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EDITORIAL

Physical health care in persons with severe mental illness: a public health and ethical priority

Mario Maj

President, World Psychiatric Association

The issue of protection and promotion of physical health in persons with severe mental illness is emerging as one of great public health and ethical relevance worldwide. If we are really concerned about the quality of life of our patients with severe mental disorders and with the protection of their civil rights, we cannot ignore that physical health is a crucial dimension of quality of life in these persons, and that the access to a physical health care of the same quality as that available to the rest of the population is a basic right of these persons as human beings and as citizens.

As reviewed by De Hert et al in this issue (1), there is now an extensive research evidence that: a) the prevalence of many physical diseases is higher in persons with severe mental illness than in the general population (2); b) the gap between these persons and the rest of the population concerning the prevalence of some of these diseases (notably, type 2 diabetes mellitus) has been increasing in the past few decades (3); c) the co-existence of one or more physical diseases has a significant impact on many quality of life and psychopathological variables in persons with severe mental illness (4); d) mortality due to physical diseases is higher in persons with severe mental illness than in the general population (5), and the gap concerning mortality due to some diseases (in particular, ischaemic heart disease) has been increasing in recent decades (6); e) the access to physical health care of persons with severe mental illness is reduced compared to the general population (6); f) the quality of physical health care received by persons with severe mental illness is poorer than the general population: recent data about mortality due to post-operative respiratory failure (adjusted odds ratio, OR=8.85) and post-operative sepsis (adjusted OR=7.14) in persons with schizophrenia are striking in this respect (7).

In order to address this situation, several lines of action can be identified. Raising awareness of the problem among mental health professionals, primary care practitioners, patients and their families is obviously a first priority. The available research information about the increased morbidity and mortality due to physical diseases in people with severe mental disorders should be much better disseminated.

Education and training of mental health professionals and primary care providers is one more essential step. Mental health professionals should be trained to perform at least basic medical tasks. They should be educated about the importance of recognizing physical illness in people with severe mental disorders. They should be encouraged to familiarize themselves with the most common reasons for underdiagnosis or misdiagnosis of physical illness in their patients (8). On the other hand, primary care providers should overcome their reluctance to treat persons with severe mental illness. They should learn effective ways to interact and communicate with these persons: it is not so much an issue of knowledge and skills; it is mostly an issue of attitudes.

Another essential step is the development of an appropriate integration between mental health and physical health care. There is some debate in the literature about who should monitor physical health in people with severe mental illness. What really matters, however, is that there is always somebody who cares: every patient should have a professional who is identified as responsible for his/her physical health care. On the other hand, mental health services should be able to provide at least a standard routine assessment of their patients, in order to identify or suspect the presence of physical health problems. Currently available guidelines about the choice of antipsychotic medication in the individual patient and the management of patients receiving antipsychotics should be known and applied by all mental health services. Mental health professionals should encourage patients to monitor and chart their own weight and should sensitize patients and their caregivers to the health risk associated with excess weight. Dietary and exercise programs should be an essential part of what mental health services provide.

Finally, further research in this area is badly needed. Physical illnesses should not be always regarded as confounding variables in studies dealing with severe mental disorders. They should be studied by specific research protocols, so that the interaction between mental disorders and the various physical diseases – in men as well as in women; in young people as well as in the elderly; in inpatients as well as in outpatients – can be better understood. This could also facilitate the development of closer working relationships between physical and mental health professionals.

The WPA will implement during this triennium an international programme on the protection and promotion of physical health in persons with severe mental illness, in collaboration with other international and national medical associations and with some organizations of users and families. One of the components of the project will be the development of an educational module to be used in training of residents in psychiatry, dealing with physical diseases and access to health care services in persons with schizophrenia.

The promotion of physical health care in people with severe mental illness is today a key issue in our field. If we do

not regard it as a priority, we will not be able to state convincingly that a better quality of life and the protection of the civil rights of our patients is really what we strive toward.

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CHOOSING PSYCHIATRY AS A CAREER

A WPA INTERNATIONAL CALL FOR RESEARCH PROPOSALS

The World Psychiatric Association (WPA) is the largest association active in the mental health field worldwide, with 134 Member Societies (national psychiatric societies), representing more than 200,000 psychiatrists, and 65 Scientific Sections.

In the WPA Action Plan 2008-2011, one of the institutional goals is to enhance the image of psychiatry worldwide among the general public, health professionals and policy makers, counteracting some negative messages – often biased by ideological prejudice – which are affecting the motivation of persons with mental disorders and their families to seek for psychiatric advice and help and to adhere to psychiatric interventions, as well as the motivation of medical students to choose psychiatry as a career.

As one of the activities pursuing this institutional goal, the WPA will fund an international project aimed to assess the factors facilitating and those hampering the choice of psychiatry as a career by medical students, and to suggest strategies to encourage this choice.

Proposals from individuals, departments or societies are welcome. They will have to include a description of the project (max. 1200 words), a list of the participating centres, a timetable, a detailed budget, and a short curriculum vitae of the proposed principal investigator(s). Proposals will have to be sent by e-mail to the WPA Secretariat (wpasecretariat@wpanet.org) by June 30, 2009.

Enhancing research and treatment of mental disorders with dimensional concepts: toward DSM-V and ICD-11

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The current versions of the DSM (DSM-IV-TR) and ICD (ICD-10) describe all mental disorders as polythetic-categorical concepts. Lists of symptoms are presented, and diagnostic category labels are assigned to patients based on observing specific patterns of symptoms. A number of notable conceptual problems emerge when using this strictly categorical system in research and in the clinic. When thorough structured diagnostic interviews are used, typical patients meet criteria for more than one specific diagnosis (a phenomenon termed "comorbidity"). In addition, groups of patients with the same putative categorical label are often heterogeneous with respect to key clinical features, such as severity and prognosis, and patients with symptomatology below diagnostic thresholds are often significantly impaired. Although categorical concepts will always be essential in official nosologies (e.g., in providing diagnostic labels for reimbursement purposes), many of the conceptual problems of a strictly categorical diagnostic system can be overcome by enhancing official nosologies with dimensional concepts. Specific dimensional approaches and directions that may be considered for upcoming revisions of both the DSM and ICD are discussed.

Key words: Diagnosis, classification, dimension, category, nosology

(World Psychiatry 2009;8:3-6)

In both DSM and ICD, all mental disorders are *polythetic-categorical* concepts.

Polythetic refers to the fact that specific mental disorders are defined by multiple symptoms, and not all listed symptoms are necessary to consider a mental disorder present in a specific individual. Rather, a specific combination and number of symptoms – less than the total number of symptoms of the disorder – must be observed to consider a diagnosis present.

Categorical refers to the fact that all mental disorders in the DSM/ICD are binary, "either/or" concepts. Disorders are considered present in individuals when the right combination and number of symptoms are present, and absent when those symptoms are not present in the correct combination and number. There are no exceptions, and gradations of present vs. absent are not allowed.

Each and every mental disorder listed in the DSM/ICD is conceptualized as both polythetic and categorical.

LIMITATIONS OF A STRICTLY POLYTHETIC-CATEGORICAL MODEL OF MENTAL DISORDERS

A number of notable problems emerge when conceptualizing mental disorders as strictly polythetic and categorical, in both research settings and in the clinic. Consider three conceptual problems that vex both research study design and clinical case conceptualization: comorbidity, within-category heterogeneity, and the validity of subthreshold symptomatology.

Comorbidity

When thorough structured diagnostic interviews are used in assessment, typical patients meet criteria for more than one specific diagnosis (2-5). This phenomenon is typically termed "comorbidity" (6). Although comorbidity is the typical concept applied to this phenomenon, it is somewhat of a misnomer. "Co-" generally refers to two things, but "multimorbidity" may actually be more prevalent, and hence, a more accurate term (7).

The terminology used to describe this phenomenon of "extensive putatively distinct mental disorder multi-occurrence" is important, because the phenomenon is an essential empirical finding about what happens when one tries to work with DSM mental disorder concepts. "Multi-morbidity" is frequently encountered and is a potent predictor of overall clinical severity (8). However, many putatively distinct disorders have etiologic factors in common. Key examples include overlapping genetic contributions to major depressive episode and generalized anxiety disorder (9,10), and overlapping genetic contributions to antisocial personality disorder and substance dependence (11,12). Such data bring into question the DSM-driven conceptualization of mental disorders as entirely categorically distinct from each other. The data indicate a lack of categorical boundaries separating disorders, suggesting instead that disorder manifestations blend into each other in a manner not well captured by the idea of polythetic categories.

Within-category heterogeneity

Another challenging problem that emerges when working with DSM mental disorder concepts is within-category heterogeneity. Consider the DSM-IV-TR personality disorders. A patient needs to meet criteria for only 5 of 9 symp-

toms to receive a diagnosis of schizotypal, borderline, or narcissistic personality disorder. As a result, patients who meet criteria for these disorders could share only one symptom. Obsessive-compulsive personality disorder involves 8 symptoms and a threshold of 4 symptoms for a diagnosis. As a result, two different diagnosed cases of obsessive-compulsive personality disorder could have no symptoms in common. In sum, a strictly polythetic-categorical approach leads to diverse diagnostic and prognostic profiles within groups of persons selected because they meet criteria for a specific mental disorder.

Consider also an illustrative example from research we pursued on DSM defined conduct disorder symptoms (13). We found that ten symptoms common to DSM-III-R and DSM-IV had an empirical structure consisting of two distinguishable dimensions, one consisting more of aggressive behaviors, and the other consisting more of rule-breaking behaviors (14). We also presented evidence that these two dimensions had distinguishable etiologies, with rule-breaking showing a greater relative contribution from the shared family environment, and aggression showing a greater relative contribution from genetic factors. DSM-IV recognizes subvarieties of conduct disorder based only on age of onset and severity of overall symptoms, and conceptualizes conduct disorder as a polythetic category consisting of 15 symptoms with a threshold of 3 symptoms for a diagnosis. The problem is that, with 15 symptoms and a threshold of 3, persons with diverse symptomatology are considered exemplars of the same, putatively homogeneous, diagnostic category. This conceptualization is incompatible with the data. For example, person A could have 3 aggressive symptoms, person B could have 3 rule-breaking symptoms, and, although the evidence suggests potentially important differences between these two persons in terms of the etiology of their psychopathology, both are considered to have "the same diagnosis".

Finally, consider an example from literature on the treatment of depression. Thase et al conducted a meta-analysis on approximately six-hundred depressed outpatients pooled from six studies (15). All patients were diagnosed with major depressive disorder based on DSM-III and DSM-IIIR (16) criteria and were on average 44 years old (31% male) (15). Patients were then stratified into less severe (a score of ≤19 on the Hamilton Rating Scale for Depression, HRSD (17)), and more severe (a score of ≥20 on the HRSD) subgroups, and were either given interpersonal psychotherapy alone, or interpersonal psychotherapy plus antidepressants (15). The combination of interpersonal psychotherapy plus antidepressants was significantly better than psychotherapy alone only in the more severe major depression subgroup (15). Thus, within a sample of patients diagnosed with major depressive disorder, there is significant variability in the way they respond to treatment.

In sum, polythetic categorical diagnostic concepts from the DSM show evidence of notable within-category heterogeneity, based on empirical studies. Interestingly, the limitations of a categorical approach, in terms of the heterogeneity problem, are described and acknowledged in the text of the DSM-IV (p. xxii). The problem is that the DSM does not describe specific strategies or concepts for overcoming the heterogeneity problem.

Validity of subthreshold symptomatology

In a polythetic-categorical framework, the extent to which a person is below or above the threshold for a diagnosis is deemed irrelevant to the diagnostic construct. Consider for example a diagnosis that consists of 10 symptoms, where the threshold is set at 5 symptoms. In this system, values from 1-4 are converted to "no diagnosis" or zero and values from 5-10 are converted to "diagnosis present" or one. The extent of symptomatology is assumed to lack clinical or public health significance.

Nevertheless, research indicates that valuable information is lost when proximity to a threshold is discarded in favor of conceptualizing disorders solely in terms of whether a threshold has been passed. A compelling example is found in research from the Christchurch Health and Development Study, a study of a longitudinally-followed birth cohort of persons in Christchurch, New Zealand (18). Fergusson et al (18) classified their research participants at ages 17-18 into three groups: asymptomatic, subthreshold (depressed mood or loss of interest for at least two weeks, but falling short of the 5 or more symptom threshold for major depression in DSM-IV) and major depression (full major depression criteria met in the last 12 months). The risk of depression and suicidal behaviors at follow-up (ages 21-25) was similar for both the subthreshold and major depression groups, and the data supported the existence of continuous, linear associations between late-adolescent depression and adverse early adult outcomes, as opposed to abrupt changes in risk at a specific threshold. In general, depression and other common mental disorders (e.g., alcohol dependence) do not appear to be empirically characterized by abrupt thresholds (19-21); these mental disorders are better characterized as continuous phenomena in nature.

DIMENSIONAL ENHANCEMENT OF MENTAL DISORDER CONCEPTUALIZATION

Future DSMs will likely continue to be framed, at least partially, by categorical mental disorder concepts. Such concepts are important for various practical purposes, such as having specific labels that can be used in facilitating third-party payments. Nevertheless, owing to the clear limitations of an exclusively categorical-polythetic diagnostic system, there is substantial interest in enhancing the next edition of the DSM (DSM-V) with dimensional concepts.

With this interest in mind, and the support of the American Psychiatric Institute for Research and Education (APIRE) and the US National Institutes of Health (NIH), we organized

a meeting to discuss dimensional options for DSM-V (22,23). Here we outline some ideas that emerged from that meeting.

Some dimensional options for official nosologies

Both categorical and dimensional approaches to diagnoses are critical to both clinicians and researchers, and the most effective classification system would offer both (24). It is also clear that dimensional scales need to reflect categorical definitions and the two must have a clear relationship to one another. Based on categorical definitions, there are numerous ways for creating continuous measures, including number of symptoms, severity of symptoms and level of illness impairment (within diagnostic entities) (24). If dimensional options for categorical diagnoses are adopted, then dimensional approaches that are most appropriate to the diagnoses defined would effectively need to be created (24).

Essentially, certain aspects of any specific disorder may be conceptualized and assessed dimensionally. Take substance use disorders for example: a categorical definition can be created based on prior categorical definitions, which sets the diagnostic threshold (25). Dimensionality can then begin at the symptom level, with each symptom being scored on (at least) a 3-point scale (25). Statistical methodology can be used to identify the dimensional score that most closely resembles the categorical (or diagnostic) threshold originally set forth. This leads to a consistent and clearer relationship between categorical and dimensional definitions (25). This method can essentially be implemented in most (if not all) parts of the DSM (e.g., personality disorders, mood disorders, psychoses, and developmental psychopathology).

The notion of a *cross-cutting* approach also becomes relevant when examining different methods for dimensional assessment. For example, the need to facilitate differential diagnosis forms the basis of grouping anxiety disorders into a single section of the DSM. Yet, symptoms such as panic attacks occur across anxiety and other psychiatric disorders (26). Evidence suggests that panic episodes are a reliable marker for higher illness severity, decreased responsiveness to treatments, and increased suicidality (27,28). Thus, panic may be considered a *cross-cutting* symptom that is defined separately and seen across several disorders (29). Implementing cross-cutting dimensions can potentially be more effective and informative than categorical diagnoses that are kept "artificially dimension-specific" (30). Another instance where a cross-cutting dimensional approach may be an effective way to conceptualize a complex illness is with children who exhibit comorbid symptoms for putatively distinct disorders (e.g., attention-deficit/hyperactivity disorder (ADHD) and oppositional defiant disorder) (31). A cross-cutting dimensional approach may be able to simplify the clinical conceptualization of intricate compound disorders by viewing those disorders as elements within a broader spectrum of interrelated conditions.

Child and adolescent disorders also highlight the need to consider sources of variance – including gender, age and development – that are generally overlooked in the current edition of DSM (31). Consider for example gender: three to seven times more boys than girls meet DSM diagnostic criteria for ADHD. By adulthood, the disparity in gender is less apparent (32). A categorical approach that fails to take gender norms into consideration may hinder the understanding of these differences. By utilizing a dimensional approach, a systematic method for selecting gender sensitive cut-offs may be put forth (31). Age and development are also sources of variance that DSM criteria do not currently take into account. Sensitivity to developmental stages and individual distinctiveness may be more straightforward with a dimensional approach rather than a categorical one which only defines a single threshold (33). When implementing a supplementary dimensional system, children can be evaluated on dimensional scales that are normed on gender, age, and ethnicity (33).

Finally, DSM has consistently employed a "top-down" approach, where clinicians consult their own expertise as well as the existing literature for a diagnosis. In contrast, a "bottom-up" approach is generally driven by empirical analyses. A large body of symptom data may be collected from the general population to be statistically analyzed in order to determine which symptoms cluster together into syndromes or facets (33). For example, Krueger et al (34) discuss the advantage of comprising core descriptive personality features as part of DSM-V, thus reducing the large number of symptoms found in DSM-IV personality disorders to a set of more manageable facets (34). Thus, one advantageous approach would be to structure the DSM-V in a way that allows the possibility to compare both top-down and bottom-up methods in order to improve the diagnostic validity of the system (33).

CONCLUSIONS

The DSM-III represented a major advance for psychopathology researchers and clinicians around the world. Clearly worded, observable criteria were presented for numerous categorical and polythetic mental disorder constructs. This clarity has been a boon to empirical research on mental disorders, because it provided consensual target constructs. The conceptual system put in place in DSM-III has essentially continued forward, through DSM-IV, with changes in specific criteria but no change in the basic conceptualization of mental disorders. As a result, extensive data and experience has accumulated regarding the limitations inherent in polythetic categories. The need to evolve our conceptualization, and to move beyond a strictly categorical and polythetic model of all mental disorders, is clear. The challenge now is how to achieve this evolution, in terms of specific strategies and approaches that can be implemented in official nosologies. This is no small task, but it is a critical one if the goal is to keep research and treatment of mental disorders on solid empirical footing.

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Relationship problems and the DSM: needed improvements and suggested solutions

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Relational problems are clinically significant behavioral or psychological syndromes or patterns that occur between or among individuals and that are associated with present distress or disability or with a significant increased risk of suffering death, pain, disability, or an important loss of freedom. Relational problems (e.g., partner relational problems, partner abuse, child maltreatment) are included as Axis I disorders in the DSM-IV as V-codes (i.e., "Other conditions that may be a focus of clinical attention"). However, there are no criteria provided in the DSM-IV for these codes. In this article, we briefly review literature that incontrovertibly documents both relational problems' syndromes/patterns and their serious sequelae. We then review a series of studies that provide evidence of content validity and inter-rater agreement for criteria to determine presence versus absence of relational problems. The most studied subset of relational problem criteria, those for partner and child maltreatment, have been shown to have remarkably high levels of reliability when disseminated broadly in the field (κ = .66-.89), at agreement levels never reached by DSM diagnoses for individuals. We conclude by arguing that science, service, families, individuals, and the DSM itself, would be well served to include diagnostic criteria for relational problems and to consider the various options for placement of relational problems/processes in the DSM-V.

Key words: Relational problems, partner and child maltreatment, diagnostic criteria, DSM-IV

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The DSM-IV-TR limits mental disorders, by definition, to problems within a person: "a clinically significant behavioral or psychological syndrome or pattern that occurs *in an individual* and that is associated with present distress (e.g., a painful symptom) or disability (i.e., impairment in one or more important areas of functioning) or with a significantly increased risk of suffering death, pain, disability, or an important loss of freedom" (1).

Clinically significant behavioral or psychological syndromes or patterns that occur *between or among individuals* and that are associated with present distress or disability or with a significant increased risk of suffering death, pain, disability, or an important loss of freedom, receive little attention in the DSM-IV. This article focuses on eleven such syndromes/patterns occurring within families – partner relational problems, parenting problems, parent-child relational problems, partner maltreatment (physical, emotional, and sexual abuse; neglect) and child maltreatment (physical, emotional, and sexual abuse; neglect) – which we will refer to as "relational problems".

We briefly review how relational problems are handled in DSM-IV. We sketch the scientific body of research that supports the importance of relational processes to individual's functioning and well-being. We provide several examples of the way criteria could be presented in a clear, structured manner. We present the series of studies that provide evidence of content validity and inter-rater agreement for criteria to determine presence versus absence of relational problems. We discuss the development of screening and diagnostic interviews for relational problems. We present recommendations for possible inclusion of relational problems/processes in the DSM-V. We conclude that criteria are available that could enhance the description of key relationship problems relevant for the provision of optimal clinical care.

HOW RELATIONAL PROBLEMS ARE HANDLED IN THE DSM-IV

The DSM-IV-TR includes relational processes in the section "Other conditions that may be a focus of clinical attention" (e.g., partner relational problem, parent-child relational problem, problems related to abuse or neglect). Further, it lists categories of psychosocial problems on Axis IV (e.g., problems with primary support group, problems related to social environment) and provides the Global Assessment of Functioning (GAF) scale on Axis V and the Global Assessment of Relational Functioning (GARF) scale in Appendix B. In addition, some relational problems have been addressed in supplemental materials, such as the discussion of abuse and neglect and other relational problems in Volume 3 of the DSM-IV Sourcebook (2). However, there are no criteria provided in the DSM-IV for relational problems (or any V-codes).

The prime reason for including criteria for relational problems in the DSM is that clinicians and researchers routinely assess and treat individuals, couples, and families with relational problems – or individual disorders related to, or exacerbated by, relational problems – but are not provided with any guidance regarding criteria. Studies using varying opera-

tionalizations of relational problems are difficult to compare (3,4); agreement among clinicians in the field is poor (5); and the content validity of typical operationalizations is debated (sometimes quite bitterly in the case of partner maltreatment) (6,7). The result is less than optimal research communication, less than optimal accumulation of research results, and less than optimal clinical practice.

The neo-Kraepelinian approach used to develop the DSM described potentially clinically significant syndromes, with an initial goal of classifying disorders reliably. The validity of such classifications then could be evaluated. As noted by Kupfer et al (8), "from the outset... it was recognized that the primary strength of a descriptive approach was its ability to improve communication among clinicians and researchers, not its established validity". In other words, DSM definitions were bootstrapped, because criteria for clinical syndromes had to precede research on prevalence, etiology, and treatment efficacy and effectiveness (9). With reliable, operationalized syndromes as a starting point, validity research is then possible.

Thus, the real question is not "should relational problems be included in the DSM-V?" but "should there be operationalized criteria?" and "should relational problems remain as V-codes or should they be placed somewhere else?" We will argue strenuously that the answer to the first question is emphatically "yes". We are agnostic on the second question; a detailed consideration of the options for placement of relational problems and relational processes in the DSM can be found elsewhere (10,11).

THE NEED FOR RELIABLE AND VALID CRITERIA FOR RELATIONAL PROBLEMS – CASE STUDY: PARTNER RELATIONAL PROBLEMS

Space constraints preclude even a cursory review of the expansive literature linking each of the eleven relational problems with significant distress, morbidity, and mortality. We have chosen, instead, to briefly present the evidence for one problem: partner relational problems. Equivalent sets of literature could be marshaled for nearly all of the other ten problems.

Partner relational problems' effects on adult mental health

The literature linking adult intimate relationships to mental health outcomes is substantial. There are documented connections between relational processes and the etiology, maintenance, relapse, and optimal treatment of many disorders. Because we do not have the space to review this literature exhaustively, we focus on briefly sampling this literature for illustrative purposes.

Serious partner relationship dissatisfaction predicts increased risk for a major depressive episode in the subsequent year, even after controlling for history of depression (12) or comorbidity (13). Both relationship conflict and physical abuse predict subsequent increases in depressive symptoms among women (14). The effect of humiliating relationship events on depression is substantial (15,16). From a behavioral-genetic perspective, the effect of partner relationship satisfaction is a nonshared environmental effect and is not well modeled as resulting from the same genetic factors that produce the vulnerability for depressive symptoms (17). Accordingly, disturbance in intimate adult relationships is key for understanding the etiology of depressive symptoms for many individuals and has the potential to supplement genetically based models (18).

Treatment approaches targeting intimate relationships have proved useful for, among other individual disorders, depression (19), alcohol abuse (20), and drug abuse (20). There are notable applications of relational interventions for individuals with severe mental illness (21). Such treatments are associated with reduced interpersonal stress, greater medication adherence, and lower rates of rehospitalization. As a result of such links, attention to relational problems has increased in the treatment of many mental health problems and is essential for the appropriate management of a number of disorders.

Partner relational problems' effects on children's mental health

Partner relationship conflict is associated with worse parenting and child adjustment, problematic attachments, and increased parent-child and sibling conflicts. Aspects of relationship conflict that have a particularly negative influence on children include frequent, intense, physical, unresolved, child-related conflicts and conflicts attributed to the child's behavior (22). Relationship and parenting problems can be mutually exacerbating and may work synergistically to create a coercive family environment. In turn, relationship and parenting problems can interact with genetic liabilities and influence gene expression to affect the etiology of many physical and mental disorders. For example, women who were adopted soon after birth and who are at high genetic risk for depression show no evidence of the disorder if reared by adoptive parents without psychopathology or relationship difficulties (23). Similarly, adoptees with a genetic risk for schizophrenia and exposure to specific communication styles in their adopted families are more likely to develop the disorder than genetically susceptible persons raised by families with more clear communication and clear roles (24). These data suggest that an interaction between the adult partner relationship environment and particular genetic diatheses may be critical to the etiology of certain major mental disorders (18).

Animal data also indicate the significance of early rearing environment; for example, poor maternal care by rat dams of their pups within the first 10 days of life influences gene expression (25). Poor maternal care leads to changes in glu-

cocorticoid receptor messenger RNA expression in the hippocampus, resulting in enhanced glucocorticoid feedback sensitivity and increased sensitivity to stress. Such changes are the basis for lifetime sensitivity to stress of the maltreated pups (25) and set the stage for the offspring's own poor maternal care of their young. Conversely, good maternal care of infant monkeys at risk for anxiety symptoms moderates symptom expression (26), suggesting that gene-family environment interactions may transform genetic liabilities into genetic assets and that disturbances in primary relationships early in life can change neural systems that control long-term emotional resilience or vulnerability (27).

EXAMPLES OF CRITERIA FOR RELATIONAL PROBLEMS

The development and validation of criteria for relational problems in the DSM-V is well advanced. The goal has been to produce clear criteria that could provide clinically useful guidance and create a basis for inter-rater agreement in clinical settings. In addition, each criteria set is based on the best available scientific understanding of the development and maintenance of these problems.

Table 1 displays the criteria for partner relational problem.

Table 1 Diagnostic criteria for partner relational problem

A. Relationship dissatisfaction during the past month, as evidenced by any of the following:
1) Pervasive sense of unhappiness with the relationship, more days than not.
2) Thoughts of divorce/separation that are more than transitory.
3) Perceived need for professional help for the relationship.

B. Significant impact of the relational dissatisfaction on behavioral, cognitive, or affective systems, as evidenced by at least one of the following for at least one of the partners:
1) Behavioral symptoms:
   a. Conflict resolution difficulties, as evidenced by either:
      i. Persistent and marked escalation of negative behavior or affect (e.g., "little" disputes quickly and frequently evolve into heated arguments).
      ii. Pervasive withdrawal so that resolution is impeded.

      (Note: Withdrawal can be either through leaving a discussion before it is resolved or through more pervasive disconnectedness that impedes bringing up or resolving problems)
   b. Pervasive lack of positive behaviors (e.g., sharing thoughts and feelings; affection) or supportive behaviors.
2) Cognitive symptoms – Pervasive pattern of negative attributions regarding the partner's intentions, as evidenced by either:
   a. Negative behaviors pervasively attributed to negative personality traits or perceived to be done voluntarily, intentionally, or with negative intent.
   b. Positive behaviors pervasively attributed to temporary states or perceived to be done accidentally, unintentionally, or with hidden negative intentions.
3) Affective symptoms – Interactions with or thoughts about the partner are frequently marked by intense and persistent levels of at least one of the following:
   a. Anger or contempt.
   b. Sadness.
   c. Apathy.

Both criteria A and B are required. Criterion A involves relationship dissatisfaction, comprising three possible presentations (similar to the depressed mood or anhedonia requirement of the major depressive episode criteria): a pervasive and persistent sense of unhappiness with the relationship; persistent thoughts of divorce or separation; a perceived need for professional help for the relationship. Criterion B comprises behavioral, cognitive, and affective symptoms that have appeared repeatedly in the empirical literature; at least one is required.

Table 2 displays the criteria for child physical abuse. Both criterion A (act) and criterion B (impact) are required, as is criterion C (lack of mitigating circumstances – that is, the acts were not committed to protect self from imminent harm, were not part of developmentally appropriate play, and were not committed to protect child from imminent harm).

As in the DSM, where the criteria for "major depressive episode" are separate from, but referenced by, the criteria for "major depressive disorder", the eleven relational disorder criteria have some sub-criteria sets that have proven essential for reliable application of the criteria. As seen in Table 2, "more than inconsequential physical injury" and "more than inconsequential fear reaction" have clarifying criteria. As we discovered during the field trials discussed below, such operationalizations are necessary to achieve high field assessor-master reviewer agreement. Finally, note that criteria B1 (more than inconsequential injury) and B3 (more than inconsequential fear reaction) involve actual impacts, whereas B2 involves potential for more than inconsequential injury. Assessors judge whether the inherent dangerousness of the act, the degree of force used and the physical environment in which the acts occurred constituted a significant potential for serious harm (e.g., pushing a child hard near the top of a flight of stairs, choking an adolescent hard but leaving no bruises).

Table 3 provides the criteria for parenting problems, which follow a similar structure to the other criteria. Criterion A involves substantial parenting difficulties and criterion B involves significant impact on the child from those parenting difficulties. Again, the criteria reflect findings in the empirical literature and provide a basis for inter-rater reliability in clinical settings. Many instances of family dysfunction for which the child now receives a diagnosis (e.g., conduct disorder, oppositional defiant disorder) could also meet criteria for parenting problem.

DEVELOPMENT AND TESTING OF CRITERIA FOR RELATIONAL PROBLEMS

Criteria have been developed for all eleven relational problems. Below we detail the creation and testing of criteria for relational problems related to partner and child maltreatment. The maltreatment criteria were developed in a multistage process described in depth elsewhere (28-30). The steps comprised: a) examining the content validity and field usability of a set of maltreatment criteria already in use; b) creat-

Table 2 Criteria for child physical abuse

A. Non-accidental use of physical force by a child's parent/caregiver. Physical force includes, but is not limited to, spanking with hand; dropping; pushing; shoving; slapping; grabbing or yanking limbs or body; throwing; poking; hair-pulling; scratching; pinching; restraining or squeezing; shaking; biting; throwing objects at; kicking; hitting with fist; hitting with a stick, strap, belt, or other object; scalding; burning; poisoning; stabbing; applying force to throat; strangling or cutting off air supply; holding under water; using a weapon.

B. Significant impact on the child as evidenced by any of the following:
1) More than inconsequential physical injury (see definition below).
2) Reasonable potential for more than inconsequential physical injury (see definition below) given the inherent dangerousness of the act, the degree of force used and the physical environment in which the acts occurred.
3) More than inconsequential fear reaction (see definition below).

C. The acts of physical force were not committed for any of the following reasons:
1) To protect self from imminent physical harm because the child/adolescent was in the act of physical force (see definition below).
2) To play with the child in a developmentally appropriate manner.
3) To protect child or another person from imminent physical harm (including, but not limited to, pushing child out of the way of a car, taking weapon away from suicidal child, stopping child from inflicting injury on another person).

(*Note:* Subsequent actions that were not directly protective – e.g., whipping child for running into the street – would not meet this criterion)

Subcriteria for "More than inconsequential physical injury"

An injury involving any of the following:
A. Any injury to the face or head.
B. Any injury to a child under 2 years of age.
C. More than superficial bruise(s) (i.e., bruise that is other than very light red in color – for example, violet, blue, black – OR bruises with total area exceeding that of the victim's hand OR are tender to light touch).
D. More than superficial cut(s)/scratch(es) (i.e., would require pressure to stop bleeding).
E. Bleeding internally or from mouth or ears.
F. Welt (bump or ridge raised on the skin).
G. Burns.
H. Loss of consciousness.
I. Loss of functioning (including, but not limited to, sprains, broken bones, detached retina, loose or chipped teeth).
J. Heat exhaustion or heat stroke.
K. Damage to internal organs.
L. Disfigurement (including, but not limited to, scarring).
M. Swelling lasting at least 24 hours.
N. Pain felt (a) in the course of normal activities and (b) at least 24 hours after the physical injury was suffered.

Subcriteria for "More than inconsequential fear reaction"

Victim's significant fear reaction, as evidenced by both of the following:
A. Fear (verbalized or displayed) of bodily injury to self or others.
B. At least one of the following signs of fear or anxiety lasting at least 48 hours:
1) Persistent intrusive recollections of the incident.
2) Marked negative reactions to cues related to incident, as evidenced by any of the following:
a. Avoidance of cues.
b. Subjective or overt distress to cues (Note: perpetrator can be a cue).
c. Physiological hyperarousal to cues (Note: perpetrator can be a cue).
3) Acting or feeling as if incident is recurring.
4) Persistent symptoms of increased arousal, as evidenced by any of the following:
a. Difficulty falling or staying asleep.
b. Irritability or outbursts of anger.
c. Difficulty concentrating.
d. Hypervigilance (i.e., acting overly sensitive to sounds and sights in the environment; scanning the environment expecting danger; feeling keyed up and on edge).
e. Exaggerated startle response.

Subcriteria for "Protection of self from imminent physical harm because child was in the act of physical force"

Acts of physical force were committed to protect self from imminent physical harm because the child was in the act of physical force, as evidenced by all three of the following:
A. Act(s) occurred while other was in the act of using physical force. "In the act" begins with the initiation of motoric behavior that typically would result in an act of physical force (for example, charging to hit him/her) and ends when the use of force is no longer imminent.
B. Sole function of act(s) was to stop other's use of physical force.
C. Act(s) used minimally sufficient force to stop other's use of physical force.

ing a unifying conceptualization for what constituted an above-threshold problem; c) reviewing and adapting (where appropriate) existing operationalizations; d) field testing and refining criteria, assessments, and decision-making process; e) testing criteria's use in wide-scale dissemination; f) creating criteria-informed screeners and structured clinical interviews; and g) examining the content validity of the final criteria.

Before describing the results of the multi-stage development/testing process, some context is necessary. First, the criteria were originally developed for use in the US Air Force and have since been adopted across all services of the US Department of Defense and the US Coast Guard. Second, all assessments and diagnostic judgments were conducted with families with maltreatment allegation lodged against them, not with a more general clinical population. Third, the processes used in this context differ slightly from that used in civilian contexts. Although all clinical assessments were conducted by credentialed providers, the decision about whether someone met the criteria was made by a committee.

Step 1: Examine content validity and field usability of existing criteria

Because we were bootstrapping our definitions using existing definitions as a starting point, we conducted two content validity studies using the family maltreatment criteria then in use by the US Department of Defense (31). To maximize the content and clinical validity of the potential criteria, we followed Haynes et al's (32) suggestion to conduct content validity studies using both civilian and military family maltreatment experts (Study 1) and those intended to use the definitions (i.e., field clinicians; Study 2).

Study 1 (28) suggested that the criteria then in force were adequate but could be improved by: a) operationalizing terms, b) eliminating the definitional overlap of emotional abuse and other forms of maltreatment, and c) eliminating the requirement that clinicians predict risk of recurrence to find that incidents met criteria for child emotional abuse or child neglect. In Study 2 (28), field clinicians shared the

Table 3 Criteria for parenting problem

A. Considering the developmental needs of the child, caregiving is markedly outside the bounds of normal, as evidenced by one of the following:
1) Pervasive caregiving difficulties involving either or both of the following:
   a. Underinvolvement (e.g., parent is not bonded to and does not provide loving relationship for the child).
   b. Overinvolvement (e.g., parent is so protective that young adolescent is not afforded any private communication with friends; child is not able to participate in choices about how they will spend their time).
2) Marked difficulties in at least one aspect of parenting, including, but not limited to:
   a. Failure to adequately monitor child (e.g., not supervising a young child's activities; being insufficiently aware of adolescent's activities).
   b. Marked lack of support of, or active interference in, a key major life activity.
   c. Excessive or inappropriate discipline (not meeting criteria for child abuse).
   d. Excessive pressure on child to engage in a single activity or interest (e.g., sport).
   e. Failure to socialize child through nonexistent or poorly enforced limits.

B. Significant impact on the child involving any of the following:
1) More than inconsequential physical injury.
2) Psychological harm, including either:
   a. More than inconsequential fear reaction.
   b. Psychiatric disorder, at or near diagnostic thresholds related to, or exacerbated by, the caregiving difficulty.
3) Stress-related somatic symptoms (related to or exacerbated by the caregiving difficulty) that significantly interfere with child's normal functioning.
4) Reasonable potential for more than inconsequential physical injury due to the inherent dangerousness of the caregiving difficulty and the child's physical environment
5) Reasonable potential for psychological harm. *Note:* The child's level of functioning and the risk and resilience factors present should be taken into consideration.
   a. Reasonable potential for the development of a psychiatric disorder (at or near diagnostic thresholds) due to the caregiving difficulty.
   b. Reasonable potential for significant disruption of the child's physical, psychological, cognitive, or social development due to the caregiving difficulty.

views of the experts that, despite being generally understandable and containing many key elements of maltreatment, the existing definitions were in need of increased operationalization. Further, regarding the process of decision-making, clinicians reported that extra-definitional issues either influenced the decision-making process or caused the decision-making committee to blatantly overrule the definitions.

Step 2: Conceptualize construct and review existing conceptualizations and operationalizations

In developing the maltreatment criteria, Heyman and Slep (28,29) adopted the DSM-like conceptual framework that partner and child physical and emotional abuse and child neglect would require both a specific type of act (e.g., use of physical force for physical abuse) and a significant impact (or high potential for significant impact, such as shooting a gun at a spouse but not hitting him or her). Because of a presumed risk for significant impact of partner sexual abuse and parent-child sexual abuse, the sexual abuse conceptual framework required only a qualifying act.

Step 3: Comprehensively survey and adapt existing legal, research, and clinical definitions and operationalizations

Step 3 involved creating the maltreatment criteria, based in part on the prior US Department of Defense criteria and on operationalizations in existing legal, research, or clinical definitions that were specific enough to promote reliability. Dozens of civilian and military definitions were comprehensively reviewed, including the following: Child Abuse Prevention and Treatment Act (33); Centers for Disease Control (CDC) partner abuse definitions (34); the Modified Maltreatment Classification System (35,36); international and domestic agencies' definitions of child sexual abuse and related terms, including, among many others, those of the NGO Group for the Convention on the Rights of the Child, Focal Point on the Sexual Exploitation of Children (37); the National Incidence Survey on Child Abuse and Neglect definitions (38); state domestic violence statutes (39); state child abuse statutes (40); the US Department of Defense definitions then in force with their proposed modifications (31,41-43); and definitions for partner maltreatment recommended by the Defense Task Force on Domestic Violence (44).

Step 4: Field tests

The next step (Study 3), a pilot field test at five sites (28), aimed to train clinical staff and other case determination committee members at five sites in the use of these definitions; improve iteratively the operationalizations during the field trial; and compare maltreatment decisions with those of master reviewers (i.e., from the Family Translational Research Group at the State University of New York at Stony Brook and from the headquarters of the Air Force Family Advocacy in San Antonio, Texas).

Agreement between committees and the master reviewers was moderate. Based on monitoring meetings prior to the field trial, Heyman and Slep (28) estimated that committee decisions followed the old definitions approximately 50% of the time. Using the new definitions, however, 76% (κ=.48) of allegations were decided by the base committees the same way as they were by master reviewers (Table 4). Although this represented an improvement, neither 76% agreement nor a Cohen's kappa of .48 could be considered adequate.

For the second field trial, Study 4 (28), several changes were made. First, to make the assessment process consistent across sites and assure that the pertinent information was being assessed, we developed a structured clinical interview that paralleled the diagnostic criteria for each form of family maltreatment. The assessing clinicians were provided with and instructed to use these questions. Second, the then-current committees (comprising primarily service providers)

Table 4 Agreement between field decisions and master reviewers

	Pilot field trial			Field trial 2			Dissemination trial		
Type of maltreatment	**κ**	**Agreement (%)**	**n**	**κ**	**Agreement (%)**	**n**	**κ**	**Agreement (%)**	**n**
Partner maltreatment (all types)	.50	74	143	.81	90	320	.85	92	549
Physical	.50	76	103	.82	91	233	.84	92	435
Emotional	.33	70	40	.76	89	79	.83	93	109
Sexual	-	-	0	.75	88	8	.62	80	5
Child maltreatment (all types)	.49	78	184	.87	94	236	.75	88	342
Physical	.55	80	46	.92	96	76	.82	91	115
Emotional	.24	59	27	.89	96	47	.73	90	60
Sexual	.67	83	12	1.00	100	12	.89	95	19
Neglect	.55	81	99	.80	91	101	.66	84	148
Total cases	.48	76	327	.84	92	556	.82	91	891

seemed to have difficulty weighing criterion-pertinent information only; our US Air Force partners decided to change the composition of who served on the determination board. Third, the presentation of information was drastically altered. The former process (used in the pilot field trial) involved a summary by the clinician who completed the assessment, which often did not straightforwardly present criteria-relevant information. In Study 4, all board members who had pertinent information presented it (e.g., assessing clinician, police, work supervisor). Fourth, votes were cast for each criterion separately, aided by a computer-guided decision matrix that presented the diagnostic decisions to be made.

As shown in Table 4, in 92% of cases (κ = .84), decisions in the field about whether or not maltreatment met or exceeded diagnostic thresholds matched those of master reviewers. This exceptional level of reliability suggested that the refinement of the criteria had been successful.

Step 5: Test diagnostic criteria's use in wide-scale dissemination

Although the second trial involved field-generated decisions under real-world conditions, it was clearly an effectiveness trial and did not speak to the performance of the diagnostic system when disseminated broadly. A dissemination trial of the diagnostic system's use under typical conditions at many sites was necessary. Because the diagnostic system was being disseminated worldwide throughout the organization, we were able to randomly select 41 communities to participate in a trial.

As shown in Table 4, agreement between the field-generated decisions and those of master reviewers remained high. The maintenance of adequate agreement is especially noteworthy, given the relative lack of expertise and training among the majority of those using the diagnostic criteria and the standard-operating-procedure nature of the participating sites (i.e., they were not "special volunteer test sites", as in the effectiveness trial). These results are quite encouraging and suggest that diagnostic systems for relational problems can indeed be reliably applied in real world settings despite the discouraging results in the general DSM literature to date (45-48).

Step 6: Select/create criteria-informed screeners and structured clinical interviews

Because clinical adoption of criteria sets is unlikely without measures to aid in screening and structured assessments, we have developed tools for two-stage screening (i.e., quick questionnaire screeners and a set of structured clinical interviews patterned after the Structured Clinical Interview for DSM-IV Axis I Disorders, SCID-I) for use in clinical practice and research for all eleven forms of relational problems listed earlier. In the coming months, we plan to field test these measures in a clinical setting.

Step 7: Examine the content validity of the final criteria

Currently, we are assessing experts' ratings of the content validity of the eleven proposed criteria sets for relational problems. Initial data from the maltreatment data sets indicated that experts had few recommendations for improvements.

CONCLUSIONS AND RECOMMENDATIONS

Nuanced, multifaceted, and content valid diagnostic criteria for relational problems have been created and can be used reliably in the field even by those with little-to-no clinical training/background. The use of definitions such as these would likely lead to more reliable decision making in the field and more consistency across studies. It is notable not just that field decisions reliably agreed with expert decisions for relational problems, but that this agreement was higher than that usually reported for DSM mental disorders. Although not conclusive, the few studies of DSM diagnoses testing the concordance of field clinicians' diagnoses and

"criterion standard" SCID diagnoses have indicated problematic levels of agreement (49). Basco et al (45) reported poor agreement (κ = .13-.45) between DSM diagnoses given by field clinicians and those by master reviewers using structured interviews (sometimes supplemented with other data sources). Kashner et al (46) reported comparable concordance between clinician's diagnoses and SCID diagnoses (κ = .20-.30), except for diagnoses of severe mental illness (κ = .52-.60). Similarly, a study of psychotic first time inpatients (47) reported decent clinician versus SCID/master reviewer agreement (κ = .51-.73), but only for academic and community hospitals; agreement between clinicians at public hospitals and researchers was poor (κ = .13-.34). Contrast this with the field-decision vs. expert reviewer agreement in the maltreatment dissemination trial (κ = .66-.89 across seven forms of maltreatment; κ = .82 overall).

Although our diagnostic criteria were used reliably and demonstrated content validity, further work is necessary to more firmly establish construct validity. We have begun such studies but do not yet have results that can shed light on the validity of the definitions, bringing relational problems in line with the rest of those in the DSM, for better and worse. The former Director of the National Institute of Mental Health, Steven Hyman, summarized nearly universally recognized sentiments about incompletely and variably validated rationally-derived diagnostic criteria: "If a relative strength of DSM is its focus on reliability, a fundamental weakness lies in problems related to validity. Not only persisting, but looming larger, is the question of whether DSM-IV-TR truly carves nature at the joints – that is, whether the entities described in the manual are truly 'natural kinds' and not arbitrary chimeras" (50). One could add relational problems to the list of reliable rationally-derived diagnoses in search of proof that they are natural kinds, and if they are, that the current criteria optimally distinguish them. Future studies must be conducted to establish the convergent, discriminate, discriminative, and predictive validity of the criteria.

Finally, taxometric methods should be used to investigate if making qualitative distinctions is empirically supportable. Some early work indicates that this is true for partner relational problems (51,52) and has been speculated in many quarters for partner maltreatment (53).

In conclusion, clinically significant behavioral or psychological syndromes or patterns occur between family members and are associated with present distress or disability or with a significant increased risk of suffering death, pain, disability, and important losses of freedom. The literature briefly reviewed above incontrovertibly documents both relational problems' syndromes/patterns and their serious sequelae. Criteria for eleven such relational problems – modeled after current DSM diagnoses – have been developed, along with screener questionnaires and SCID-like structured clinical interviews that operationalize the criteria for each problem. The most studied subset of relational problem criteria – those for partner and child maltreatment – have been shown to have remarkably high levels of reliability when used in the field, at agreement levels never reached by DSM diagnoses for individuals.

Science, service, families, individuals, and the DSM itself, would be well served to include diagnostic criteria for relational problems and to consider the various options for placement of relational problems/processes in the DSM-V.

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Metabolic syndrome in people with schizophrenia: a review

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Metabolic syndrome and other cardiovascular risk factors are highly prevalent in people with schizophrenia. Patients are at risk for premature mortality and overall have limited access to physical health care. In part these cardio-metabolic risk factors are attributable to unhealthy lifestyle, including poor diet and sedentary behaviour. But over recent years it has become apparent that antipsychotic agents can have a negative impact on some of the modifiable risk factors. The psychiatrist needs to be aware of the potential metabolic side effects of antipsychotic medication and to include them in the risk/benefit assessment when choosing a specific antipsychotic. He should also be responsible for the implementation of the necessary screening assessments and referral for treatment of any physical illness. Multidisciplinary assessment of psychiatric and medical conditions is needed. The somatic treatments offered to people with severe and enduring mental illness should be at par with general health care in the non-psychiatrically ill population.

Key words: Metabolic syndrome, schizophrenia, antipsychotics

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People with severe mental illnesses (SMI), such as schizophrenia, have a reduced life expectancy compared to the general population (1-13). They have a 2-3 fold increased risk of dying, and this mortality gap associated with mental illness compared to the general population has widened in recent decades (13). People with severe mental illness have nearly twice the normal risk of dying from cardiovascular disease (CVD) (1-13).

In the psychiatric community, this has led in recent years to a growing concern about physical illness in people with SMI, specifically CVD risk (14-24). People with SMI are more likely to be overweight, to smoke and to have hyperglycaemia/diabetes, hypertension and dyslipidaemia (Table 1). With an overall increased risk of somatic comorbidities, patients with schizophrenia have poorer access and quality of physical health care (7,25-27).

In part these cardio-metabolic risk factors are attributable to unhealthy lifestyle, including poor diet and sedentary behaviour. But over recent years it has become apparent that antipsychotic agents (AP) can have a negative impact on some of the modifiable risk factors (7,14,15-42) (Table 2). Part of this negative impact can be explained by the liability of some antipsychotics to induce significant weight gain. A recent study indicates that these metabolic changes are dose independent (42).

Metabolic syndrome (MetS) brings together a series of abnormal clinical and metabolic findings which are predictive of CVD risk, though there is continuing debate around the use of the term (44-50). The causes of MetS are not fully understood, but there is a central role of visceral adiposity and insulin resistance. The most commonly used definitions for the MetS are the Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program (NCEP) (46), and the adapted ATP III-A proposed by the American Heart Association following the American Diabetes Association lowering of the threshold for impaired fasting glucose to 100 mg/dl (45,47). A more recent definition, by the International Diabetes Federation (45,49), stressed the importance of waist circumference, using both more stringent and ethnic/race specific criteria (Table 3).

In the general population, the presence of MetS is a strong predictor of CVD, CVD mortality and diabetes (50-58).

Table 1 Estimated prevalence and relative risk (RR) of modifiable cardiovascular disease risk factors in schizophrenia and bipolar disorder compared to the general population (from 16)

	Estimated prevalence, % (RR)	
Modifiable risk factors	**Schizophrenia**	**Bipolar disorder**
Obesity	45-55 (1.5-2)	21-49 (1-2)
Smoking	50-80 (2-3)	54-68 (2-3)
Diabetes	10-15 (2)	8-17 (1.5-2)
Hypertension	19-58 (2-3)	35-61 (2-3)
Dyslipidaemia	25-69 (≤5)	23-38 (≤3)
Metabolic syndrome	37-63 (2-3)	30-49 (1.5-2)

Table 2 Second generation antipsychotic agents and metabolic abnormalities (14,41,107-109)

Antipsychotic	Weight gain	Risk for diabetes	Worsening lipid profile
Clozapine	+++	+	+
Olanzapine	+++	+	+
Risperidone	++	?	?
Quetiapine	++	?	?
Aripiprazole	±	No report	No report
Ziprasidone	±	No report	No report
Amisulpride	±	No report	No report

Table 3 Definitions of metabolic syndrome (45-48)

	ATP III (3 out of 5 criteria required)	ATP III A (3 out of 5 criteria required)	IDF (waist plus 2 criteria required)
Waist (cm)	M >102, F >88	M >102, F >88	M ≥94, F ≥80
Blood pressure	≥130/85*	≥130/85*	≥130/85*
HDL (mg/dl)	M <40, F <50	M <40, F <50	M <40, F <50
Triglycerides (≥150 mg/dl)	≥150	≥150	≥150
Glucose (mg/dl)	≥110**	≥100**	≥100**

ATP – Adult Treatment Protocol; IDF – International Diabetes Federation
*or treated with antihypertensive medication; **or treated with insulin or hypoglycaemic medication.

A joint statement from the American Diabetes Association and the European Association for the Study of Diabetes concluded recently that the metabolic syndrome has been imprecisely defined, there is a lack of certainty regarding its pathogenesis, and there is considerable doubt regarding its value as a CVD risk marker. They recommended that, until further research has been carried out, clinicians should evaluate and treat all CVD risk factors whether or not patients meet the criteria for diagnosis of the MetS (59,60).

The concept of MetS has found its way into the psychiatric literature, helping psychiatric clinicians to focus more on CVD risk in patients treated with antipsychotics (34,35,61).

We conducted a systematic review on the prevalence and incidence of metabolic syndrome in patients suffering from schizophrenia. A literature search for relevant articles was carried out in two steps. First, articles published until August 1, 2008 were identified by PubMed search, using metabolic syndrome, antipsychotic(s), psychotic disorder and schizophrenia as key words. Second, a hand search was conducted based on the bibliography of the identified articles.

Since the first paper on MetS in patients with schizophrenia published in 2003, more than 30 studies have become available. Prevalence and incidence studies using different MetS criteria are shown in Tables 4 and 5 (62-99). Studies in different ethnic groups consistently show elevated prevalences of MetS in patients with schizophrenia. If population comparison data are available, the rates of MetS are 2 to 3 fold higher in patients. In studies where a comparison was possible between antipsychotic medications, a differential relative metabolic risk between agents was confirmed.

In the largest study, the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), approximately one third of patients met NCEP criteria for metabolic syndrome at baseline (82,83). A troubling finding was that 88% of patients with dyslipidaemia were not receiving treatment, as were 62% of the hypertensive patients and 38% of those with diabetes (100). Some antipsychotic agents were associated with more significant adverse effects on weight, lipids, and glucose metabolism than others (25,41,84).

A large Belgian study found similar rates of MetS, which were 2 to 3 fold higher than in an age-adjusted population sample (71,72). The prevalence of diabetes per age-band was 4-5 times higher in schizophrenia patients than in the general population.

In a recent study of metabolic syndrome in patients diagnosed with schizophrenia in 2000-2006 compared to 1984-1995, those started on second generation antipsychotics (SGA) had over twice the rate of new incident cases of metabolic syndrome after three years, compared to those treated with first generation antipsychotic agents (27.8% vs. 9.8%) (73). In patients without metabolic syndrome at baseline, the risk of developing this combination of metabolic abnormalities was significantly greater in patients started on SGA (odds ratio 3.6).

For the increased risk of MetS and other metabolic abnormalities in patients with schizophrenia, three complementary and partially overlapping causes are put forward in the literature: lifestyle factors, aspects of the psychotic disorder and antipsychotic medication. A number of recent studies explore the underlying genetic risk for the development of metabolic abnormalities (76,85,101). Future studies will need to address possible gene-environment interactions with specific antipsychotic agents (101).

People with schizophrenia on average have a lifestyle which increases their risk for the development of MetS: sedentary lifestyle, lack of regular physical activity, poor food intake, substance use and high rates of smoking (25,38,39). Part of these lifestyle factors are influenced by aspects of the illness such as negative symptoms and vulnerability to stress. Older studies have showed an increased liability for people with schizophrenia to develop metabolic abnormalities in the absence of antipsychotic medication, and there are indications of an increased risk for diabetes in first-degree relatives (21,25,39). Also, some studies have showed increased visceral adiposity, elevated glycaemia and higher cortisol levels in first-episode patients before treatment (25,40,41). A recent study showed that people with schizoaffective disorder have a higher vulnerability to develop MetS compared to people with bipolar disorder or schizophrenia (99).

The increased risk to develop MetS under antipsychotic agents is in part related to their propensity to induce weight gain. Although all antipsychotics can induce weight changes, the relative risk to induce clinically relevant weight changes (>7% increase) is clearly different between antipsychotic agents (25,29,31). In up to 25% of cases of MetS under antipsychotic treatment, no weight gain or increased abdominal adiposity was present, suggesting a direct link between

Table 4 Prevalence of metabolic syndrome (MetS) in people with schizophrenia

Study	Country	N	Design	Mean age	% MetS	Criteria
Heiskanen et al (78)	Finland	35		44.5	37.1	ATP III
Almeras et al (62)	Canada	42	Olanzapine	31.7	33.0	ATP III
	Canada	45	Risperidone	28.4	11.0	ATP III
Basu et al (65)	USA	33	Schizoaffective disorder	44.5	42.4	ATP III
Cohn et al (68)	Canada	240		42.7	44.6	ATP III
Kato et al (80)	USA	48		40.3	63.0	ATP III
Straker et al (96)	USA	89		39.8	29.2	ATP III
Meyer et al (83)	USA	1231		42.8	35.8	ATP III
McEvoy et al (82)	USA	342	White males	39.8	40.9	ATP III
		92	White females	44.2	56.2	ATP III
Saari et al (88)	Finland	31		31.0	19.4	ATP III
Correll et al (69)	USA	367		42.9	37.3	ATP III
De Hert et al (71)	Belgium	430		36.5	32.3	ATP III-A
De Hert et al (72)	Belgium	415		37.7	33.3	IDF
		100	First episode (maximal duration 2 year illness)	25.7	17.0	IDF
		130	Duration illness <10 years	29.0	28.5	IDF
		106	Duration illness 10 to 20 years	39.0	42.4	IDF
		79	Duration illness >20 years	49.8	49.4	IDF
Hagg et al (77)	Sweden	269		46.0	34.6	ATP III
Lamberti et al (81)	USA	93	Clozapine	34.4	53.8	ATP III
Meyer et al (84)	USA	80		49.0	51.2	ATP III
Bobes et al (66)	Spain	1452		40.7	24.6	ATP III
Correll et al (70)	USA	294	Antipsychotic monotherapy	43.6	34.3	ATP III
De Hert et al (73)	Belgium	208	3 months after start antipsychotics	33.7	27.9	ATP III-A
		23	3 months after start amisulpride	33.7	13.0	ATP III-A
		31	3 months after start aripiprazole	33.7	9.7	ATP III-A
		25	3 months after start clozapine	33.7	56.0	ATP III-A
		54	3 months after start olanzapine	33.7	33.3	ATP III-A
		25	3 months after start quetiapine	33.7	32.0	ATP III-A
		50	3 months after start risperidone	33.7	24.0	ATP III-A
L'Italien et al (79)	USA	155	Placebo trials, placebo endpoint	41.4	25.8	ATP III
		267	Placebo trials, aripiprazole endpoint	40.7	19.9	ATP III
		373	Active comparator trials, olanzapine endpoint	37.7	41.6	ATP III
		380	Active comparator trials, aripiprazole endpoint	37.6	27.9	ATP III
Mulder et al (85)	Netherlands	112		36.0	25.0	ATP III
Sicras-Mainar et al (94)	Spain	742	Different diagnosis treated with antipsychotics	55.1	27.0	ATP III
		57		37.5	35.0	IDF
Srisurapanont et al (95)	Thailand	38		53.7	36.2	ATP III
		44		44.3	31.8	ATP III-A
Suvisaari et al (97)	Finland	108		34.6	34.0	ATP III-A
Teixeira and Rocha (98)	Brazil	122	First episode, before treatment with FGA	23.1	5.7	ATP III-A
		122	First episode, 3 year FGA	26.8	13.1	ATP III-A
Cerit et al (67)	Turkey	108	First episode, before treatment with SGA	21.9	5.6	ATP III-A
De Hert et al (74)	Belgium	108	First episode, 3 year SGA	25.1	31.6	ATP III-A
		2270		41.0	33.9	ATP III-A
De Hert et al (75)	Europe	58		36.3	40.0	ATP III-A
Ellingrod et al (76)	USA	99	First episode after treatment	26.1	18.2	IDF
Saddichha et al (90)	India	433		38.0	34.0	ATP III
Schorr et al (91)	Netherlands	53		35.0	45.0	ATP III
Schorr et al (92)	Netherlands	260		28.0	35.0	ATP III
Schorr et al (93)	Netherlands	503	Schizophrenia	34.8	28.8	ATP III-A
van Winkel et al (99)	Belgium	92	Schizoaffective disorder	40.7	50.0	ATP III-A

FGA – first-generation antipsychotic; SGA – second generation antipsychotic; ATP - Adult Treatment Panel; IDF - International Diabets Federation

the antipsychotic agent and the development of metabolic abnormalities (25). Some authors link the receptor profile of antipsychotics to their differential liability to induce weight gain and other metabolic changes (25,29,33,41). Antagonism for muscarinergic receptors could lead to more pronounced weight gain. Antipsychotics can lead to increased appetite by interfering with the dopamine reward system (32). There is emerging data that glucose abnormalities can occur soon after initiation of treatment and that these can be reversible after discontinuation of medication, indicating a direct effect on pancreatic function (25,38, 39,42).

Growing evidence suggests that children and adolescents who take antipsychotic medication are at higher risk of weight gain and metabolic effects than adults who use the same drugs (102-104).

Table 5 Incidence of metabolic syndrome (MetS) in people with schizophrenia

Study	Country	N	Design	Mean age	% MetS	Criteria
De Hert et al (71)	Belgium	31	Baseline aripiprazole	36.7	61.3	ATP III-A
			Endpoint aripiprazole	36.7	29.0	ATP III-A
Attux et al (64)	Brazil	44	First episode 6 months	26.3	6.8	ATP III
De Hert et al (73)	Belgium	155	After 3 months SGA	33.7	18.7	ATP III-A
		16	After 3 months amisulpride	33.7	6.3	ATP III-A
		16	After 3 months aripiprazole	33.7	0.0	ATP III-A
		20	After 3 months clozapine	33.7	45.0	ATP III-A
		45	After 3 months olanzapine	33.7	24.4	ATP III-A
		21	After 3 months quetiapine	33.7	19.1	ATP III-A
		37	After 3 months risperidone	33.7	10.8	ATP III-A
L'Italien et al (79)	USA	91	Placebo trials, placebo	41.4	14.3	ATP III
		151	Placebo trials, aripiprazole	40.7	5.3	ATP III
		212	Active comparator trials, olanzapine	37.7	27.4	ATP III
		198	Active comparator trials, aripiprazole	37.6	15.7	ATP III
Saddichha et al (89)	India	30	First episode 6 weeks	26.9	27.5	IDF
Srisurapanont et al (95)	Thailand	35	Naturalistic 1 year follow-up	34.7	20.0	IDF
De Hert et al (74)	Belgium	122	First episode, 3 year FGA	26.8	9.8	ATP III-A
		108	First episode, 3 year SGA	25.1	27.8	ATP III-A
		8	First episode, 3 year amisulpride	25.1	12.5	ATP III-A
		10	First episode, 3 year aripiprazole	25.1	0.0	ATP III-A
		12	First episode, 3 year clozapine	25.1	50.0	ATP III-A
		34	First episode, 3 year olanzapine	25.1	41.3	ATP III-A
		24	First episode, 3 year quetiapine	25.1	12.6	ATP III-A
		20	First episode, 3 year risperidone	25.1	10.2	ATP III-A
Meyer et al (84)	USA	164	Baseline olanzapine	40.9	34.8	ATP III-A
			After 3 months olanzapine	40.9	43.9	ATP III-A
		147	Baseline risperidone	40.9	30.6	ATP III-A
			After 3 months risperidone	40.9	30.6	ATP III-A
		143	Baseline quetiapine	40.9	37.8	ATP III-A
			After 3 months quetiapine	40.9	37.1	ATP III-A
		77	Baseline ziprasidone	40.9	37.7	ATP III-A
			After 3 months ziprasidone	40.9	29.9	ATP III-A
		129	Baseline perphenazine	40.9	37.2	ATP III-A
			After 3 months perphenazine	40.9	38.0	ATP III-A
Schorr et al (93)	Netherlands	260	12 months incidence	41.0	14.0	ATP III
			12 months reversibility	37.0	33.0	ATP III

FGA – first-generation antipsychotic; SGA – second generation antipsychotic; ATP - Adult Treatment Panel; IDF - International Diabetes Federation

GUIDELINES FOR SCREENING AND MONITORING

Prevention should be key. Clinicians should take into account both the present CVD risk as well as the metabolic risk profile of the antipsychotic chosen. To avoid weight gain, diet and lifestyle interventions should be started early after treatment initiation.

Despite the risks, many patients with SMI have limited access to general healthcare, with less opportunity for cardiovascular risk screening and prevention than would be expected in a non-psychiatric population (7,25-27). There is a lack of consensus over who should take responsibility for the general healthcare needs of mental health patients, which has resulted in a continuing failure to provide appropriate services. General health care needs in this population are commonly neglected and psychiatrists mainly focus on efficacy of treatment of psychotic symptoms.

Over recent years, both national and international groups have developed screening and monitoring guidelines (14,105-112), but these have not made their way to routine clinical care for patients (113,114).

Before start of treatment, the cardio-metabolic risk profile of a patient should be assessed. At the start of treatment, patients should be closely monitored for the relevant metabolic parameters. An easy screening tool for MetS is the measurement of waist circumference in combination with fasting glucose (sensitivity 100%) (96).

Lifestyle interventions, with diet, increased physical activity and smoking cessation, are the first-line treatments to decrease the risk for CVD in people with MetS (8). The Adult Treatment Panel guidelines recommend a reduced intake of saturated fat and cholesterol, increased intake of fibres and increased physical activity (46). A reduction of 10% of cholesterol levels results in a 30% reduction of CVD risk. A lowering of blood pressure of 4 to 6% decreases CVD risk 15%. Smoking cessation would result in a 50 to 70% lowering of CVD prevalence. Maintaining a body mass index below 25 lowers CVD risk 35 to 55%, and having active lifestyle (20 minutes brisk walk a day) results in a similar decrease of risk (8). These data also apply for people with severe mental illness, but no studies are available that confirm that short-term beneficial effects of lifestyle interventions result in long-term

changes (115,116). However, there is growing evidence that lifestyle interventions can be effective for groups of patients with schizophrenia.

There is a general consensus that physical activity has a mild to moderate favorable effect on many metabolic and cardiovascular risk factors that constitute or are related to the MetS (117). Regular physical activity is effective in prevention and treatment of hypertension (118,119), obesity (120), impaired glucose tolerance and diabetes (121) and dyslipidaemia (122). Therefore, it should be an important component in multidisciplinary programs for people with schizophrenia. At the moment, identifying an optimal dose or intervention strategy for physical activity programs in people who have schizophrenia is not possible (123). The current guidelines for the general population of accumulating 30 min of moderate lifestyle physical activity, five days a week (124) should also be applied to people who have schizophrenia. Compliance with these guidelines appears to markedly decrease the likelihood of MetS especially in high risk groups (117). In physical activity related treatment programs for people who have schizophrenia, special attention could be given to the specific cardio-metabolic comorbidities by using the physical activity recommendations for chronic somatic diseases (125). A physical activity program should be adapted to the patients' previous experiences, their attitude towards physical activity, their personal preferences and objectives.

If a patient develops metabolic abnormalities (e.g., weight gain, increased blood pressure, glucose or lipid levels) following initiation of antipsychotic therapy, consideration should be given to switching the patients to an SGA which has not been associated with significant weight gain or diabetes. Initiation of appropriate blood pressure, glucose or lipid lowering therapy should also be considered, in consultation with the patient's general practitioner when that is possible, or with a specialist physician when this is considered appropriate. Until recently, there was no data on the safety and efficacy of statins in patients also exposed to antipsychotics. In patients with schizophrenia, statins were an effective and safe treatment for severe dyslipidaemia but they did not succeed in reversing MetS (126, 127).

A European current update of screening and monitoring guidance is being produced (128,129) and an update of the ADA/APA 2004 consensus document is expected to be published this year (14).

CONCLUSIONS

MetS and other CVD risk factors are highly prevalent in people with SMI. The psychiatrist needs to be aware of the potential metabolic side effects of antipsychotic medication and to include them in the risk/benefit assessment when choosing a specific antipsychotic. He should also be responsible for the implementation of the necessary screening assessments and referral for treatment of any physical illness. Multidisciplinary assessment of psychiatric and medical conditions is needed. Psychiatric treatment facilities should offer and promote healthy lifestyle interventions. The somatic treatments offered to people with severe and enduring mental illness should be at par with general health care in the non-psychiatrically ill population.

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Effectiveness as an outcome measure for treatment trials in psychiatry

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There is at present some confusion about the relative value of clinical trials performed to investigate efficacy vs. those designed to investigate effectiveness. This is particularly challenging when studies performed as experiments for regulators by companies are used to shape and inform clinical practice, especially if studies conducted under more real life conditions fail to support predicted benefits. We review the field in relation to the new antipsychotics, in particular. Other indications, including mood disorders, which are also briefly touched upon, have so far received less definitive attention, but are likely to encounter the same difficulties. We conclude that, where the results of efficacy trials are positive and an effectiveness trial is negative, one should not necessarily prefer the effectiveness trial – it may simply have failed. Where efficacy trials and effectiveness trials point to similar conclusions, then the findings are mutually supportive.

Key words: Clinical trials, methodology, schizophrenia, mood disorders, bipolar disorder, depression, antipsychotics, antidepressants, mood stabilizers, efficacy, effectiveness, pragmatic trials

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In recent years, our field has experienced a growing difficulty in translating the results of randomized controlled clinical trials (RCTs) into clinical practice concerning the clinical usefulness of new medications for the treatment of schizophrenia and mood disorders. This difficulty has been accentuated by the fact that meta-analyses and systematic reviews have often delivered discrepant messages. For instance, Leucht et al (1), following a meta-analysis of RCTs comparing first-generation to second-generation antipsychotics, concluded that "risperidone and olanzapine are more effective than haloperidol against global symptomatology and negative symptoms" and that all tested second-generation antipsychotics cause less extrapyramidal symptoms and lead to lower use of anticholinergics. However, analysing more or less the same data set, Geddes et al (2) came to the conclusion that "there is no clear evidence that atypical antipsychotics are more effective or are better tolerated than conventional antipsychotics". Davis et al (3), analysing data from 142 studies, suggested that some second-generation antipsychotics but not others show superior efficacy over the traditional medications, while Tandon and Fleischhacker (4), on the basis of a qualitative review of the available evidence, concluded that "meta-analytic studies of the comparative efficacy of non-clozapine second-generation antipsychotics do not provide undisputed evidence of differential efficacy".

For mood disorders, the controversy has been especially about the drug-placebo difference in efficacy trials of antidepressants (5), with media hype presenting the conclusion that these drugs are no more effective than sugar pills in unipolar depression. The issue in common with the antipsychotic debate has been the extrapolation to everyday practice of studies completed in rather artificial circumstances for regulatory purposes.

Clearly, these publications have provided conclusions which could be read as being mutually contradictory. The field has been therefore challenged to find reasons behind these discrepancies and remedies which would improve the usefulness of clinical trials for everyday practice.

Patient selection has been identified as one of the main culprits for discrepant findings. Clinical trials of antipsychotics in schizophrenia patients have included highly selected patient populations (6-8), not truly representative of the patients these drugs would be used for in ordinary practice. Increasingly large drop-out rates in RCTs, sometimes linked to specific methodologies (9), have called into question analyses which in one way or another must impute results for missing values, and jeopardized simple conclusions – for example that a single treatment is likely to be effective in treating the target condition. The latter is difficult to claim when almost half the patients in the active arm of a three week trial of mania may fail to complete it. Furthermore, it has been questioned whether the traditional outcome criteria, such as improvements on the total score of rating scales measuring psychopathological symptoms, have ecological validity for true patient outcomes (10,11).

The same problems are even more pronounced for trials in depression. Many patients entering RCTs for depression are attracted by advertisement and may be paid to participate. This is most notably true in the United States, where many such trials have been completed. Moreover, inflation of the depression ratings required for entry is widely believed to occur and so confound subsequent effects attributed either to active treatment or placebo (5).

This discontent has brought the concept of effectiveness into play. Effectiveness studies aim to include an unselected or less selected group of patients by using broad inclusion criteria and few reasons for exclusion. Simple trial methodology may be employed to keep

drop-out rates low. Rather than measuring the effects of therapeutic interventions on fairly specific outcomes in psychopathology, effectiveness studies aspire to measure something more tangible. In the case of large scale trials in cardiovascular medicine, the outcome is often death. In psychiatry, death is too rare an outcome to consider, but admission to hospital or drug discontinuation are regarded as clinically relevant outcomes. In slight defiance of the impulse to measure hard outcomes, there is also a parallel desire to find outcomes relative to the patient experience – often subsumed under the clichéd term "quality of life". Moreover, there are pressures to include an economic evaluation of treatment choices. All of this is geared towards producing results which can be translated into everyday clinical practice, but it also sounds deceptively straightforward.

In the following sections, we will provide some examples of large pragmatic clinical trials in patients suffering from schizophrenia and mood disorders and thereafter discuss the pros and cons of effectiveness studies vis-a-vis traditional RCTs.

EFFECTIVENESS TRIALS IN SCHIZOPHRENIA

Various effectiveness trials in schizophrenia have been performed over the last decade. We focus on studies which have been carried out in large scale samples. Both blinded and open trials are reviewed, provided they have used random treatment allocation. We regard this random allocation, with adequate control and concealment of the allocation process, as the key property allowing fair comparison between two treatments.

Clinical Antipsychotic Trials in Intervention Effectiveness (CATIE)

The CATIE was a clinical trial sponsored by the US National Institute of Mental Health (NIMH) following a bid for a research contract. This large pragmatic trial included three phases. In the first, five new generation antipsychotics were compared to the first generation drug perphenazine. After phase I, patients had the option to switch into two different arms of phase II. One was originally planned to compare clozapine to other new-generation antipsychotics in patients found treatment resistant in phase I, and the other one to include patients who had tolerability problems. Treatment allocation in phase I and II was randomized and double blind, with the exception of the clozapine arm. Following phase II, patients could be switched to open treatment trials of various older or newer antipsychotics. All cause discontinuation was the primary treatment outcome measure (12).

In some way this represents a hybrid methodology, as inclusion criteria and outcome measures followed an effectiveness principle, while the rest of the trial design was that of a traditional RCT. Moreover, this type of staged design may encourage early treatment discontinuation in phase I, as it allows graduation into a second phase of the investigation.

Several papers providing results of phases I and II and more specific treatment outcomes have been published (13-15). With the exception of a significantly lower all cause discontinuation rate with olanzapine, second-generation antipsychotics had no efficacy advantages over perphenazine in any of the analyses published so far. Perphenazine was chosen for pragmatic reasons, to increase the sense of equipoise. A more typical drug such as haloperidol was judged not to be a feasible choice, because of the preconceptions of patients and investigators. It was commented that perphenazine was chosen "because of its lower potency and moderate side-effect profile". Whether it fairly represented the classical antipsychotic group is open to doubt.

Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study (CUtLASS)

This study, sponsored by the UK National Health Services, also attempted to compare the effectiveness of newer to older antipsychotics. Clinicians who wanted to enter a patient into this study had to decide at first whether patients had been resistant to previous treatments (in which case they were entered into an arm comparing clozapine to other new-generation antipsychotics) or whether a switch was indicated for other reasons (in which case they were randomly assigned to receive either a first- or a second-generation antipsychotic). Within those two medication groups, clinicians were free to choose the drug of their preference. Quality of life was chosen to be the primary outcome measure.

By the end of this one year open study, clozapine was found to be advantageous over other second-generation drugs in the treatment resistant arm, while there was no advantage of second-generation antipsychotics (46% had been treated with olanzapine) compared to the group of older medications (49% of patients had received sulpiride in this group) (16,17). Pharmacologically speaking, the inclusion and excessive representation of sulpiride in the "first-generation" treatment arm is unhelpful. Sulpiride is pharmacologically very close to amisulpiride, which was included in the second-generation group. This decision in part may have reflected recruitment difficulty, and indeed the trial did not reach its pre-defined recruitment targets. The reason for this was probably a failure of equipoise. The perception of clinicians may have favoured "atypicals" and it was difficult to persuade clinicians to use the older (and more "typical") antipsychotics.

The failure to detect a contrast between first- and second-generation drugs hence becomes questionable. Moreover, the patients entered the study as a consequence of the need to change medication, so potentially selecting patients who were either less responsive (18) or more intolerant of medication (or both).

Comparison of Atypicals in First Episode of psychosis (CAFE)

All cause discontinuation was the primary outcome measure in this dou-

ble-blind clinical trial comparing quetiapine to risperidone and olanzapine (19). Discontinuation rates were high in all three groups, but did not differ from each other. This was also true for changes in scores on the Positive and Negative Syndrome Scale (PANSS). As in the CATIE, olanzapine led to a higher prevalence of weight gain.

European First Episode Study in Schizophrenia (EUFEST)

This one year randomized yet unblinded study, conducted in 13 European countries and Israel, studied the effectiveness of the new-generation antipsychotics amisulpride, quetiapine, olanzapine and ziprasidone in comparison to low-dose haloperidol in patients with a first episode of schizophrenia (20). Loss of retention on the drug to which the patients were originally randomized was the primary outcome. All new-generation drugs performed better than haloperidol. In addition, even a low dose of haloperidol produced more extrapyramidal side effects than the newer agents. The PANSS total scores, one of the secondary outcomes, were not different between groups (21). However, the PANSS scores was measured less often than other outcomes.

The findings of the EUFEST contradict the conclusions often claimed for the CATIE and the CUtLASS – that the atypicals show no important advantage over the older compounds. Low-dose haloperidol was less acceptable than second-generation medications and translated into significantly shorter treatment adherence in first-episode patients. The atypicals in both the CATIE and the EUFEST behaved differently in relation to each other, and do not appear to be equivalent at the doses employed. The comparison with perphenazine in the CATIE, and of one heterogeneous group of compounds with another in the CUtLASS, limits the conclusions that can be reached from these studies.

It needs to be clear that naturalistic clinical trials also reflect naturalistic treatment practice, which may not always follow generally accepted evidence and guidelines. For instance, in the CATIE, only about 40% of all patients in phase I received the maximally allowed doses. On the other hand, pragmatic studies which allow researchers more leeway in including patients and modifying treatment are advantageous for improving retention rates, as exemplified by the CUtLASS and the EUFEST. Blinding also has an impact upon discontinuation rates: in general, higher drop-out rates are encountered in double-blind studies, such as the CATIE and the CAFE.

EFFECTIVENESS TRIALS IN MOOD DISORDERS

Sequenced Treatment Alternatives to Relieve Depression (STAR*D)

The STAR*D did not address efficacy of an antidepressant against a comparator in its initial stage. Instead, all participants were treated with a single selective serotonin reuptake inhibitor, citalopram, and outcomes were systematically determined for over 2000 unipolar patients with a major depressive episode.

Overall, remission rates were probably lower than expected, and the side effect burden higher. Thirty percent of subjects obtained remission and the time required was over 8 weeks. Sub-group analysis was useful in suggesting particular efficacy for women with strong personal backgrounds of achievement. The poorest outcomes were in those patients with longer index episodes, more concurrent psychiatric disorders (especially anxiety disorders or drug abuse), more general medical disorders, lower baseline function and quality of life (18).

The original intention of the STAR*D was to compare strategies of treatment after monotherapy with citalopram had been judged insufficient. Unfortunately, a too permissive approach to patient choice resulted in a disappointing rate of true randomization to competing treatments. After failure on citalopram, level 2 options in STAR*D were a switch to another medication (bupropion, sertraline or venlafaxine) or cognitive therapy, or augmentation of citalopram with bupropion, buspirone or cognitive therapy. Only 21 of 1439 patients accepted to be randomized to any of these options. The vast majority had preferences that were allowed in the study design. Thus, comparisons between augmentation and switch strategies were of great clinical interest, but were subverted by allowing patient preference for one of these approaches. About 30% of patients in all groups treated with medication remitted after change in treatment, whatever the type (22,23). The rate for cognitive therapy was substantially lower (but not statistically different because of lack of power) (24). Further steps in the treatment algorithm suffered from falling numbers, and most outcomes were not statistically discriminable one from another.

There are conflicting interpretations of the STAR*D programme. Nihilists will say that we have learned nothing from it. Optimists claim that the treatment strategies showed reasonable overall remission rates if the algorithm was followed. Whether this represented an improvement on real life treatment could not be decided. The strengths of the study were the sample size and some preliminary pharmacogenetic findings.

Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD)

The STEP programme was a major effort, in parallel with the STAR*D, to examine a variety of treatment pathways for bipolar patients. Of the five proposed trials, only that enrolling depressed bipolar patients yielded useful randomized results. The acute depression study addressed in 366 patients the response to adding antidepressants or placebo to ongoing mood stabilizers (in practice this was very liberally interpreted and almost any non-antidepressant co-medication was permitted). The findings were negative, with no evidence for remission (or for switch to mania) occurring preferentially in the antidepressant arm (25).

The result can be interpreted either as a negative study (antidepressants do not

work in bipolar depression) or a failed study (we do not know if antidepressants work in bipolar depression). In the absence of a positive control treatment, the answer remains moot. A lesson from the antidepressant study of STEP-BD is perhaps not to combine the inexactitude of real life with the unreality (placebo) of the regulatory trial.

Bipolar Affective disorder: Lithium/ Anticonvulsant Evaluation (BALANCE)

The BALANCE is a study completing in mid 2008 to compare the combination of lithium plus valproate (as Depakote) with lithium or valproate monotherapy. The question it was designed to address was the superiority of combination treatment over monotherapy in the long-term treatment of bipolar disorder. This was felt to have generic value in bipolar disorder, because combination of different medicines for long-term treatment has become very common, although almost unsupported by independent evidence of benefit. Secondarily, the study was designed to compare lithium with valproate as monotherapy.

The study was initially intended to assess re-admission as the primary outcome, but the size of the sample required would have been very large (over 1000 participants) and, in the absence of adequate funding, recruitment was likely to take too long. In fact, successful placebo controlled studies of lamotrigine (25,26) and the lessons of the failed study of valproate (27) (which had planned to use re-admission as primary end-point also), resulted in a rethink and the adoption of time to intervention for a new mood episode as the primary outcome. Final recruitment numbers were over 400, with 330 successfully randomized. The study outcomes will be analysed later in 2008. Event rates are compatible with adequate assay sensitivity.

Like the EUFEST, the BALANCE was a randomized open study. This conserves the primary advantage of any RCT: random and concealed allocation to different treatments. However, clinician or patient bias could contaminate the study. In practice, a significant run-in on combination therapy helped to protect the study from poor adherence and to some extent mitigated against bias for or against a particular treatment. Nevertheless, treatment could have been driven in part by bias, especially for early interventions. These factors will limit but not invalidate the findings of the study, since the absence of a blind is obviously closer to real clinical practice. In particular, we are not convinced that a single prevailing bias against any one of the study treatments could be detected among participating clinicians or patients.

DISCUSSION

When balancing the merits of efficacy and effectiveness studies, one will have to weigh the advantages of studying well-defined homogeneous patient samples with state-of-the-art double-blind methodology against obtaining data closer to everyday clinical practice. This means recruiting more representative samples and using potentially more relevant outcome measures. But it also means, when unblinded as in normal practice, risking bias from patients and clinicians who determine the outcomes. As open, unblinded studies are always at risk for observer bias, this disadvantage needs to be balanced against the fact that generalizability of results is higher with lower drop-out rates. From a methodological perspective, randomization appears to be a *condicio sine qua non* if one chooses to compromise for an unblinded study.

The definition of relevant outcome measures has also been a source of heated debate. On the one hand, it is argued that all cause discontinuation, even if split into discontinuation due to lack of efficacy, tolerability issues or patient choice, is an unsophisticated and crude outcome measure. On the other, it can be argued that a minor change in PANSS total scores or even more specific factors of a rating scale may only be of marginal clinical relevance.

There is a kind of uncertainty principle at work here. The more rigorous and controlled an experiment, the more confident we become of the treatment effect, but the less a trial corresponds to real life; the closer to real life an effectiveness study becomes, the less it offers confidence of efficacy. In principle, we believe that both kinds of study are desirable, but always together, not as alternatives. Moreover, we are most secure when both types of study indicate similar directions of effect.

CONCLUSIONS

When considering all evidence available to date, we suggest that both the experimental RCT and the more pragmatic effectiveness design have an important place in clinical psychopharmacology. Ideally, drug development, after an exploratory phase I, which more and more includes patients, at risk samples or healthy volunteers in proof of concept studies, will proceed with blinded well-controlled studies with rigorously defined outcomes. Such studies can demonstrate efficacy, but the magnitude of the benefit cannot be simply extrapolated to real life.

Results from these phase II and III studies should then be complemented, perhaps as early as phase IIIb, by larger pragmatic clinical trials. Such trials must be designed to ask the key pragmatic clinical questions in the patient population at large. In the examples we have considered, this could range from head-to-head comparability with earlier generation compounds to use in combination with other drugs or psychological interventions. Very complex designs reduce the acceptability of trials to patients (and investigators). Moreover, all pragmatic studies need to be undertaken before extensive marketing of new compounds has occurred and opinions about them have already hardened in the minds of investigators. We believe that the licensing of new drugs currently seems to demand too much (and increasing) evidence from early stage trials of poor generalizability. A provisional licence harnessed to the implementation of large scale clinical trials might meet some of the needs we perceive for the development of new medicines.

Effectiveness studies need to be planned using key properties of clinical trial methodology, namely randomization and concealment of allocation. They will be assured by statistical planning, clear *a priori* hypotheses and necessary good clinical practice standards. Reporting of adverse events in such trials could provide early indications of unexpected problems with safety. Employing these trial designs earlier in drug development may diffuse some of the controversy around the applicability to ordinary practice of trials completed for drug registration and also allow for a quicker appreciation of a drug's usefulness in meeting real clinical needs.

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Clinical trial design: horses for courses

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Fleischhacker and Goodwin contribute to the ongoing debate around the relative value of so-called "efficacy" and "effectiveness" trials. Comparisons between trials need to take into account the fact that different trials are designed to answer different clinical questions and that methodological choices inevitably involve compromises (1,2). Various approaches to describing the different priorities, and designs, of clinical trials have been suggested: e.g., explanatory vs. pragmatic (3), practical vs. large simple vs. efficacy (2) and large simple vs. small complex (4).

Explanatory ("efficacy") trial designs tend to have a greater degree of control over internal validity and a higher signal-to-noise ratio, but will typically tend to sacrifice external validity (i.e., applicability to real world patients) (3,5). The aim of explanatory trials is to determine if the experimental intervention *can* work in controlled, optimized, circumstances (6). By contrast, the objective of more pragmatic ("effectiveness") trials is to determine if the intervention *does* work in the real world of clinical practice, which is, almost by definition, a more noisy and less controlled environment. While pragmatic trials include less selected and more representative patients and clinical sites and use less standardized, more routine, measure of clinical outcomes, the design compromises inherent in effectiveness trials will tend to increase variability (and hence statistical noise) and, frequently, bias.

Fleischhacker and Goodwin are right, therefore, to highlight the problem that arises when there appears to be a discrepancy between the results of explanatory and more pragmatic trials. Are the explanatory or the pragmatic trial(s) intrinsically more reliable and likely to produce a closer estimate of the "true" effect of the investigational agent? This question is chimerical. In fact, the vast majority of trials lie on a continuum between idealised explanatory and pragmatic designs. Every trial needs to be critically appraised on its own merits for likely sources of bias and noise.

Fleischhacker and Goodwin consider that randomisation with adequate concealment of allocation is the *sine qua non* of a fair comparison of two (or more) treatments. However, empirical studies suggest that other design characteristics, such as blinding, can also have substantial effects on the chances of a trial producing an unbiased result (7). Indeed, for trials with subjectively assessed outcomes, absence of blinding seems to be as important a cause of bias as inadequate allocation concealment (8). Lack of blinding can lead to both *performance bias* (knowledge of allocation leads to systematically different behaviour of physician and patient) and *ascertainment bias* (knowledge of allocation leads to systematically different assessment of outcomes between treatment and control groups). One might predict that blinding will be particularly important when both the possibility and the likelihood of these biases is high. This will be the case when behaviour and outcomes are easily modifiable and when true equipoise is absent and the investigator and/or participants have clear preferences between the compared treatments.

A good example of the need to take the designs of individual trials into account is provided by the trials comparing first generation (FGAs) with second generation antipsychotics (SGAs). By way of context, there was considerable hope that SGAs would provide a substantial step forward in the treatment of schizophrenia. This led to an early tendency to overlook the methodological limitations of the industry conducted trials (which were towards the explanatory end of the design spectrum) (9), to overrate the advantages of the SGAs (10) and for a rapid clinical shift to using SGAs in preference to FGAs (11). Systematic reviews and meta-analyses of the industry-sponsored trials essentially found similar results (12-14), although the authors of one of the reviews drew notably more favourable conclusions concerning SGAs than the others (14,15).

A number of non-industry randomised controlled trials comparing FGAs and SGAs have now been reported (16-19). This number of independent trials is unusual in psychiatry: it is both a critically important development and a reflection of the rare degree of continuing uncertainty and importance of this issue. Taken as a group, these independent trials seem to indicate that, although there may be minor differences in efficacy between drugs, such benefits cannot be shown to be cost-effective and appear to be counterbalanced by an increased rate of certain adverse effects. However, this broad conclusion should not obscure the fact that these trials have very different designs and that they were aimed at different, although complementary questions. Space prevents a full critical appraisal of each of these trials and so I will discuss only some selected issues.

The CATIE trial, termed a "practical" trial by its designers, had some pragmatic characteristics (representative patients, variable dosing, reasonably long follow-up) but maintained blinding and high quality assessment of outcome (2). The results of CATIE were unsurprising although very valuable in that they confirmed a picture that was emerging from disparate strands of evidence, including both the meta-analyses and emerging observational data on safety (20).

CUtLASS was further along the pragmatic continuum, being unblinded and allowing choice of both SGA and FGA (18). Out of context, it inevitably remains unclear to what extent the lack of observed differences in CUtLASS mean that there were truly no differences or that the trial was too "noisy" to detect them. However, the CUtLASS cost-effectiveness findings are highly consistent with the other independent trials.

EUFEST was an ambitious trial of first episode patients, but its open design made it highly susceptible to performance bias (and consequently ascertainment

bias), which led to its authors being unable to draw any clear conclusions (19), although Fleischhacker and Goodwin seem now more prepared to do so.

Space precludes a discussion of the other effectiveness trials in other disorders discussed by Fleischhacker and Goodwin, but similar issues apply. It is clearly the case that neither "efficacy" or "effectiveness" trials are more likely to estimate the "truth". All trials are susceptible to limitations and trial design is the art of compromise. All trials should therefore be critically appraised. Despite the various methodological shortcomings in the new generation of independent trials, their resurgence – and the willingness of government and charities to fund them – is long overdue. Many important clinical questions remain unanswered by trials designed solely to meet the narrow needs of industry and their regulatory authorities (1,21). Those designing trials with a more pragmatic focus need to make sure that important sources of bias are identified for each individual trial. It is crucial that the trial design is robust enough to make the results both credible and useful – otherwise the hard-earned results will be vulnerable to the criticisms of those who do not like them!

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Much ado about small differences

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Fleischhacker and Goodwin note that "meta-analyses and systematic reviews have often delivered discrepant messages" regarding comparisons across antipsychotic medications; they refer to these discrepancies as "mutually contradictory". A more parsimonious explanation is that, when only a small difference exists between one drug and another, and numerous studies compare the two drugs, some, but not all, of the studies "detect" the difference. If no difference exists, only a rare, anomalous study "detects" a difference. These are fundamental tenets of probability.

Fleischhacker and Goodwin also state that "where the results of efficacy trials are positive and an effectiveness trial is negative, one should not necessarily prefer the effectiveness trial – it may simply have failed". Others have cautioned that one should not necessarily prefer the efficacy trials – they may simply be biased (1,2). "Failed" implies that a trial was done so poorly that it was incapable of detecting a difference between treatments when a difference exists. "Failed" is fighting words. The use of such a pejorative term is usually accompanied by detailed delineation of the trial's purported deficits.

Regarding CATIE, the authors state that "this type of staged design may en-

courage early treatment discontinuation in Phase I, as it allows graduation into a second phase of the investigation". Investigators and patients involved in single phase trials have financial incentives to continue on assigned treatments when they would otherwise switch; payment from sponsors to investigators and free care for patients cease when treatment is discontinued. By having subsequent phases available we did not "encourage" discontinuation; we simply avoided discouraging discontinuation. The CATIE design resembles usual clinical care, wherein alternative treatments are readily available and switches are common. The CATIE survival curves correspond closely to the antipsychotic switch curves in large administrative databases.

Fleischhacker and Goodwin also question whether the selection of perphenazine in CATIE "fairly represented the classical antipsychotic group". This is a puzzling comment. Should we have selected haloperidol to maximize extrapyramidal side effects, or thioridazine to maximize weight gain and anticholinergic side effects? We chose perphenazine because we believed it offered the best package of therapeutic benefit relative to side effects among the classical antipsychotic agents (3,4). Should one insist that ziprasidone most fairly represents the second-generation antipsychotic medications?

Finally, Fleischhacker and Goodwin state that in CATIE "only about 40% of all patients in Phase I received the maximally allowed doses". They seem to imply that the randomized and blinded design of CATIE somehow restricted clinicians from increasing doses. CATIE clinicians could adjust dose at their discretion, just as they could utilize adjunctive medications (e.g., mood stabilizers or antidepressants) and concomitant medications (e.g., anti-parkinson drugs or anti-hypertensive agents) at their discretion. We surmise that these clinicians saw no reason to increase dose in patients who did well, or who developed dose-related side effects, at low doses. Should everyone have been pushed to the highest available dose irrespective of such indicators?

Fleischhacker and Goodwin fault CUtLASS because "the perception of clinicians may have favoured 'atypicals' and it was difficult to persuade clinicians to use the older (and more 'typical') antipsychotics". This same concern about clinician biases must, of course, be applied to the EUFEST results, where un-blinded clinicians were quicker to discontinue haloperidol than atypical comparators, even though no differences in Positive and Negative Syndrome Scale (PANSS) outcomes were apparent across the drugs. The equivalent survival curves for haloperidol and risperidone in large blinded first episode trials (5,6) are noteworthy.

An over-arching view of all available comparisons (many of which are poorly characterized by an "efficacy/effectiveness" dichotomy) across antipsychotic medications suggest that any therapeutic advantages for second-generation antipsychotic medications (other than clozapine) are small (compared to their differential pricing) and restricted to amisulpride, olanzapine, and perhaps risperidone; any therapeutic advantages of these drugs must be weighed against their potentials for producing metabolic abnormalities and/or prolactin elevations.

Many patients have excellent therapeutic outcomes, and avoid metabolic side effects and prolactin elevations, if treated with inexpensive, low-dose perphenazine (or loxitane, or thiothixene). The under-utilization of such agents reflects marketing rather than evidence.

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The silver lining of recent effectiveness trials

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Effectiveness trials have played an increasingly prominent position in the evaluation of the comparative benefits or adverse events of various psychotropic agents. Fleischhacker and Goodwin review results of several recent trials in psychiatry and discuss their pros and cons. They argue for the need for such effectiveness studies in late Phase III or post approval Phase IV of the drug development cycle, but with some key caveats, emphasizing the need for incorporating key elements of traditional randomized clinical trials (RCT): randomization and concealment allocation. These would have strengthened many of the recent studies that have been wanting in terms

of what they have really taught us about optimal treatment. This was an unfortunate consequence of STAR*D, where Phase II inpatients could themselves choose to switch to a new agent or augment with the addition of a second one (1,2). While Fleischhacker and Goodwin's observations and suggestions are warranted, perhaps it might be wise to pause a moment and reflect on what we are trying to accomplish, where we have come from, and where should we be heading.

Clinical drug development in psychiatry has become largely focused on demonstrating efficacy by achieving two or more positive, pivotal trials in which an investigational agent is shown to be statistically more effective than placebo in alleviating a specific disorder (e.g., major depression) or less commonly specific symptoms across several syndromes (e.g., agitation in dementia, depression, etc.). Companies generally conduct 4-8 studies to yield at least two positive trials. A filing with the regulatory agencies often includes one or more failed or negative trials but, with enough positive trials and a side effect profile that was not severe or dangerous, an agent would likely be approved. A typical development program trial might include 1,000-1,500 patients exposed to the agent. Phase III trials may include active comparators, but rarely in sufficiently large numbers to allow for enough power to demonstrate superiority of an investigational agent over an available therapy. They are used largely for so-called assay sensitivity to assess the reasons for a so-called failed trial.

This type of efficacy approach has provided a pathway to approval but not for helping the clinician decide when to use a drug, particularly in relationship to older, available compounds that are frequently less expensive. Hence, this divide between efficacy and effectiveness.

To remedy this problem, the field in recent years has embarked on a number of effectiveness trials that many hoped would answer key questions and justify their costs. Unfortunately, many have argued that the studies have taught us little we had not known already and that the cost has not been justified. These trials have not answered the key question for us: which medication strategy is best for a particular patient's disorder.

Yet the studies may have been useful for other reasons. They have allowed us as a field for perhaps the first time to conduct relatively large-scale trials. These have been common in treatment of patients with cancer or cardiovascular disease but have been rare in psychiatry. Indeed, several of these studies did recruit relatively large samples of subjects. Protocol development, study implementation, data collection and analysis were well coordinated and well implemented. And, while the lack of randomization and at times blinding has prevented many important questions to be answered, the foundation has been laid to conduct large-scale, true comparison studies in the future. They have also demonstrated that DNA samples can be collected to assess for genetic predictors of response.

A few comments on where we should be heading. Future studies can build on these new infrastructures but still require that we build in key features. As Fleischhacker and Goodwin point out, randomization is key to make real comparisons. This needs to be routinely built into trials. Comparing two known active strategies should make it easier for both patients and investigators to feel comfortable building in this essential feature in the trial.

Setting entry criteria to allow inclusion of as many representative patients is also essential. Here we may need to do some research and have active discussion regarding risks and ethics involved in re-exposure to a specific agent or class of agents. There has been a tendency to exclude subjects based on a past history of adverse event or lack of response to a specific agent or class. Not uncommonly we may exclude patients whose previous response – particularly if it were long ago – had been complicated by other factors (e.g., concomitant flu-like symptoms), or in whom adverse events were not particularly severe. All too often with studies in more chronic conditions we are confronted with the issue of previous treatment response. If we do include such patients, we may need to stratify in the randomization on the basis of positive or negative response.

With more experience, large scale studies need to be reassessed as to optimal design. Should we be nesting substudies that compare two agents A vs. B, C vs. D within larger trials? Should we be employing adjustments of the randomization based on results to date (e.g., so-called play the winner strategies) (3)? These could all add power to the study design.

DNA samples for pharmacogenetics should be routinely collected in large scale studies or even in smaller studies within large scale drug development programs. Indeed, this is a plus of the recent studies, with several of them having already reported interesting genetic prediction data (4-6). Unfortunately, some DNA samples were not collected at baseline, prior to drug initiation, such that important data on dropouts or drug intolerance may have been lost. Thus, genetic samples should truly be routine parts of the design – i.e., collected in all subjects at baseline (7). These types of data can then be combined with clinical measures to develop moderators or predictors of response (8). As we collect more data, the field can develop criteria for assessing the utility of such predictors for drug selection and for determining when to adopt them clinically. This will help move us beyond a conclusion that the newer agents are not more beneficial than are older ones to a recommendation that a particular patient would best be treated with one or another drug. That is ultimately what we want out of these studies: greater beneficial effects for the patient in our office or in our waiting room. We then will need to all be prepared for a more individual-based practice. The recent effectiveness trials need to be seen as a step in the evolution of our clinical specialty, both in terms of research and treatment applications.

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Do "real world" studies on antipsychotics tell us the real truth?

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In recent years, the so-called "effectiveness" or "real world" studies ("pragmatic trials") have gained increasing importance, claiming that they can give a better answer to questions related to efficacy and side effects of psychopharmacological treatment than phase III studies. However, the actual advantage of these "effectiveness" studies on antipsychotics remains questionable (1). This does not deny, though, that effectiveness studies, as well as other kinds of phase IV studies, can give a complementary view of the results of phase III studies. Some effectiveness studies appear to have a different kind of selection of patients than phase III trials, but they are not at all representative for average clinical samples. Often, patients with milder or more chronic symptoms may be selected than is the case in phase III studies, thus making it more difficult to demonstrate drug effects, and in particular differences between drugs, because a relevant subgroup of patients might be partially unresponsive to a drug.

In contrast to phase III studies, the "real world" approach allows more comorbidity, comedication, etc., so that a broader range of information may be obtained than from the respective phase III studies. However, there is often no differentiated analysis of the influence of these variables. Thus, no advantage is taken of the chance to learn more about these "confounders". On the other hand, the inclusion of such "confounders" (from the perspective of a phase III trial) increases the variance and results in a reduced signal-to-noise ratio, which makes it more difficult to find differences between two groups (beta error problem), even if these factors are adequately considered in the statistical analysis. It might sometimes even be difficult to judge without placebo conditions whether there is a real drug effect, especially if the pre-post difference is unexpectedly low and if there are no differences between two active comparators. It should be questioned whether so-called pragmatic primary outcome criteria such as "discontinuation", or similar categorical endpoints like "level of caring", really are ideal outcome criteria, given the fact that they can easily be influenced by the investigators (who may be biased by their expectations if they are not blinded) and are of poorer psychometric value than dimensional ones.

Another measure of global outcome used as a primary outcome criterion in effectiveness studies is "quality of life". There is no doubt that this is an important outcome criterion, which reflects the subjective dimension of the patient's experience. The classical approach assesses quality of life using a self-rating scale in order to guarantee the subjective perspective. There are pros and cons for the use of self-rating scales. They give a complementary view to the observer rating of the same construct/dimension (1). The correlation between the observer ratings and self ratings might not be high and may be quite changeable, depending on the psychopathological state in terms of severity and type of symptoms. It is often unclear what exactly self ratings of quality of life reflect. If such a scale is used as the primary outcome criterion of a study, it is doubtful whether it is sensitive enough to detect inter-group differences of treatment-induced changes, given the high variance of self rating in general and of self ratings of quality of life in particular.

In summary, because of the less restrictive methodology, effectiveness studies are not able to falsify the results of carefully designed phase III studies, but they can only give a complementary view. Despite the amount of attention being paid to them, we should not start to doubt earlier findings from phase III studies on antipsychotics, but should continue to consider the full array of evidence and use it to guide an evidence-based approach to treatment (2).

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The quest for a meaningful evidence base in psychiatry

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While the rest of the medical profession moved swiftly and confidently into the era of evidence-based medicine, psychiatry was initially reluctant to follow, and slow to warm to its principles. However, more and more psychiatrists are now enthusiastically embracing an evidence-based approach and demanding "the evidence" for all therapeutic interventions. The trouble with this approach is that the evidence is often inconclusive, inconsistent and even contradictory, giving rise to the danger that those with specific interests can select the evidence to suit their needs.

Studies failing to show advantages for newer agents are pounced upon by funding bodies and used to argue for the return to (cheaper) first generation antipsychotics (FGAs). At the same time these studies are disregarded by proponents of the newer agents, who point out the methodological flaws that are inherent in all clinical trials.

Because much psychiatric symptomatology remains subjective, accumulating evidence based on objective measures is that much more difficult. Despite the encouraging progress in our ability to treat effectively most psychiatric disorders, there remain major shortcomings in clinical practice, and "real world" treatment outcomes are frequently unsatisfactory. Part of the problem lies in determining best practice based on the available evidence. The array of "evidence" being published each month in scientific journals can be bewildering.

The article by Fleischhacker and Goodwin provides a timely and insightful discussion of some of the difficulties that psychiatrists experience when attempting to translate research findings into best practice. Thus, the randomized controlled trial (RCT) – the cornerstone of evidence-based medicine – is under siege in psychiatry, and has been criticized for, amongst other things, not accurately reflecting "real world" conditions (1). The high and increasing placebo response and dropout rates associated with randomized controlled trials have become the statisticians' recurring nightmare, casting serious doubt on the validity of trial results. In an attempt to counter the shortcomings of RCTs, so-called "pragmatic" trials are appearing in the literature more frequently. However, these studies, with alluring acronyms that seem to promise much, such as CATIE (2), CUtLASS (3), CAFE (4), EUFEST (5) and STAR*D (6), are threatening to confuse the picture even more. They are proving just as difficult to interpret and are creating considerable controversy. It seems that, with each new study conducted, an additional batch of unanswered questions is generated.

Fleischhacker and Goodwin argue for the retention of both RCTs and pragmatic trials, the latter at an earlier stage of drug development, before fixed opinions have been formed. By combining the advantages of the scientifically rigorous RCTs with those of the closer-to-real-world-practice experience of pragmatic trials, we can hopefully come closer to establishing which treatments are best for our patients. While this clearly makes sense, it alone might not be enough, as the difficulty is not just in obtaining evidence but also in interpreting the findings. Part of the problem may be that we have too many expectations from each individual trial – these trials are usually designed to address one or two questions – yet we often attempt to extrapolate the findings to other issues and other populations of patients. For example, the CATIE study found that the first generation antipsychotic (FGA) perphenazine performed surprisingly well against the second generation antipsychotics. However, it is potentially dangerous to generalize this finding to other FGAs such as haloperidol. No individual clinical trial, be it a randomized controlled or a pragmatic one, is designed to answer all the questions or to provide a basis for definitive treatment protocols – each study adds a little to the knowledge base. This means that the "evidence" on which practice is based will comprise a large pool of sometimes inconsistent knowledge. Clinicians need to be able to integrate justifiable conclusions from each new piece of knowledge into their daily practice, and accurate interpretation and translation will require a long-term cumulative approach, not a rash and sometimes opportunistic exclusive focus on each new piece of emerging data.

However, we would argue that approaching the *status quo* with caution is not enough; that we need to do more to remove bias. Publication bias needs to be urgently addressed. The consequences of selective publication of positive results have become painfully clear in the controversy surrounding the use of antidepressants and other related drugs in adolescents (7). The various recently established clinical trial registers should go some way to preventing a recurrence of this situation, in which internationally accepted and implemented treatment guidelines appear to have been unknowingly based on incomplete data. The influence of the pharmaceutical and medical device industries, accused of impugning the integrity of medical science, needs to be carefully regulated (8,9).

The quality of clinical data from RCTs may be improved by minimizing recruitment incentives (especially those for rapid recruitment), ensuring unimpeachable methodology, and using appropriate outcome measures. The rigorous training of investigators may improve the accuracy of clinical data collected. The usefulness of pragmatic trials may be increased by a broader selection of clinical contexts, including patient populations in developing countries and other low income settings. Perhaps most importantly, clinicians will need to maintain a non-dogmatic approach, a thorough knowledge of *all* of the evidence and sound clinical judgement, for which there is still no substitute.

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The role of efficacy and effectiveness trials

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Fleischhacker and Goodwin raise some important points about the roles of efficacy and effectiveness studies, in the context of reviewing recent large pragmatic trials. They initially suggest that, should the efficacy and effectiveness trials result in different conclusions, we have to trust the efficacy trials. They also note that findings from the efficacy trials, if positive, may be valid for a limited subset of patients (i.e., those who meet often restrictive entry criteria used in efficacy trials or those who are being treated under "research conditions" in which vigorous treatment is provided). Later in their conclusion, however, they are a bit more forgiving of effectiveness trials, saying they are as needed, and they even suggest requiring effectiveness trials before full market availability is allowed for the manufacturer. So which is it? Are effectiveness trials of use or not?

My view is in some but not complete agreement with theirs. I do not believe there are two types of trials (i.e., efficacy vs. effectiveness). Particular designs are formulated to answer specific questions. Different questions beget different designs. Different designs will give different answers as they should, since they are answering different questions.

The efficacy studies (Phase II - III) are designed with maximal internal validity to answer questions like: what is the efficacy, safety and tolerability of treatment "X" as compared to placebo (i.e., to isolate the clinical effects of the molecule or device *alone* on the patient (as expressed by side effects) and on the disease (as expressed as therapeutic or worsening effects).

Effectiveness trials entail a host of different designs, that address a range of different questions. Specifically, as noted by Fleischhacker and Goodwin, these trials enroll a wider range of patients, employ a wider range of "clinically relevant" outcomes, and provide treatment under "usual" vs. "research" conditions (which may or may not increase retention whilst risking underdosing). When an efficacy trial reveals efficacy, the magnitude of the effect may well be different in practice, depending on *who* is being treated (i.e., which patients) and *how* they are being treated. For depression, patients with anxious symptom features may do less well (1) than less anxious patients, even when equivalently treated. Indeed, as STAR*D showed, the time at which, in a sequence of interventions, a treatment is used will affect the chances of remission (2).

I am in substantial agreement with their conclusion: that both "types" of trials are useful. Each contributes to our understanding. No one design provides a unique path to the truth. Rather, the first question is: does the potential treatment actually work for not very complicated patients and at what cost or risk (e.g. adverse events) to patients? If the benefit outweighs the negative effects (as evaluated in efficacy trials), then where, how, and for whom is the treatment to be recommended? These latter questions are partially addressed by so called "effectiveness" trials. The designs may hold constant or allow variance in the nature and types of patients (e.g., comorbidities, concomitant medications, etc.), treatment procedures (e.g., visit frequency, dose to titration, etc.), where the treatment is used in a sequence of treatments (i.e., levels of treatment resistance), etc.

In addition, effectiveness trials can address other practical issues. In STAR*D, for example, patients could select among treatment strategies. Substantial numbers chose to augment, while others chose to switch treatments. The different switch and augmentation medication treatments did not differ in remission rates – a clear answer to the question about the comparative efficacy of "in class", "out of class" or "dual action" agents as second step switch treatments, for example. That far fewer patients chose to both switch and augment is not surprising. Patients with high side effects and poor efficacy from step 1 would logically want a switch. Those with some benefits and tolerable side effects from step 1 would logically not want to lose the benefit and therefore preferred augmentation. What was most interesting was the STAR*D finding that greater levels of resistance have a major effect on outcomes – both

acutely and in follow up. Thus, when a treatment is used is as important as how and for which patients it is to be used. This finding should affect the subsequent designs in efficacy trials.

Efficacy studies can only evaluate efficacy under specific conditions. If effectiveness studies differ in outcomes, then logically, it is *not* the case that the treatment will *never* work. Rather, the treatment is likely to work only under select conditions defined by patient subgroups, treatment methods, or at where in the sequence of treatments the treatment is used for example.

In conclusion, each type of trial (efficacy/effectiveness) provides essential contributions to how best to treat our patients.

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Social functioning and quality of life as measures of effectiveness in the treatment of schizophrenia

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From the perspective of health care practitioners, the most useful clinical trials are those that assess the effectiveness of a drug, that is, determine how well the drug works under conditions of actual clinical practice. Clinical trials designed to determine effectiveness should use outcome measures that have the greatest clinical significance for practitioners, with the goal of maximizing generalizability and addressing practical questions about the risks, benefits, and costs of an intervention in routine clinical practice (1). Here we would like to emphasize the importance of social functioning and quality of life (QOL) as outcome variables in clinical trials in patients with schizophrenia.

Recent research has shown that atypical antipsychotics improve QOL in patients with schizophrenia (2). However, studies that incorporate QOL in the assessment of long-term effectiveness are limited and inconsistent. Fleischhacker and Goodwin summarize the results of the Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study (CUtLASS) (3), which employed the Quality of Life Scale (4) as the primary outcome measure for evaluating the effectiveness of treatment. The CUtLASS found no disadvantage of first-generation antipsychotics in comparison to non-clozapine second-generation antipsychotics. Similarly, in a double-blind, randomized controlled trial, Rosenheck et al (5) reported that measures of effectiveness demonstrated no advantage for olanzapine compared with haloperidol in overall QOL. In contrast, a naturalistic observational study on patients with schizophrenia undergoing usual care indicated that ziprasidone treatment resulted in improved satisfaction with general activity as measured by the Quality of Life Enjoyment and Satisfaction Questionnaire (6).

When measuring QOL in patients taking antipsychotics, it is important to acknowledge that a variety of factors may influence QOL outcomes: these include side effects and daily dosage of the antipsychotic, depressive and negative symptoms, duration of treatment, and subjective tolerability. In a naturalistic comparative study, Ritsner et al (7) found no significant difference in general QOL between patients using atypical vs. typical antipsychotics. However, after adjusting for daily dosage, duration of treatment, and subjective tolerability, QOL measures indicated that atypical antipsychotics (olanzapine and risperidone) were superior to typical ones.

Some randomized controlled trials of antipsychotics have used a social functioning scale as an outcome measure, such as the Social and Occupational Functioning Assessment Scale (8,9), the Medical Outcomes Study Short-Form 36 Health Survey (10), or the Personal and Social Performance scale (PSP) (11). However, these trials have largely involved short-term interventions, limiting their ability to detect meaningful changes in the social functioning of patients. We are currently undertaking a randomized, controlled, open-label clinical trial in Korea to evaluate improvement in social functioning in patients with schizophrenia or schizoaffective disorder. The study compares long-acting injectable vs. oral risperidone using a hybrid model to assess both efficacy and effectiveness after one year of treatment. Primary outcome measures in this study are the PSP and the Social Functioning Scale.

The scales used to assess social functioning and QOL in clinical trials must be appropriate to the study population and the clinical condition, and should measure several dimensions of social functioning and QOL. Furthermore, we need to develop scales that measure functioning independently from symptoms, and that are sensitive to changes over the course of the illness.

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Migraine in affectively ill Mexican adolescents

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The objective of this cross-sectional study was to determine the prevalence of migraine headache among depressed Latino adolescents of Mexican American origin. This is, to the best of our knowledge, the first study of the prevalence of migraine among depressed adolescents of any ethnic/racial background. In a mental health clinic for the indigent, 132 consecutive Latino adolescents fulfilling the DSM-IV criteria for major depressive episode were compared with a sample of adolescents with other mental disorders. Logistic regression was used to test for associations and control for confounding effects. The prevalence of migraine headache among depressed adolescents was 6 times greater than that of the comparison patients (OR = 5.98, z = 2.35, p = 0.019). This finding is consistent with previously published reports involving adult samples, in which the prevalence of migraine was found to exceed that in the general population. However, contrary to what we previously found in Latino adults, the prevalence of migraine was not higher in bipolar than in unipolar adolescents.

Key words: Migraine, depression, Latino, mood disorders, comorbidity

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Migraine is the most common form of chronic, episodic headache (1). The results of a major epidemiological study revealed that the annual prevalence of migraine headaches among men and women in the United States is 6% and 15-17%, respectively (2).

Zwart et al (3) measured the 12-month prevalence of migraine among adolescent subjects living in a Norway county during the period 1995-1997. Their database included 8,255 subjects between 13 and 18 years of age. Of these, 5,487 were evaluated by a personal interview, in which they were asked whether they experienced recurring headaches in the previous 12 months. Those answering in the affirmative were classified as having tension, migraine or unclassifiable headaches. The 12-month prevalence of migraine was 7%.

Fendrich et al (4) ascertained the 3-month prevalence of migraine among subjects between the ages of 12 and 15 years in a population-based cross-sectional study in Germany. All students attending the 7th, 8th and 9th grades were eligible for inclusion. Of the 3,699 eligible students, 3,324 participated in the study. The prevalence of migraine was 6.9%.

The prevalence of migraine headache among adults with mood disorders exceeds that of adults in the general population (5-13). Mahmood et al (5) were, to the best of our knowledge, the first investigators to report that migraine is common among persons with bipolar disorder. The lifetime prevalence of migraine among bipolar patients in their sample was 30%.

In a population of Latino adults, we found that those with bipolar disorder were nearly three times more likely to suffer from migraine headache than those with major depressive disorder (54% vs. 29%, OR=2.9, p<0.0001) (14). Fasmer and Oedegaard (7) found that the lifetime prevalence of migraine headaches among bipolar and unipolar patients was, respectively, 57% and 45%, while Fasmer (6) reported that the lifetime prevalence of migraine headaches among bipolar and unipolar patients was 44% and 46%, respectively.

We recently reported that 76% of Latino adolescents meeting the criteria for major depressive disorder had at least one of four pain complaints (15). The difference in prevalence of pain complaints between these patients and psychiatric controls was dramatic.

In that previous study (15), we did not explore the possibility that the prevalence of migraine headache among depressed adolescents exceeded that of controls. We now endeavor to explore this possibility, and to investigate whether the prevalence of migraine is higher in adolescents with bipolar disorder than in those with major depressive disorder. This is, to the best of our knowledge, the first study with these objectives.

METHODS

The study was carried out at a public sector psychiatric outpatient clinic for the destitute situated in the rural expanse of Starr County, Texas, a very impoverished region of the United States resting on the Rio Grande River. The county had a population of 53,597 persons in the 2000 census. Its racial composition is 99% Latino of Mexican American origin and 1% other.

One hundred thirty-two consecutive adolescents (between 12 and 17 years of age) fulfilling the DSM-IV criteria for major depressive episode, as ascertained by the Structured Clinical Interview for DSM-IV (SCID-CV) (16), were recruited for the study. Any physical illness which could be a possible basis for headache, as ascertained by medical history and review of systems, was an exclusion criterion.

Forty-seven adolescents without major depression and without any physical illness which could be a possible basis for headache composed the control group. The diagnoses in the control group, ascertained by the SCID-CV, were adjustment disorder, attention-deficit/hyperactivity disorder or substance use disorder.

The diagnostic interview included the query "Have you been having headaches in the last week?".

Patients answering this question in the affirmative were asked explicit questions about the characteristics of the cephalalgia. Our definition of migraine included pain worse on one side of the head and simultaneous concurrent pounding, pulsating or throbbing pain at that site. This method of classifying migraine has a sensitivity of 87% and a specificity of 50% for migraine as defined by the International Headache Society (17).

Written informed consent was not required, since the data were obtained in the course of the delivery of routine clinical services.

Logistic regression was used to test associations and to control for confounding effects. P values were two-tailed, and the critical value of alpha was set at 0.05.

RESULTS

The sample of depressed adolescents included 88 patients with a DSM-IV diagnosis of major depressive disorder (29 males and 59 females, mean age 14.3±1.6 years) and 44 patients with a DSM-IV diagnosis of bipolar disorder (21 males and 23 females, mean age 14.4±1.6 years). The control group included 47 patients (14 males and 33 females, mean age 14.6±1.5 years).

Of the depressed patients, 60.6% had tension or migraine headache, compared to 14.9% of the control group. This difference is highly significant (OR=8.14, z=4.89, p<0.0001, 95% CI = 3.33-19.94).

The prevalence of migraine headache among the patients with major depressive disorder and bipolar disorder was 26.5% and 25.0%, respectively (OR=1.04, z=0.09, p=0.93, 95% CI = 0.44-2.45). The prevalence of migraine headache in the control group was 4.3%. The patients with major depressive episode were more likely to have migraine than those in the control group (OR=5.98, z=2.35, p=0.019, 95% CI = 1.34-26.59). Those with major depressive disorder (OR=5.92, OR, z=2.28, p=0.023, 95% CI = 1.28-27.34) and those with bipolar disorder (OR=6.15, z=2.23, p=0.026, 95% CI = 1.25-30.4) were both more likely to have migraine headache than those in the control group.

DISCUSSION

This is the first study of the prevalence of migraine headache among depressed Latino adolescents of Mexican American origin. It is also, to the best of our knowledge, the first study to reveal a higher prevalence of migraine headache among depressed adolescents of any ethnic/racial background relative to a comparison group.

The focus of the study was a Latino population living in a semi-closed community. This raises questions about the generalizability of the results. However, the Latino population of Mexican American origin is the most rapidly growing segment of American society. This demographic shift dictates that health care professionals become increasingly aware of the health care attitudes, problems and needs of this population.

Our findings are consistent with results involving adult samples, indicating that the rate of migraine among persons with mood disorders substantially exceeds that of non-affectively ill individuals (5-13).

We previously reported that among adults in Starr County those with bipolar disorder are nearly three times more likely to suffer from migraine headache than those with major depressive disorder (54% vs. 29%, OR=2.9, p<0.0001) (14). We did not find this difference in the present population of adolescents, where the prevalence of migraine in those with major depressive disorder and those with bipolar disorder was 26.5% and 25.0%, respectively. Since an age of onset of major depression in childhood and adolescence is a strong predictor of the eventual emergence of bipolar disorder (18,19), it is possible that a significant fraction of our adolescents classified as having major depressive disorder actually have a "latent" bipolar disorder. This could explain the above discrepancy. The hypothesis could be put forward that migraine among youths with early onset major depressive disorder is a trait placing a subset of them along the bipolar spectrum.

Pain in the context of a depressive syndrome is often state-dependent. We were not able to conduct a longitudinal study in our sample of adolescents. Further studies are warranted in order to investigate the long-term course of migraine and its response to antidepressant treatment.

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Indexation of psychiatric journals from low- and middle-income countries: a survey and a case study

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There is a marked underepresentation of low- and middle-income countries (LAMIC) in the psychiatric literature, which may reflect an overall low representation of LAMIC publications in databases of indexed journals. This paper investigates the worldwide distribution of indexed psychiatric journals. A survey in both Medline and ISI Web of Science was performed in order to identify journals in the field of psychiatry according to their country of origin. Two hundred and twenty-two indexed psychiatric journals were found. Of these, 213 originated from high-income countries and only nine (4.1%) from middle-income countries. None were found in low-income countries. We also present the experience of a LAMIC psychiatric journal, the Revista Brasileira de Psiquiatria, in its recent indexation process. This case study may serve as an example for other LAMIC journals to pursue indexation in major databases as a strategy to widen the international foundation of psychiatric research. There is an important need for the inclusion of LAMIC psychiatric publications in the major indexation databases. This process will require multiple agents to partner with journals from LAMIC to improve their quality and strengthen their chances of being indexed.

Key words: Indexed psychiatric journals, low- and middle-income countries, psychiatric research

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Low- and middle-income countries (LAMIC), where over 80% of the global population live, bear the greatest burden of mental disorders. The level of submission from LAMIC in high-impact indexed journals is, however, less than 20% (1), and the proportion of papers published is even lower (2): a search in the Institute of Scientific Information (ISI) Web of Science database from 1992 to 2001 (3) reported that low- and middle-income countries (n=152) contributed only 6% of the international mental health research. A recent review of all original contributions during the 2002-2004 period in the six highest impact factor journals in the field of psychiatry revealed that only 3.7% of the published papers were submitted by authors from LAMIC (4). Moreover, a survey of the editorial and advisory boards of ten leading psychiatry journals showed a low representation of LAMIC (5). A major obstacle to disseminating LAMIC research is the scarcity of indexed journals with a strong LAMIC focus - such as, for example, journals published in LAMIC (3).

Local initiatives to develop information networks between researchers and mental health professionals are evident in some developing countries. An extensive survey published in 1999 identified 977 psychiatry journals being edited worldwide; of these, 413 were not listed in any abstracting or indexing service (6). Retrieving the best information in this scenario has become increasingly difficult and requires researchers to use indexation databases. The use of indexation databases, equally, is now a requirement for any publication that pursues adequate visibility and impact of research published in the journal. Two of the most relevant indexation systems for psychiatric journals are Medline, a bibliographic database developed by the US National Library of Medicine, and the citation indexes of the ISI, now part of Thomson Scientific, available online under the name Web of Science.

This paper aims to describe the worldwide distribution of indexed psychiatric journals, and identify the number published by LAMIC. It also aims to present information from a variety of sources about unindexed journals in the field, and to describe the recent experience of indexation of the Revista Brasileira de Psiquiatria as a case study. We use this study to provide suggestions for editors of journals in LAMIC to achieve better levels of indexations, so as to improve representation of these countries in the global literature databases.

METHODS

We performed a survey in both Medline and ISI databases to identify journals in the field of psychiatry according to their country of origin. The search in Medline was done by entering the expressions "psychiatry" and "substance abuse" in the journals database. Only journals that were currently both indexed and published were included. Psychiatric and substance abuse journals in the ISI were identified through the Journal Citation Reports (JCR). We included all journals listed in both Science and Social Sciences editions of the JCR for the category Psychiatry. For each journal, we collected information on title, ISSN, country of origin, publisher, and publication start year as provided by the databases. For publications indexed in ISI, we also collected citation data (e.g., impact factors, total cites). The assignment of a journal to a country was done based on registries from both databases; in

case of disagreement, priority was given to information obtained in ISI.

We sought information about unindexed journals in two ways. First, we contacted the 18 WPA Zonal Representatives (ZRs). We asked them to identify, with the help of their Member Societies, journals published in the Zone countries, but missing from the list. We also asked them to identify journals published by countries in each Zone and wrongly attributed to another. This may occur for example when a journal published on behalf of a Member Society by an international publisher is attributed to the country where the publisher's head office is located, often in Europe or USA. Second, we obtained permission to use information from a recent initiative of the World Forum for Global Research and the World Bank, a survey conducted to map out the research production in mental health from LAMIC for the period 1993 to 2003, in which researchers from 114 countries of Africa, East and South Asia, and Latin America and the Caribbean were identified through their publications in two databases (Medline and PsycInfo) and from local grey literature (7).

RESULTS

As of July 2007, for the category Psychiatry (including substance abuse), there were 209 journals indexed in Medline and 175 in ISI. Evidently, there is some degree of overlap between these two databases, and the number of journals indexed in any of these two systems is 222.

As shown in Table 1, there is a high concentration of indexed psychiatric journals in high income countries. We observed a significant correlation between per capita income and the number of indexed journals published ($r=0.75$, $p<0.001$). Two hundred and thirteen journals from high-income countries represent 95.9% of the total publications; the remaining nine publications (4.1%) were from upper-middle income countries. No psychiatric journal from any low-income country was identified in Medline or ISI databases.

As shown in Table 2, there is a clear geographical agglomeration of psychiatric journals, with 13 out of the 18 WPA Zones having three or less indexed journals, and six of them

Table 1 Number of journals indexed in Medline and/or the Institute of Scientific Information (ISI) Web of Science according to country of origin

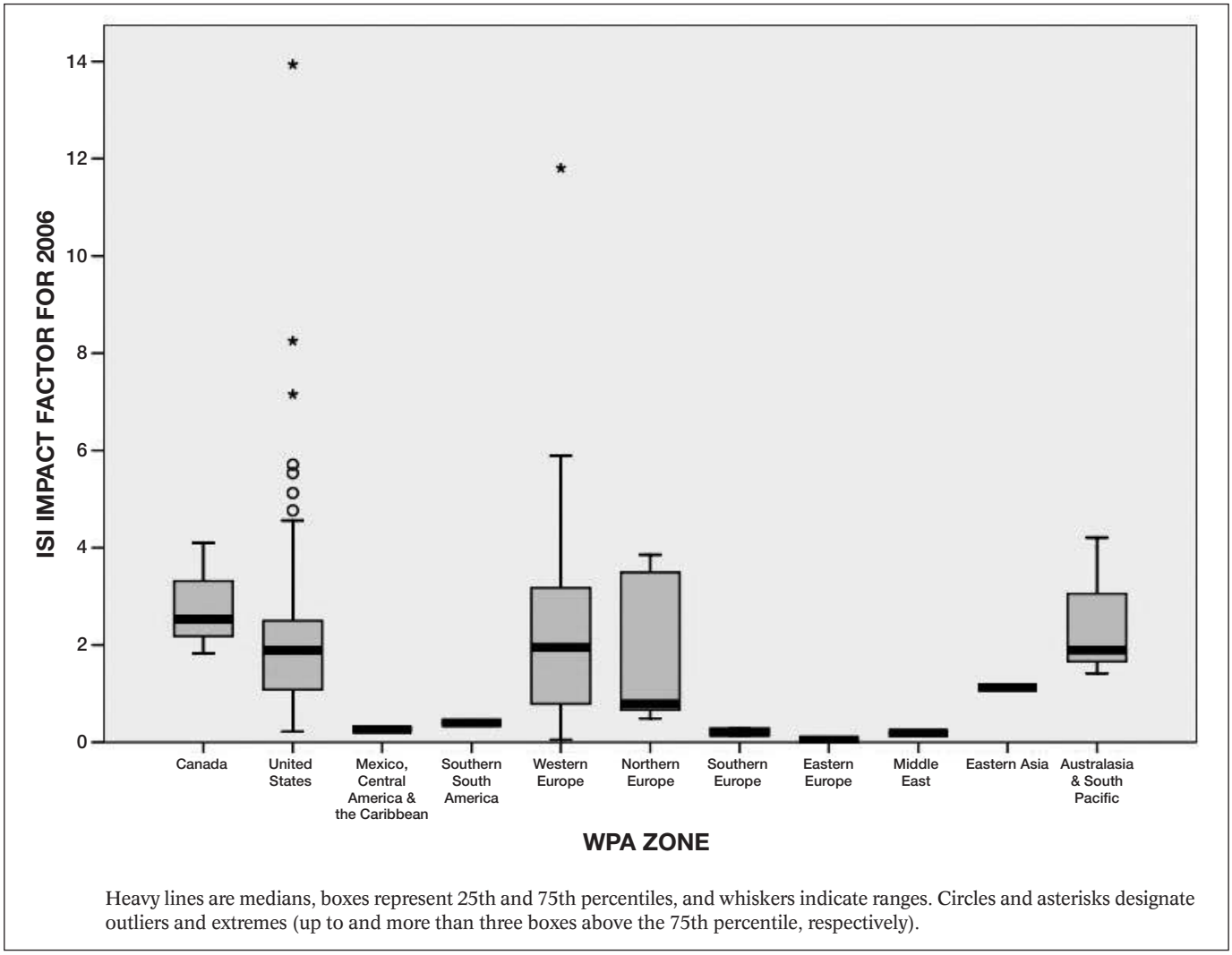
Country	Medline	ISI	Total
Argentina*	1	0	1
Australia	3	2	3
Brazil*	2	2	2
Canada	4	3	4
Croatia*	1	0	1
Denmark	2	3	3
England	40	37	44
France	5	3	5
Germany	12	14	15
Hungary*	1	0	1
Israel	1	1	1
Italy	2	2	2
Japan	3	1	3
Netherlands	8	7	9
New Zealand	1	1	1
Norway	1	2	2
Mexico*	0	1	1
Poland*	1	0	1
Russia*	1	1	1
Spain	2	2	3
Switzerland	10	10	11
Turkey*	1	0	1
United States	107	83	107

* Middle-income countries

Table 2 Number of journals indexed in Medline and/or the Institute of Scientific Information (ISI) Web of Science according to the WPA Zone distribution and of unindexed psychiatric publications from LAMIC

WPA Zone	Medline	ISI	Total indexed	Unindexed LAMIC journals
Canada	4	3	4	NA
United States	107	83	107	NA
Mexico, Central America and the Caribbean	0	1	1	6
Northern South America	0	0	0	13
Southern South America	3	2	3	56
Western Europe	75	71	84	NA
Northern Europe	3	5	5	NA
Southern Europe	5	4	6	2
Central Europe	3	0	3	11
Eastern Europe	1	1	1	NA
Northern Africa	0	0	0	2
Middle East	1	1	1	NA
Western and Central Africa	0	0	0	1
Southern and Eastern Africa	0	0	0	3
Western and Central Asia	0	0	0	1
Southern Asia	0	0	0	7
Eastern Asia	3	1	3	16
Australasia and South Pacific	4	3	4	NA

NA - not available and/or not applicable



Heavy lines are medians, boxes represent 25th and 75th percentiles, and whiskers indicate ranges. Circles and asterisks designate outliers and extremes (up to and more than three boxes above the 75th percentile, respectively).

Figure 1 Median impact factors for psychiatric journals indexed in the Institute of Scientific Information (ISI) Web of Science according to the WPA Zone distribution

having no journals at all (Northern South America, Northern Africa, Western and Central Africa, Southern and Eastern Africa, Western and Central Asia, and Southern Asia). Information obtained from ten WPA ZRs indicated the existence of another 46 unindexed psychiatric publications from LAMIC, while the Global Forum survey led to the identification of additional 87 LAMIC journals. Together, 118 LAMIC psychiatric journals not indexed in Medline or ISI were identified (Table 2).

Based on impact factors released in 2007 (regarding the year 2006), the 167 journals indexed in ISI had a median impact factor of 1.85 (ranging from 0.05 to 13.94). Only three of these publications were from middle-income countries (Brazil, Mexico, and Russia - ranked 154th, 161st and 166th in the final list, respectively).

Figure 1 shows the median impact factor for psychiatric journals according to WPA Zones. Of note, only two regions, namely United States and Western Europe, present outlier publications, with an impact factor higher than five.

A case study: the indexation of the Revista Brasileira de Psiquiatria

The Revista Brasileira de Psiquiatria has been published since 1966 as the official journal of the Brazilian Psychiatric Association (ABP). In 1984, the ABP and the Latin American Psychiatric Association (APAL) conducted a joint venture to publish the journal Revista da Associação Brasileira de Psiquiatria/APAL, with the acronym Revista ABP-APAL. In 1998, two new editors received the mission to re-structure the journal by the presidents of the Brazilian Psychiatric Association.

The first steps of the new editors were to invite two associate editors, to set up the missions of the journal, and to recover the original label Revista Brasileira de Psiquiatria. The missions of the journal were to give visibility to the scientific production of Latin American and Caribbean countries in the field of mental health and related sciences, and to provide continued medical education in the context of

evidence based information for mental health professionals in these countries. The journal was published quarterly, and two yearly supplements enhanced its educational role.

The editorial board was completely reformulated, increasing the representation of international investigators. To deal with political pressures, scientific productivity was included as a criterion to select participants in the board. The first major operational achievement was to include the journal in the Scientific Electronic Library Online (SciELO). This database is sponsored by Brazilian public funding agencies and aggregates the best available publications in Latin America and Caribbean countries, providing free online access to journals. The system is now also allowing for the electronic submission of manuscripts and for the bibliometric evaluation of journals.

To reach a wider audience and to promote the dialogue with other publications, the editorial board decided that it was essential for the journal to be indexed in the major scientific databases. In 2001, its first application to the ISI was refused on the grounds of a very low citation activity, from both authors and most editorial board members, and because "the journal would have low impact and less relevance for coverage in [Thompson Scientific's] products compared to other journals in this very competitive category".

Continuing the process of indexation, the journal was included in Medline in 2003 (8). At this time, all original research in the journal started to be published in English, with most of the review and special articles (which have a very important role in continuing education) being published in Portuguese or English, depending on the language in which they were submitted. This editorial decision found a degree of resistance among some readers, but this was an essential step for increasing the visibility of original articles in the journal and subsequently attracting high-quality research from authors from Brazil and many other countries.

A second application for the inclusion in ISI was attempted on the following grounds: the strengthening of the quality of the editorial board, attested by the number of their citations in the literature; the previous evaluation by the US National Library of Medicine and inclusion of the journal in Medline; and the growing presence of Brazil in health and mental health research (9,10), with each Brazilian article receiving a mean of 4.5 citations according to the ISI JCR (11). Another argument was that the inclusion of the journal in ISI would *per se* augment its citability. In 2005, the journal was finally indexed in ISI (8).

The Revista Brasileira de Psiquiatria is now a quarterly publication with two additional supplements dealing with topics of clinical practice and directed to update clinicians and mental health professionals. Supplements are printed in Portuguese only and published electronically in both English and Portuguese. The journal can be accessed online at SciELO (www.scielo.br/rbp), and at its own website (www.rbpbrasil.org.br), where free full-text articles can be downloaded. The number of article requests via SciELO has been 230,919 in 2004; 487,508 in 2005; and 762,794 in 2006. The first impact factor for the journal is going to be released in 2008, but projections reveal a steady growth in its citation rate, with an unofficial impact factor of 0.512 for the year 2006 (12). The journal costs around US$ 200,000 yearly, and 90% of these costs are covered by the pharmaceutical industry (the remaining comes from the Brazilian Research Council). By the end of 2006, the editorial board comprised 71 members: 37 from Brazil, 12 from United States, nine from England, and four from other Latin American countries. By comparison, the leading national psychiatric journal of United States has no international members on its editorial board, while a quarter of the editorial board of the leading journal of the UK is international.

DISCUSSION

Despite the rapid growth of global mental health research and the profile of global mental health, there is a marked underepresentation of LAMIC in the psychiatric literature. This underepresentation is also reflected in the proportion of psychiatric journals from LAMIC which are indexed in major international databases; we report that of all psychiatric journals indexed in either Medline or the ISI Web of Science just 4% are from middle-income countries. No indexed psychiatric journals from low-income countries were found. In addition, several WPA zones presented with no indexed journal (Northern South America, Northern Africa, Western and Central Africa, Southern and Eastern Africa, Western and Central Asia, and Southern Asia).

A joint statement by psychiatric journal editors and the World Health Organization in 2004 recognized the pivotal role of scientific journals in production and dissemination of research, as well as in the establishment and expansion of clinical services and in the education of investigators in research skills (13). By addressing the mental health needs of LAMIC and enhancing the international and multicultural aspects of psychiatric research, LAMIC journals emerge as a crucial vehicle for the promotion of mental health. Major difficulties met by these publications include limited visibility to the scientific community and consequent limited submission of high quality research.

Journal editors from LAMIC can ideally aspire to have their journals among the highest quality publications. The example of the Revista Brasileira de Psiquiatria demonstrates that such an ambition demands considerable local initiative to restructure the journal, sometimes in the face of opposition from vested interests. The main modifications implemented in this journal to achieve indexation in major databases were: a) an uncompromising criterion to include members in the editorial board based on scientific productivity in the last five years; b) an international board consisting of recognized investigators truly related to the journal activities; c) a rigid publishing timetable supported by a reliable income and stable editorial staff including clear succession plans; d) publishing original articles in English with free

electronic access, and e) publishing educational and review articles in the original language. Another important procedure was to invest in training current staff as well as future members of editorial teams. Since 2004, the journal created three junior editor positions for young investigators. Each of them works together with two senior editors learning the skills of scientific and peer review editing.

The number of unindexed journals identified in several regions attests to the activity and aspirations of researchers and readers across the world. The figures presented were derived from only two information sources and do not intend to be exhaustive – future work is necessary to identify additional psychiatric journals around the globe. We also acknowledge that the absence of psychiatric journals does not mean lack of scientific productivity in the field of mental health. Many countries not mentioned here may have indexed general medical journals in which mental health research may be published. However, it also likely that only a fraction of mental health research carried out in a LAMIC will be published in general journals, as they compete for space with all other medical specialties – thus, a substantial amount of research will never be disseminated. Apart from the overall low representation of LAMIC journals, we also acknowledge the marked intraregional and intranational disparities, which we have not investigated. In the case of South America, for example, only Argentina, Brazil and Mexico, out of 12 countries, have indexed journals. A recent survey that included only LAMIC mental health investigators revealed that researchers and indexed publications output were concentrated in just 10% of the countries, confirming the heterogeneity among emergent nations (14). Disparities inside countries are also present: in Brazil there is a geographical cluster of funding and scientific productivity, with most research being conducted in the South Eastern and Southern states (15).

In order to close the 10/90 gap in mental health research, LAMIC need not only to improve the quality of research, but also find ways to increase the dissemination of their scientific production. In LAMIC where financial resources are especially limited, the development of dissemination strategies to support evidence based knowledge is critical to influence mental health policies and programs in order to reduce the burden of mental health disorders.

The WPA has 130 Member Societies in 110 countries, and through its ZRs is working to establish a database of journals in all parts of the world as a basis for advocacy and action (16,17). We call on journals with a record in achieving high standards, together with funding agencies, to partner with journals from LAMIC, particularly regions which are not represented in the international scientific databases, to improve their quality and strengthen their chances of being indexed.

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Mental health policies on reporting child sexual abuse and physician-patient sexual relationships

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The reporting of child sexual abuse (CSA) and physician-patient sexual relationships (PPSR) are currently the focus of professional, legal and media attention in several countries. This paper briefly reviews mental health policies on these issues and reports on a WPA survey of them. While the WPA Madrid Declaration permits breaching confidentiality for mandatory reporting of CSA and clearly prohibits PPSR, it is not known how or to what extent these policies are implemented in WPA Member Societies' countries. It is also not known whether policies or laws exist on these topics nationally or to what extent psychiatrists and the public are aware of them. Representatives of WPA Member Societies were e-mailed a survey about issues pertaining to CSA and PPSR. Fifty-one percent of 109 countries replied. All reporting countries had laws or policies regarding the reporting of CSA, but this was often voluntary (63%) and without protection for reporting psychiatrists either by law (29%) or by Member Societies (27%). A substantial number of psychiatric leaders did not know the law (27%) or their Society's policy (11%) on these matters. With respect to PPSR, some reporting countries lacked laws or policies about PPSR with current (17%) or past (56%) patients. Fewer than half of responding representatives believed that their Society's members or the public were well informed about the laws and policies pertaining to CSA or PPSR. There is clearly a wide range of laws, policies and practices about CSA and PPSR in WPA Member Societies' countries. There is a need in some countries for laws or supplemental policies to facilitate the protection of vulnerable child and adult patients through clear, mandatory reporting policies for CSA and PPSR. Mechanisms to protect and support reporting psychiatrists should also be developed where they do not already exist. There is also a need in some countries to develop strategies to improve the education of psychiatrists, trainees, and the public on these issues.

Key words: Child sexual abuse, psychiatrist-patient sexual relationships, Madrid Declaration

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Ethical standards for psychiatric practice are delineated in the WPA Madrid Declaration and its later supplements (1-3). Two ethical issues, the reporting of child sexual abuse (CSA) and the prohibition of physician-patient sexual relationships (PPSR), have recently been the focus of professional, legal and media attention in several countries (4,5). It is unknown how ethical standards on these two issues are implemented in WPA Member Societies' countries.

There is strong evidence that CSA is harmful to the mental health of children, and this harm may extend into adulthood (6). Many countries mandate the disclosure by health professionals to relevant authorities when CSA is suspected, and failure to report may result in sanctions (7). However, questions arise as to the level of certainty the health professional should have before reporting CSA. The manner in which information about CSA is elicited by the health professional is also contentious, especially if leading suggestions of CSA have been made to the child (8). While the welfare of the child is foremost in psychiatrists' minds, the damage of false CSA allegations to the accused adult are enormous, and must also be considered. Ultimately establishing the veracity of allegations of CSA falls to legal authorities, but psychiatrists may be called as expert witnesses and/or left to treat the child victims, or adult perpetrators.

Increasingly, physicians, including psychiatrists, find that falsely accused adults seek revenge against them through legal channels, or by complaints to medical licensing authorities (4,9). Consequently, CSA reporting to protect their vulnerable child patients may place the reporting physician in jeopardy (9). As a result, paediatricians and psychiatrists are becoming apprehensive about what support they can expect legally and professionally in these precarious situations (9). The WPA Madrid Declaration says little about this issue, but does state that "breach of confidentiality may only be appropriate when required by law (as in obligatory reporting of child abuse or when serious physical or mental harm to the patient or a third party would occur if confidentiality were maintained)" (3).

Sexual relationships between doctors and patients were generally hidden from professional and public gaze until the late 1970s and 1980s, when case reports and surveys began to emerge which suggested that the problem was much larger than previously thought (10,11). Over the next 20 years, the deleterious effects of doctor-patient sex on patients, public trust in physicians, and the offending physician and his family were documented (12,13). While this problem is certainly not unique to physicians, and numerous cases of psychologists, social workers, nurses and non-medical professionals have been reported, it is concerning that the majority of cases against physicians in North America have involved psychiatrists. Policies have been established in many countries and smaller jurisdictions clearly prohibiting sexual behaviour between doctors and patients (14,15).

The WPA Madrid Declaration explicitly states that "under no circumstances should a psychiatrist get involved with a patient in any form of sexual behaviour, irrespective of whether the behaviour is initiated by the patient or the therapist. Consent on the part of a patient is considered vitiated

by the knowledge the psychiatrist possesses about the patient and by the power differential that vests the psychiatrist with special authority over the patient" (1).

This statement is unambiguous with regard to current patients, but silent on relationships with past patients, in which transference issues and power imbalances often, if not always, persist beyond formal treatment (16). In some countries, mental health policies have clearly proscribed sexual relationships between psychiatrists and past patients (14,17), but in other countries mental health policies have remained silent on the whole issue of these relationships with current or past patients.

In an attempt to understand more clearly how WPA Member Societies and the corresponding countries address issues pertaining to CSA and PPSR, we undertook an e-mail survey to: a) assess the presence of national laws and psychiatric societies' policies, including those that could increase the reporting of CSA and protect psychiatrists who reported CSA in good faith, and b) explore the presence of policies that explicitly prohibit PPSR, promote its reporting, and provide treatment for victims and perpetrators. Finally, the survey sought the opinions of national psychiatric leaders about the educational needs of their societies' psychiatrists and the public on these topics.

THE SURVEY

The questions from this 21-question survey were based on the WPA Madrid Declaration and its supplements (1), internationally-respected reports, policies and laws published on these issues (5,7,14,16), and input from the WPA Review Committee. Four questions concerned respondents' demographics, seven questions addressed CSA, and ten questions addressed PPSR. Respondents had the option of completing the survey anonymously by not completing the demographics portion. Respondents could also provide additional anonymous comments.

Representatives of 128 WPA Member Societies (usually the President or Secretary), representing 109 distinct countries, were invited by e-mail to complete the survey. They were also reminded to participate by follow-up e-mails and personally by one of the authors at WPA meetings. If more than one person from a country responded, the respondent's answers that were the most informative, that is, provided the fewest "don't know" responses, were used. The University Health Network Research Ethics Board approved the administration of this survey.

Fifty-six separate countries completed the survey (response rate 51%). The proportion of countries responding from each WPA region was 54% for Europe, 50% for the Americas, 48% for Africa/Middle East, and 35% for Asia/Australasia. Using the World Bank's classification of countries by income, 73.6% of responses came from upper-middle income countries, and 26.4% from lower-middle or low-income countries.

REPORTING OF CHILD SEXUAL ABUSE

Ninety-six percent of responders reported that their country had laws that prevented adults from having sexual relations with minors under a specified age. Of the countries that had laws prohibiting sexual relationships with minors, 7 (13%) did not require health professionals, including psychiatrists, to report knowledge or suspicion of CSA. Of the countries that required reporting of CSA, 8 (15%) did not have laws that penalized persons for not reporting CSA, while an additional 22% of respondents did not know their country's requirement. When asked whether their country's law protected health professionals who reported sexual abuse in good faith if the allegation later proved to be false, 16 respondents (29%) said no and 15 (27%) did not know. Fifteen respondents (27%) reported that their national society did not support psychiatrists who reported CSA in good faith, if the allegation was later shown to be false. Moreover, 6 (11%) did not know their society's policy.

Only 25 representatives (45%) believed that their professional members were well informed about the law and professional requirements on this topic. The public were thought by 18 representatives (33%) to be much less aware about these standards than psychiatrists.

PSYCHIATRIST-PATIENT SEXUAL RELATIONSHIPS

Twenty-eight respondents (52%) reported that their country had laws, and 42 (78%) that their national societies or medical licensing authorities had specific rules prohibiting PPSR with current patients. Only six (11%) representatives' countries and associations did not have either laws and/or policies prohibiting PPSR with current patients, and an additional two (4%) representatives did not know. Thirteen (24%) of the representatives' psychiatric organizations had rules prohibiting PPSR with past psychotherapy patients.

Eleven representatives (21%) reported that their medical licensing authority required one physician to report if another physician was known to be having sex with a current patient. For the countries that had laws or policies prohibiting PPSR with current patients, 26 representatives (57%) reported that psychiatrists lost their licenses to practice if found guilty. For these countries, 13 representatives (50%) were aware of psychiatrists in their association in the last five years losing their licence to practice for this reason. A wide range of time was reported for loss of license, including permanently or discretionary, from one to ten years, depending on the offence. Other sanctions mentioned included death, written reprimands, public reprimands, criminal proceedings, fines, ethics education, professional bad opinion, condemnation, losing job, restrictions on license, supervision and compulsory therapy. Eighteen representatives (18%) reported programs to help physicians disciplined for PPSR, and an equal number reported provision of free counselling to patients of psychiatrists found guilty of sexual misconduct.

Twenty-two representatives (42%) thought their members were well informed about the law and professional standards on PPSR. Of those who thought that their members were not well informed, 19 (86%) believed that education would be useful. Only 11 representatives (21%) perceived that their country's public was well informed on this topic.

DISCUSSION

CSA and PPSR probably occur globally, but the prevalence within many countries is unknown. A Lancet review placed the prevalence of CSA at 2 to 62% in females and 3 to 16% in males, with a wide range of negative physical, social, and psychological consequences for the victims (18). Though studies are more limited on PPSR, one review reported that 7.1 to 10.9% of male psychiatrists and 1.9% to 3.5% of female psychiatrists admitted to intimate sexual contact with current patients (11), with a range of deleterious effects on patients (12).

Most countries and/or WPA Member Societies have laws that prohibit CSA and PPSR with current patients. Basic policies are vital, but enforcement may require supplemental policies to facilitate compliance. This survey revealed that 13% of representatives' countries did not require health professionals to report CSA, and that even in countries that required reporting, several did not have penalties for not reporting. Even countries that have these laws may not enforce them, as one respondent stated: "There are some penalties subscribed in law, but they don't apply in reality. In fact, (these) are just theoretical".

Moreover, psychiatrists may be reluctant to report CSA, especially if they practice in the almost 30% of countries without laws that protect physicians who report it in good faith or if they perceive that their national association will not support them. One respondent wrote: "There is fear among professionals to report sexual abuse because there's no legal or professional protection". Clearly, this has a chilling effect on psychiatrists' abilities to protect their vulnerable child patients.

Suboptimal rates of implementation or supplemental policies were also present for PPSR. One respondent stated "we do not even talk about these things". While 85% of associations had laws or policies prohibiting PPSR with current patients, less than a quarter of representatives reported that their association or medical licensing authority had policies prohibiting PPSR with past psychotherapy patients. This is despite the opinion of many experts on this topic that the nature of the psychotherapy relationship and long lasting effects of transference may always make PPSR with past patients unethical (16). One respondent stated "the psychiatric diagnosis of the patient makes it unlikely she will be believed". Over half the representatives reported that there was not a duty in their country for a physician to report another physician to a medical licensing authority if the latter physician was known to be having a sexual relationship with a patient.

Victims of PPSR suffer many negative health effects, and may require psychotherapy, counselling and other treatment (12). Unfortunately, only a small percentage of representatives reported that their association provided free counselling to patients of psychiatrists found guilty of sexual misconduct or to physicians who are disciplined for engaging in sexual misconduct. One clear finding was that although over half of country representatives reported that, physicians lost their license if found guilty of PPSR, almost half of these representatives were not aware of any psychiatrist in their association losing his or her license to practice for this reason in the previous five years. The wide range of sanctions for PPSR was striking, and ranged from death to education, but loss of license for variable time periods was clearly the most common.

Cultural attitudes toward appropriate boundaries in interpersonal, including professional, relationships likely differ. For example, collectivist cultures (basically Eastern and traditional cultures) and individualist cultures (North America, most of Europe, Australia and New Zealand) may have different views on boundary-keeping practices that affect the psychiatrist-patient relationship (19,20). While some cultural differences are to be expected, what is clear is that all physicians must do no harm, act in the patients' best interests and never exploit patients for their own gratification. Residency training programs and continuing education for clinicians need to include explicit training on PPSR, as suggested by many representatives (13,20).

This study does have some limitations. Responses were received from only 51% of countries, though this rate is greater than in many physician surveys (21). Consequently, the survey may have been subject to responder bias. Responding representatives' associations may have been more likely to be compliant with the Madrid Declaration, and to have broader national policies, as almost three quarters were in countries with greater resources. Social desirability bias may have resulted in more positive responses to questions. Additionally, some representatives may have lacked proficiency in English, which deterred them from responding. Although we assumed that the representatives gave answers that reflected the status of their country and association, it is possible that they were incorrect.

Limitations aside, the results of the survey clearly indicate that problems exist in reporting CSA and in PPSR in several countries. While nearly all the WPA Member Societies have laws or policies for reporting CSA, this practice may be hampered by the voluntary nature of reporting and the lack of legal and professional association support for reporting psychiatrists. The lack of Member Societies' policies and enforcement procedures in some cases indicates the need for further work.

Finally, representatives expressed a need for more education for psychiatrists, trainees, and the public about these issues. One respondent captured this need well: "Since sex in general and professional sexual misconduct in particular is a taboo in this part of the world, patients (mostly women

and minors) need to be empowered to know their rights and be able to bring the perpetrators to justice". We hope that the results of this survey will aid in bringing about necessary changes.

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Community mental health care in the Asia-Pacific region: using current best-practice models to inform future policy

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The vast experiences from the community mental health care models in the Asia-Pacific region can serve as valuable lessons and inspiration for future development. For positive change to occur, it is clear that innovative, culturally sensitive and economically sustainable pathways for community treatment models need to be explored and developed. The Asia-Pacific Community Mental Health Development (APCMHD) project has been established to explore diverse leading models or approaches to community mental health service delivery in the Asia-Pacific region. It aims to illustrate and promote best practice in mental health care in the community through use of information exchange, current evidence and practical experience in the region. The project is based on the work of an emerging network of mental health leaders from 14 countries or regions in the Asia-Pacific, working to build culturally appropriate mental health policy frameworks and workforce in the implementation of community mental health services. Some of the key guiding principles of developing community mental health care in the region are highlighted. Such collaborative exchange based on local practices will help enhance regional solutions to challenges in building capacity and structures for community-based mental health systems in the future.

Key words: Community mental health, local models, principles of care, culture and service delivery

(World Psychiatry 2009;8:49-55)

The Asia-Pacific region has close to half of the estimated 450 million people affected by mental illness globally (1).

Based on international mental health care benchmarks, many Western health systems have established contemporary health policy and guidelines which include the provision of mental health care in the community. However, the delivery of quality and appropriate community mental health care remains an ongoing challenge for countries of both high and low socio-economic level. Difficulties and obstacles in implementation of comprehensive community service models include inadequate funding, availability of trained mental health workforce, integration with primary care services and community agencies, and collaboration between public and private health systems (2,3). As community mental health service system depends on sufficient workforce for service delivery, the critical shortage of adequately trained mental health staff continues to impede the progress of mental health reform.

In response to such global trends, many countries in the Asia-Pacific region have begun to establish mental health policy and guidelines to move from institutional care to community mental health services. While these reforms are supported by recommendations from the World Health Organization (WHO) governing bodies, such as the Western Pacific Regional Mental Health Strategy (4), social, economic and cultural factors in Asia-Pacific countries often do not allow ready translation of Western community mental health models of care. Governments and service providers commonly face challenges in the development and implementation of locally appropriate community mental health care and services. Additionally, it would be unrealistic or undesirable to produce rigid recommendations for a singular community mental health care model, due to the diversity across the Asia-Pacific region. Hence, for constructive change to occur in the region, innovative, culturally appropriate and economically sustainable pathways for community treatment models need to be explored, developed and shared. Community mental health service reform appears to be gaining momentum in this region, despite the obstacles. Valuable lessons and inspiration for further development can be gained from both the successes and difficulties in reforming mental health systems and practices in the region.

An emerging network of representatives from governments, peak bodies and key organizations is emerging in the Asia-Pacific region to build supportive relationships in order to facilitate the implementation of locally appropriate policy frameworks for community mental health service reform. The network is supported by the Asia-Pacific Community Mental Health Development (APCMHD) project, which involves 14 countries/regions in the Asia-Pacific region. Initiated in collaboration with the WHO Western Pacific Regional Office, the APCMHD project is led by Asia-Australia Mental Health, a consortium of the University of Melbourne Department of Psychiatry and Asialink, and St. Vincent's

Health, which is a part of the WHO Collaborating Centre for Mental Health (Melbourne). The project, which brought many key mental health organizations to work collaboratively, is consistent with the WHO Global Action Programme for Mental Health (5).

The project aims are to promote best practice in community mental health care through exchange of knowledge and practical experience in the Asia-Pacific region. The key outcome is the documentation of the current status, strengths and needs of community mental health services in the region, in the hope to translate current understanding into practical changes in the future.

STAGES OF THE PROJECT

The project involved a three stage process of development over three years. Best practices in community mental health care in the Asia-Pacific region were identified and examined through collection of national data, existing evidence, information exchange, and practical experience. A total of 14 countries/regions participated in the project, including (in alphabetical order) Australia, Cambodia, China, Hong Kong, India, Indonesia, Japan, Korea, Malaysia, Mongolia, Singapore, Taiwan, Thailand, and Vietnam. A network of representatives from ministries of health and key mental health organizations in the region worked to produce guiding principles for the development of culturally appropriate practices of community mental health care. Significant progress was made as a result of the good will and enthusiasm of the participants, who valued sharing real-life practices and solutions. Asia-Australia Mental Health, WHO and the project partners provided technical support and continuously reviewed the progress of the participating countries in this project.

Stage 1: Developing the framework for data collection

Preparatory work meetings with key country representatives were held in 2005-2006 at key conferences in Asia to scope the project, plan directions and agree on working methodology to ensure consistency of documentation of existing community mental health resources, policy and practice across the countries and regions.

Stage 2: Producing resources for best practice

A draft report template was developed by the country representatives, based on the project goals, to assist each country or region to document mental health policies, strategies, and the diverse local models or approaches to community mental health service delivery. A consensus meeting was convened at the WPA International Congress in Melbourne in November 2007 to clarify the methodology and report the information collected from participating countries.

Stage 3: Publication, dissemination and implementation

A regional report has been published (6), based on experiences and learning gained, to provide a resource to inform future policy development and implementation of community based services. Publication of the report and dissemination of information to the regional countries will be followed by implementation of planned outcomes. Full reports for each country/region are available on www.aamh.edu.au.

KEY PRINCIPLES FOR BUILDING COMMUNITY MENTAL HEALTH CARE IN THE ASIA-PACIFIC REGION

Cost-effective models of community mental health care need to be scaled up throughout the region. A number of focal approaches are deemed to be particularly relevant for the local environment, culture, and mental health system in the Asia-Pacific countries. The following key guiding principles are distilled from the analyses of different regional exemplars of best practice, some of which are briefly outlined below together with the corresponding principles.

Emphasis on community-based care in the hospital system

The concept of community mental health service takes different meanings in different cultures and varies throughout the region. Community-based care can be developed within a mental health hospital system. Many hospitals have developed community outreach teams to provide specialist mental health services in local settings, and to train primary health workers and community agencies. While adequate beds for acute care must still be provided, alternative community mental health services are needed to facilitate early discharge, optimize treatment and rehabilitation outside the hospital, and prevent relapses of illness or re-hospitalisation. Community-based care must be incorporated within a balanced mix of service components, ranging from psychiatric hospital care to general hospital and primary care.

The Hospital Bahagia Ulu Kinta in Perak, Malaysia, is a large psychiatric hospital which has developed home care services offering individualized rehabilitation in the community. The large tertiary hospital is the "hub" which administers and resources the "spokes", which are the community mental health centres. Resources are gradually moving from the hospital's bed-based services to the community-based services. Relapse and re-admission rates have been reduced from 25% to 0.5%.

The Kyonggi Provincial Mental Health Program in Korea established 14 community mental centers across the Kyonggi province in 1998, providing essential services such as day care services, case management, family support,

community education, and linkage to various community resources. Owing to its successful implementation, the Ministry Division of Mental Health adopted Kyonggi's model project in starting a national mental health project in 1999.

Equitable access to mental health care

Access to basic mental health care usually means access to practitioners with mental health training, basic medications and family support. To support basic mental health care, access to specialist services, including acute care, and to rehabilitation and vocational programs is also needed. Access may be restricted for many reasons, including geographical barriers, a shortage of trained staff and medication, social stigma, a lack of financial support, and poor patient advocacy. The transition from institution-based care to community-based care has resulted in innovative approaches to address gaps in care across the region.

The National Mental Health Service Model Reform Program or "686 Program" in China was developed by the National Centre for Mental Health to increase access to mental health care through the development of 60 demonstration areas in 30 provinces. Free clinical care and medications have been provided to thousands of disadvantaged patients. Each site covers a population of about 400,000, with a total coverage of 42.9 million. Over 600 training sessions have been conducted for psychiatrists, community doctors, allied health workers, policemen, community workers, and patients' families, resulting in more than 50,000 people being trained. Globally, this has been one of the largest mental health reforms ever seen.

The Community Mental Health Nursing (CMHN) project in Indonesia increased access to mental health care in rural areas through the use of a mobile outreach service made up of nursing staff, community health workers and medical doctors with mental health training. The CMHN provided a range of services in terms of education, support and treatment targeting patients, their families and the greater community. Through education given by this project, the community can also support mental health care and vocational rehabilitation.

Support in the transition of care from institution to community

The process of shifting from institution-based care to the community is particularly difficult for people with chronic and severe mental illnesses who have spent many years in institutions. This may be due to a paucity of resources, both personal and external, that may result from their disability and institutionalization. However, the values of autonomy, self efficacy, personal strengths and good quality of life are no less important in these patients. Patients leaving institution-based care require not only strong psychiatric support, but also practical support, such as housing assistance and vocational and life skills training, to ensure good mental health outcomes.

The Extended-Care Patients Intensive Treatment, Early Diversion and Rehabilitation Stepping Stone (EXITERS) project in Hong Kong achieves supported transition of care of long-stay patients using a 3-phase system including flexible matching of resources, active community supports and follow-up structures utilising multidisciplinary staff. Intensive rehabilitation and case-management is provided to improve social and vocational functioning.

The Flight From The Nest Group (Sudachi-kai) in Japan is a social welfare corporation with an active role in both mental health staff and peer-led discharge promotion. Further, it places a strong emphasis on vocational training and providing housing support to ensure successful discharge from hospital-based care. This community based discharge programme run by a non-governmental organization (NGO) in Japan has discharged over 126 people since the program begun.

The Ger Project in Mongolia, fostered by the WHO and SOROS Foundation, utilizes traditional portable round houses and tents called "gers" to deliver education and training in life and social skills to people with mental illness in the community. The Ger Project also provides psycho-education, counselling, family support and continuing psychiatric treatment.

Consumer and carer roles

Empowering users and carers, and the inclusion of their agenda, are critical to the planning and development of community mental health care. Many of the projects reviewed place a strong emphasis on patient autonomy. Patients' involvement in decision making regarding their care is not only in accordance with their human rights, but may also contribute to better compliance and may therefore result in better health outcomes. This is just as pertinent for people with mental illness as for those with other forms of illness. The role of a patient as consumer is powerful as it can be used to guide the future of care for people with mental illness through sharing of experience and advocacy. The role of consumer also extends beyond mental health care alone, and can be used to further validate the role of people with mental illness in the greater community.

The House of Bethel in Japan is a complex of services, self-help groups, and private firms that was established by a group of consumers. It places a strong emphasis on con-

sumer-focussed meetings, during which consumers discuss issues that they have faced, use problem-solving techniques to resolve these issues, and record their progress for the future benefit of other consumers.

Community networks and partnerships

The formation of community networks and partnerships increases the resources available to people with mental illness who are living in the community. Community partners such as community agencies, NGOs and volunteers bring valuable experience and resources that allow the development of projects which are appropriate to the patient group and their local community. They are also key partners in developing community linkages with local agencies and stakeholders.

The Mental Health Care model in Cambodia highlights the importance of effective patient advocacy by strengthening community links, and the role of families, NGOs and community agencies in mental health care. By putting emphasis on integrating mental health issues into all levels of medical training, the mental health knowledge and skills base of general health workers can be increased.

The Community-based Mental Health (CSSKTT) Project in Vietnam, by the establishment of an integrated mental health network between the provinces, initiated the development of mental health services in the community. The priority is to increase public awareness of mental illness, early detection, and access to treatment centres, therefore benefiting patients and families from underprivileged backgrounds and remote areas. This project received support from the provinces, districts, and villages.

Integration into existing health care resources

In all countries, community mental health services should be integrated with primary care and the general health system, to ensure a seamless and more cost-effective system of care, and ready access to treatment and care for those with mental illnesses. Integration will maximize holistic care of mentally ill patients who frequently have medical as well as psychological problems. In the context of limited resources in many countries, there is a need to maximize available resources and adapt to the socio-economic reality in developing appropriate community mental health services. Integration may be achieved by locating mental health workers in primary care settings or by training the primary care and community workers in basic mental health care and ensuring they receive continuing support from mental health specialists.

The District Mental Health Programme (DMHP) Model in India, launched under the National Mental Health Program, aimed to create a decentralized mental health service through the integration of mental health into the primary health care system. This is supported by the extensive network of trained health staff in the general health care system. In doing so, the DMHP also aims to raise community awareness and subsequently improve early detection, provide treatment and reduce stigma of mental illness.

The "Taipei Model", developed by the Taipei City Psychiatric Center (TCPC) in Taiwan, aims to build up a network between the hospital and the public health sector, and to facilitate follow-up visits by public health workers from 12 district health institutes to patients with severe mental illness discharged from the Center. Public health nurses are involved in the assessment, planning, implementation, and evaluation of the community psychiatric services.

Community awareness and promoting the value of mental health

The process of shifting the locus of care from institutions to the community runs parallel with stigma reduction and mental health promotion, as the very presence of mentally ill people in the community raises community awareness of mental health and illness. However, stigma is still present in many communities and acts as a barrier to accessing services. Promoting the value of mental health can be a positive and pro-active way to promote acceptance of mental illness care services, raising the community's awareness and understanding of mental health issues.

The DMHP in India employed a variety of techniques to improve mental health awareness, including the production and distribution of information booklets to youth clubs, volunteer organisations, teachers and government staff, screening of films on mental health in villages, and the creation of cinema slides to bring awareness of mental health issues to a broad audience.

The Community Based Mental Health Program (CMHP) in Thailand increases mental health awareness through the involvement of communities and their leaders in mental health promotion and prevention of mental illness in their own populations.

The primary objective of the Mental Health Promotion Project in Mongolia was to create an environment of mental health promotion, through an integrated strategy involving schools, families, NGOs and community agencies, to increase mental health awareness in the population. The use of this strategy aimed to increase community participation in mental health promotion activities, to improve the knowledge and attitude of policy makers regarding mental health, and to build inter-sectoral collabora-

tions in mental health awareness and the prevention of mental illness.

Crisis intervention

A key component of community mental health care is the provision of adequate and timely crisis intervention services to respond to people with acute psychiatric conditions or psychiatric emergencies. The crisis service should be part of a strong community mental health infrastructure which can provide ongoing care and support to reduce the incidence of psychiatric emergencies. Early intervention in acute episodes of psychiatric illness may decrease the need for hospital admission or prevent the development of chronic psychiatric disorders.

The Seoul Metropolitan Mental Health Centre (SMMHC) in Korea delivers comprehensive care to people with mental illness in the metropolitan community, using four distinct teams specializing in coordination of mental health centres, crisis intervention, providing care to homeless people with mental illness, and mental health promotion. The crisis management system also coordinates related agencies to prevent suicide and build social safety networks.

The Crisis Mental Health Intervention (CMHI) in Thailand, rapidly developed in response to the 2004 Tsunami, utilized models of community care and links with community networks and other organizations to deliver care in three phases to a large population, many of whom were displaced. Through the use of mobile mental health teams, and with the participation of primary care workers, village health volunteers and community leaders such as teachers and monks, all villages received timely and appropriate mental health care.

Early intervention

Early intervention aims to prevent chronic illness course and disability as a result of mental disorders. This can result in improved mental health outcomes, including reductions in the incidence of illness relapses, long-term complications and the need for inpatient care. Early intervention is especially critical for young people. Social withdrawal and disengagement from schooling often occur early in the illness and can have a significant impact on the young person's quality of life.

The Early Psychosis Intervention Programme (EPIP) in Singapore aims to increase early detection of mental health problems, including psychosis, through improved mental health literacy in schools. The EPIP also promotes early intervention through the training of primary care physicians in screening and the ongoing management of young people with mental illness.

The Early Assessment Service for Young People (EASY) in Hong Kong promotes early intervention by raising awareness through an extensive information campaign, assists early detection through the use of an open referral system, and provides optimal care through the use of pharmacological and psychosocial management delivered using a case management structure.

Adopting a patient-centred approach

Patients' needs are complex and vary from person to person, from group to group, and over time. A comprehensive and flexible mental health service that includes in-patient, community outreach, rehabilitation and home-based care is needed to cater for both acute episodes and long-term care for people with mental illness. Integration of various types of service provision is required to ensure continuity of care, so that patients can move between inpatient, community and home as their needs change. In meeting the variety of individual needs, services also need to be culturally sensitive and recovery oriented.

The Prevention and Recovery Care (PARC) services based in Victoria, Australia provide early intervention in the relapse process and post-acute support, and interventions to promote comprehensive care, self-management, relapse prevention and rehabilitation. Such services have both clinical and rehabilitation components, to close the gap between inpatient care and the community support system provided through the psychiatric disability rehabilitation and support sector. They reduce inpatient admissions by assisting those with acute mental illness (step up), and providing an early discharge alternative from inpatient units (step down).

A multi-disciplinary team approach, where clinicians of various mental health disciplines work collaboratively in the care of patients, is likely to provide higher quality, integrated care in the community. The team approach enables a more comprehensive care as it draws on the training and experience of all the staff involved. A multidisciplinary approach to care also promotes coordination, with all members of the treating team participating in planning comprehensive delivery of care. Community-based programs would also work closely with primary health care practitioners, NGOs and community resources, in achieving good mental health care outcomes.

The Community Psycho-Geriatric Programme (CPGP) in Singapore is a home-based clinical service that uses a multidisciplinary team approach to increase patients' access to services and the early detection of mental illness.

The CPGP places a strong emphasis on building community networks by actively engaging NGOs and community agencies. The programme provides training and support to these agencies in areas such as screening and early diagnosis of mental illness, and the ongoing management of older people with mental illness in the community.

To ensure that each patient is able to access the services they need and when they need them, it is essential to provide mental health professionals with skills to better manage and co-ordinate their activities. A co-ordinated patient-centred service is referred to as case management, which includes assessment, planning, implementation, coordination and monitoring aspects. Case management needs to be practiced differently depending on cultural contexts, resources and system preparedness. However, there are some principles that remain constant, and can be implemented generically (for example, individual service plans).

The National Mental Health Service Model Reform Program or "686 Program" in China has among its priorities to build workforce capacity to deliver a comprehensive mental health system, by up-skilling the mental health staff to enhance the practice of community care and case management. A tripartite training program is currently being conducted between mainland China, Hong Kong and Australia. Over 500 trainers have been trained in basic case management to deliver coordinated mental health care in 60 sites.

DISCUSSION

The Asia-Pacific region is characterized by great diversity of people, culture, ethnicities, languages, socioeconomic development, climate, geographical features and government systems. There is also wide variation among the countries in terms of population, gross national product, social infrastructures, health systems, education resources, and employment rates. In recent times, rapid socioeconomic development, population growth, propensity for natural disasters, threat of viral epidemics, shifts in social and family structures occurring in many countries in the region have resulted in significant challenges and impact on their health systems.

Throughout the region, the proportion of health budget expenditure on mental health is generally low compared to Western countries. While mental health funding is provided mostly by government budgets or insurance systems, in a number of countries the private sector, NGOs and international aid contribute significantly to the mental health resources. A common issue across nearly all countries has been the relative lack of resources in mental health, in terms of funding, workforce, facilities, availability of psychotropic drugs and research provisions. While most countries have mental health policies and plans, and many have mental health legislation, the standards and quality of mental health service provision vary widely between and within countries. Stigma associated with psychiatric conditions and lack of community acceptance of mental illness remain a major barrier throughout the region.

Community psychosocial rehabilitation facilities provide better and earlier care for people with mental disorders, help preserve the human rights of mental illness sufferers, and limit the stigma of mental health treatment. Globally, however, community care facilities exist only in 68.1% of countries, and in several regions, including South-East Asia, such facilities are only available in about half the countries (7). Where present in Asian countries, community mental health services are not equally available and are often restricted to a few well-resourced areas within urban centres in the country. Therefore, it is necessary to develop innovative approaches to scale up and expand community mental health resources, services and facilities (8), while not negating the need to improve the standards of existing psychiatric services in psychiatric hospitals and general hospitals.

Most recently, there is evidence of new ways of thinking about community mental health in our region. Significant efforts have been made to develop locally appropriate community-based mental health services in line with the recommendations in the World Health Report (9) and WHO Policy and Service standards (5). However, the different socioeconomic and cultural factors of mental health systems in Asia-Pacific countries often do not necessarily lend direct application of a standard or Western-based approach to community mental health models of care. Locally and culturally appropriate models of care are needed to implement sustainable mental health services that can be embedded in local community and health infrastructures.

The APCMHD project has been set up to explore diverse local models or approaches to community mental health service delivery in the region. The project has found that, although there is wide diversity in the models of community mental health care across and within Asia-Pacific countries and regions, consensus derived from these experiences is useful. The exchange of information about regional practices and solutions to challenges is useful in creating locally appropriate community mental health services and care models that could be implemented within each country. Many examples of best practice models of community-based services or care can be found across the Asia-Pacific. The examples present local modifications of community mental health models, highlighting successes and gaps, as well as some of the strategies used to overcome challenges encountered.

The APCMHD project provides impressive evidence that throughout the Asia-Pacific region there is increasing emphasis on system-wide reform in community mental health care rather than a series of localized and uncoordinated initiatives. Legislation, government policy and service standards are being established to support such mental health reform. Increasing resources are being directed to the provision of community-based services, including the expansion of mental health workforce training (medical practitioners, nursing and allied

health workers) in community-based services, as well as training and support of primary health care and community workers in basic mental health care. There is increasing recognition of the human rights of mentally ill people throughout the region, while steps are being taken to increase consumer and carer involvement. Emphasis is also given to strengthening inter-sectoral links such as social welfare, housing, employment and education. There is a strong underlying enthusiastic commitment from each country to move towards best practice community mental health care with the development of innovative, locally relevant programmes to transcend the acknowledged inherent obstacles within each country.

As local successful models are analysed and better understood in terms of future practical improvements in service delivery, there are positive implications and potential for constructive development for the rest of the region. However, the process has in fact only just begun, and much more needs to be done. There is considerable consensus in the region on the guiding principles and ingredients for successful implementation of community mental health care and also what is necessary and essential to meet future challenges.

APPENDIX

The Editorial Group of the Asia-Pacific Community Mental Health Development project includes: H.M. Aminullah, R. Calder, M.L. Somchai Chakrabhand, S. Chhit, J. Fraser, M. Goding, Se-Fong Hung, Tae-Yeon Hwang, Jin Liu, Than Thai Phong, R.N. Salhan, S. Singh, T. Takeshima, G. Tsetsegdary, Kim Eng Wong, E. Chia-Husan Wu.

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Embodiment and schizophrenia

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The essential feature of schizophrenic existence is its being disembodied. This is the feature that unifies the varied dimensions of that existence. The disembodiment of the self, of the self-object relation and of interpersonal relationships all lead to a kind of world in which the schizophrenic person lives and behaves like a soulless body or a disembodied spirit.

Key words: Cenesthesia, intersubjectivity, lived body, schizophrenia, self-awareness

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Since the beginning of the 20th century, phenomenology has developed a distinction between lived body (*Leib*) and physical body (*Koerper*), or body-subject and body-object. The first is the body experienced from within, my own direct experience of my body in the first-person perspective, myself as a spatiotemporal embodied agent in the world. The second is the body thematically investigated from without, as for example by natural sciences as anatomy and physiology, a third person perspective. Phenomenology conceives of the lived body as the center of three main dimensions of experience: a) the experience of my self, and especially of the most primitive form of self-awareness; b) object-experience and meaning-bestowing; c) the experience of other people, i.e. intersubjectivity.

MINIMAL SELF-AWARENESS

I experience myself as the perspectival origin of my experiences (i.e., perceptions or emotions), actions and thoughts. This primordial access to myself, or primitive form of egocentricity, must be distinguished from any explicit and thematic form of I-awareness, since it is tacit and implicit, although experientially present. This primitive experience of myself does not arise in reflection, i.e. from a split between an experienced and an experiencing self, but is a pre-reflexive phenomenon. It is also immediate, since it is an evidence not inferentially and criterially given. This form of primitive self-awareness is not a conceptual or linguistic representation of oneself, but a primordial contact with oneself or *self-affection* in which who feels and who is felt are just one thing (1). Last but not least, it must be also distinguished from a kind of object-awareness, since it is does not arise from an objectifying or observational perception of oneself. Henry uses the term *ipseity* to express this basic or minimal form of self-awareness (1). Thus, *ipseity* is the implicit, pre-reflexive, immediate, non-conceptual, non-objectifying and non-observational sense of existing as a subject of awareness. It is prior to, and a condition of, all other experience.

Two basic and closely related aspects of minimal self-awareness are self-ownership and self-agency (2). Self-ownership is the pre-reflexive sense that I am the one who is undergoing an experience. Self-agency is the pre-reflexive sense that I am the one who is initiating an action. The immediate awareness of the subjectivity of my experience or action involves that these are in some sense owned and generated by myself. These are the basic components of the experienced differentiation between self and non-self, my self and the object I perceive, and my representation of that object and the object itself. Merleau-Ponty (3) emphasized that this basic form of self-experience is rooted in one's bodily experience and its situatedness amongst worldly objects and other people. Ipseity, to Merleau-Ponty, is indiscernible from "inhabiting" one's own world, i.e. being engaged and feeling attuned to one's own environment. It is the lived body that provides this engagement and attunement. Being conscious – says Merleau-Ponty (3) – is dwelling in (*être-à*) the world through one's own lived body. There is good empirical evidence in developmental psychology that newborn infants are already equipped with this minimal form of self-awareness that is embodied and attuned to the world; for instance, Rochat (4) argues that children, long before they have developed a conceptual image of themselves, have a proprioceptive and ecological sense of their bodily self.

OBJECT-AWARENESS AND MEANING BESTOWING

The power of organizing experience is grounded in motility and perception. Husserl (5) showed that a modification in one's lived body implies a modification in the perception of the external world. To Husserl, the shape of material things, just as they stand in front of me in an intuitive way, depends on my configuration, on the configuration of myself as an experiencing embodied subject. By means of the integrity of kinaesthesia – the sense of the position and movement of voluntary muscles – my own body is the constant reference of my orientation in the perceptive field. The perceived object gives itself through the integration of a series of prospective appearances.

The lived body is not only the perspectival origin of my perceptions and the locus of their integration, it is the means by which I own the world, insomuch as it structures and organizes the chances of participating in the field of experience.

The living body perceives worldly objects as parts of a situation in which it is engaged, of a project to which it is committed, so that its actions are responses to situations rather than reactions to stimuli. The body – as Merleau-Ponty would put it – seeks understanding from the objects with which it interacts; the lived body is silently at work whatever I do. I understand my environment as I inhabit it, and the meaningful organization of the field of experience is possible because the active and receptive potentials of my own body are constantly projected into it (6). Knowledge is enacted (7) or action-specific, and perception is always tangled up with specific possibilities of action (8). Perception is constantly geared up to tracing possibilities for action; these possibilities for action are what we call "meaning", since the meaning of an object is how we put it at use. As Heidegger (9) put it, the basic kind of knowledge I have of objects I encounter in the world is not a kind of mere theoretical cognition, but rather a kind of concern which manipulates things and "puts them to use". Objects appear to my embodied self as something "in-order-to", as "equipment", "ready to hand", for manipulating reality and so for cutting, sewing, writing, etc. I literally *grasp* the meaning of one thing, since this meaning is exactly the specific "manipulability" (*Handlichkeit*) of one thing.

INTERSUBJECTIVITY

Merleau-Ponty places the lived body also at the center of the problem of intersubjectivity, setting the stage for the understanding of intersubjectivity as intercorporeality, i.e. the immediate, pre-reflexive perceptual linkage between my own and the other's body through which I recognize another being as an alter ego and make sense of his actions. From the angle of intercorporeality, intersubjectivity is a communion of flesh and not a relationship between separate persons. Intercorporeality means the transfer of the corporeal schema, the primary bond of perception by which I recognize others as being similar to myself. This phenomenon is the phenomenal basis of syncretic sociability, i.e., of pathic identification with the other; in a word, of intersubjectivity (10). Intercorporeality is never fully evident, but it is the bearing support of all interaction connected with behaviour, already active and present ahead of any explicit communication. The perceptive bond between myself and another person is based on my possibility to identify with the other person's body by means of a primary perceptive tie. Developmental psychologists support the hypothesis that proprioception is involved in understanding other persons through body-to-body attunement (11). Scientific evidence from neuroimaging also seems to corroborate this view: mirror neurons are a set of visuo-motor neurons in the pre-motor cortex of primates that are supposed to be the neurophysiological substratum for intersubjectivity as intercorporeality. Mirror neurons fire both when a given action is performed by the self and when, performed by another individual, it is simply observed, and as such they are involved in action understanding: meaning is assigned to an observed action by matching it on the same neuronal circuits that may generate it (12,13).

CENESTHESIA

Cenesthesia is the word by which psychopathologists, and sometimes philosophers, talk of the internal perception of one's own body, whereas cenesthopathy refers to abnormal bodily sensations. Both are quite neglected subjects in mainstream contemporary psychopathology, but they have represented a fundamental topic in French and German 19th and early 20th century psychiatry. The historian Starobinski (14) speaks of an "imperialism of cenesthesia" in the last century. It was Reil in 1794 who coined this term, indicating "the means by which the soul is informed of the state of its body". Cenesthesia (deriving from Greek *koiné aesthesis,* common sensation) is defined as the global experience in which all the single bodily sensations are synthesized, the crossroads of all sensibility on which consciousness is grounded, including the feeling of existing, of being a self and of being separated from the external world. Affections of cenesthesia are, especially to French early 20th century psychopathologists, the origin of psychoses. For instance, Dide and Guiraud (15) thought that hebephrenia is characterized by the specific impairment of those cellular nervous systems presiding to the cenesthetic and kynesthetic synthesis and to instinctual vital activity. Athymormia – the global disorder of instinct (*hormé*) – is considered "the spring of delusions" since delusions are supposed to be disorders of the "primordial psychic activity", complicated and masked by the intellectual and affective superstructures of human thinking (16).

In a quite different vein, Huber (17) defined as the fourth subtype of schizophrenia – next to paranoid, catatonic and simplex-hebephrenic forms – a clinical syndrome called *cenesthetic schizophrenia,* characterized by abnormal bodily sensations. These are disorders of the lived body, painful and uncanny, that occur abruptly, and often migrate from one organ or bodily zone to another. Typical examples are feelings of extraneousness, or numbness, or non-existence of parts of one's own body, sensations of paralysis, heaviness, abnormal lightness, of shrinking or enlargement, of movement or traction, etc. These abnormal bodily sensations may lead to psychotic symptoms, such as hypochondriac delusions and more typically delusions of being controlled. Sass (18) remarked that these bodily sensations are not abnormal per se, but remarkably similar to those reported by normal subjects adopting a detached introspective stance toward their bodies. Schizophrenic cenesthopathies are normal bodily sensations that are always present, even though we do not usually attend to them; what is abnormal is the way schizophrenic persons attend to them – they are abnormal since they are "lived in the perfectly abnormal condition of hyperreflexive awareness and diminished self-affection" (17). The final result is an experience of increasing distance between subjectivity and bodily experience.

Others remarked that schizophrenic cenesthopathies are typically quasi-ineffable. Huber (17) observed that a key feature of schizophrenic bodily disesthesias is that they challenge the ordinary capacity for linguistic representation: in our language, the expressive possibilities and adequate categories concerning these peculiar bodily sensations are completely lacking. The issue of the relations between abnormal bodily sensations and language has a long tradition. Blondel (19), a forerunner in this field, postulated that cenesthopathies occur when the mind is not able to categorize bodily sensations, i.e. to express them through the impersonal system of socialized discourse. Ey (20) remarked that bodily hallucinations crop up when the subject cannot express linguistically a bodily sensation. To Ey, the expression of bodily sensations always needs a metaphor. Hallucinating, in the field of this peculiar sense, is perceiving one's own body completely or partially as an object or a living entity outside oneself, i.e., as an object transformed by the very impossibility of metaphorical expression.

SCHIZOPHRENIA AND DISEMBODIMENT

The essential feature of schizophrenic existence is its being disembodied. This is the feature that unifies the varied dimensions of schizophrenic existence. The disembodiment of the self, of the self-object relation and of interpersonal relationships all lead back to a kind of world in which the schizophrenic person lives and behaves like a soulless body or a disembodied spirit (21,22).

Disembodiment of the self

The crisis of ipseity is the clearest expression of the shape schizophrenic life assumes as a deanimated body (i.e., a body deprived of the possibility of living personal experiences – perceptions, thoughts, emotions – as *its own*) and also as a disembodied spirit (i.e., as a sort of abstract entity which contemplates its own existence from outside – a third-person perspective view, or a view from nowhere). As a deanimated body, the schizophrenic person experiences a specific feeling of *loss of presence*. In the lightest cases, he feels detached from himself and his actions and experiences. The seam between mind and body seems to have been torn apart. In the severest cases, he describes himself as empty, hollow: "There's nothing inside my body; it's just a frame", "Inside my chest nothing's there, just a big hole" (23). The hollowness manifests itself, in movements, as a lack of contact between the various parts of the body: "When I move I seem to lose something, like my whole body is leaving me. The spinal column or something goes invisibly through the flesh" (23). Organs lose their mass, and with this, their ability to have a reciprocal bond that acts as a force to tie them together. This state is marked by a total mechanization of the body: "I'm blessed with a bladder-emptier that I can turn on and off, and an anal expeller". They feel like mechanical replicas of living organisms: "I'm a psycho-machine" – says a patient of Kimura (24). These experiences and expressions must be taken literally and not metaphorically.

A second way people with schizophrenia experience their own body is that of disembodied spirit or incorporeal, purely theoretical awareness. They live as mere spectators of their own perceptions, actions, and thoughts: "The world is an illusion because it's seen through a brain"; "If the mind is empty it functions like a plotter or a camera". This radical dualism between a *subject* who's thinking and an *object* that is conceived of in its pure and simple extensive externalness – pure consciousness and pure materialness – is the fundamental phenomenon of schizophrenic anomalies of embodied self-awareness.

Disembodiment of self-object relations

The global crisis of embodiment involves anomalies of self-object relations and meaning-bestowing. If my body-based involvement in the world is switched off, my *grasp* onto the world will fade away too. Objects in the world will not immediately relate to my body as existentially relative utensils. They become non-utilizable and appear devoid of practical meanings. There is a loss of *ready-to-hand meanings* to be attached to things in the world, which paradigmatically occurs in pre-delusional perplexity. Here the expression "ready-to-hand" must be taken literally, not metaphorically: since things cannot be *grasped*, they appear as *devoid of their ordinary meaning*, i.e. the way one usually puts them to use (25). New meanings may emerge (as in delusional perceptions) that are not practical meanings in the ordinary sense, i.e. geared up with survival and drive-based ordinary life; rather, they are geared up with idiosyncratic concerns that arise from a background of ontological incompleteness and abnormal constitution of intersubjectivity. The quest for personal identity and one's place in the world and metaphysical concerns typically provide a new and peculiar kind of enactment in schizophrenic disembodied self-world relationship. For instance, a patient described by K. Schneider (26) may take a dog lifting its leg in front of him as "a true revelation". What comes into view in delusional perceptions is a perceptive detail that speaks to the person and in so doing discloses a new understanding of the world or a new identity that is deeper and more personal (27). An emblematic example of metaphysical enactment is the following: a schizophrenic person says that, when he seats at the theatre, he is not focused on what happens on the stage, since he cannot help thinking of what's going on backstage, what "makes the scene possible". An unusual perspective unto the world takes place and new meanings (the quest for what is real vs. unreal) emerge (28).

A further feature of disembodiment is the inclination to abstraction of schizophrenic cognition: words escape the situation to which they are referred and the meaning they

take on according to the context in which they are used. Words too become disembodied and de-situated and acquire an existence of their own. They themselves may get an object-like existence, undistinguishable from "real" objects (these too disembodied and thus more similar to concepts and representations than to material objects). Words are no longer used to share a world, but to create an alternative one, or a world on its own. Therefore, words and objects may become interchangeable: paradigmatically, metaphors become flesh-and-blood things; the catachresis (concrete expression) of metaphors flings open the door to delusions.

Disembodiment of intersubjectivity

In the relations between the disorders of embodied self-awareness and intersubjectivity-intercorporeality, we can recognize a circular relationship. The defective structuring of selfhood, particularly through the phenomena of somato-psychic depersonalization (bodily perception disorders) and auto-psychic depersonalization (detachment from one's own emotions and thoughts), can become an obstacle to the intercorporeal attunement between the self and the other persons. Schizophrenic autism may derive from the incapacity to enter into emotional attunement with others and recognizes as *primum movens* a different quality of bodily performance.

Schizophrenic autism reflects the fundamental constitutional fragility of selfhood, that is its fundamental incompleteness, which results in problematic relations, meetings and confrontations with the other. Detachment from the social world appears to derive from the lack of this fundamental structure, of this ontological setting, necessary and indeed crucial to be a self and thus to take part in the self/other-from-self dialectic of social relations. Looking at it from the opposite angle, that is, from the interpersonal dimension of the ontogenesis of consciousness, a disorder in early relationships can heavily damage the maturing process of full corporeal self-awareness.

The *attunement crisis* conveys this third-person perspective to the interpersonal world. This social world loses its characteristic as a network of relationships among bodies moved by emotions, and turns into a cool, incomprehensible game, from which the schizophrenic person feels excluded, and whose meaning is sought through the discovery of abstract algorithms, the elaboration of impersonal rules.

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Letter to the Editor

Hospitalization in a psychiatric ward is a complex experience that requires patients to cope with new situations and interact with previously unfamiliar people, such as staff members and fellow patients. Living together 24 hours a day in a ward and participating in group therapeutic interventions facilitates an atmosphere where patients can discuss their problems and may sometimes develop close, intimate relationships. Contact with peers from within the mental health system is likely to provide opportunities for ventilation of emotions, reassurance and social approval, problem solving and reality testing (1).

The issue of sexual relations between psychiatric inpatients is more problematic. Though 75% of sexual relationships in acute wards are by reciprocal consent (2), dilemmas arise regarding patients' rights, mental conditions, suicidality, impulsivity, cultural, familial and social norms. The situation becomes more complicated when the involved patients have spouses, come from different ethnic backgrounds, or face adversity due to political strife between two ethnicities.

Here we report the problematic case of an emotional involvement which developed between a young man with schizophrenia and a young woman with borderline personality disorder with different ethnic backgrounds.

Mr. P is a 21 year-old Jewish Israeli, diagnosed with DSM-IV schizophrenia. While in an open psychiatric ward, P met a 20 year-old Arab Israeli woman and they became deeply involved in an emotional relationship. The relationship's process was very dramatic and unstable, partly because of the strong opposition from both families. The hospital staff was faced with the impact of this situation on P's mental condition, including suicidal thoughts, wedding plans and resistance to discharge. Rehabilitation programs did not progress due to lack of cooperation. The problematic emotional circumstances of the relationship interfered with his chances of achieving a complete remission. He was very tense and at one point was transferred to a closed ward after he exhibited aggressive behavior following a fight with his girlfriend. When his mental condition improved he was discharged, but he refused to participate in any rehabilitation program in the community. Once again, he was admitted to the ward because of his reports of "suicidal thoughts". It was clear that he came back in order to stay with his girlfriend in the only place where they were able to be together without fear of their families' reactions.

Ms. M is a 20 year-old Israeli Arab woman. She was admitted to the same open psychiatric ward as Mr. P because of depression and suicidal thoughts. Her behavior in the ward was characterized by emotional lability, anxiety, a pattern of dramatic and unstable relationships and short psychotic episodes. She was diagnosed with borderline personality disorder.

After her first discharge, she was re-admitted several times, because of violent confrontations with her family, partly because of her resistance to behave according to Arab social norms. The situation became more complicated because of her romantic relationship with Mr. P. M didn't want to return home, even for week-ends, as she was constantly involved in her relationship with Mr. P. The violence at home worsened, so the department staff decided that M's rehabilitation should take place away from her home. However, M did not cooperate, her family was clearly against this program, and finally after nine months she returned home.

The relationship between the two patients had several implications for the treatment of each as an individual, as well for management by the professional staff.

Considering the fact that Mr. P has schizophrenia, a disorder usually associated with feelings of loneliness and isolation, his emotional and sexual relationship with Mrs. M may suggest a degree of success. However, he was so involved with M, that he lost all motivation to participate in rehabilitation programs and therapeutic activities that did not include her. In his psychotherapy sessions, he did not talk about anything other than his girlfriend. His mood was very unstable and his responses to various situations in the relationship were unpredictable.

Although P and M did not have sexual contact in the ward, the staff strongly suspected that they found discreet places to be together. When the families pressured the couple to sever the relationship, P reported suicidal thoughts.

During P's long hospitalization, the staff had to reframe the goals of his treatment. P's mental condition was not improving. Although he was not in a psychotic state, he refused to participate in occupational therapy and therapeutic groups, and he exhibited a functional deterioration. The staff faced the dilemma of respecting P's rights but at the same time protecting him from becoming a victim of some level of emotional abuse by M. Decisions regarding discharge were complicated, because outside of the ward he felt that he had nothing and reported that he was feeling alive only in the ward with M. In addition, M's family threatened to murder him and his family if he did not terminate the relationship.

M is a young Arab Muslim woman. She acted against the social and religious norms of her society, provoking rage in her parents, even to the point of murder threats. In the psychiatric ward she felt very liberated, and was very popular among young patients. The staff wondered if she was not manipulating Mr. P's feelings, using him as a weapon against her family, or using her disorder to escape the home life which she experienced as oppressive. In her case it was very difficult to establish treatment goals, to cope with her suicidal thoughts, and to appropriately manage her interactions with her family.

After several months of trying to define the treatment objectives for each patient, P was discharged and continued visiting M. As far as we know, they are trying to keep in touch, in spite of great difficulties.

We evaluated the mental conditions of both patients involved in the emotional relationship, especially the reality judgments concerning the relationship and its consequences. We concluded that both individuals decided to continue with their relationship by exercising their free will, with full understanding of the situation's complexity due to the families' opposition and political adversities.

We decided to respect the patients' autonomy and not to disturb the process of their relationship. Nevertheless, with the consent of both patients, we met the families and communicated to them our position and the importance of respecting the patients' rights. Considering the patient's condition, P, for the first time in his life, fell in love and that love was returned by M. M, on her part, received love and empathy from P, which may have been a type of corrective experience, after being a neglected and maltreated child. The treating staff concluded that forbidding the relationship would damage the mental condition of each of the patients.

In our opinion, the major aspects that have to be evaluated, when the staff is dealing with emotional relationships between psychiatric inpatients, are included in the Georgetown principles of ethics in medicine (3): benefit the patient's condition; first of all don't damage (non-maleficence; *primum non nocere*); respect patient's autonomy; keep the principle of justice in conflict situations between benefits to the individual and society.

Evaluation of patient's judgment is essential in order to respect autonomy, and also to protect patients that are at risk of being abused by other patients. The staff has to be aware of not evaluating and judging situations according to their own cultural norms. The staff can also consider getting advice from the hospital ethics committee, including about the legal aspects of the situation.

Every case of emotional relationships between patients in an acute ward demands an individual evaluation, taking into consideration the Georgetown principles of medical ethics and the importance of a good therapeutic alliance with the treatment staff of each of the patients.

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The WPA General Assembly in Prague and the new WPA leadership

The WPA General Assembly was held in Prague on September 22, 2008, within the 14th World Congress of Psychiatry.

The Assembly approved unanimously the admission of five new Member Societies: the Jamaican Psychiatric Association; the Montenegrin Psychiatric Association; the Libyan Association of Psychiatry, Neurology and Neurosurgery; the Saudi Psychiatric Association; and the Psychiatrists' Association of Nepal. The WPA Member Societies are now 134: 28 in the Americas; 62 in Europe; 23 in Africa and the Middle East; and 21 in Asia and the Australasia.

The WPA Action Plan 2008-2011 was unanimously approved. The Association's institutional goals during the triennium will be the following: 1. To enhance the image of psychiatry worldwide among the general public, health professionals and policy makers. 2. To partner with Member Societies in their efforts to improve the quality of mental health care, education and research in their countries and regions, and in their attempts to upgrade their own structure, governance and organizational capacity. 3. To promote the dissemination of information on recent clinical, service and research developments in such a way that it can be assimilated by psychiatrists of all regions of the world. 4. To promote the professional development of young psychiatrists worldwide. 5. To promote the development of mental health care in low-income countries and its integration into primary care. 6. To foster the participation of psychiatrists from all regions of the world in the international dialogue on clinical, service and research issues. 7. To promote the highest ethical standards in psychiatric practice and advocate for the rights of persons with mental disorders in all regions of the world. 8. To promote the establishment of networks of scientists conducting collaborative research in the mental health field. 9. To increase the visibility and credibility of the Association at the international level. 10. To build up a long-term, solid and transparent partnership with potential donors.

Resulting from the elections which were held during the General Assembly, the composition of the new Executive Committee of the WPA is the following:

President: Mario Maj (Italy)
President-Elect: Pedro Ruiz (USA)
Secretary-General: Levent Küey (Turkey)
Secretary for Finances: Tsuyoshi Akiyama (Japan)
Secretary for Meetings: Tarek Okasha (Egypt)
Secretary for Education: Allan Tasman (USA)
Secretary for Publications: Helen Herrman (Australia)
Secretary for Sections: Miguel Jorge (Brazil)

The composition of the new Board of the Association is the following:

Zone 1 (Canada): Raymond Tempier (Canada)
Zone 2 (United States of America): Michelle B. Riba (USA)
Zone 3 (Mexico, Central America and the Caribbean): Mauricio Sanchez (Nicaragua)
Zone 4 (Northern South America): Fabrizio Delgado (Ecuador)
Zone 5 (Southern South America): Luis Risco (Chile)
Zone 6 (Western Europe): Linda Gask (UK)
Zone 7 (Northern Europe): Henrik Wahlberg (Sweden)
Zone 8 (Southern Europe): Miguel Roca Bennasar (Spain)
Zone 9 (Central Europe): Dusica Lecic-Tosevski (Serbia)
Zone 10 (Eastern Europe): Armen Soghoyan (Armenia)
Zone 11 (Northern Africa): Driss Moussaoui (Morocco)
Zone 12 (Middle East): Charles Baddoura (Lebanon)
Zone 13 (Central and Western Africa): Joseph Adeyemi (Nigeria)
Zone 14 (Eastern and Southern Africa): Solomon Rataemane (South Africa)
Zone 15 (Central and Western Asia): S. Ahmad Jalili (Iran)
Zone 16 (Southern Asia): E. Mohandas (India)
Zone 17 (Eastern Asia): Naotaka Shinfuku (Japan)
Zone 18 (Australasia and the South Pacific): Julian Freidin (Australia)

The WPA International Congress "Treatment in Psychiatry: A New Update" (Florence, April 1-4, 2009)

The WPA International Congress "Treatments in Psychiatry: A New Update" will take place in Florence, Italy, from 1 to 4 April, 2009. It will be the follow-up to the 2004 WPA International Congress "Treatments in Psychiatry: An Update", which was the second most attended psychiatric congress worldwide in that year, with almost 7,000 participants. This time, more than 8,000 participants are expected.

The Congress aims to provide a high-quality, comprehensive overview of all evidence-based treatments currently available for all mental disorders. Many of the most renowned experts in the various treatment areas will be among the speakers.

The Congress will consist of the following components: a) ESI[SM] Top-Cited Scientist Lectures (delivered by the scientists who attracted the highest total citations to their papers in indexed journals of psychiatry and psychology over the past 10 years, according to the Essential Science Indicators); b) Update Lectures (providing a comprehensive update on some of the most significant aspects of current treatments in psychiatry); c) Update Symposia (focusing on specific treatment issues, with an active interaction between speakers and participants); d) Advanced Courses (in which a well-renowned expert will interact with no more than 50 participants); e) Regular Symposia (high-quality Symposia selected from those submitted by April 30, 2008); f) Workshops (high-quality sessions dealing with very specific treatment issues, selected from those submitted by April 30, 2008); g) Section and Zonal Symposia or Workshops (organized by WPA Scientific Sections or Zones); h) New Research Sessions; i) Poster Sessions.

Please find below the list of the ESI[SM] Top-Cited Scientist Lectures, Update Lectures, Update Symposia and Advanced Courses. The final programme of the Congress is available on the website www.wpa2009florence.org.

ESI[SM] Top-Cited Scientist Lectures

TL1. *R.C. Kessler* – The treatment gap in psychiatry

TL2. *K.S. Kendler* – Psychiatric genetics: a current perspective

TL3. *H.S. Akiskal* – Bipolarity: a broad spectrum (spectra) in search of treatment

TL4. *S. McElroy* – Pharmacotherapy of binge eating disorder

TL5. *M. Rutter* – Environmental causes of mental disorder

TL6. *R.M. Murray* – The causes of schizophrenia: the striatum and the street

TL7. *M.E. Thase* – Long-term management of depression: the role of pharmacotherapy and psychotherapies

TL8. *P.E. Keck* – What is a mood stabilizer?

TL9. *D.J. Kupfer* – Medical burden in bipolar disorder

TL10. *A.J. Rush* – Getting the evidence for evidence based care of depression: how to narrow the knowledge gap

Update Lectures

UL1. *R.J. Baldessarini* – Disorders, syndromes, target symptoms: how do we choose medications?

UL2. *P. Fonagy* – Psychotherapies: what works for whom?

UL3. *K.W.M. Fulford* – Values-based practice and psychiatric diagnosis: bringing values and evidence together in policy, training and research

UL4. *S.G. Resnick* – Recovery and positive psychology: empiricism or attitude?

UL5. *G. Thornicroft* – Steps, challenges and mistakes to avoid in the development of community mental health care: a framework from experience

UL6. *P.D. McGorry* – Early intervention in psychiatry

UL7. *M.F. Green* – Improving cognitive performance and real-world functioning in people with schizophrenia

UL8. *E. Vieta* – Evidence-based comprehensive management of bipolar disorder

UL9. *R.E. Drake* – Management of patients with co-occurring substance abuse and severe mental disorder

UL10. *M. Stone* – Comprehensive management of borderline personality disorder in ordinary clinical practice

UL11. *W.W. Fleischhacker* – Comparative efficacy, effectiveness and cost-effectiveness of antipsychotics in the treatment of schizophrenia

UL12. *P.J. Weiden* – The art and science of switching antipsychotic medications

UL13. *G.A. Fava* – Combined and sequential treatment strategies in depression and anxiety disorders

UL14. *K.A. Halmi* – Multimodal management of anorexia and bulimia nervosa

Update Symposia

US1. The evolving science and practice of psychosocial rehabilitation (*Chairperson: R. Warner*)

US2. Anxiety disorders: from dimensions to targeted treatments (*Chairperson*: *J. Zohar*)

US3. Treatment advances in child psychiatry (*Chairperson*: *J.L. Rapoport*)

US4. Outcome in bipolar disorders: new findings and methodological findings *(Chairperson: M. Tohen)*

US5. Management of medically unexplained somatic symptoms (*Chairperson*: *O. Gureje*)

US6. The future of psychotherapies for psychoses (*Chairperson*: *P. Bebbington*)

US7. Advances in the management of treatment-resistant depression (*Chairperson*: *S. Kasper*)

US8. ICD-11 and DSM-V: work in progress (*Chairperson*: *M. Maj*)

US9. Gender-related issues in psychiatric treatments (*Chairperson*: *D. Stewart*)

US10. Suicide prevention: integration of public health and clinical actions (*Chairperson*: *Z. Rihmer*)

US11. Brain imaging in psychiatry: recent progress and clinical implications (*Chairperson*: *L. Farde*)

US12. Advances in the management of treatment-resistant bipolar disorder (*Chairperson*: *G.B. Cassano*)

US13. Partnerships in mental health care (*Chairperson*: *B. Saraceno*)

US14. Genomics and proteomics in psychiatry: an update (*Chairperson*: *N. Craddock*)

US15. Patterns of collaboration between primary care and mental health services (*Chairperson*: *V. Patel*)

US16. Effectiveness and cost-effectiveness of pharmacological treatments in psychiatry: evidence from pragmatic trials (*Chairperson*: *J. Lieberman*)

US17. Cognitive impairment: should it be part of the diagnostic criteria for schizophrenia? (*Chairperson*: *R. Keefe*)

US18. Cultural issues in mental health care (*Chairperson*: *P. Ruiz*)

US19. Advances in the management of treatment-resistant psychotic disorders (*Chairperson*: *H.-J. Möller*)

US20. Violence, trauma and victimization (*Chairperson*: *A. McFarlane*)

US21. The challenge of bipolar depression *(Chairperson: J. Calabrese)*

US22. Novel biological targets of pharmacological treatment in mental disorders (*Chairperson*: *G. Racagni*)

US23. Intermediate phenotypes in psychiatry (*Chairperson*: *D. Weinberger*)

US24. Current management of mental disorders in old age (*Chairperson*: *C. Katona*)

US25. Prevention and early intervention strategies in community mental health settings (*Chairperson*: *S. Saxena*)

US26. Managing comorbidity of mental and physical illness (*Chairperson*: *N. Sartorius*)

US27. Mental health care in low-resource countries (*Chairperson*: *P. Deva*)

US28. Prevention of substance abuse worldwide (*Chairperson*: *M.E. Medina-Mora*)

Advanced Courses

AC1. Interacting with families of people with severe mental disorders *(Director*: *C. Barrowclough)*

AC2. Management of the suicidal patient (*Director: D. Wasserman*)

AC3. The therapeutic alliance in psychiatric practice (*Directors: A. Tasman, J. Kay*)

AC4. Management of mental disorders during pregnancy and post-partum (*Director*: *I. Brockington*)

AC5. How to organize a comprehensive community mental health service (*Directors: G. Thornicroft, M. Tansella*)

AC6. Prevention and management of burnout in mental health professionals (*Director*: *W. Rössler*)

AC7. Measures of outcome in schizophrenia (*Director: R. Kahn*)

AC8. Assessing and training neurocognitive functions in patients with chronic psychoses (*Director*: *S. Galderisi*)

AC9. Consultation-liaison psychiatry: learning from experience (*Director*: *F. Creed*)

AC10. Relevance of phenomenological psychiatry to clinical practice (*Director*: *G. Stanghellini*)

AC11. The psychiatrist in court (*Director*: *J. Arboleda-Florez*)

AC12. Management of the "difficult" child (*Director*: *S. Tyano*)

AC13. The public health approach: what psychiatrists need to know (*Directors*: *H. Herrman, S. Saxena*)

AC14. Interpersonal psychoterapy of depression (*Director*: *T. Gruettert*)

CALL FOR PROPOSALS OF RESEARCH PROJECTS TO BE SUPPORTED BY THE WPA AND CONDUCTED BY ITS SCIENTIFIC SECTIONS

The World Psychiatric Association (WPA) is the largest association active in the mental health field worldwide, with 134 Member Societies (national psychiatric societies), in 122 countries, representing more than 200,000 psychiatrists.

The scientific backbone of the Association is represented by its 65 Scientific Sections, covering practically every aspect of psychiatry. According to the WPA statutes, one of the purposes of these Sections is the promotion and conduction of international collaborative research, a purpose which has been only partially achieved up to now, mainly due to financial constraints.

The WPA is going to fund two high-quality research projects proposed by its Scientific Sections. The projects will have to deal with one of the following issues highlighted in the WPA Action Plan 2008-2011: 1. Depression in persons with physical diseases. 2. Stigmatization of psychiatry and psychiatrists. 3. Integration of mental health care into primary care. 4. Protection and promotion of physical health in persons with severe mental disorders. 5. Assessment and development of talents and strengths of persons with mental disorders.

Proposals from individual Sections or networks of Sections are welcome. They will have to include a description of the project (max. 3000 words, including an introduction, the objectives, the methodology and some references), a list of the participating centres, a timetable, and a detailed budget. A short curriculum vitae of the proposed principal investigator(s) is also requested (no more than one page). Proposals will have to be sent by e-mail to the WPA Secretariat (wpasecretariat@wpanet.org) by June 30, 2009.

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