

# 29 - First episode of psychosis

## First episode of psychosis

28 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 1 Antipsychotic prophylaxis First episode of psychosis Antipsychotics provide effective protection against relapse, at least in the short to medium term,<sup>1</sup> and the introduction of antipsychotics in the 1950s seems to have improved outcomes overall.<sup>2</sup> A meta-analysis of placebo-controlled trials found that 26% of patients with first-episode schizophrenia on maintenance antipsychotic relapsed after 6–12 months compared with 61% on placebo.<sup>3</sup> Although the current consensus is that antipsychotics should be prescribed for 1–2 years after a first episode of schizophrenia,<sup>4,5</sup> one study<sup>6</sup> found that withdrawing antipsychotic treatment in line with this view led to a relapse rate of almost 80% after 1 year medication-free and 98% after 2 years. A 2019 Swedish population study revealed that the longer the treatment with antipsychotics, the lower the risk of hospitalisation (e.g. those with 5 years' treatment had half the hospitalisation rate of those treated for less than 6 months).<sup>7</sup> Other studies in first-episode schizophrenia confirmed that only a small minority of patients who discontinue remain well 1–2 years later<sup>8–11</sup> (e.g. a small study found 94% of patients with first-episode schizophrenia relapsed within 2 years of stopping risperidone long-acting injection; 97% at three years).<sup>12</sup> A 2018 meta-analysis of eight RCTs was rather more optimistic and found relapse rates averaged 35% (treated) and 61% (discontinued) at 18–24 months.<sup>13</sup> A 5-year follow-up of a 2-year RCT, during which patients either received maintenance antipsychotic treatment or had their antipsychotic dose reduced or discontinued completely, found that while there was a clear advantage for maintenance treatment with respect to reducing short-term relapse this advantage was lost in the medium term. Further, the dose-reduction/discontinuation group were receiving lower doses of anti psychotic drugs at follow-up and had better functional outcomes.<sup>14</sup> There are numerous interpretations of these outcomes but the most that can be concluded is that dose reduction is a possible option in first-episode psychosis. The study has been heavily criticised<sup>15</sup> and there are certainly other studies showing disastrous outcomes from antipsychotic discontinuation,<sup>16</sup> albeit over shorter periods with fewer patients. Nonetheless, some patients with first-episode psychosis will not need long-term anti psychotics to stay well – figures as high as 18–30% have been put forward.<sup>17</sup> There are no reliable patient factors linked to outcome following discontinuation of antipsychotics in patients with first-episode psychosis (other than cannabis use)<sup>18</sup> and there remains more evidence in favour of continuing antipsychotics than for stopping them.<sup>19</sup> There are indications that very prolonged discontinuation regimens using hyperbolic tapering (see section on stopping antipsychotics in this chapter) may offer the best chance of successfully withdrawing from antipsychotic treatment.<sup>20,21</sup> Definitions of relapse usually focus on

the severity of positive symptoms and largely ignore cognitive and negative symptoms: positive symptoms are more likely to lead to hospitalisation while cognitive and negative symptoms (which respond less well, and in some circumstances may even be exacerbated by antipsychotic treatment) have a greater overall impact on quality of life. With respect to antipsychotic choice, in the context of an RCT, clozapine did not offer any advantage over chlorpromazine in the medium term in patients with first-episode non-refractory schizophrenia.<sup>22</sup> However, in a large naturalistic study of patients with

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Revision #1

Created 2026-01-04 20:13:39 UTC by Omar Ayman

Updated 2026-01-04 20:13:39 UTC by Omar Ayman