

## Breast cancer screening in women receiving antipsychotics

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Women with severe mental illness (SMI) are more likely to develop breast cancer and often have more advanced stages of breast cancer when it is detected.<sup>1</sup> Antipsychotics have a wide variety of FDA-approved indications and many important life-saving properties. However, patients treated with antipsychotic medications that increase prolactin levels require special consideration with regards to referral for breast cancer screening. Although no clear causal link between antipsychotic use and breast cancer has been established, antipsychotics that raise serum prolactin levels (haloperidol, iloperidone, lurasidone, olanzapine, paliperidone, risperidone) are associated with a higher risk of breast cancer than antipsychotics that produce smaller increases in prolactin levels (aripiprazole, asenapine, brexpiprazole, cariprazine, clozapine, quetiapine, and ziprasidone).<sup>2,3</sup> Risperidone and paliperidone have the highest propensities to increase prolactin (45 to >100 ng/mL), whereas other second-generation antipsychotics are associated with only modest elevations.<sup>4</sup> Prolonged exposure to high serum prolactin levels should be avoided in women due to the increased risk for breast cancer.<sup>2,3</sup> Although there are no clear rules regarding which number or cluster of personal risk factors necessitates a further risk assessment for breast cancer, women receiving antipsychotics (especially those age ≥40) can be referred for further assessment. An individualized, patient-centered approach should be used.

### Recognize risk factors

Patients with SMI often need to take a regimen of medications, including antipsychotics, for weeks or months to stabilize their

symptoms. Once a woman with SMI is stabilized, consider referral to a clinic that can comprehensively assess for breast cancer risk. Nonmodifiable risk factors include older age, certain genetic mutations (*BRCA1* and *BRCA2*), early menarche, late menopause, high breast tissue density as detected by mammography, a family history of breast cancer, and exposure to radiation.<sup>5,6</sup> Modifiable risk factors include physical inactivity, being overweight or obese, hormonal exposure, drinking alcohol, and the presence of certain factors in the patient's reproductive history (first pregnancy after age 30, not breastfeeding, and never having a full-term pregnancy).<sup>2,3</sup> When making such referrals, it is important to avoid making the patient feel alarmed or frightened of antipsychotics. Instead, explain that a referral for breast cancer screening is routine.

### When to refer

All women age ≥40 should be offered a referral to a clinic that can provide screening mammography. If a woman has pain, detects a lump in her breast, has a bloody discharge from the nipple, or has changes in the shape or texture of the nipple or breast, a more urgent referral should be made.<sup>4</sup>

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The most important thing to remember is that early breast lesion detection can be life-saving and can avert the need for more invasive surgeries as well as exposure to chemotherapy and radiation.

## What to do when prolactin is elevated

Ongoing monitoring of serum prolactin levels can help ensure that the patient's levels remain in a normal range (<25 ng/mL).<sup>2,3,5,6</sup> If hyperprolactinemia is detected, consider switching to an antipsychotic less likely to increase prolactin. Alternatively, the addition of aripiprazole/brexipiprazole or a dopamine agonist as combination therapy can be considered to rapidly restore normal prolactin levels.<sup>2</sup> Such changes should be carefully considered because patients may decompensate if antipsychotics are abruptly switched. An individualized risk vs benefit analysis is necessary for any patient in this situation. Risks include not only the recurrence of psychiatric symptoms but also a potential loss of their current level of functioning. Patients may need to continue to take an antipsychotic that is more likely to increase prolactin, in which case close monitoring is advised as well as collaboration with other physicians and members of the patient's care team. Involving the patient's support system is helpful.

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