

Major Depressive Disorder (MDD)

A plain-English guide for you and your family

WHAT IS HAPPENING

Major depressive disorder is more than feeling sad. For at least two weeks, nearly every day, the person has at least five of these: low mood (in children it can look like irritability instead), losing interest or pleasure in almost everything, appetite or weight changes, sleeping too little or too much, moving or speaking noticeably slower or being restless, exhaustion, feeling worthless or excessively guilty, trouble thinking or deciding, and thoughts of death or suicide. At least one of the five must be the low mood or the loss of pleasure. It is treated with talk therapy (especially cognitive behavioral therapy and interpersonal therapy) and antidepressant medicines (such as SSRIs like sertraline or escitalopram), which usually take four to six weeks to work. Close follow-up is needed, especially in the first few weeks of treatment, because energy sometimes returns before hope does, raising the risk of suicide.

What you might feel

- Sad, empty, or hopeless mood almost all day, nearly every day (or grouchy, angry mood in kids and teens)
- Loss of interest or pleasure in almost everything you used to enjoy (anhedonia)
- Big change in weight or appetite (gain or loss of more than 5% of your body weight in a month, or not gaining weight as expected in a growing child)
- Trouble sleeping or sleeping way too much, almost every night
- Moving or talking much slower than usual, or being so restless and fidgety that other people can see it
- Feeling exhausted or drained of energy nearly every day, even after rest
- Feeling worthless, or guilty in a way that's way out of proportion to anything you actually did
- Hard time concentrating, remembering things, or making even small decisions
- Repeated thoughts of death, wishing you were dead, thinking about suicide, planning suicide, or trying suicide

Call the doctor right away if...

- Suicidal thoughts with a specific plan, intent to act, or access to a gun, pills, or other lethal means — needs emergency evaluation the same day, usually in an ER or crisis center
- Psychotic features — delusions (false beliefs, like 'I'm rotting inside' or 'I've lost all my money when I haven't') or hallucinations (hearing voices, often cruel ones) — requires combined medication and therapy or electroconvulsive therapy (ECT), and urgent psychiatry referral
- Refusing to eat or drink, or catatonia (frozen, unresponsive, or bizarre posturing) — medical emergency that can be life-threatening; ECT is often the fastest, most effective treatment
- Any history of a manic or hypomanic episode (days of sky-high mood, racing thoughts, risky behavior, little need for sleep) — STOP: this is bipolar disorder, not simple depression. Giving an antidepressant alone can flip the person into mania. Must treat with a mood stabilizer first.
- New or worse suicidal thoughts in the first few weeks after starting an antidepressant, especially in anyone under 25 — FDA black-box warning: the medicine can briefly increase suicide risk before it helps. Needs close follow-up.
- Started right after having a baby, with scary intrusive thoughts about harming the infant — same-day assessment to rule out postpartum psychosis, which is a psychiatric emergency

What the care team will do

- Assess suicide risk directly at every encounter — ideation, plan, means, intent
- Teach the 4–6 week medication timeline and book follow-up within 1–2 weeks of starting
- Screen every depressed patient for lifetime mania/hypomania BEFORE antidepressants
- Mobilize behavioral activation early: small scheduled activities, sleep regularity, daylight
- Involve family/supports in the safety plan and means restriction
- Never stop antidepressants abruptly; plan continuation 6–12 months past remission

Medicines you may be given — and why

Sertraline / Escitalopram / Fluoxetine (SSRIs — first choice)

Blocks the pump that sucks serotonin (a brain messenger that steadies mood, sleep, and appetite) back into the nerve cell. More serotonin stays in the gap between nerve cells. Over weeks, the brain adjusts its receivers and grows new connections, and the dark cloud slowly lifts.

Venlafaxine / Duloxetine (SNRIs)

Blocks the pumps for two brain messengers: serotonin (which steadies mood and sleep) and norepinephrine (which fuels energy, focus, and the body's get-up-and-go). Used when an SSRI did not work well enough, or when exhaustion and body pain are big parts of the depression.

Bupropion

Blocks the pumps for norepinephrine (which fuels alertness and drive) and dopamine (which powers motivation, pleasure, and focus). Targets the 'zombie' symptoms — no energy, no joy, foggy thinking. Does not harm sex drive like SSRIs do. Also helps people quit smoking.

Mirtazapine

Blocks the brake pedal (alpha-2 autoreceptors) on nerve cells that release norepinephrine and serotonin, so those messengers flood out. Also blocks histamine receivers (causes sleepiness) and certain serotonin receivers that trigger nausea. Perfect when depression steals sleep and appetite.

Tricyclic antidepressants (amitriptyline, nortriptyline)

Older drugs that block serotonin and norepinephrine pumps like the newer drugs do, but they also hit many other receivers — acetylcholine (causes dry mouth, blurry vision, constipation, confusion), histamine (drowsiness), alpha receptors (dizziness when standing), and heart sodium channels (dangerous in overdose). Effective but messy, so now second or third choice.

MAOIs (phenelzine, tranylcypromine) — specialist use only

Blocks monoamine oxidase, the enzyme that breaks down serotonin, norepinephrine, and dopamine inside nerve cells and in the gut and liver. All three messengers build up. Very powerful for depression that has not responded to anything else, but comes with strict food and drug rules because the gut enzyme that normally destroys tyramine (a chemical in aged foods) is also blocked.

Where this information comes from

- American Psychiatric Association DSM-5-TR (2022)
- NIMH Major Depression fact sheet
- FDA black-box warning on antidepressants and suicidality
- Rush et al. STAR*D trial (NEJM 2006)

Last reviewed: 2026-06-01