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The Grey Drizzle of Horror-Depression



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ABSTRACT

Depression as a disorder has always been a focus of attention of researchers in India. Over the last 50-60 years, large number of studies has been published from India addressing various aspects of this commonly prevalent disorder. The various aspects studied included epidemiology, demographic and psychosocial risk factor, neurobiology, symptomatology, comorbidity, assessment and diagnosis, impact of depression, treatment related issues and prevention of depression in addition to the efficacy and tolerability of various antidepressants. Here, we review data on various aspects of depression, originating from India.





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INTRODUCTION

Depression

In the language of clinical psychology, depression is a syndrome, a cluster of emotional, physical, and behavioural symptoms characterized by sadness, low self-esteem, loss of pleasure, and sometimes, difficulty functioning. If these problems persist for more than two weeks, cause real suffering, and interfere with the business and pleasure of daily life you may have a clinical depression. In everyday conversation people say they are depressed when they are feeling unhappy, down, blue, sad, or hopeless. Almost everyone has experienced these emotions, and many people eventually suffer some adversity or loss that could give them reason to be anxious or depressed at time. These feelings are just one part of everyday life for most people. However, if the feelings are overwhelming or persistent, you may benefit from psychological evaluation and treatment. Depression of this type can be effectively reduced or even eliminated with treatment that is often relatively simple. Professional intervention in serious depression can reduce suffering and improve the quality of life. [1-5]

Causes of depression

Scientific research proves that the mother's depression and her anxiety during pregnancy can be inherited and can cause anxiety and depressive disorders in the newborns [6].

It is estimated that the people, whose first-degree relatives suffer from depression are 1.5 to 3 times more likely to develop depression. According to some studies, depression can be associated with genes occupying a fixed position can be associated with genes occupying a fixed position on chromosome 8, 15 and 17 [7].

Social factors and lifestyle

This can include family problems, traumatic experiences, all kinds of stress, addiction, being overwhelmed with daily duties, insomnia, etc.

Influence of family

Here, it is both the relationships between parents them-selves, as well as their relation with children. There might be conflicts, divorce, alcoholism in the family, including the mental health disorders and domestic violence of a sexual or moral nature. According to an article published by Journal of the American Academy of Child and Adolescent Psychiatry in 2004,

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a family history of susceptibility to depression and the level of parental education has a

significant impact on the occurrence of depressive symptoms among adolescents. They are at

three-fold higher risk of developing depressive symptoms [8].

Sociocultural Factors

Factors such as education, religion, value systems, social conditions, behavioural patterns

also play a significant role in the development of depression [9].

Other factors

Changing the place of residence, school, as well as the sense of hopelessness and

meaninglessness of life are also predisposing factors for developing depression. Also, this-

rings true for other issues related to sexuality, somatic disorders, trauma.

It has been proven that more than two-fold higher depressive symptoms affect young people

implicated in bullying, both in the concept in the concept of the perpetrator and the victim.

The consumption of psychoactive substance by adolescents seems to be also a significant

problem. [10]

Diagnosis

The diagnosis of anxiety disorders is made by symptoms, triggers, and a person's personal

and family histories. There are no objective biomarkers or laboratory tests that can diagnose

anxiety [11].

It is important for a medical professional to evaluate a person for other medical and mental

causes of prolonged anxiety because treatments will vary considerably.[11]

Numerous questionnaires have been developed for clinical use and can be used for an

objective scoring system. Symptoms may vary between each sub-type of generalized anxiety

disorder. Generally, symptoms must be present for at least six months, occur more days than

not, and significantly impair a person's ability to function in daily life. Symptoms may

include: feeling nervous, anxious, or on edge; worrying excessively; difficulty concentrating;

restlessness; and irritability. [11][13]

Differential diagnosis

Anxiety disorders differ from developmentally normal fear or anxiety by being excessive or

persisting beyond developmentally appropriate periods. They differ from transient fear or

anxiety, often stress-induced, by being persistent (e.g., typically lasting 6 months or more), although the criterion for duration is intended as a general guide with allowance for some degree of flexibility and is sometimes of shorter duration in children.[11]

The diagnosis of an anxiety disorder requires first ruling out an underlying medical cause.[14][15][16]

Diseases that may present similar to an anxiety disorder include certain endocrine diseases hyperthyroidism, hyperprolactinemia),[17][14][18] metabolic (diabetes),[14][19] deficiency states (low levels of vitamin D, B2, B12, folic acid),[14] gastrointestinal diseases (celiac disease, non-celiac gluten sensitivity, inflammatory bowel disease),[20][21][22] heart diseases,[23][14] blood diseases (anaemia),[14] and brain degenerative diseases (Parkinson's disease, dementia, multiple sclerosis, Huntington's disease).[14][24][25][26] Several drugs can also cause or worsen anxiety, whether through intoxication, withdrawal, or chronic use. These include alcohol, tobacco, cannabis, sedatives (including prescription benzodiazepines), opioids (including prescription painkillers and illicit drugs like heroin), stimulants (such as caffeine, cocaine, and amphetamines), hallucinogens, and inhalants. [17][11]

Prevention of diagnosis

Focus is increasing on the prevention of anxiety disorders.[27] There is tentative evidence to support the use of cognitive behavioural therapy. [27]

and mindfulness therapy.[28][29] A 2013 review found no effective measures to prevent GAD in adults.[31] A 2017 review found that psychological and educational interventions had a small benefit for the prevention of anxiety.[31][32]

Research indicates that predictors of the emergence of anxiety disorders partly differ from the factors that predict their persistence.[29]

Treatment of diagnosis

Treatment options include therapies, medications and lifestyle changes. There is no clear evidence as to whether therapy or medication is most effective; the specific medication decision can be made by a doctor and patient with consideration for the patient's specific circumstances and symptoms.[33]

If, while on treatment with a chosen medication, the person's anxiety does not improve, another medication may be offered.[33]

Specific treatments will vary by sub-type of anxiety disorder, a person's other medical conditions, and medications.

Role of antidepressants

Antidepressants are drugs used for the treatment of major depressive disorder and other conditions, including dysthymia, anxiety disorders, obsessive compulsive disorders, chronic pain, neuropathic pain and in some cases, dysmenorrhoea, snoring, migraine, attention-deficit hyperactivity disorder (ADHD), substance abuse and sleep disorders. They can be used alone or in combination with other medications but only when prescribed.

The most important classes of antidepressants are the selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), tetracyclic antidepressants (TECAs), and noradrenergic and specific serotonergic, antidepressant (NASSAs). Other drugs used or proposed for the treatment of depression include buprenorphine, low-dose antipsychotics, and St John's wort. [34]

While antidepressant drugs are widely prescribed to treat depression and anxiety disorder, only one-third of drug- treated patients exhibit a beneficial therapeutic response. Response and tolerability to medication are highly variable, with some patients responding to one treatment but not another. There are several potential explanations for these poor drug-response rates, including clinical heterogeneity and diagnostic uncertainty, environmental and social factors. If it were possible to isolate variables that could predict a greater likelihood of positive response to the medication, it would be possible to use the medication with greater certainty and efficiency. This forms the basis of much of the contemporary effort in the field of personalized medicine.

Early studies suggested that specific clinic phenotypes, such as melancholic or anxious depression, might predict differential responses to antidepressants; however, the clinical phenotypes were often variable and difficult to translate into clinical practice. Pharmacogenetics, which is the identification and development of genetic biomarkers that predict therapeutic response and the risk of side effects, take a different approach to

ultimately help the practitioner in choosing effective and safe treatment for patients suffering from psychiatric disorders.

This discovery of monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants (TCAs) in the 1950s spurred on research into developing new antidepressant medications with a better safety and tolerability profile. Following a serotonin (5-HT) hypothesis of depression, the selective 5-HT reuptake inhibitors (SSRIs) were discovered to be more effective antidepressants, with there improved safety and tolerability profile.

More recently, dual-acting antidepressants such as 5-HT-norepinephrine (NE) reuptake inhibitors (SNRIs) have presented clinicians with a wider range of antidepressants that are effective, safe and easy to prescribe. Currently, SSRIs are usually the first method of treatment, with dual-acting TCAs and SNRIs used as second-line treatment. [35-37]

There has been a recent increase in the use of antidepressants across the antidepressants across the USA, particularly for major depressive (MDD), but also for other disorders such as anxiety, bipolar disorder and adjustment-related disorders.

Chronic pain and bipolar depression. With MDD affecting 10-15% of the population and anxiety disorders affecting approximately 25% of the population, a large percentage of the population use antidepressants for pharmacotherapy. However, response and tolerability to medication are highly variable, with some patients responding to one treatment but not another. Pharmacogenetics research attempts to use genetic factors to predict some of the variability in treatment response. Early studies showed a correlation between relatives with depression in antidepressant-treatment responses. One small study found pairs of related people with depression responded equally well to antidepressants, while another study found that depressed probands and depressed relatives had favourable responses to the same class of antidepressants. Such studies indicated a role for genetics in antidepressant-treatment outcome, spurring on pharmacogenetic research in this field. This article will review current pharmacogenetic studies of antidepressants in mood and anxiety disorders and discuss the clinical future of the current research.

Antidepressant medications are most commonly used to help relieve the distress of depression or anxiety. They are also used to help with other condition, such as bulimia and chronic pain. These medications help many people with mental health problems. However, they don't work for everyone, and even when they do work well, they can only do so much. They often work best when they are combined with talk therapy, support from family and

friends, and self-care, such as regular exercise, a nutritious diet and getting enough sleep. Learning how to live well in spite of your distress is also important. Antidepressant medications can take up to several weeks to be fully effective. Early signs that the medication is working include improved sleep, appetite and energy. Improvement in mood usually comes later.

Side-effects of antidepressants

All medications can have side-effect. Some people experience no side-effect. Others may find the side-effects distressing. In most cases, side- effects lessen as treatment continues. Treatment is usually started at a low dose, to minimize side-effects, and then slowly increased until the ideal dose is found. The ideal dose is one that provides the greatest benefit with minimum side-effect. One of the main reasons why people stop talking these medications is the side-effect. Check the information given to you by your doctor or pharmacist on the specific effects of any drug you have been prescribed. If side-effects are not mild and tolerable, it is best to continue talking your medication as let your doctor know as soon as possible. Your doctor may:

- Encourage you to wait a little longer for the side-effects to fade
- Adjust your dose
- Suggest you take the medication at a different time of day
- Prescribe other medication to help control side-effects
- Change your medication
- Stop medication treatment and suggest a different type of treatment approach.

Types of antidepressants

There are several classes of antidepressants: within each class there are many individual medications. While all antidepressants work overall, no drug or type of drug works equally well for everyone who takes it. You may be advised to try another type of antidepressant or to use a combination of antidepressants to seek relief from your distress. The different types of antidepressants are listed below in the order in which they are most commonly prescribed. [38]

• SSRIs-Selective Serotonin Reuptake Inhibitors

This group of drugs, including fluoxetine (Prozac), paroxetine (Paxil), fluvoxamine (Luvox), citalopram (Celexa), escitalopram (CIPRALEX) and sertraline (Zoloft), is usually the first choice for treatment of depression and anxiety problems. These medications are known to have milder side-effects than some other antidepressants. Buspirone (Buspar) is similar to SSRIs and has been found to help with anxiety but not depression. Common side-effects include nausea, vomiting, diarrhoea, weight gain, dry mouth, headaches, anxiety, sedation and a decrease in sexual desire and response. This group of drugs may also cause a jittery or restless feeling and sleep difficulties, such as problems falling asleep, walking in the night, vivid dreams or nightmares. [39]

• SNRIs-Serotonin and Norepinephrine Reuptake Inhibitors

This class of medications includes venlafaxine (Effexor), duloxetine (Cymbalta) and desvenlafaxine (Pristiq). These drugs are used to treat depression, anxiety problems and chronic pain. Common side-effects include nausea, drowsiness, dizziness, nervousness or anxiety, fatigue, loss of appetite and sexual problems. In higher dosage, these medications may increase blood pressure. [40]

• NDRIs-Norepinephrine and Dopamine Reuptake Inhibitors

The medication available in this class is bupropion (Wellbutrin. Zyban). When used to treat depression, it is often given for its energizing effects, in combination with other antidepressants. It is also used to treat attention-deficit/hyperactivity disorder and as a smoking cessation aid. Common side-effects are jitteriness and insomnia. [41]

• NASSAs-Noradrenergic and Specific Serotonergic Antidepressants

Mirtazapine (Remeron), the medication available in this class, is the most sedating antidepressant, making it a good choice for people who have insomnia or who are very anxious. This medication also helps to stimulate appetite. Common side-effects are drowsiness and weight gain. [42]

• Cyclic Antidepressants

This older group includes amitriptyline (Elavil), maprotiline (LUDIOMIL), imipramine (Tofranil), desipramine (NORPRAMIN), nortriptyline (Novo-Nortriptyline) and clomipramine (Anafranil).

Because these drugs tend to have more side-effects than the newer drugs, they are not often a first choice for treatment. However, when other drugs do not provide relief from sever depression, these drugs may help.

Common side-effects include dry mouth, tremors, constipation, sedation, blurred vision, difficulty urinating, weight gain and dizziness. Because cyclic may cause heart rhythm abnormalities, your doctor should give you an electrocardiogram (ECG) before you take this medication. [43]

MAOIs-Monoamine Oxidase Inhibitors

(PAENATE) were the first class of antidepressants. MAOIs are effective, but they are not often Used because people who take them must follow a special diet. A newer MAOIs,

Monoamine oxidase inhibitors, or MAOIs, such as phenelzine (NARDI) and tranylcypromine

moclobemide (MANERIX), can be used without dietary restriction; however, it may not be as effective as other MAOIs. Common side-effects include a change of blood pressure when

moving from a sitting to a standing position (orthostatic hypotension), insomnia, swelling and

weight gain. [44]

Commonly used antidepressants

Antidepressants use is considerable, especially in the Western world, and is on the rise in several countries. (45)

Data from the National Health and Nutrition Examination Survey published in 2017 showed that during 2011-2014 about one in eight people aged 12 and over in the USA reported taking antidepressants during the previous month. (46)

Antidepressant use increased nearly 65% over a 15- year time frame, (46) and more than 60% of people in the USA taking antidepressants have been taking them for more than 2 years. (46)

A number of different drugs, referred to as antidepressants, are used to treat depression. Antidepressants belong to several different categories. They affect the function of certain neurotransmitters in the brain, although the process is not completely understood.

The medications that currently are most widely used to treat both major depression and dysthymia belong to categories referred to as SSRIs, "selective serotonin reuptake inhibitors"

or SNRIs "serotonin/norepinephrine reuptake inhibitors. They take their name from the effect they have on a neurotransmitter in the brain known as serotonin and norepinephrine, which are believed to play a role in causing depression. There are currently six SSRIs (drugs that affect serotonin) available in the united state:

- Prozac (fluoxetine)
- Paxil (paroxetine)
- Zoloft (sertraline)
- Luvox (fluvoxamine)

Common with Lexapro. At the same time, Prozac, Zoloft, Paxil, Luvox, and Wellbutrin may cause temporary loss of appetite and consequent weight loss when they are started [47].

REFERENCES

- 1.Rush AJ Trivedi MH, Wisniewski SR et al. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report. Am. J. Psychiatry 163, 1905-1917 (2006).
- 2. Joyce PR, Paykel ES. Predictors of drug response in depression. Arch. Gen. Psychiatry46(1),89-99(1989).
- 3. Lieberman J. History of the use of antidepressants in primary care. Primary Care Companion: J. Clin. Psychiatry5,6-10(2003).
- 4. Olfson M, Marcus SC. National patterns in antidepressant medication treatment. Arch. Gen. Psychiatry66(8),848-856 (2009).
- 5. Ballenger JC, Davidson JR, Lecrubier Y et al. Consensus statement on social anxiety disorder from the International Consensus Group on Depression and Anxiety. J Clin. Psychiatry59(Suppl.17),54-60(1998).
- 6. Weissman M, Pilowsky D, Wickramaratne P, et al. Remissions in maternal depression and child psychopathology: A STAR* D-child report.
- 7. Holmans P, Weissman M, Zubenko G, et al. Genetics of recurrent early-onset major depression (GenRED): final genome scan report. Am J Psychiatry. 2007; 164(2):248-58.
- 8. Eley TC, Lian H, Plomin R, et al. Parental Familial Vulnerability, Family Environment, and Their Interactions as Predictors of Depressive Symptoms in Adolescents. J Am Acad Child Adolesc Psychiatry. 2004;43(3):298-306.
- 9. Pillay A, Bundhoo H, Bhowon u. Depression-related distress in Mauritian and South African adolescent girls: an exploratory investigation. Psychol Rep. 2010;107(1):87-94.
- 10. Saluja G, Iachan R, Scheidt PC, et al. Prevalence of and risk factors for depressive symptoms among young adolescents. Arch Pediatr Adolesc Med. 2004;158(8):760-5.
- 11. Diagnostic and statistical manual of mental disorders 5th edition: DSM-5. Arlington, VA Washington, D.C: American Psychiatric Association. 2013. p. 189–195 (https://archive.org/details/diagnosticstatis0005unse/page/189). ISBN 978-0-89042-555-8. OCLC 830807378 (https://www.worldcat.org/oclc/830807378).
- 12. Aspden P (20 April 2012). "So, what does 'The Scream' mean?" (https://www.ft.com/content/42414792-8968-11e1-85af-00144feab49a). Financial Times. ProQuest 1008665027 (https://search.proquest.com/docview/1008665027)
- 14. Testa A, Giannuzzi R, Daine S, Bernardini L, Petrongolo L, Gentiloni Silveri N (February 2013). "Psychiatric emergencies (part III): psychiatric symptoms resulting from organic diseases"

- (https://www.europeanre view.org/wp/wp-content/uploads/86-99.pdf) (PDF). European Review for Medical and Pharmacological Sciences. 17 (Supple 1): 86–99. PMID 23436670 (https://pubmed.ncbi.nlm.nih.gov/2343 6670).
- 15. Kessler, et al. (2007). "Lifetime prevalence and age-of-onset distributions of mental disorders in the World Health Organization's World Mental Health Survey Initiative" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2174588). World Psychiatry. 6 (3): 168–76. PMC 2174588 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2174588) PMID 18188442 (https://pubmed.ncbi.nlm.nih.gov/18188442).
- 16. Pharmacological treatment of mental disorders in primary health care. World Health Organization. 2009. hdl:10665/44095 (https://hdl.handle.net/10665%2F44095). ISBN 978-92-4-154769-7.
- 17. Craske MG, Stein MB (December 2016). "Anxiety". The Lancet. 388 (10063): 3048–3059.doi:10.1016/S01406736(16)303816(https://doi.org/10.1016%2FS01406736%2816%2930381-6) .PMID 27349358 (https://pubmed.ncbi.nlm.nih.gov/27349358). S2CID 208789585 (https://api.semanticscholar.org/CorpusID:208789585).
- 18. Aspden P (20 April 2012). "So, what does 'The Scream' mean?" (https://www.ft.com/content/42414792-8968-11e1-85af-00144feab49a). Financial Times. ProQuest 1008665027 (https://search.proquest.com/DocView/1008665027)
- 19.Psychological Disorders (http://www.psycho-prat.fr/index.php?module=webuploads&func=download &fileId=2963_0) Archived (https://web.archive.org/web/20081204123458/http://www.psycho-prat.fr/index.php?module=webuploads&func=download&fileId=2963_0) 4 December 2008 at the Wayback Machine, Psychologies Anglophone.
- 20. Rose M, Devine J (June 2014). "Assessment of patient-reported symptoms of anxiety" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4140513). Dialogues in Clinical Neuroscience. 16 (2): 197–211. doi:10.31887/DCNS.2014.16.2/morse (https://doi.org/10.31887%2FDCNS.2014.16.2%2Fmrose). PMC 4140513
- 21. Birmes P, Coppin D, Schmitt L, Lauque D (2003). "Serotonin syndrome: a brief review". CMAJ 168(11): 1439-42.
- 22. Moore RA, Derry S, Aldington D, Cole P, Wiffen PJ (2012). "Amitriptyline for neuropathic pain and fibromyalgia in adults". Cochrane Database Syst Rev 12: CD008242.
- 23. Craske MG, Stein MB (December 2016). "Anxiety". The Lancet. 388 (10063): 3048–3059. doi:10.1016/S0140-6736(16)30381-6 (https://doi.org/10.1016%2FS0140-6736%2816%2930381-6) PMID 27349358 (https://pubmed.ncbi.nlm.nih.gov/27349358). S2CID 208789585 (https://api.semanticscholar.org/CorpusID:208789585).
- 24. Mason PJ, Morris VA, Balce Zak TJ (2000). "Serotonin syndrome. Presentation of 2 cases and review of the literature". Medicine (Baltimore) 79 (4): 201-9.
- 25. Sampson E, Warner JP (1999). "Serotonin syndrome: potentially fatal but difficult to recognize". Br J Gen Pract 49 (448): 867-8.
- 26. Nik far S, Rahimi R, Hendoiee N, Abdollahi M (2012). "Increasing the risk of spontaneous abortion and major malformations in newborns following use of serotonin reuptake inhibitors during pregnancy: A systematic review and updated meta-analysis". Daru 20 (1): 75.
- 27. Bienvenu OJ, Ginsburg, GS (December 2007). "Prevention of anxiety disorders". International Review of Psychiatry. Abingdon, England. 19 (6): 647–54. doi:10.1080/09540260701797837 (https://doi.org/10.10 80%2F09540260701797837). PMID 18092242 (https://pubmed.ncbi.nlm.nih.gov/18092242). S2CID 95140 (https://api.semanticscholar.org/CorpusID:95140).
- 28. Khoury B, Lecomte T, Fortin G, et al. (August 2013). "Mindfulness-based therapy: a comprehensive meta-analysis". Clinical Psychology Review. 33 (6): 763–71. doi:10.1016/j.cpr.2013.05.005 (https://doi.org/10.1016%2Fj.cpr.2013.05.005). PMID 23796855 (https://pubmed.ncbi.nlm.nih.gov/23796855).
- 29. Sharma M, Rush SE (July 2014). "Mindfulness-based stress reduction as a stress management intervention for healthy individuals: a systematic review" (https://doi.org/10.1177%2F215658721454314 3). J Evid Based Complementary Altern Med. 19 (4): 271–86. doi:10.1177/2156587214543143 (https://doi.org/10.1177%2F2156587214543143). PMID 25053754 (https://pubmed.ncbi.nlm.nih.gov/2505375 4).
- 30. Patel G, Fancher TL (3 December 2013). "In the clinic. Generalized anxiety disorder". Annals of Internal Medicine. 159 (11): ITC6–1, ITC6–2, ITC6-3, ITC6-4, ITC6-5, ITC6-6, ITC6-7, ITC6-8, ITC6-9, ITC6-10,

- ITC6- 11, quiz ITC6-12. doi:10.7326/0003-4819-159-11-201312030-01006 (https://doi.org/10.7326%2F0003-4819-159-11-201312030-01006). PMID 24297210 (https://pubmed.ncbi.nlm.nih.gov/24297210). S2CID 42889106 (https://api.semanticscholar.org/CorpusID:42889106).
- 31. Moreno-Peral P, Conejo-Ceron S, Rubio-Valera M, Fernández A, Navas-Campana D, Rodríguez-More Jón A, Motrico E, Riga Bert A, Luna JD, Martín-Pérez C, Rodríguez-Bayón A, Ballesta-Rodríguez MI, Luciano JV, Billon JÁ (1 October 2017). "Effectiveness of Psychological and/or Educational Interventions in the Prevention of Anxiety: A Systematic Review, Meta-analysis, and Meta-regression" (https://www.ncbi.nl m.nih.gov/p.m.c/articles/PMC5710546). **JAMA** Psychiatry. 74 (10): 1021-1029. doi:10.1001/jamapsychiatry.2017.2509 (https://doi.org/10.1001%2Fjamapsychiatry.2017.2509). PMC 5710546 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5710546). **PMID** 28877316 (https://pu bmed.ncbi.nlm.nih.gov/28877316).
- 32. Schmidt NB, Allan NP, Knapp AA, Capron D (2019). "Targeting anxiety sensitivity as a prevention strategy". The Clinician's Guide to Anxiety Sensitivity Treatment and Assessment. pp. 145–178. doi:10.1016/B978-0-12-813495-5.00008-5 (https://doi.org/10.1016%2FB978-0-12-813495-5.00008-5). ISBN 978-0-12-813495-5. S2CID 8178211 (https://api.semanticscholar.org/CorpusID:8178211 9).
- 33. Stein MB, Sareen J (19 November 2015). "Generalized Anxiety Disorder". New England Journal of Medicine. 373 (21): 2059–2068. doi:10.1056/nejmcp1502514 (https://doi.org/10.1056%2Fnejmcp150251 4). PMID 26580998 (https://pubmed.ncbi.nlm.nih.gov/26580998).
- 34. Stein DJ, McAnda N. Pharmacotherapy of posttraumatic stress disorder: a review of meta-analyses and treatment guidelines. CNS Spectr.14(I Suppl. I), 25-31 (2009).
- 35. Lynch M. Antidepressants as analgesics: a review of randomized controlled trials. J. Psychiatry Neurosci.26,30 (2001).
- 36. Fountoulakis KN, Vieta E. Siamouli M et al. Treatment of bipolar disorder: a complex treatment for a multifaceted disorder. Ann. Gen. Psychiatry6,27 (2007).
- 37. Wittchen H. Generalized anxiety disorder: prevalence, burden, and cost to society. Depress. Anxiety.16, 162-171 (2002).
- 38. Akerblad AC, Bengtsson F, von Knorring L, et al. (2006) Response, remission and replace in relation to adherence in primary care treatment of depression: A 2-year outcome study. Int Clin psychopharmacology 21: 117-124.
- 39. Akiskal HS, Maser JD, Zeller PJ, et al. (1995) Switching from 'unipolar' to bipolar II. An 11-year prospective study of clinical and temperamental predictors in 559 patients. Arch Gen Psychiatry 52: 114-123.
- 40. Lunn MP, Hughes RA, Wiffen PJ (2014). "Duloxetine for treating painful neuropathy, chronic pain or fibromyalgia". Cochrane Database Syst Rev 12: CD008242.
- 41. Moore RA, Derry S, Aldington D, Cole P, Wiffen PJ (2012). "Amitriptyline for neuropathic pain and fibromyalgia in adults". Cochrane Database Syst Rev 12: CD008242.
- 42. Birmes P, Coppin D, Schmitt L, Lauque D (2003). "Serotonin syndrome: a brief review". CMAJ 168(11): 1439-42.
- 43. Boyer EW, Shannon M (2005). "The serotonin syndrome" (PDF). N. Engl. J. Med. 352 (11): 1112-20.
- 44. Mason PJ, Morris VA, Balce Zak TJ (2000). "Serotonin syndrome. Presentation of 2 cases and review of the literature". Medicine (Baltimore) 79 (4): 201-9.
- 45. Fountoulakis KN, Vieta E. Siamouli M et al. Treatment of bipolar disorder: a complex treatment for a multifaceted disorder. Ann. Gen. Psychiatry6,27 (2007).
- 46. Wittchen H. Generalized anxiety disorder: prevalence, burden, and cost to society. Depress. Anxiety.16, 162-171 (2002).
- 47. Angst J. clinical analysis of the effects of Tofranil in depression. Longitudinal and follow-up studies. Treatment of blood-relations. Psychopharmacologia2,381-407 (1961).
- 48. Kok, Rob M., and Charles F. Reynolds. "Management of depression in older adults: a review." *Jama* 317.20 (2017): 2114-2122.
- 49. Bottino, Cássio MC, Ricardo Barcelos-Ferreira, and Salma RI Ribeiz. "Treatment of depression in older adults." *Current psychiatry reports* 14 (2012): 289-297.
- 50. Zivin, Kara, and Helen C. Kales. "Adherence to depression treatment in older adults: a narrative review." *Drugs & aging* 25.7 (2008): 559-571.

- 51. Gellis, Zvi D., and Bonnie Kenaley. "Problem-solving therapy for depression in adults: a systematic review." *Research on social work practice* 18.2 (2008): 117-131.
- 52. Ijaz, Sharea, Philippa Davies, David Kessler, Glyn Lewis, and Nicola Wiles. "Psychological therapies for treatment-resistant depression in adults." *Cochrane database of systematic reviews* 5 (2018).
- 53. Van Der Wurff, F. B., Stek, M. L., Hoogendijk, W. J. G., & Beekman, A. T. F. (2003). The efficacy and safety of ECT in depressed older adults: a literature review. *International journal of geriatric psychiatry*, 18(10), 894-904.
- 54. Snowden, Mark, Lesley Steinman, and John Frederick. "Peer reviewed: treating depression in older adults: challenges to implementing the recommendations of an expert panel." *Preventing Chronic Disease* 5, no. 1 (2008).
- 55. Brosse, Alisha L., et al. "Exercise and the treatment of clinical depression in adults: recent findings and future directions." *Sports medicine* 32 (2002): 741-760.
- 56. Scogin, Forrest, Douglas Welsh, Ashley Hanson, Jamie Stump, and Adriana Coates. "Evidence-based psychotherapies for depression in older adults." *Clinical Psychology: Science and Practice* 12, no. 3 (2005): 222-237.
- 57. Walker, J., et al. "Treatment of depression in adults with cancer: a systematic review of randomized controlled trials." *Psychological medicine* 44.5 (2014): 897-907.
- 58. Drew, Michael R., and Rene Hen. "Adult hippocampal neurogenesis as target for the treatment of depression." CNS & Neurological Disorders-Drug Targets (Formerly Current Drug Targets-CNS & Neurological Disorders) 6, no. 3 (2007): 205-218.
- 59. Andersson, Gerhard, and Pim Cuijpers. "Internet-based and other computerized psychological treatments for adult depression: a meta-analysis." *Cognitive behaviour therapy* 38, no. 4 (2009): 196-205.
- 60. Gaynes, Bradley N., et al. "Nonpharmacologic interventions for treatment-resistant depression in adults." (2011).
- 61. Anglin, Rebecca ES, Zainab Samaan, Stephen D. Walter, and Sarah D. McDonald. "Vitamin D deficiency and depression in adults: systematic review and meta-analysis." *The British journal of psychiatry* 202, no. 2 (2013): 100-107.
- 62. McKendree-Smith, Nancy L., Mark Floyd, and Forrest R. Scogin. "Self-administered treatments for depression: A review." *Journal of clinical psychology* 59.3 (2003): 275-288.
- 63. Steinbruck, Susan M., Scott E. Maxwell, and George S. Howard. "A meta-analysis of psychotherapy and drug therapy in the treatment of unipolar depression with adults." *Journal of Consulting and Clinical Psychology* 51.6 (1983): 856.
- 64. Stein-Shvachman, Ifat, Dikla Segel Karpas, and Perla Werner. "Depression treatment non-adherence and its psychosocial predictors: differences between young and older adults?" *Aging and disease* 4.6 (2013): 329.
- 65. Champaneri, Shivam, Gary S. Wand, Saurabh S. Malhotra, Sarah S. Casagrande, and Sherita Hill Golden. "Biological basis of depression in adults with diabetes." *Current diabetes reports* 10 (2010): 396-405.
- 66. Zalaquett, Carlos P., and Andrea N. Stens. "Psychosocial treatments for major depression and dysthymia in older adults: A review of the research literature." *Journal of Counseling & Development* 84, no. 2 (2006): 192-201.
- 67. Noonan, Sanjay, Meena Zaveri, Elaine Macan inch, and Kathy Martyn. "Food & mood: a review of supplementary prebiotic and probiotic interventions in the treatment of anxiety and depression in adults." *BMJ nutrition, prevention & health* 3, no. 2 (2020): 351.
- 68. Quirk, Shae E., Lana J. Williams, Adrienne O'Neil, Julie A. Pasco, Felice N. Jacka, Siobhan Housden, Michael Berk, and Sharon L. Brennan. "The association between diet quality, dietary patterns and depression in adults: a systematic review." *BMC psychiatry* 13 (2013): 1-22.
- 69. Farragher, Janine F., Helene J. Polatajko, and Sarbjit V. Jassal. "The relationship between fatigue and depression in adults with end-stage renal disease on chronic in-hospital haemodialysis: a scoping review." *Journal of pain and symptom management* 53, no. 4 (2017): 783-803.
- 70. Walker, Jane, et al. "Prevalence of depression in adults with cancer: a systematic review." *Annals of oncology* 24.4 (2013): 895-900.
- 71. Teri, L., McKenzie, G., & LaFazia, D. (2005). Psychosocial treatment of depression in older adults with dementia. *Clinical Psychology: Science and Practice*, 12(3), 303.

- 72. Elias, Sharifah Munirah Syed, Christine Neville, and Theresa Scott. "The effectiveness of group reminiscence therapy for loneliness, anxiety and depression in older adults in long-term care: A systematic review." *Geriatric nursing* 36.5 (2015): 372-380.
- 73. Simmonds-Buckley, Melanie, Stephen Kellett, and Glenn Waller. "Acceptability and efficacy of group behavioural activation for depression among adults: a meta-analysis." *Behaviour Therapy* 50, no. 5 (2019): 864-885.
- 74. Maj, Mario, et al. "The clinical characterization of the adult patient with depression aimed at personalization of management." *World Psychiatry* 19.3 (2020): 269-293.
- 75. Sclar, David A., Linda M. Robison, Jennifer M. Schmidt, Kurt A. Bowen, Leigh V. Castillo, and Ambartsum M. Oganov. "Diagnosis of depression and use of antidepressant pharmacotherapy among adults in the United States: does a disparity persist by ethnicity/race?" *Clinical drug investigation* 32 (2012): 139-144.
- 76. Jayasekara, Rasika, Nicholas Procter, Julie Harrison, Kerim Skelton, Sally Hampel, Russell Draper, and Kate Deuter. "Cognitive behavioural therapy for older adults with depression: a review." *Journal of mental health* 24, no. 3 (2015): 168-171.
- 77. Morimoto, Sarah Shizuko, Theodora Kanellopoulos, and George S. Alexopoulos. "Cognitive impairment in depressed older adults: implications for prognosis and treatment." *Psychiatric annals* 44.3 (2014): 138-142.
- 78. Paige, Lisa A., Matthew W. Mitchell, K. Ranga R. Krishnan, Rima Kaddurah-Daouk, and David C. Steffens. "A preliminary metabolomic analysis of older adults with and without depression." *International Journal of Geriatric Psychiatry: A journal of the psychiatry of late life and allied sciences* 22, no. 5 (2007): 418-423.
- 79. Unitizer, Jürgen, Wayne Katon, Mark Sullivan, and Jeanne Miranda. "Treating depressed older adults in primary care: narrowing the gap between efficacy and effectiveness." *The Milbank Quarterly* 77, no. 2 (1999): 225-256.
- 80. Deuschle, Michael. "Effects of antidepressants on glucose metabolism and diabetes mellitus type 2 in adults." *Current opinion in psychiatry* 26, no. 1 (2013): 60-65.
- 81."Anxiety disorders— Symptoms and causes" (https://www.mayoclinic.org/diseases-conditions/anxiety/s ymptoms-causes/syc-20350961). Mayo Clinic. Retrieved 23 May 2019.