Major depression invites major concerns

Depressão maior suscita questionamento maior

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Abstract

Objective: *To overview limitations to the concept and construct of major depression.* ***Method****: The objectives in initially conceptualizing major depression are examined against its subsequent utility and relevance to clinicians and researchers.* ***Results:*** *It is argued that, as defined, major depression does not differentiate clinical depression well from expressions of non-clinical depression or sadness, that its criteria set do not generate reliable diagnoses, that a diagnosis of major depression means little in and of itself (as it effectively comprises multiple types of depression) and that it fails to inform us about cause, natural history or differential treatment response.* ***Conclusion:*** *Limitations to the concept of major depression would benefit from wider appreciation to advance changes to the clinical diagnosis of depressive sub-types.*

Descriptors: *Depression; Depressive disorder; Psychotherapy; Clinical trials as topic; Treatment outcome*

Resumo

Objetivo*: Revisar as limitações do conceito e do construto da depressão maior.* ***Método:*** *Os objetivos na conceitualização inicial da depressão maior são examinados em relação à sua subseqüente utilidade e relevância para os clínicos e pesquisadores.* ***Resultados:*** *Afirma-se que, como definida, a depressão maior não diferencia bem a depressão clínica das expressões de depressão não clínica ou de tristeza; que seu conjunto de critérios não gera diagnósticos confiáveis; que um diagnóstico da depressão maior pouco significa por si só (na medida em que compreende efetivamente múltiplos tipos de depressão); e não nos informa sobre a causa, histórico natural ou resposta diferenciada ao tratamento.* ***Conclusão:*** *As limitações do conceito de depressão maior poderiam se beneficiar de uma avaliação mais ampla para impulsionar alterações no diagnóstico clínico dos subtipos depressivos.*

Descritores: *Depressão; Transtorno depressivo; Psicoterapia; Ensaios clínicos como assunto; Resultado de tratamento*

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Introduction

This paper will consider the status and utility of 'major depression', a multi-purpose construct that is commonly equated with 'clinical depression'. It dominates categorical assignment in studies pursuing the 'causes' of depression and is viewed by many clinicians as sufficient to dictate treatment of the individual depressed patient. Before challenging the utility of this construct ('major depression'), it is first useful to ask what we want of a classificatory system for the depressive disorders.

As considered elsewhere,[1] in addition to a valid underlying model, requirements of such a classificatory system might be expected to include: 1) distinguishing clinical depressed mood states from 'normal' depressed mood states (i.e. differentiating 'cases' and 'non-cases'); 2) defining and differentiating a limited set of meaningful categories or syndromes; 3) distinguishing unipolar and bipolar disorders, and their principal subtypes, from each other; 4) defining research and clinical samples sufficiently precisely to ensure replication; 5) generating reliable diagnoses; 6) delineating diagnostic groupings that show differential and prioritized treatment approaches for each of the defined conditions; and 7) assisting communication among clinicians. We will shortly consider how well DSM-defined 'major depression' meets such requirements.

The concept of major depression was introduced nearly thirty years ago in the DSM-III manual. The subsequent DSM-IV criteria (and cut-off decision rules) differ only slightly from the original DSM-III definition. While the features are well known, let's overview them before considering how useful a diagnosis of major depression is to researchers and clinicians.

DSM-IV defines major depression as requiring a) at least 2 weeks of depressed mood or loss of interest or pleasure in nearly all activities, accompanied by b) at least four additional symptoms of depression drawn from a list that includes changes in appetite or weight, sleep (insomnia or hypersomnia) or psychomotor activity (either observable retardation or agitation); decreased energy; feelings of worthlessness or inappropriate guilt; difficulty thinking, concentrating or making decisions; or recurrent thoughts of death or suicidal ideation, plans, or attempts. Such symptoms must c) either be newly present or must have clearly worsened compared with the person's pre-episode status. The symptoms must d) persist for most of the day, nearly every day, for at least two consecutive weeks and cause e) clinically significant distress or impairment in social, occupational, or other important areas of functioning. Further, the symptoms are f) not caused by bereavement, by substance abuse or by a medical condition.

In essence, major depression requires a new depressive episode that has been present for at least two weeks, with a minimum number of prescribed symptoms which persist across the day and are impairing. It differs from grief (i.e. bereavement) and the inference is that it is a primary condition – that is, it is not secondary to substance abuse or to a medical condition – but no statement is made about it being primary or secondary in relation to psychiatric conditions (e.g. anxiety) or psychosocial problems (e.g. personality disorder). Major depression is sub-divided into multiple sub-groups – some categorical (e.g. psychotic, melancholic, catatonic), some aetiologically (e.g. postpartum, seasonal, atypical) and some dimensionally (involving severity, chronicity and persistence) weighted. The only other principal DSM-IV depressive condition is dysthymia, positioned as less severe but lasting longer than major depression, while there are a number of secondary disorders.

Does major depression clearly distinguish clinical depressed mood states from 'normal' depressed mood states?

The DSM-IV model of major depression is primarily dimensional – with 'caseness' status defined by severity (the presence of a certain number of symptoms), persistency and recurrency parameters. However, any dimensional model requires the imposition of a cut-off score which is intrinsically imprecise and risks both 'false positive' diagnosis (i.e. 'non-cases' being defined as 'cases') and 'false negative' assignment (i.e. 'cases' being defined as 'non-cases').

Theoretically, disorders are better characterized by categorical features – subject to the underlying condition having such pathognomonic features – as method error is reduced (i.e. features are present in true cases only). Here major depression has immediate problems. Firstly, none of its criteria are specific to major depression, to clinical depression or even to depression itself. Sad people will have a depressed mood, while appetite and sleep disturbance can reflect multiple conditions (e.g. anxiety) and states (e.g. stress).

Secondly, some DSM features are not described with clarity, and some DSM criteria are quite concatenated. For example "feelings of worthlessness or excessive or inappropriate guilt (which may be delusional)" captures a construct that might include those with modest depressed mood-driven guilt through to those with overwhelming psychotic guilt, allowing a positive rating to emerge from quite differing depressive expressions. Rating issues also cloud clarity. The initial descriptive profile of major depression within the DSM-III system (and perpetuated within the DSM-IV model) effectively described the melancholic subtype of depression. However, the DSM-III guiding principle – as stated on page seven - was to have clinical criteria described at the "lowest order of inference necessary to describe the characteristic feature of the disorder", so that 'pathological guilt' (which might be a marker of psychotic or non-psychotic melancholia) illustrates the attenuation of such a categorical feature to the "lowest order of inference" (i.e. mood-related guilt).

Thirdly, the relatively non-specific (and certainly non-categorical) criterion features do not lend themselves to clear operationalising. In addition, their intrinsic dimensionality risks measurement error.

Fourthly, 'impairment' is operationalised as "clinically significant distress or impairment". Significant? Is significance as judged by the clinician valid, particularly when depression is very much an experiential or subjective mood state?

Thus, the relatively low number of symptom criteria, their 'low inference' level and a relatively soft definition of mandated impairment has made it relatively easy to reach criteria for a diagnosis of major depression. As Horwitz and Wakefield argue "the recent explosion of putative depressive disorder… is not… a real rise in this condition.[2] 'Instead, it is largely a product of conflating the two conceptually distinct categories of normal sadness and depressive disorder… made possible by a changed psychiatric definition of depressive disorder that often allows the classification of sadness as a disease, even when it is not".

Spitzer, writing in the forward to the Horwitz and Wakefield book observed that "the authors argue that to be human means to naturally react with feelings of sadness to negative events in one's life[3]. When the symptoms of sadness have no apparent cause or are grossly disproportionate to the apparent cause…something important in human functioning has gone wrong". He noted that Horwitz and Wakefield argued that "contemporary psychiatry confuses normal sadness with depressive mental disorder because it ignores the relationship of symptoms to the context in which they

emerge. The psychiatric diagnosis of major depression is based on the assumption that symptoms alone can indicate that there is a disorder; this assumption allows normal responses to stressors to be mischaracterized as symptoms of disorder".

Does major depression join with a relatively small set of other depressive conditions to capture 'a limited set of meaningful categories or syndromes'?

The answer is an unequivocal 'no'. There are multiple categorical and dimensional 'specifiers' to the DSM-IV mood disorder section, and we have estimated[4] that there are more than 200 DSM depressive categories. Yet how many are used by day to day clinicians, let alone by medical records or researchers? The risk then is for clinicians to avoid the specifiers and apply a diagnosis of major depression as a generic summary diagnosis - so making an intrinsically nebulous diagnosis even less 'clinically meaningful'.

Do major depression and its specifiers generate meaningful sub-types or syndromes?

As noted, the DSM-IV model is primarily dimensional, so that major depression is largely positioned as differing from other depressive conditions by severity (e.g. duration and symptom numbers distinguish major depression and dysthymia), and by persistence and recurrence.

While some of the 'specifiers' would appear categorical (e.g. melancholia), this is less evident when decision rules are inspected. For example, a patient with anhedonia, early morning wakening, psychomotor agitation or retardation and weight loss would meet criteria for both major depression and the melancholic specifier. This is illogical if the 'specifier' is seeking to identify a sub-set or sub-type of major depression. Logic would argue that there should be one set of criteria for the general category (here major depression) and a second and independent criterion set for the specified sub-category (here 'melancholia'). Thus, any study seeking to show how and why melancholia may be a distinct category (either on the basis of clinical features, aetiology or treatment differentiation) will be doomed to failure if DSM-IV criteria are used, so discouraging any view that melancholia is a meaningful depressive sub-type.

Is major depression a reliable and precise diagnosis, so allowing replication studies?

As detailed previously,[4] "the architects of the DSM-III classificatory system argued that one of the principal advantages of their criterion-based approach to diagnosis was to promote and achieve reliable diagnosis". Yet according to Kirk and Kutchins, the field trial reliability data for DSM-III depressive diagnoses were so poor that they were never formally reported.[5] Following the release of the DSM-III system, independent post-release studies formally demonstrated poor reliability for DSM categories such as major depression. For example Anthony et al. quantified a kappa coefficient of 0.25 for major depression.[6] Subsequently, other commentators (see[1]) noted that major depression was one of the most unstable diagnoses in terms of reliability. Thus, while the DSM architects claimed high reliability for the system, such claims were never substantiated, leading Kirk and Kutchins to conclude that "It was the claims of success, however, that were successful".[5]

Does major depression allow differential treatment effects to be specified?

As reviewed elsewhere,[1] the evidence base in relation to treatments for major depression is the largest database we have in psychiatry. In one meta-analysis' by Williams et al., 'old' and 'new' antidepressants were compared (150 studies, 160,000 subjects), with quantified response rates of 54% for each group.[7] In another meta-analysis, undertaken by Anderson,[8] comparing exemplar old antidepressants (i.e. tricyclic or TCA drugs) and new antidepressants (selective serotonin re-uptake inhibitors or SSRI's) no difference in efficacy rates was determined. In a meta-analysis by Robinson et al. comparing psychotherapy trials against pharmacotherapy, only trivial superiority of pharmacotherapy was demonstrated.[9] In another meta-analysis of 28 randomized control trials for psychotherapies, response rates of 50% for cognitive behaviour therapy (CBT), 52% for interpersonal psychotherapy (IPT), and 55% for behaviour therapy (BT) were derived.[10] In essence, meta-analyses have quantified similar response rates for all antidepressants and all tested psychotherapies, allowing an 'equipotency' model, where all treatments appear equally effective for major depression.

The consequences of the randomized control trial efficacy database failing to demonstrate any single treatment as being superior to any other for major depression – and with a similar overall non-differential treatment finding generated in regard to the other DSM-IV category, dysthymia – is that the evidence base is actually of no help at all. This reality then leads to treatment being more likely to be determined by the background training or interest of the professional rather than by the characteristics of the disorder.[1] Logically, it might be assumed that treatment would be tailored to the specific pathological process contributing to the particular depressive condition rather than applying a single treatment modality as if it has universal application – a consequence of a dimensional model rather than a sub-typing model. The overlap between criteria used to define major depression and melancholia in DSM-IV builds to such a risk.

Does major depression assist communication?

There is little doubt that major depression has had wide 'take up' by clinicians and that it has cachet value amongst other groups (contributing to medico-legal reports, allowing hospitalization and insurance rights). This identifies high status, but it does not establish validity or true utility. Its utility could reflect no more than lazy thinking or communication.

Of greater concern, is its positioning – before the public and in the eyes of many professionals – as reflecting entity status. Major depression is commonly described as an 'it', with professionals then offering views about its status (e.g. "It reflects a chemical imbalance") and its treatment. In reality, a diagnosis of major depression tells us nothing about causes or best treatment at the individual patient level and even at the group level. Why?

In essence, major depression is no more a meaningful diagnosis than (say) 'major dyspnoea' - without qualifying whether the differing symptoms reflect pneumonia, asthma or a pulmonary embolism. As major depression is a non-aetiological diagnosis, its capacity to truly inform the clinician – or the patient – is limited. In essence, it is no more than a domain diagnosis – that the patient has some degree of depression, which may or may not be at the level of clinical 'caseness'.

While major depression has become an 'it', being commonly interpreted as representing an entity – it is more a 'pseudo-entity', lacking specificity, and meaning differing things to differing people. It risks promotion of a 'one size fits all' model where differing practitioners apply quite differing treatments for 'it', with the view that 'it' is alone sufficient to shape treatment. Thus, it disallows the alternate model that clinical depression comprises differing

constituent disorders and syndromes (e.g. psychotic, melancholic and non-melancholic depression) with quite contrasting symptom patterns and with distinctive disorders benefitting from differential treatments – be they drugs, ECT or specific psychological interventions.

Consider the following analogy. You are driving along and you car makes some ghastly noise, the engine seizes and you and your car are towed to a garage where there is a sign stating 'Specialist Car Engineering'. The mechanic looks under the bonnet for a while, looks up and states: "Right. You've got a Major Engine Problem". You ask for more details. If it is the engine, has it run out of oil or has some part malfunctioned? "No Sir. Major Engine Problem is the diagnosis. Don't need to know anymore". You then ask how the engineer is going to fix it. "Well here, Sir, we recommend a retune for Major Engine Problem but there's a bloke over the road who always recommends cleaning the valves, while there's another service down the road that reckons changing the oil will always fix Major Engine Problem".

A simple analogy perhaps but one that illustrates the risk of regarding major depression as a diagnosis sufficient in and of itself to dictate treatment. The homogenizing of multiple conditions into a single dimensionally-based 'diagnosis' does not offer an effective tool for clinical communication amongst practitioners or researchers. By itself, major depression provides no specific information about cause or neurobiological underpinnings and no information to advance treatment specificity. It is a sterile construct risking sterile clinical practice, while its research sterility does little to inform clinical practice.

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** Modest*
*** Significant*
**** Significant. Amounts given to the author's institution or to a colleague for research in which the author has participation, not directly to the author.*
For more information, see Instructions for authors.

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