.
- A risk assessment for all the involved parties.
- Possible benefits and adverse effects from the proposed intervention(s).
- The likely effect of the proposed intervention(s) on the person's and her/his family's quality of life.

A proper assessment and formulation will often depend on input from the person with ID and/or her/his family and carers. This input should continue at every stage of management. It is important to share information with the person with ID in a way that he/she can understand. This may require additional time and effort on the part of the health professionals and other members of the multidisciplinary team. It may also involve using other methods of information sharing, such as pictures.

Multidisciplinary input may also be needed during implementation and monitoring of the management options. This may not always be possible to achieve, because of lack of resources or expertise in this field. Where relevant and if possible, an attempt should be made to secure multidisciplinary input throughout the process of assessment and management.

When to consider medication

If there is an obvious physical or psychiatric cause for the behaviour, this should be managed appropriately. The relevant guides governing the use of medication in the treatment of the particular psychiatric disorder should be followed (32,33).

If no treatable physical or psychiatric disorder can be recognized, then non-medication based management such as behavioural strategies should be considered first. Sometimes, after considering non-medication based management options, medication may be needed either on its own or as an adjunct to non-medication based management. However, it may also be possible to improve the PB of the person by providing counselling or addressing some adverse social and environmental factors, for example by finding more enjoyable

activities to do during the day, and using medication simultaneously to make the person concerned less anxious. This may be seen as an interim strategy, which then needs to be monitored carefully at regular intervals to assess its effectiveness.

The exact situation under which medication and/or non-medication based management strategies should be implemented will depend on individual circumstances. Below are some of the situations under which the clinicians may consider using medication:

- Failure of non-medication based interventions.
- Risk/evidence of harm/distress to self.
- Risk/evidence of harm/distress to others or property.
- High frequency/severity of PB.
- To treat an underlying psychiatric disorder or anxiety.
- To calm the person to enable implementation of non-medication based interventions.
- Risk of breakdown to the person's placement.
- Good previous response to medication.
- Person/carer choice.

The lack of adequate or available non-medication based interventions should not be the only reason for using medication, although in practice this may happen. Under such circumstances, the medication should be used for as short a period as possible.

The management of PB should always be person-centred. The plan should be discussed with the person with ID and/or her/his carers and should be designed according to the person's best interests. The prescribing should not take place in isolation but should always be part of a much broader person-centred care plan.

Monitoring the effectiveness of medication

The effectiveness and possible adverse effects of the prescribed medication should be monitored at regular intervals. This should include collecting objective information from family members, carers, staff of the multi-disciplinary team as well as the person with ID, where necessary and possible. Physical examination and relevant investigations such as blood tests and ECG/EKG should also be performed when necessary.

The medication should be prescribed at the lowest possible dose and for the minimum duration. Non-medication based management strategies and the withdrawal of medication should always be considered at regular intervals. If the improvement of the PB is unsatisfactory, an attempt should be made to revisit and re-evaluate the formulation and the management plan.

Communication issues

The management plan should be communicated clearly to the person with ID and/or her/his family and carers and all other relevant professionals involved on a need-to-know basis. This process should be updated at regular intervals. Accessible format may be needed when communicating with adults with ID. The prescribing should be carried out according to the country's legal framework and clearly documented in medical records.

In Figure 1 we present a flow chart summarising the main activities involved in the process of prescribing and monitoring of its effect.

General principles for prescribing psychotropic medications

Anyone prescribing medication to manage PBs in adults with ID should keep the following good practice points in mind:

- Medication should be used only in the best interests of the person.
- All non-medication management options should be considered, and medication should be seen as necessary under the circumstances, or alongside non-medication management.
- If possible, evidence to show that the medication is cost-effective should be taken into account.
- Information about which medications worked before and which did not should be noted.
- If medication used previously produced unacceptable adverse effects, the details should be noted.
- The effect of availability or non-availability of certain services and therapies on the treatment plan should be taken into account.
- Relevant local and national protocols and guidelines should be followed.

Once the decision to prescribe is taken, the following points should be followed:

- Ensure that the appropriate physical examinations and laboratory investigations are carried out at regular intervals.
- Explain to the person and/or her/his family or carers if the medication is being used outside its licensed indications. In this case, they should be told about the evidence that is available to demonstrate its effectiveness.
- Identify a key person who will ensure that medication is administered appropriately and communicate all changes to the relevant parties.
- If possible, provide the person and/or her/his family or carers with a copy of the agreed recommended treatment plan at the time of prescribing.
- As far as possible, there should be an objective way to assess outcomes, including adverse effects (where possible the use of standardized scales or the monitoring of the

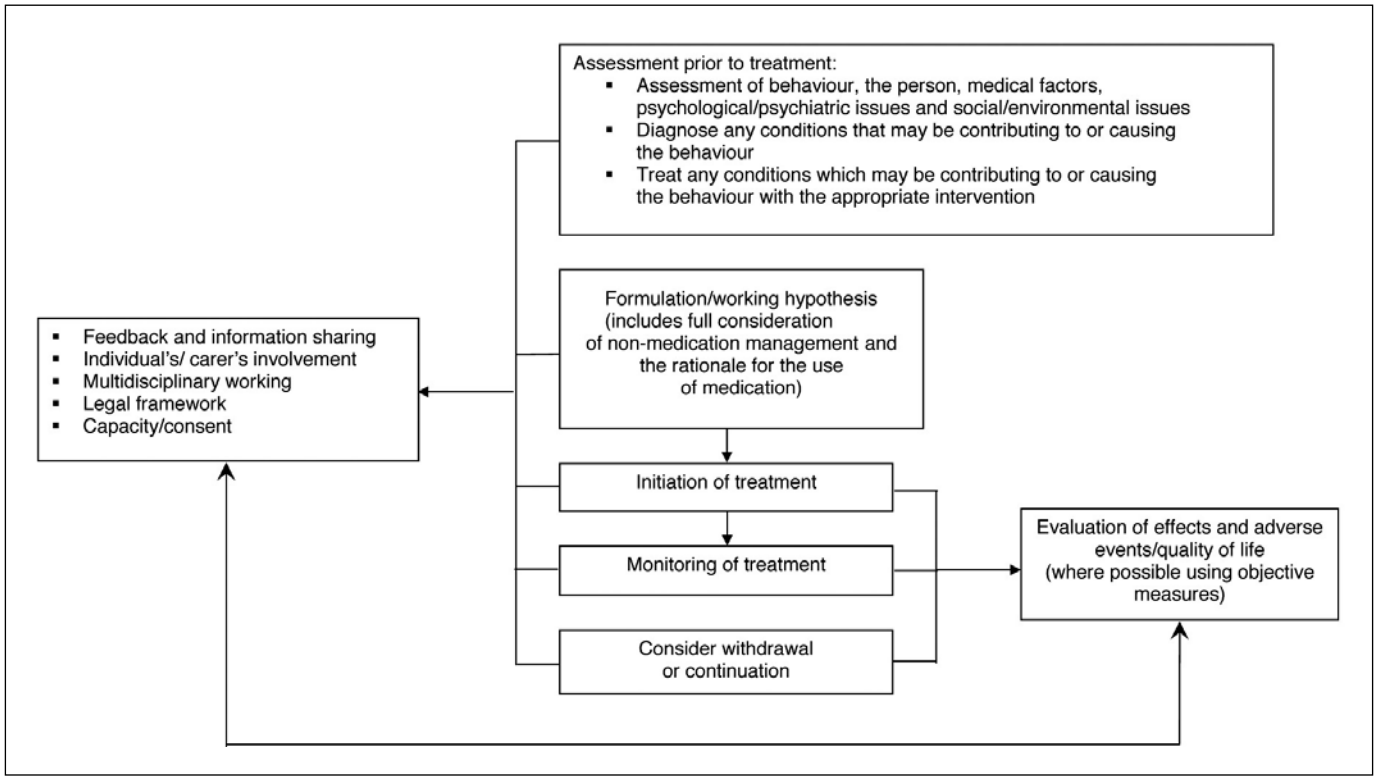

Figure 1 Key processes associated with using medication to manage problem behaviours in adults with intellectual disability

severity and frequency of the target behaviour is recommended) (34).
- Ensure there will be follow-up assessments for continued monitoring.
- As far as possible, one medication for the PB should be prescribed at a time.
- As a general rule, the medication should be used within the standard recommended dose range.
- A dose of medication above the maximum recommended should only be used in exceptional circumstances after full discussion with all the relevant stakeholders under appropriate safeguards and regular reviews.
- Start with a low dose and titrate the dose up slowly.
- Medication should be used at the lowest required dose for the minimum period of time necessary.
- Consideration for withdrawing medication and exploring non-medication management options should be ongoing.

Currently, it is not possible to recommend the type of medication for the treatment of specific PBs because there is no evidence to support such specificity (35).

Risks associated with prescribing medication in adults with ID and PB

Most medications carry a potential risk associated with adverse events. However, evidence is largely gathered from studies among patients who do not have ID. For example, current evidence shows that several newer antipsychotic medications may produce weight gain and some metabolic abnormalities related to glucose tolerance, lipid metabolism and prolactin secretion (36).

There is no good-quality evidence to either support or refute concerns that people with ID may be at greater risk of the adverse effects of medication than people from the general population who do not have ID. The shortage of good-quality evidence does not mean that medication is associated with an unacceptable risk specifically for adults with ID.

In view of the above, the following general points should be kept in mind:

- Discuss with the person and/or her/his family or carers about both common and serious adverse events related to the medication (where possible provide accessible information in writing).
- Advise what action should be taken if a serious adverse event occurs.
- All adverse events should be recorded properly.
- Once a medication is prescribed, the risk-benefit profile should be evaluated regularly, with particular emphasis on the person's and her/his family or carers' quality of life.

Withdrawing medication that has been prescribed for a long period

Studies of withdrawing medication show that, in some people with ID, the medication can be successfully withdrawn after a long period of use (37,38). In another group, the dose can be reduced, but total withdrawal is not possible. Lastly, there remain certain cases where medications cannot be reduced even after a very long period of use. Many factors affect the success of withdrawal of medication, including social and environmental factors such as the training and the attitude of care staff. However, on the basis of such evidence, it is not possible to recommend which medication to withdraw and the rate of withdrawal, but the following general recommendations are proposed:

- Try to stabilise the person's PB on a minimum number of medications prescribed at the lowest possible dose.
- Withdraw one medication at a time.
- Withdraw medication slowly.
- If necessary, allow time (sometimes a few weeks) after withdrawing one medication and before starting to withdraw another.

FUTURE DIRECTIONS

There are plans to publish this guide in other languages as it has been done with previous guides produced by the WPA Section on Psychiatry of Intellectual Disabilities. Spanish and Italian translations will be available this year. The Section also plans to develop training materials on assessment of PBs among adults with ID, and to enhance links with other international organizations on this topic.

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Mental patients in prisons

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Mental conditions usually affect cognitive, emotional and volitional aspects and functions of the personality, which are also functions of interest in law, as they are essential at the time of adjudicating guilt, labeling the accused a criminal, and proffering a sentence. A relationship between mental illness and criminality has, thus, been described and given as one of the reasons for the large number of mental patients in prisons. Whether this relationship is one of causality or one that flows through many other variables is a matter of debate, but there is no debating that prisons have become a de facto part, and an important one, of mental health systems in many countries. This paper deals with the issue of the relationship and provides estimates of prevalence of mental patients in prisons culled from many studies in different countries. It also provides some direction for the management of mental patients as they crowd correctional systems.

Key words: Mental illness, prisons, epidemiology, mental health systems

(World Psychiatry 2009;8:187-189)

The association between some mental conditions and an increased risk for criminal behaviour has been repeatedly reported. In a series of 100 murderers, 29% had a diagnosis of "psychosis" (21% of schizophrenia and 8% of affective disorders) and 35% had a diagnosis of substance abuse (1). Among alcoholics, the prevalence of violent behaviour is much higher than among non-alcoholics (2). Psychopathy is strongly associated with a high risk for criminal and violent behaviour (3). Factors that seem to mediate the interaction between mental illness and crime include gender (4), age (5), socio-economic status (6), previous criminality (7), and previous forensic psychiatric involvement (8). In a 30-year follow-up of a birth cohort in Sweden, men who had a mental disorder were 2.5 times more likely to have been registered for a criminal offense and 4 times more likely to have been registered for a violent offense, compared to men not mentally ill or intellectually handicapped (9).

The level of convergence, however, varies according to the mental condition. Firstly, there are mental disorders whose very behavioural manifestations are *ipso facto* criminal offenses, such as in the case of paraphilias, pyromania, kleptomania and others. In these cases, the relationship between mental disorder and criminality is one-to-one.

Secondly, disorders such as psychopathic personality, antisocial personality, borderline personality, pathological gambling, and impulse control disorders connote a criminological element, but the degree of convergence is not one-to-one, in that symptoms could be expressed without necessarily breaking the law. For example, alcoholism carries a high risk of law breaking in the form of victimization at the time of intoxication, and drug dependencies are known to lead to income-generating crimes in order to finance the habit, but only if the addicted person does not have the financial means to support it.

Finally, the level of convergence is less straightforward among some other mental conditions. For example, persons suffering from schizophrenia may get involved in serious unexplainable violent crime (10), and persons suffering from major depression may display violent behaviour against self or others (11,12). However, the relationship between these conditions and criminal offenses is not a one-to-one, as many mentally ill persons suffering from schizophrenia or major depression never commit a criminal offense, in spite of the high prevalence of these mental disorders in the general population.

Looked at from a different angle, it may be that the association between criminality and mental illness flows not from a causal relationship, but is only the result of inadequate health systems. Lack of adequate number of hospital beds and inexistent community alternatives would be expected to create pressures in the alternate systems of correction (13) and community crime of the mentally ill may be reactive and defensive within the context of exposure to victimization (14).

Finally, while the relative risk is elevated for some mental conditions, it should be remembered that, for public health purposes, the measure to be concerned about is the attributable risk. Despite a high relative risk, violence due to mental illness is not that frequent once all other causes of violence in society are taken into account. This risk has been estimated at about 3% and, when substance abuse and alcoholism are included, at about 10% (15). Other estimates place the risk at 4.3% (16) or as low as 1% (17).

Furthermore, when a mental condition is suspected in relation to a crime, the unstated assumption is that the condition *preceded* the crime, and hence, may have actually *caused* the crime. In reality, it could have been that the mental condition that was present much earlier in life was not a factor in the present crime, or the mental condition developed after the crime had been committed.

PREVALENCE OF MENTAL ILLNESS IN CORRECTIONS

Correctional psychiatry in the strictest sense refers to psychiatric practice in the corrections system (18). More

amply, correctional psychiatry is the branch of forensic psychiatry that studies the incidence, prevalence, determinants and management of mental disorders in prisons, the response of correctional systems to the mentally ill offender, and the relationship between criminality and mental illness (19).

Reluctantly, prisons have accepted the mentally ill ever since their invention over 200 years ago. Despite multiple government commissions and voluminous parliamentary reports in many countries, and the introduction of several alternatives to care, the problem persists and appears to be getting worse. In many cities, the large number of mental patients in the local jails has made the jail a practical extension of the general mental health services. The trans-institutionalization of mentally ill persons from hospital to prisons has been documented in a plethora of studies that have also estimated their numbers at different points of the justice-correctional system (20).

In jails, also known as remand centres in some countries, research reports on the prevalence of mental illness date back many years, as do reports from longer term prisons. A systematic review of 62 surveys in 12 countries involving 22,790 inmates found that, among males, 26% were violent offenders, 3.7% had psychotic illnesses, 10% suffered from major depression and 65% had a personality disorder, of which 47% antisocial and, among females, 4% had a psychotic illness, 12% had major depression and 42% had a personality disorder, of which 21% antisocial (21).

About 7% of sentenced males, 10% of men on remand, and 14% of women in both categories had been affected by a psychotic illness in the previous year; and among women on remand, 75% reported neurotic symptoms, and 20% of men and 40% of women had attempted suicide at least once (25% of women in the previous year and 2% of women and men in the previous week) (22). Lifetime history of abuse of substances or dependence disorders has been estimated to be present among 74% of inmates, and about 37% had abused or were dependent on alcohol or drugs in the previous 30 days (23). Furthermore, among 104 sentenced inmates arriving at a therapeutic prison in England, 26% had Psychopathy Checklist-Revised (PCL-R) scores of 30 or more and were, therefore, identified as psychopaths (24).

Overall, prevalence estimates of mentally ill in correctional facilities vary widely, from 7% (25) to 90% (26). Many reasons have been given to explain these disparities, including methodological problems, type of institutions where the studies have been carried out, kind and size of samples used, and how mental conditions are defined (27,28).

Violence in prison is both against others and, frequently, against self. Most people die by suicide than from any other reason in prison and, given that the majority of suicides occur within the first days of detention in jails or remand centres, special precautions and screening methods are highly recommended (29). Substance misuse, previous suicidal behavior and single-cell accommodation were considered risk factors for suicide (30).

MANAGEMENT

Prevention is the best policy. To make sure that patients do not drift into criminal behaviour by virtue of need or because of symptomatology, mental health systems should be flexible enough to provide adequate number of beds in acute psychiatric units in general hospitals, rehabilitation beds in tertiary hospitals and a red of services in the community that provide treatment, support and social rehabilitation to patients and their families (31). The police, as the caregiver of first instance, should participate in efforts to decriminalize the mentally ill (32). In many situations involving mental patients, the police should also have legislative authority to redirect patients to psychiatric services in cases where criminal offences have been minor or to make sure that patients are routed to mental health courts as found in several large urban centres (33).

When prevention fails and mental patients end up in prison, correctional systems should have protocols for their management and treatment. From the start, and to follow a principle of equivalence, treatment options in prison should not be second to quality to similar services in the community (34) and should address both the immediate mental health needs of the inmate and, in communication with mental health systems in the community, develop adequate post-release plans. Consent to treatment and other ethical safeguards pertaining to psychiatric treatment and research (35) should be the same as those that apply in the community, and regulatory bodies or research watchdogs should exercise their authority in overseeing that these regulations apply behind the prison walls as well (36).

CONCLUSIONS

Jails are not only "the most important of all our institutions of imprisonment" (37); they are also the mental health asylums of our times by the number, the diversity and the complexity of cases among the mentally ill persons they serve (38). Jails also seem to have assumed part of the burden of treatment for substance abuse and alcoholism. Whether this is a more humane or even a more economical alternative to community interventions would be highly debatable.

Despite many efforts and initiatives to minimize the plight of the mentally ill in prison and to prevent deterioration and imprisonment and especially to prevent reincarcerations (39,40), their numbers do not cease to climb. Close cooperation among agencies, new service modalities and better treatment approaches may be necessary to stop the transfer of mental patients from hospitals to prisons. Given that back in the early 1800s and afterwards, in many countries, prisons were the usual place for mental patients in lieu of asylums, despite all that has been done, little seems to have changed and their plight remains the same. *Plus ça change, plus c'est la même chose.*

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The WPA Train-the-Trainers Workshop on Mental Health in Primary Care (Ibadan, Nigeria, January 26-30, 2009)

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A 5-day WPA training workshop for the teachers of mental health in community health officers' training institutions in the southwest of Nigeria took place at the University of Ibadan Conference Centre, Ibadan from 26 to 30 January, 2009. There were 25 participants selected from the 6 southwestern states (Lagos, Ogun, Ondo, Osun, Oyo, and Ekiti) and the two Yoruba speaking north-central states (Kogi and Kwara).

The workshop aimed to provide the participants with:

- Knowledge, skills and competencies around mental health and mental disorders as well as common neurological disorders, and their contribution to physical health, economic and social outcomes.
- Understanding of linkages between mental health and child health, reproductive health, malaria and HIV.
- Understanding of the general policy and implementation contexts for primary care.
- Understanding of mental health policy and legislation.
- Skills about working with the community, and supporting volunteer community health workers.
- Skills about disaster management.

Selection of participants was made through the National Primary Health Care Development Agency working with the heads of the various institutions. The selected participants were experienced, senior teachers serving in colleges of health technology, community health officers' training programs in teaching hospitals, and community health officer tutors' courses in the University College Hospital Ibadan. There were also representatives of the Community Health Officers' Registration Board (the agency responsible for developing community health officers' curriculum and licensing of practitioners) and the National Primary Health Care Development Agency.

The program ran daily from 8.00 a.m. to 5.00 p.m. using an adapted curriculum, following a general health systems approach and compatible with the World Health Organization Primary Health Care (WHO-PHC) guidelines. The curriculum had been previously developed by R. Jenkins for Kenya, and subsequently adapted for and used in Ghana (V. Doku), Malawi (F. Kauye) and Pakistan (R. Taj and R. Jenkins). Short didactic lectures were augmented with 23 role plays and case vignette discussions. The resource persons were O. Gureje, R. Jenkins and V. Doku. Participants were administered a pre- and post-workshop questionnaire to assess their knowledge of mental health issues and evaluate the changes due to the training. The analysis of the tests will be conducted in due course.

An important highlight of the workshop was the requirement for the participants to develop specific plans of action that build on the outcome of the training. The following were the plans collectively agreed upon:

- Provision of written report on the workshop to the authorities at their institutions within one week of completion of workshop.
- Plan to incorporate the contents of the WHO-PHC guidelines into their lecture notes on mental health within the next academic session.
- Plan to improve their teaching skills by employing role plays and discussions by their students.
- Having understood the relationship between mental health and reproductive health, malaria, HIV/AIDS and child health, the participants resolved to sensitize teachers of other subjects in their institutions to the relevance of mental health to the other courses and subjects.
- Specific plan to forward to Ibadan the academic timetable of their institutions indicating when mental health courses would be taught so as to facilitate monitoring and support visit by O. Gureje and his team in Ibadan.

It was agreed to have periodic monitoring, evaluation and boosting of the knowledge already acquired through scheduled visits to the participants in their respective institutions to observe them teaching their students using the skills acquired during the training.

This initiative is part of the WPA Action Plan 2008-2011 (1).

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Update on WPA Education Programs, 2009

Allan Tasman
WPA Secretary for Education

It is incumbent upon those involved in training the next generation of psychiatrists and other physicians to ensure that trainees and practitioners are exposed to the widest possible range of medical and psychiatric knowledge and clinical settings, so that they can develop ap-

propriate clinical skills based on cutting edge knowledge. It is within this context that the WPA has developed an array of educational programming geared toward ensuring that psychiatrists, other physicians, and the general public, no matter where in the world they live or train, will have the advantage of the latest understanding of psychiatric illness etiologies, diagnosis, and treatment. A variety of educational materials are available on the WPA website (www.wpanet.org).

A recent education project is the WPA/International Society for the Study of Personality Disorders program on personality disorders (1,2). E. Simonsen and colleagues have produced a work that is comprehensive, but organized in a way that makes access to the material easy for individuals at any stage of their professional careers.

Soon after the publication of this issue of *World Psychiatry*, readers will find that a new and completely revised edition of the educational program on depressive disorders (3) is available on the WPA website. An important aim of the revision is to make the new materials useful in the primary care setting. Thus, an important part of the overall project will include collaboration with other organizations to develop material for use in primary care.

A newly approved Education Committee statement, entitled "Recommended roles for the psychiatrist in first episode psychosis", is available on the WPA website under "Educational Resources". This document was prepared to provide psychiatrists with guidance about the most recent developments regarding knowledge of psychosis onset, and the implications of these findings for early detection and intervention.

Another important component of the WPA Action Plan 2008-2011 is a complete revision of the WPA curricular recommendations for medical student and resident education (4). The goal of this project is to ensure that the material is useful for those teaching in a wide range of programs around the world, with extremely variable resources. In addition, the project will include sections on advances in various educational approaches, such as competency based education and evaluation, which were not covered in the previous works because these approaches did not exist at the time.

Another important component of future educational programs will be to develop ways to take advantage of existing and future technologies, such as interactive computer based education and telemedicine based educational programming. As a starting point to assess the use of technology in WPA education initiatives, we plan to develop a series of online continuing medical education (CME) programs based on lectures presented at WPA World and International Congresses. We also intend to develop online, interactive continuing medical education (CME) review questions, so that psychiatrists will have the opportunity to gain CME credits.

Another example of plans to use technology in education is an ongoing project of the WPA Education Committee to develop a Wikipedia based medical student textbook of psychiatry. Wikipedia is an online, free encyclopedia which has now expanded its scope to include books and textbooks. While this program has not yet received official WPA endorsement, because it is not yet complete and submitted for approval, interested individuals can visit the Wikipedia website for the present draft version, which is http://en.wikibooks.org/wiki/Textbook_of_Psychiatry.

To address the ongoing concern about stigma regarding mental illnesses and psychiatrists, we have initiated the development of a new project on public education. The eventual product will be a separate section of the WPA website with materials available in the major WPA languages and with links to public education materials from WPA Member Societies, all in the languages of the home country. In addition, it is envisioned that these links will also contain WPA developed public education materials in the native language of the local country.

We have an extensive and ambitious agenda for the development of our educational programs over the coming years. This is essential for the field, as the pace of change within psychiatry is rapid and dramatic. Anyone interested in assisting with any aspect of our projects is encouraged to contact me, Allan Tasman, WPA Secretary of Education, at allan.tasman@louisville.edu. These are exciting times for the future of psychiatric education, and collaboration with as many of you as possible will make our progress even more impressive.

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WPA forthcoming scientific meetings

Tarek Okasha
WPA Secretary for Meetings

Since my election as WPA Secretary for Meetings during the 14th World Congress of Psychiatry last September, I have had the opportunity to continue the work of the past Secretary for Meetings Pedro Ruiz (1) and to add new initiatives with the help of the newly appointed Standing Committee on Meetings. This Committee, which I am honoured to chair, includes W. Gaebel as co-chair; H. Chaudhry, A. Monchablon, and R. Cordoba as other members, and F. Antun and J. Raboch as consultants. All the members of this Committee have been involved in the organization of many WPA regional and thematic meetings, as well as the World Congresses held in Hamburg 1999, Cairo 2005 and Prague 2008 (2), which I believe makes all of

them able to add more and more to the improvement of WPA sponsored and co-sponsored meetings, thus contributing to raise the image of the WPA worldwide.

The Committee decided to implement and improve the tasks and functions of the WPA related to sponsored and co-sponsored meetings, by: a) improving the scientific quality of WPA scientific meetings; b) working in close collaboration with the WPA Secretary for Education to obtain CME credits for WPA meetings as much as possible; c) working in close collaboration with the WPA Secretary for Finances to improve the financial income and stability of the WPA through sponsored meetings; d) increasing the number of WPA co-sponsored meetings to involve all the 4 Regions and 18 Zones of the WPA, reaching high, middle and low income countries; e) disseminating WPA information, knowledge, educational programmes and expertise to all the different WPA Regions; f) preparing and organizing symposia in as many WPA meetings as possible on "how to organize a scientific meeting"; g) focusing as much as possible on evidence based knowledge by research oriented and educationally oriented presentations.

The WPA held a very successful International Congress in Florence, Italy last April, with more than 9,000 delegates from all over the world (3). For the triennium 2008-2011, eight Regional Meetings have been planned in Isla Margarita, Venezuela (2008), Dhaka, Bangladesh (2010), St. Petersburg, Russia (2010), Beijing, China (2010), Cairo, Egypt (2011), Yerevan, Armenia (2011) and Taipei, Taiwan (2011), and two Thematic Conferences will take place in Toledo, Spain (2009) and Istanbul, Turkey (2011).

We will also have at least 54 co-sponsored WPA Meetings, co-organized with WPA Member Societies or Affiliated Associations as well as other associations whose goals and objectives are in harmony with the WPA. The number of WPA co-sponsored meetings is increasing at a steady rate.

As usual, this triennium will end with the World Congress of Psychiatry, which will be held in Buenos Aires, Argentina, in September 2011.

The WPA meetings are going to include, present and disseminate scientific aspects of the Action Plan presented by the WPA President Mario Maj for the triennium 2008-2011 (4).

Since the Prague Congress in 2008, the WPA sponsored and co-sponsored meetings have been attended by nearly 34,000 mental health professionals from all over the world.

With the strong interest of the WPA Member Societies and Affiliated Associations to hold WPA sponsored and co-sponsored meetings, it seems that we will not only have the same success with WPA meetings as in the last triennium, but we will surpass that level. If these expectations and efforts are properly met, the WPA will have a major role in contributing to the quality of scientific knowledge and psychiatric care offered across the world, in particular to middle and low income countries.

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CALL FOR APPLICATIONS FOR A WPA RESEARCH FELLOWSHIP

AT THE INSTITUTE OF PSYCHIATRY OF LONDON

The World Psychiatric Association, as part of its Action Plan 2008-2011, has launched a programme of research fellowships for early-career psychiatrists from low- or lower-middle income countries, in collaboration with internationally recognized centers of excellence in psychiatry. Within this programme, the World Psychiatric Association is funding a one-year international mental health research fellowship at the Institute of Psychiatry, King's College London.

Applications are invited from psychiatrists less than 40 years of age or with less than five years elapsed since completion of residency training. The list of eligible countries (low- or lower-middle income countries) is available on the World Bank website (http://www. worldbank.org).

The fellowship holder will receive a subsidy of 30,000 Euros plus coverage of travel expenses (economy class). He/she will commit himself/herself to report to the World Psychiatric Association about the results of his/her activity, and to apply in his/her country of origin what he/she has learnt.

Applicants should submit by e-mail their curriculum vitae to the WPA Secretariat (wpasecretariat@wpanet.org). The deadline for applications is November 30, 2009.

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