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Conceptualization about internalizing problems in children and adolescents

O conceito de problemas internalizantes em crianças e adolescentes

Paul Wilkinson [1]

Abstract *This review will discuss the concept of internalizing disorders. It will describe the two main types of internalizing disorder: depressive and anxiety disorders. It will discuss how they have much in common, but that there are also key differences. The review will use data from modern studies of symptom factor analysis, aetiology, treatment and prognosis to illustrate the commonalities and differences. It will conclude by trying to answer where internalizing disorders should be placed in future diagnostic classification schemes.*

Key words *Internalizing disorders, Symptom factor analysis, Diagnostic classification*

Resumo *Esta revisão discute o conceito de transtornos internalizantes, descrevendo os dois principais tipos deste problema: depressão e ansiedade. Será discutido o quanto eles têm em comum, mas também as principais diferenças entre eles. Para ilustrar estas características em comum e as diferenças, serão usados dados de estudos modernos usando análise fatorial de sintomas, etiologia, tratamento e prognóstico. Na conclusão, será feita uma tentativa de responder a questão onde os problemas internalizantes deveriam ser inseridos nos esquemas futuros de classificação diagnóstica.*

Palavras-chave *Internalização, Análise fatorial de sintomas, Classificação diagnóstica*

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The first attempt to classify child psychopathology was made by Hewitt and Jenkins in 1946[1]. They carried out a factor analysis of symptoms and linked factors with social situation. This led to the differentiation of "emotional disturbance" and two classes of disruptive disorders, based both on intercorrelations between symptoms within each factor and different patterns of psychosocial variables in the three factors. Since then, there has developed infinitely greater complexity to psychiatric diagnosis. Yet a similar split between emotional (or "internalizing", where the patients feel distress inside themselves) and behavioural (or "externalizing", where the patients cause distress to people external to themselves) problems is still often made.

This article will look in detail at the conceptualization of internalizing disorders in children and adolescents. It will explain the main disorders, looking at what separates the disorders, but also at what these disorders have in common, validating Hewitt and Jenkins' original classification. It will discuss the aetiology of these disorders, and how modern scientific technology has been able to demonstrate differences and commonalities within this group of disorders. It will finish by discussing whether the concept of internalizing disorders (and the sub-classification of internalizing disorders) is helpful and valid.

Classification of internalising disorders

The two main emotions suffered by patients with emotional disorders are sad (or depressed) mood and worry (or anxiety). These emotions form the basis of the two main types of internalizing disorders: depressive and anxiety disorders. The third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III,1980) reflected this, and was the first diagnostic classification that made a major separation between "affective" and "anxiety" disorders.

This article will focus on these two main groups of disorders. It will not include bipolar disorder and obsessive-compulsive disorder. The phenomenology, biology and genetics of these disorders demonstrate that while these disorders have much in common with internalizing disorders, they share many features of, respectively, schizophrenia[2] and tic disorders[3]. This overlap demonstrates part of the difficulty of a simple split of psychiatric disorders into a small number of discrete groups.

Depressive disorders

Depressive disorders are about more than feeling sad. They are syndromes of persistent emotional, biological and psychological symptoms, accompanied by impaired social functioning. The most important of the depressive disorders is major depression.

For a DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, fourth edition[4]) diagnosis of major depression, at least five depressive symptoms must have been present most of the time for two weeks and represent a change from previous functioning. At least one of the symptoms must be:

. Depressed or irritable mood

. Markedly diminished interest or pleasure in almost all activities (anhedonia).

Other possible symptoms are:

. Decreased or increased weight or appetite

. Increased or decreased sleep

. Psychomotor agitation (fidgetiness) or retardation (slowed down speech/movements)

. Reduced energy

. Worthlessness or excessive guilt

. Reduced concentration or indecisiveness

. Recurrent thoughts of death or suicidal ideation.

In addition, there must be significant distress or impairment in functioning (such as at school, with friends or with the family). Symptoms must not be due to a medical condition, medication, illicit substances or bereavement. Onset is rare before adolescence.

However, here we have the first of our problems with the conceptualisation of internalising disorders. As clinicians, it is convenient to be able to say whether or not people have a diagnosis, a categorical approach. This makes it easy at a superficial level to decide what treatment we should use, and whether somebody is eligible for treatment at all. However, human biology and psychology is not so simple. In the same way as blood pressure lies on a continuum, and at one end of this, the doctor and patient must decide whether to treat "high" blood pressure, depressive symptoms and the associated social dysfunction lie upon a continuum. The American Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV)[5] defines a threshold of five symptoms. But this is fairly arbitrary, and is not based on any empirical data. It has been shown that there is a gradual reduction in social functioning with more symptoms in children and adolescents[6] and in adults[7] and that older adolescents with subthresh-

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old depressive symptoms are as likely as those with the full depressive syndrome to develop a subsequent depressive disorder[8]. So it is not helpful to clinicians to use a simple yes/no approach to treatment. Instead it is better to consider the number of symptoms, the social context, the level of dysfunction, the duration of symptoms and the views of the patient on treatment. The more symptoms, the more likely it is that we should use treatments.

Clinicians do not feel it right to ignore the patients who are clearly suffering but only have four depressive symptoms. In some healthcare systems, it is not even possible to get treatment without a "diagnosis". Other depressive disorders have since been described. Dysthymic disorder is a more chronic, less severe condition, consisting of depressed mood for most of the time, with at least two other depressive symptoms, lasting at least one year, and in which criteria for a major depressive episode are not met for the first year. Many children with dysthymia later develop major depression.

DSM-IV discussed "minor depression" as 2-4 depressive symptoms, including depressed/irritable mood or anhedonnia, over a two week period, but concluded there was not sufficient evidence to include minor depression as a formal diagnosis. Instead, depressive disorder, not otherwise specified, was included, to refer to people with depressive problems, but not enough criteria for the full diagnosis. Minor depression has been shown to have financial costs intermediate between those of major depression and no depression in adults[9].

Randomised controlled trials have demonstrated that the standard treatments for depression, antidepressants and psychological therapies, are effective for minor depression[10] and dysthymia[11,12] in adults. This again demonstrates the dimensional nature of depression, and the inappropriateness of using the cut-off of 5 symptoms for major depression in deciding upon suitability for treatment.

Adjustment disorder is emotional and/or behavioural symptoms within 3 months of an identified stressor. Caseness is determined by either marked distress or social dysfunction in excess of what would be expected from such a stressor. One subtype is "with depressed mood". Such a diagnosis cannot be made if full criteria for major depression are met.

Anxiety disorders

Anxiety can be useful and adaptive, warning us that we should avoid somewhere dangerous. The simultaneous adrenergic response (high heart rate, fast breathing, sweating) would help our body function optimally in a fight-or-flight dangerous situation. Sometimes anxiety is maladaptive, and it is here that we see anxiety disorders. People may have excess anxiety around situations that they need to be in to function normally (such as school or shops). This anxiety can be very distressing and can be so overwhelming that it affects normal function in these arenas (such as stopping children from concentrating on their schoolwork). In extreme cases, anxiety can be so overwhelming that people cannot face the feared situation, and avoid it completely. This avoidance leads to a great feeling of relief and anxiety levels fall. Sadly, this benefit is greatly reinforcing, and makes it even harder for that person to face the feared situation on the next occasion. Anxiety is often accompanied by physical symptoms, such as heart racing, stomach pains and sweating. These are mediated by the sympathetic nervous system/adrenergic response, that would be useful in a fight-flight dangerous situation, but which often makes feelings even worse in the non-dangerous anxiety producing situation.

As with depressive disorders, anxiety disorders lie on a spectrum, from the common feeling of slight anxiety at the start of a new school year, to children unable to leave their house for many years because of fear of what people may think of them. We do not have a simple symptom count to help us divide people into those with and without a disorder (some may say this is a blessing!). Instead, diagnosis is determined by the level of distress and how impaired the patient is by the anxiety, in particular whether it leads to avoidance. Of course, normal development must be taken into account. Great anxiety and protest at being left by the mother in a shop would be normal, indeed adaptive, for 15 month olds. It is not for a 15 year old.

Anxiety disorders can be further subclassified by the stimuli which the patient is anxious about. Some anxiety disorders present at earlier ages than others, reflecting the normal anxieties children have at different ages. Many children have more than one anxiety disorder at the same time, in particular generalized anxiety disorder is often found alongside another anxiety disorder[13].

Specific phobic disorder is anxiety around a specific object (e.g., spiders) or situation (e.g., flying), and is present whenever the person encounters the specific object. Onset is often in early childhood.

Separation anxiety disorder is anxiety at separation from caregivers, either when the child leaves the caregiver (e.g., to go to school) or when the caregiver leaves the child at home when they go out. It sometimes leads to school refusal. Onset peaks in late childhood.

Social phobia (sometimes called social anxiety disorder) is anxiety in social situations due to fear of other people´s evaluations and reactions and the possible resultant embarrassment or humiliation. It can be generalized, present in most social settings, or non-generalized, such as only present at parties, or when speaking or eating in front of others. The generalized form may have earlier age of onset, a worse prognosis and more psychopathology in parents[14]. Onset is often in adolescence or adulthood.

Agoraphobia is anxiety about being away from home especially in crowds, where they cannot leave easily, such as in shops or on buses. It is often comorbid with panic disorder, and the main focus of the anxiety may then be worry that the person will have a panic attack in public and not be able to escape. Onset is often in adolescence or adulthood.

Panic disorder is the repeated experience of sudden, unprovoked panic attacks, with intense anxiety and physical symptoms. It sometimes leads to agoraphobia. Onset is often in adolescence or adulthood.

Generalized anxiety disorder is multiple worries about many aspects of life, rather than about specific stimuli, with resultant distress and reduced functioning. Worry is the main symptom, and avoidance is not common. It is often found with other psychiatric disorders. When found only within a depressive episode, the diagnosis cannot be given, as these symptoms are also part of depression. Onset is often in adolescence or adulthood.

Comorbidity between depressive and anxiety disorders

It is common for people to have more than one psychiatric disorder at the same time, a phenomenon called "comorbidity". It has been demonstrated that in people with one psychiatric disorder, the presence of a second disorder is more than can be accounted for by the prevalence of the second disorder in the healthy population and chance[15].

Comorbidity is certainly a feature of anxiety and depressive disorders. In a large meta-analysis of community epidemiology studies, 32% of children/adolescents with major depression also had an anxiety disorder and 24% of adolescents with an anxiety disorder had major depression[16]. The odds ratio for the other disorder to be present in probands with one disorder compared with probands without that disorder was 8.2. However, comorbidity is not specific to internalizing disorders: there is also great comorbidity between internalizing and externalizing disorders.

Comorbidity may occur for several reasons. It may be an artifact of imperfect diagnostic systems. Some symptoms are present in depressive and anxiety disorders, such as insomnia, poor concentration and fatigue, therefore not many symptoms are needed of a second disorder to make it a full comorbid disorder. However, non-overlapping symptoms are also present for both disorders in comorbid patients, and so this can only be a partial explanation at best.

Secondly, one disorder may "cause" the other. For example, a chronic anxiety disorder with its distress and the effects on socializing with friends and going to school may make a person sad, then depressed. Anxiety disorders precede depression in two thirds of cases where both are present[17,18].

Thirdly, common predisposing factors may increase the risk of both disorders. An adult twin study demonstrated that the liability to major depression and generalized anxiety disorder is influenced by the same genetic factors, and that different environmental factors must therefore determine which disorder an individual develops[19]. This shared genetic liability is partially mediated by the personality trait of neuroticism[20]. It has been demonstrated in adults that the life events of humiliation, bereavement and respondent-initiated separation predicted major depression but not generalized anxiety, while dangerous life events predicted generalized anxiety but not depression. Life events that predicted mixed major depression and generalized anxiety were the sum of those that predicted the individual disorders[21]. A smaller study in children also demonstrated that loss events, family and friendship problems and schoolwork stress were significantly associated with high depressive, but not anxiety, symptoms; threat events were associated with high anxiety, but not depressive, symptoms[22]. However it has been demonstrated that one genetic factor underlies phobic and panic disorders while a separate factor may underly depressive and generalized anxiety disorders[23].

Fourthly, comorbid depression and anxiety may be a different syndrome to each of the individual diagnoses. Tyrer in particular has argued for the existence of a "cothymia", a disorder with both anxiety and depression present at a syndromal level[24]. In a meta-analysis of studies of adults, such "cothymia" has worse prognosis than either disorder alone [25]. In adolescents, comorbid depression has been shown to worsen the outcome of anxiety disorders [26]. It is possible that the worse prognosis of combined depression is because risk factors for both are present, and so this is simply a more severe illness, rather than a different illness.

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However, there may be differences at a biological level. High salivary cortisol has been demonstrated in the evening in depressed people in several studies[27], but in one of these groups, evening cortisol level was similar to that of healthy controls in depressed adolescents with comorbid panic or phobic disorder[28].

Depressive and anxiety disorders – two truly different disorders?

DSM-III separated depressive and anxiety disorders. Was this the correct thing to do? The main distinction between the disorders is the core emotion – depressed mood vs. anxiety. Yet the secondary symptoms may be seen in both types of disorder. And there is great overlap, with many people with one disorder also having the other. There may be a common genetic basis underlying the two disorders. Are we best keeping this distinction? Or would we be better changing to a common depressive/anxiety disorders classification, with patients lying on a depressed-both-anxiety spectrum? Or should we separate the classification further into depression only, anxiety only, and mixed anxiety-depression?

One way to answer this question is to use more modern statistical techniques than Hewitt and Jenkins to investigate which symptoms cluster in very large samples of children with psychiatric disturbance. Such studies have also shown a split between internalizing and externalizing disorders[29]. They have also demonstrated two correlated subfactors within internalising disorders: "fear", including simple phobia, social phobia, panic disorder and separation anxiety disorder; and "distress/misery", including depressive disorders and generalized anxiety disorder. A study of young adults showed that there is an underlying latent "internalising" trait responsible for some of the variance in anxiety and depressive disorders but also additional disorder-specific traits responsible for some of the variance[30].

The best way to answer this question is to think about what would help us as we see our patients. There are three main ways a diagnosis is useful. It should guide us towards specific treatments. It should help us to advise our patients on what their prognosis is likely to be. It helps communication (to patients and fellow professionals) if we can use a word or two to sum up the main problem(s) of a patient. I shall consider these three uses of a diagnosis to help us to decide on the most appropriate classification system.

Treatment

There are three main areas to consider when making a treatment plan: biological, psychological and social. Social treatment, the improving of a patient´s environment, should always be guided by the problems in that specific environment, more than by the diagnosis. Therefore I shall not consider it further in this discussion on whether separation of anxiety and depressive disorders is helpful.

The most basic level of psychological treatment is psychoeducation and non-specific supportive listening. Again, this is not diagnosis-specific. The most widely used specific psychological therapy, with the greatest evidence-base, for both anxiety[31, 32] and depressive[33,34] disorders is cognitive-behavioural therapy (CBT). However, the techniques used in CBT are rather different in the two disorders. In anxiety disorders, the focus is on facing the feared situations, moving up a hierarchy of more difficult and anxiety provoking situations, while dealing with any inappropriate and maladaptive thoughts about the anxiety-provoking stimuli. In depression, the focus is on encouraging taking part in pleasurable activities, rather than ruminating about problems, and challenging inappropriate, maladaptive and negative thoughts about the self, the world and the future. Meta-analysis has demonstrated that remission rates in depressed adolescents randomized to CBT are 48% and to placebo 34%[35]; the respective figures for anxiety disorders are 57% and 35%[32]. Different statistical methods make it not possible to compare relative effectiveness of the two treatments.

The other specific psychological therapy with proven effectiveness against paediatric depression is interpersonal therapy[36, 37]. It was specifically designed to treat depression, and looks at the relationship between affect and interpersonal relationships, and tries to improve relationships, thus improving mood. While effective against depression in many adults and child studies, it did not demonstrate greater effectiveness against anxiety disorders than supportive therapy, in the only study to date (with adults)[38].

The name of the medication class "antidepressants" suggests they are for treating depression. Research has demonstrated one antidepressant, the selective serotonin re-uptake inhibitor (SSRI) fluoxetine, to be more effective than placebo in treating childhood and adolescent depression[39-41]. However, SSRIs are also effective against anxiety disorders in children and adolescents[42-45]. The most recent meta-analysis[46] of SSRI and other new generation antidepressants showed that for depression,

61% of adolescents responded to antidepressants and 50% to placebo; while for non-OCD anxiety disorders, 69% responded to antidepressants and 39% to placebo. Effect sizes using continuous measures also demonstrated greater drug-placebo differences for anxiety disorders (0.69) than for depressive disorders (0.20). 95% confidence intervals for drug-placebo differences did not overlap between the two disorders in either recovery rate or continuous measures analyses, suggesting that the antidepressant-placebo difference is significantly greater for anxiety disorders than depressive disorders. Some caution should be made when comparing the results of different studies, as differences may be due to different methodologies and remission criteria. In addition, meta-analyses did not differentiate between the different anxiety disorders.

In conclusion, the same pharmacological treatment is effective for anxiety and depressive disorders, while different psychological treatments are effective. This partly reflects genetic findings that similar genes may underly the two types of disorder (in particular generalized anxiety disorder), reflecting similar biological vulnerability, while different psychosocial events lead to the two disorders[19]. However, antidepressants may be relatively more effective compared with placebo for anxiety than depressive disorders.

Prognosis

It is difficult to compare the prognosis of different disorders, as the prognosis in a sample very much depends on the severity of illness of individuals in that sample. Different studies, with different disorders, differ greatly in recruitment, inclusion and exclusion criteria. Outcome is also affected by treatment in clinic samples, and cohort effects are important: later studies may be at times when better treatments are available, appearing to demonstrate a better prognosis for the disorder. A sample of depressed adolescents recruited in the early 1990s and followed up prospectively demonstrated that community-ascertained cases had a median time to full remission of 3 months for community-recruited cases and two years for clinic-recruited cases[47]. A sample of adolescents asked retrospectively about past and present anxiety disorders in the late 1980s, who were mainly recruited from the community, had a median time of recovery of 8 years[48]. Of course, a major confound with prospective studies is that ascertainment may lead to treatment.

Of more interest to our patients than spontaneous recovery in community cases is what their prognosis will be like if they receive optimum treatments in clinic. The most recent meta-analysis of psychological treatments for depression showed that 50% of those randomised to psychological treatments "responded" after a course of treatment[35]. Meta-analysis of CBT for anxiety disorders demonstrated remission rate of 57%[32]. The most recent meta-analysis of SSRI and other new generation antidepressants showed that for 61% of depressed adolescents and 69% of adolescents with non-OCD anxiety disorders responded to antidepressants[46]. Again, caution must be taken in comparing studies due to different methodologies and definitions of response.

A way to compare outcome that avoids the confounds of different methodologies between studies is to look at those with co-morbid anxiety and depressive disorders in the same study, and compare outcome of each disorder. Anxiety precedes depression in 2/3 of cases where both occur together, and often persists after remission of depression[17,18], suggesting anxiety disorders have worse prognosis.

People with internalizing disorders have high recurrence rates of both the initial disorder and other internalizing disorders[49]. When followed up over 7 years, continuity of all internalizing disorders was mediated by the common latent "internalising disorder" trait. There was also disorder-specific continuity for depressive and phobic disorders, but not panic and generalized anxiety disorders [30].

In summary, people with anxiety disorders may have longer time to recovery than those with depressive illnesses if left untreated; however, those with anxiety disorders may be more likely to recover if treated. Long-term follow up suggests that while recurrence of the index illness is high, there is also a greater incidence of other internalizing disorders than people who have not had any internalizing disorder.

Communication

It may be tempting at this point to think that all internalizing disorders lie on a spectrum from no disorder to very ill; and that as internalizing disorders may overlap, then we can say that people lie on the "internalising disorders spectrum". So why not just assign people scores on the different dimensions? While this may be scientifically quite pure, it is of little help when talking to real people! It helps people to know whether or not they have an illness, and to give a name to that illness. Moreover, this name should bear some relation to what

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the illness feels like. People know what "depressed" and "anxious" moods are, and so depressive and anxiety disorders make sense to them. People can also understand that they have both types of disorder, and being given a dual diagnosis of an anxiety and a depressive disorder may make more sense than "cothymia". While fellow academic psychiatrists may understand a dimensional system of classification, many professionals we speak with about the children we are trying to help have very different trainings, for example as teachers or social workers. Again, a straightforward and logically-named classification system will make communication far easier. While severity lies on a spectrum, we can talk about disorders as being mild, moderate and severe, which people can understand. DSM-IV even gives us a list non-major depressive disorders. While using symptom counts to assign a diagnosis can be fairly arbitrary, deciding whether somebody is significantly impaired, and so has an "illness", has greater face validity.

Conclusion: the future of conceptualization about internalizing problems in children and adolescents

Internalizing and externalizing disorders were proposed as separate entities 60 years ago. Is this separation still valid today? The answer is a resounding yes. Research has demonstrated anxiety and depressive disorders to have much in common. Modern factor analytic studies have demonstrated that symptoms of these disorders cluster together, and separately to those of externalizing disorders. There is great overlap between individual symptoms amongst diagnoses and between diagnoses amongst individuals. There may be shared genetic liability to internalizing disorders, particularly depression and generalized anxiety disorders. Internalising disorders all respond to similar treatments, in particular selective serotonin re-uptake inhibitor antidepressants and different types of cognitive-behavioural therapy. People who develop one internalizing disorder have a high risk of developing any internalizing disorder in future.

What is less clear cut is classification within the internalizing disorders. With so much in common, should anxiety disorders and depressive disorders be separated? I would argue that they should, for several reasons.

1. While there are common aetiological factors (in particular genetic), separate life events lead to the different disorders;

2. Outcome appears different. Despite the limitations of comparing the results of different studies, it appears that:

a. People take longer to recover from anxiety disorders than depressive disorders if untreated in the community, or are treated with inactive placebo in clinic;

b. Conversely, there is a slightly better response to active treatment (whether pharmacological or psychological) among those with anxiety disorders;

c. In people with both anxiety and depressive disorders, the anxiety disorder has a worse prognosis;

d. While there is non-specific risk of future internalizing disorders, there is also some specific risk of recurrence of the index disorder.

3. Different forms of psychological treatment are needed for the different disorders;

4. People understand anxiety and depression as different emotions, which may of course both be present. We need a very good reason to go against people's understanding and say they are part of the same disorder.

Both types of disorder may be present in the same individual at the same time. Rather than call this a different disorder, I would argue that the patient has a real problem of two different illnesses, which may worsen each other and worsen overall prognosis. Treatment of both disorders is necessary, particularly if psychological treatment is used.

Of course, no classification system is perfect. In particular, generalized anxiety disorder poses some problems: it may share more genetic liability with major depression, yet outcome may be more similar to anxiety disorders.

Current classifications are currently being revised, so that we shall soon benefit from the improved 5th version of the Diagnostic and Statistical Manual of Mental Disorders, and the 11th version of the International Classification of Diseases. My own opinion is that depression and anxiety disorders should be brought together into the same chapter, as they have much in common, in particular when they are compared against other types of disorders, such as externalizing and psychotic disorders. I still think Hewitt and Jenkins were correct back in 1946. However, the distinction between the diagnoses should still remain. In particular depressive and anxiety disorders should remain separate.

References

1. Hewitt LE, Jenkins RJ. ***Fundamental Patterns of Maladjustment: the Dynamics of Their Origin***. Springfield, Illinois: State of Illinois Publications; 1946.
2. Craddock N, Owen MJ. Rethinking psychosis: the disadvantages of a dichotomous classification now outweigh the advantages. ***World Psychiatry*** 2007; 6(2):20-7.
3. Leckman JL, Cohen DJ. Tic Disorders. In: Rutter M, Taylor E, editors. ***Child and Adolescent Psychiatry***. 4th ed. Oxford: Blackwell; 2002.
4. American Psychiatric Association. ***Diagnostic and statistical manual of mental disorders*** (4th edition). Washington, D. C.: American Psychiatric Association; 1994.
5. American Psychiatric Association. ***Diagnostic and statistical manual of mental disorders.*** 4th edition. Washington, D. C.: American Psychiatric Association; 1994.
6. Pickles A, Rowe R, Simonoff E, Foley D, Rutter M, Silberg J. Child psychiatric symptoms and psychosocial impairment: relationship and prognostic significance. ***Br J Psychiatry*** 2001; 179:230-235.
7. Cuijpers P, de Graaf R, van Dorsselaer S. Minor depression: risk profiles, functional disability, health care use and risk of developing major depression. ***J Affect Disord*** 2004; 79(1-3):71-79.
8. Fergusson DM, Horwood LJ, Ridder EM, Beautrais AL. Subthreshold depression in adolescence and mental health outcomes in adulthood. ***Arch Gen Psychiatry*** 2005; 62(1):66-72.
9. Cuijpers P, Smit F, Oostenbrink J, de Graaf R, Ten Have M, Beekman A. Economic costs of minor depression: a population-based study. ***Acta Psychiatr Scand*** 2007; 115(3):229-236.
10. Fogel J. Recognising Minor Depression. ***Medscape Psychiatry and Mental Health***. [serial on the Internet] 2006;11(2). Available from: http://www.medscape.com/viewarticle/528985_1
11. Dunner DL. Treatment of dysthymic disorder. ***Depress Anxiety*** 1998; 8(Suppl 1):54-58.
12. Lima MS, Moncrieff J. Drugs versus placebo for dysthymia. ***Cochrane Database Syst Rev*** 2000; (4):CD001130.
13. Klein RG, Pine DS. Anxiety Disorders. In: Rutter M, Taylor E, editors. ***Child and Adolescent Psychiatry***. Oxford: Blackwell; 2002.
14. Wittchen HU, Stein MB, Kessler RC. Social fears and social phobia in a community sample of adolescents and young adults: prevalence, risk factors and comorbidity. ***Psychol Med*** 1999; 29(2):309-323.
15. Caron C, Rutter M. Comorbidity in child psychopathology: concepts, issues and research strategies. ***J Child Psychol Psychiatry*** 1991; 32(7):1063-1080.
16. Angold A, Costello EJ, Erkanli A. Comorbidity. ***J Child Psychol Psychiatry*** 1999; 40(1):57-87.
17. Kovacs M, Gatsonis C, Paulauskas SL, Richards C. Depressive disorders in childhood. IV. A longitudinal study of comorbidity with and risk for anxiety disorders. ***Arch Gen Psychiatry*** 1989; 46(9):776-782.
18. Alpert JE, Maddocks A, Rosenbaum JF, Fava M. Childhood psychopathology retrospectively assessed among adults with early onset major depression. ***J Affect Disord*** 1994; 31(3):165-171.
19. Kendler KS, Neale MC, Kessler RC, Heath AC, Eaves LJ. Major depression and generalized anxiety disorder. Same genes, (partly) different environments? ***Arch Gen Psychiatry*** 1992; 49(9):716-722.
20. Kendler KS, Gardner CO, Gatz M, Pedersen NL. The sources of co-morbidity between major depression and generalized anxiety disorder in a Swedish national twin sample. ***Psychol Med*** 2007; 37(3):453-462.
21. Kendler KS, Hettema JM, Butera F, Gardner CO, Prescott CA. Life event dimensions of loss, humiliation, entrapment, and danger in the prediction of onsets of major depression and generalized anxiety. ***Arch Gen Psychiatry*** 2003; 60(8):789-796.
22. Eley TC, Stevenson J. Specific life events and chronic experiences differentially associated with depression and anxiety in young twins. ***J Abnorm Child Psychol*** 2000; 28(4):383-394.
23. Kendler KS, Walters EE, Neale MC, Kessler RC, Heath AC, Eaves LJ. The structure of the genetic and environmental risk factors for six major psychiatric disorders in women. Phobia, generalized anxiety disorder, panic disorder, bulimia, major depression, and alcoholism. ***Arch Gen Psychiatry*** 1995; 52(5):374-383.
24. Tyrer P. The case for cothymia: mixed anxiety and depression as a single diagnosis. ***Br J Psychiatry*** 2001;179:191-193.
25. Emmanuel J, Simmonds S, Tyrer P. Systematic review of the outcome of anxiety and depressive disorders. ***Br J Psychiatry Suppl*** 1998; 34:35-41.
26. Lewinsohn PM, Rohde P, Seeley JR. Adolescent psychopathology: III. The clinical consequences of comorbidity. ***J Am Acad Child Adolesc Psychiatry*** 1995; 34(4):510-519.
27. Goodyer IM, Herbert J, Altham PM, Pearson J, Secher SM, Shiers HM. Adrenal secretion during major depression in 8- to 16-year-olds, I. Altered diurnal rhythms in salivary cortisol and dehydroepiandrosterone (DHEA) at presentation. ***Psychol Med*** 1996; 26(2):245-256.
28. Herbert J, Goodyer IM, Altham PM, Pearson J, Secher SM, Shiers HM. Adrenal secretion and major depression in 8- to 16-year-olds, II. Influence of comorbidity at presentation. ***Psychol Med*** 1996; 26(2):257-263.

29. Clark LA, Watson D. Distress and fear disorders: an alternative empirically based taxonomy of the "mood" and "anxiety" disorders. ***Br J Psychiatry*** 2006; 189:481-483.
30. Fergusson DM, Horwood LJ, Boden JM. Structure of internalising symptoms in early adulthood. ***Br J Psychiatry*** 2006;189:540-546.
31. NICE NIfHaCE. ***Anxiety (amended). Management of anxiety (panic disorder, with or without agoraphobia, and generalised anxiety disorder) in adults in primary, secondary and community care***. London: NICE; 2007.
32. Cartwright-Hatton S, Roberts C, Chitsabesan P, Fothergill C, Harrington R. Systematic review of the efficacy of cognitive behaviour therapies for childhood and adolescent anxiety disorders. ***Br J Clin Psychol*** 2004; 43(Pt 4):421-436.
33. NICE. ***Depression in Children and Young People: identification and management in primary, community and secondary care***. London: British Psychological Society, Royal College of Psychiatrists; 2005.
34. Weisz JR, McCarty CA, Valeri SM. Effects of psychotherapy for depression in children and adolescents: a meta-analysis. ***Psychol Bull*** 2006; 132(1):132-149.
35. Watanabe N, Hunot V, Omori IM, Churchill R, Furukawa TA. Psychotherapy for depression among children and adolescents: a systematic review. ***Acta Psychiatr Scand*** 2007; 116(2):84-95.
36. Mufson L, Dorta KP, Wickramaratne P, Nomura Y, Olfson M, Weissman MM. A randomized effectiveness trial of interpersonal psychotherapy for depressed adolescents. ***Arch Gen Psychiatry*** 2004; 61(6):577-584.
37. Mufson L, Weissman MM, Moreau D, Garfinkel R. Efficacy of interpersonal psychotherapy for depressed adolescents. ***Arch Gen Psychiatry*** 1999; 56(6):573-579.
38. Lipsitz JD, Gur M, Vermes D, Petkova E, Cheng J, Miller N, Laino J, Liebowitz MR, Fyer AJ. A randomized trial of interpersonal therapy versus supportive therapy for social anxiety disorder. ***Depress*** s ***Anxiety*** 2008; 25(6):542-553.
39. Emslie GJ, Rush AJ, Weinberg WA, Kowatch RA, Hughes CW, Carmody T, Rintelmann JW: A double-blind, randomized, placebo-controlled study of fluoxetine in depressed children and adolescents. ***Arch Gen Psychiatry*** 1997; 54:1031–1037.
40. Emslie GJ, Heiligenstein JH, Wagner KD, Hoog SL, Ernest DE, Brown E, Nilsson M, Jacobson JG. Fluoxetine for acute treatment of depression in children and adolescents: a placebo-controlled, randomized clinical trial. ***J Am Acad Child Adolesc Psychiatry*** 2002; 41(10):1205-1215.
41. March J, Silva S, Petrycki S, Curry J, Wells K, Fairbank J, Burns B, Domino M, McNulty S, Vitiello B, Severe J; Treatment for Adolescents With Depression Study (TADS) Team. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents With Depression Study (TADS) randomized controlled trial. ***Journal of the American Medical Association*** 2004; 292(7):807-820.
42. Rynn MA, Siqueland L, Rickels K. Placebo-controlled trial of sertraline in the treatment of children with generalized anxiety disorder. ***Am J Psychiatry*** 2001; 158(12):2008-2014.
43. Wagner KD, Berard R, Stein MB, Wetherhold E, Carpenter DJ, Perera P, Gee M, Davy K, Machin A. A multicenter, randomized, double-blind, placebo-controlled trial of paroxetine in children and adolescents with social anxiety disorder. ***Arch Gen Psychiatry*** 2004; 61(11):1153-1162.
44. PPASG. Fluvoxamine for the treatment of anxiety disorders in children and adolescents. The Research Unit on Pediatric Psychopharmacology Anxiety Study Group. ***N Engl J Med*** 2001; 344(17):1279-1285.
45. Birmaher B, Axelson DA, Monk K, Kalas C, Clark DB, Ehmann M, Bridge J, Heo J, Brent DA. Fluoxetine for the treatment of childhood anxiety disorders. ***J Am Acad Child Adolesc Psychiatry*** 2003; 42(4):415-423.
46. Bridge JA, Iyengar S, Salary CB, Barbe RP, Birmaher B, Pincus HA, Ren L, Brent DA. Clinical response and risk for reported suicidal ideation and suicide attempts in pediatric antidepressant treatment: a meta-analysis of randomized controlled trials. ***Jama*** 2007; 297(15):1683-1696.
47. Dunn V, Goodyer IM. Longitudinal investigation into childhood- and adolescence-onset depression: psychiatric outcome in early adulthood. ***Br J Psychiatry*** 2006; 188:216-222.
48. Keller MB, Lavori PW, Wunder J, Beardslee WR, Schwartz CE, Roth J. Chronic course of anxiety disorders in children and adolescents. ***J Am Acad Child Adolesc Psychiatry*** 1992; 31(4):595-599.
49. Pine DS, Cohen P, Gurley D, Brook J, Ma Y. The risk for early-adulthood anxiety and depressive disorders in adolescents with anxiety and depressive disorders. ***Arch Gen Psychiatry*** 1998; 55(1):56-64.

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