| Citation | Abstract | Takeaway |
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| Lian, Y., Xu, Y., Li, H., Wang, J., Chen, J., Wei, X., & Tang, Y. (2022). Efficacy of long-acting injectable versus oral antipsychotic drugs in early psychosis: A systematic review and meta-analysis. Early Intervention in Psychiatry, 16(5), 508–520. https://doi.org/10.1111/eip.13202 | Aim<br>Long-acting injectable antipsychotic drugs (LAIs) are often used as an alternative to oral antipsychotics (OAPs) in individuals with psychosis who demonstrate poor medication adherence. Previous meta-analyses have found mixed results on the efficacy of LAIs, compared to OAPs, in patients with psychotic disorders. The objective of this meta-analysis was to compare the effectiveness of using LAIs versus OAPs in the early stages of psychosis.<br>Methods<br>Major electronic databases were used to search for any studies examining the comparative effectiveness (i.e., relapse, adherence, hospitalization, and all-cause discontinuation) of any LAIs versus OAPs in early stages of psychosis. Studies published up to 6 June, 2019 were included and no language restriction was applied. Inclusion criteria were a diagnosis of schizophrenia or related disorder, where patients were in their first episode or had a duration of illness ≤5 years. Data were analysed using a random-effects model.<br>Results<br>Fifteen studies (n = 10 584) were included, of which were 7 RCTs, 7 observational studies, and 1 post-hoc analysis. We found that LAIs provided advantages over OAPs in terms of relapse rates. No significant differences were found between LAI and OAP groups in terms of all-cause discontinuation, hospitalization, and adherence rates. However, considering only RCTs revealed advantages of LAIs over OAPs in terms of hospitalization rates.<br>Conclusions | LAIs may benefit patients over OAPs in relapse and hospitalizations, but further studies are needed to elucidate full benefit due to heterogeneity of studies and risk of bias in included trials.<br><br>LAIs provide significant advantages in ability to support adherence to medication, but many clinicians are reluctant to prescribe it. |

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| | LAIs may provide benefits over OAPs with respect to reducing relapse and hospitalization rates in early psychosis patients. There is a need for larger and better-designed studies comparing OAPs and LAIs specifically in early psychosis patients. | |
| Kane JM, Schooler NR, Marcy P, et al. Effect of Long-Acting Injectable Antipsychotics vs Usual Care on Time to First Hospitalization in Early-Phase Schizophrenia: A Randomized Clinical Trial. JAMA Psychiatry. 2020;77(12):1217–1224. doi:10.1001/jamapsychiatry.2020.2076 | Key Points<br>Question Compared with usual care, does the use of a long-acting formulation of antipsychotic medication reduce the risk of hospitalization in early-phase schizophrenia?<br>Findings In this cluster randomized trial of 489 participants, use of long-acting injectable aripiprazole monohydrate was associated with a significant delay in time to first hospitalization, with the number needed to treat to prevent 1 hospitalization of 7.<br>Meaning Long-acting formulations are infrequently used in early-phase treatment, and the association between their use and decreased hospitalization risk can have implications for individual treatment decisions and public health efforts.<br>Abstract<br>Importance Long-acting injectable antipsychotics (LAIs) can potentially reduce hospitalization risk by enhancing medication adherence but are rarely considered for early-phase schizophrenia treatment.<br>Objective To determine whether encouraging use of a LAI compared with usual care delays the time to first hospitalization with patients with early-phase illness.<br>Design, Setting, and Participants The Prevention of Relapse in Schizophrenia (PRELAPSE) trial was cluster randomized with a follow-up duration of 2 years. The study began in December 2014, was completed in March 2019, and was conducted in 39 mental health centers in 19 US states. Site randomization | Comparing usual care (clinician choice) to once monthly apriprazole injection -> reduced hospitalization for early phase schizophrenia<br><br>Many think low LAI use is due ot patient refusal – however, with sufficient training in educating patients about LAIs and engaging in shared decision making conversations around medication choices, LAIs can be powerful tool for many who require ongoing treatment |

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| | assigned 19 clinics to encourage treatment with long-acting aripiprazole monohydrate (aripiprazole once monthly [AOM] condition) and 20 to provide treatment as usual (clinician's choice [CC] condition). Participant eligibility criteria included (1) schizophrenia diagnosis confirmed by a structured clinical interview, (2) fewer than 5 years of lifetime antipsychotic use, and (3) age 18 to 35 years. The AOM sites identified 576 potentially eligible participants, of whom 234 (40.6%) enrolled; CC sites identified 685 potentially eligible participants, of whom 255 (37.2%) enrolled.<br>Interventions There were no restrictions on treatment at CC sites (including using LAIs) or at AOM sites with the exception that aripiprazole monohydrate had to be prescribed within US Food and Drug Administration–approved guidelines.<br>Main Outcomes and Measures The primary outcome was time to first psychiatric hospitalization based on participant interviews every 2 months, the service use resource form administered every 4 months, and other sources (eg, health records) as available. Potential events were adjudicated by an independent committee masked to treatment assignment.<br>Results The 489 participants (368 men [75.3%]) had a mean (SD) age of 25.2 (4.2) years and 225 (46.0%) had 1 year or less lifetime antipsychotic use. Fifty-two AOM (22%) and 91 CC participants (36%) had at least 1 hospitalization. The mean survival time until first hospitalization was 613.7 days (95% CI, 582.3-645.1 days) for AOM participants and 530.6 days (95% CI, 497.3-563.9 days) for CC participants. For time to first hospitalization, the hazard ratio was 0.56 (95% CI, 0.34- 0.92; P = .02), favoring AOM. Survival probabilities were 0.73 (95% CI, 0.65-0.83) for AOM participants and 0.58 (95% CI, 0.50-0.67) for CC participants. The number needed to treat to prevent 1 | |

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| | additional hospitalization was 7 participants treated with AOM compared with CC.<br>Conclusions and Relevance Long-acting injectable antipsychotic use by patients with early-phase schizophrenia can significantly delay time to hospitalization, a personally and economically important outcome. Clinicians should more broadly consider LAI treatment for patients with early-phase illness. | |
| Strube W, Wagner E, Luykx JJ, Hasan A. A review on side effect management of second-generation antipsychotics to treat schizophrenia: a drug safety perspective. Expert Opin Drug Saf. 2024 Jun;23(6):715-729. doi: 10.1080/14740338.2024.2348561. Epub 2024 May 6. PMID: 38676922. | Introduction<br>Effective side effects management present a challenge in antipsychotic treatment with second-generation antipsychotics (SGAs). In recent years, most of the commonly used SGAs, except for clozapine, have been shown to differ only slightly in their effectiveness, but considerably regarding perceived side effects, safety profiles, and compatibility to preexisting medical conditions.<br>Areas covered<br>The current state of available evidence on side-effect management in SGA treatment of patients with schizophrenia spectrum disorders (SSD) is reviewed. In addition, current guideline recommendations are summarized, highlighting evidence gaps.<br>Expert Opinion<br>SGA safety and side effects needs to be considered in treatment planning. Shared decision-making assistants (SDMA) can support patients, practitioners and relatives to orient their decisions toward avoiding side effects relevant to patients' adherence. Alongside general measures like psychosocial and psychotherapeutic care, switching to better tolerated SGAs can be considered a relatively safe strategy. By contrast, novel | SGA treatment should be oriented towards lowest dose and avoiding possible side effects<br><br>General health measures (physical activity) are considered first line options in approaching side effects, in addition to psychotherapeutic and psychosocial interventions<br><br>Does reduction below standard treatment doses appears to increase risk of relapse. Should only be considered for select cases in the list of side effect impact, risk of nonadherence and risk of relapse.<br><br>Switching from one SGA to another shown through recent meta-analysis to be considered fairly safe. |

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| | meta-analytical evidence emphasizes that dose reduction of SGAs can statistically increase the risk of relapse and other unfavorable outcomes. Further, depending on the type and severity of SGA-related side effects, specific treatments can be used to alleviate induced side effects (e.g. add-on metformin to reduce weight-gain). Finally, discontinuation should be reserved for acute emergencies. | Abrupt discontinuation of SGA should be reserved for acute emergencies |
| Bao Y, Papp MA, Lee R, Shern D, Dixon LB. Financing Early Psychosis Intervention Programs: Provider Organization Perspectives. Psychiatr Serv. 2021 Oct 1;72(10):1134-1138. doi: 10.1176/appi.ps.202000710. Epub 2021 Mar 4. PMID: 33657841; PMCID: PMC8417142. | Objective: The authors aimed to identify prominent financing approaches for coordinated specialty care (CSC) of patients with first-episode psychosis, alignment or misalignment of such approaches with sustained CSC implementation, and CSC provider perspectives on ideal payment models.<br>Methods: Semistructured interviews were conducted with informants from CSC provider organizations. Purposeful sampling of CSC program directors, team leaders, and other administrators from a national e-mail Listserv was supplemented by snowball sampling via participant recommendations. Interview data from 19 CSC programs in 14 states were analyzed by using an integrated (inductive and deductive) approach to derive themes.<br>Results: The results indicated that financing approaches to CSC were patchwork and highly varied. Three major sources of funding were cited: insurance billing (largely fee for service [FFS] to Medicaid and private insurance), set-aside funding from the federal Mental Health Block Grant (MHBG) program, and state funding. The findings revealed limited coverage and restrictive rules associated with FFS insurance billing that were misaligned with CSC implementation. The grant nature of MHBG and other public funding was seen as a threat to long-term CSC sustainability and deployment. CSC stakeholders endorsed a bundled-payment approach by public and private | Most stakeholders endorsed bundled approach and tying payment to client outcomes reflecting CSC's recovery goals<br><br>Bundled payment could be utilized to cover costs of the program operation, and grant/state funds could support program start up, capacity building and network expansion<br><br>Bundled payments should be linked to credentialing and certification of CSC programs to ensure fidelity to the program model |

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| | payers and supported tying payment to client outcomes to reflect CSC's recovery orientation.<br>Conclusions: Reliance on FFS insurance billing and public funding is likely to be unsustainable. Additionally, FFS billing is misaligned with CSC goals. Because of the diversity in CSC programs, populations, and existing funding mechanisms and rules, payer-provider collaboration will be essential in designing a bundled-payment model that meets local needs. | |