Weight Gain

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Characteristics: Typically, patients will report food craving and binging. Weight gain is rapid in the first three months, more gradual over the following year, then often plateaus. Rapid initial weight gain is correlated with greater eventual cumulative weight gain. FDA definition of weight gain is ≥7% increase in weight from baseline.

Meds That Cause It: Antipsychotics, especially clozapine, olanzapine, and quetiapine. Somewhat less weight gain with risperidone and paliperidone. Least weight gain with aripiprazole, haloperidol, ziprasidone, and lurasidone. Antidepressants: Mirtazapine, tricyclics, paroxetine. Mood stabilizers: Lithium, valproic acid.

Mechanism: Blockade of histamine and serotonin 2A receptors, leading to increased hunger.

General Management:

- Monitoring: Weight, BMI, waist circumference every four weeks for three months, then every three months.
- Lifestyle modification, including exercise and dietary changes, is helpful for patients who are motivated; several studies have shown some benefit, but in actual clinical settings it may be difficult to match their results.
- Switch to a medication that is more weight neutral.

First-Line Medications (some evidence specifically for reducing psychotropic-induced weight gain):

- Topiramate (Topamax) 100–300 mg/day; SE: Cognitive dulling.
- Metformin XR (Glucophage XR, Glumetza) 500–2000 mg: Take with largest meal, split into two doses if needed (based on GI side effects).
- Olanzapine/samidorphan (Lybalvi) as an alternative to olanzapine alone to reduce weight gain.
- Orlistat (Xenical) 120 mg three times daily after meals. Interferes with fat absorption; SE: Diarrhea.
- Aripiprazole (Abilify) 15 mg/day. Antipsychotic. May be useful for olanzapine-induced weight gain as adjunct.
- Glucagon-like peptide-1 agonists (GLP1 agonists), such as liraglutide (Saxenda) or semaglutide (Ozempic).

Second-Line Medications (effective for weight loss, but little or no evidence specifically for psychotropic-induced weight gain):

- Bupropion SR (Wellbutrin SR) 300–400 mg daily.
- Any psychostimulant of the methylphenidate or amphetamine class.
- Naltrexone/bupropion (Contrave) 8 mg/90 mg up to two tabs twice daily. Anti-obesity drug.
- Phentermine (Adipex-P, Lomaira)) 15–37.5 mg daily. Anti-obesity drug.
- Phentermine/topiramate (Qsymia) 7.5 mg/46 mg up to two tabs daily. Anti-obesity drug.
- Nizatidine (Axid) 150–300 mg daily. Antacid, H2 blocker, available over the counter.
- Amantadine (Symmetrel) 100–300 mg/day.

Clinical Pearls:

- Weight gain is most likely in the first six weeks of taking an antipsychotic, and it's difficult for patients to ever lose this weight. As such, you should monitor weekly initially and switch to a more weight-neutral agent at the first sign of weight gain.
- If patient gains 5% or more of body weight, switch to a different drug.
- Ziprasidone and aripiprazole are probably the most weight-neutral antipsychotics and may even cause weight loss, especially if switching from another agent.
- Weight gain tends to be most severe in patients who are taking an antipsychotic for the first time.
- Ask weight-gaining patients about dry mouth; many psychotropics cause this, and such patients may gain weight from drinking sugary beverages to deal with this side effect.

Fun Fact:

Some researchers have hypothesized that treatment-emergent weight gain is related to and predictive of clinical response, but others argue it may be a marker for medication adherence instead.