A Systematic Literature Review of Economic Evaluation Studies for Schizophrenia

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Background

- Schizophrenia is a chronic psychiatric disorder associated with substantial clinical, social, and economic burden worldwide (1).

- The illness typically emerges in early adulthood and often requires lifelong treatment and support, leading to high healthcare costs and indirect productivity losses (2,5).

- Economic evaluations—particularly cost-effectiveness analyses (CEAs)—help determine how best to allocate scarce mental health resources and assess the value of interventions such as antipsychotics, long-acting injectables, or psychosocial therapies (3).

- In schizophrenia, treatment adherence and relapse prevention are major determinants of both patient outcomes and costs (4).

Objective

This systematic review synthesizes economic evaluation studies of schizophrenia interventions to map evidence trends, methodological diversity, and key cost drivers.

Methods

Search strategy
Systematic searches were performed in PubMed (6), Medline (via NCBI) (7), and the Cochrane Library (8), supplemented by grey literature and manual review of bibliographies.
Search terms included: schizophrenia, psychosis, hallucination, paranoia, dementia praecox, cost, economic, burden

Screening & extraction
Two independent reviewers performed study selection, data extraction, and quality assessment; disagreements resolved by consensus.
Each record included study details (author, title, country, year, model type, perspective, time horizon, intervention, comparator, and DOI).

Time-frame
1990 – 2024

Inclusion criteria
Original full-text studies in English or Greek reporting full economic evaluations (e.g. cost-effectiveness, cost-utility, cost-benefit) targeting schizophrenia.
Excluded: abstracts, reviews, meta-analyses, letters, editorials, presentations.

Results

Study selection
- The systematic search initially identified a total of 10,573 records from electronic databases and 39 additional records from other sources (e.g., reference lists, grey literature).
- An updated supplementary search in 2025 yielded an additional 18,441 records, ensuring inclusion of the most recent economic evaluations.
- After removal of duplicates, 23,961 unique records were retained for screening.
- Titles and abstracts were screened for relevance, resulting in the exclusion of 23,595 records that did not meet the predefined inclusion criteria (e.g., non-schizophrenia studies, non-economic outcomes, incomplete analyses).
- A total of 366 full-text articles were retrieved and assessed for eligibility according to the PICOS framework (Population, Intervention, Comparator, Outcomes, Study design), of which 248 were excluded.
- Finally, 110 studies (8-118) fulfilled all inclusion criteria and were included in the qualitative synthesis of this systematic literature review (**Figure 1**).

Study characteristics
- The majority of identified studies were conducted in high-income countries, primarily the United States (n=31), the United Kingdom (n=11) and Spain (n=8), while an increasing number of analyses have emerged in the past decade from Asia and other middle-income regions (n=8), particularly China, South Korea, and Vietnam, reflecting the geographical expansion of economic evaluation evidence in schizophrenia (**Figure 2**).
- Antipsychotic treatments, particularly long-acting injectables, dominated the economic literature, with few evaluations of psychosocial or community-based programs (20,39,43,50,53,65,83,87,90,91).
- Most evaluations addressed adult populations with established schizophrenia, while only a limited number specifically focused on early-intervention (45,61,71) or first-episode psychosis (26).

Analytical and methodological overview
- Decision-analytic and Markov models were the most commonly applied analytical frameworks, reflecting their suitability for chronic disease modeling and relapse cycles.
- Microsimulation models (14,21,37,38,94) appeared in a limited number of studies, mainly for capturing adherence dynamics and individualized treatment pathways.
- Time horizons typically ranged from 1–5 years, while only a minority of studies used lifetime horizon to capture long-term cost offsets (13,54,59,72,106,108,117) (**Table 1**).
- Cost-effectiveness analyses (CEAs) were predominant, followed by cost-utility analyses (CUAs), and fewer cost-benefit (65) or cost-minimization/comparison evaluations (10, 23, 74) (**Table 1**).
- Healthcare or payer perspectives were adopted in over 80% of cases, whereas societal perspectives, which include productivity losses and informal caregiver costs, remained underrepresented (46,50,54,56,59,82,83,87,88,90,91,106,118) (**Table 1**).

Economic evaluation findings
- Olanzapine, risperidone, and aripiprazole were the most frequently assessed, driving nearly half of all evaluations (**Figure 3**).
- Long-acting injectable antipsychotics (LAIs), including risperidone LAI, aripiprazole LAI, paliperidone palmitate, and olanzapine pamoate, were also identified, showing strong evidence of economic advantage through improved adherence and reduced relapse rates (**Figure 3**).
- LAIs consistently demonstrated generally tended to show superior cost-effectiveness compared with oral or other depot formulations, mainly through reductions in relapse rates, emergency visits, and hospitalizations (29,30,38,52,99,100,103,113,116).
- Paliperidone palmitate (PP-LAI) frequently emerged as a cost-effective or dominant option across various settings, outperforming risperidone and olanzapine LAIs in cost-utility analyses conducted in Finland, Norway, Croatia, South Korea, and the United Arab Emirates (31, 34, 52, 55, 66).
- Olanzapine was often reported as the most cost-effective oral antipsychotic, occasionally dominating alternatives such as aripiprazole, risperidone, or haloperidol for relapse prevention and long-term maintenance, with high consistency across Serbia and Singapore (101, 117).
- Haloperidol and risperidone, among first-generation and low-cost options, remained cost-saving or dominant in several analyses from low- and middle-income countries, especially in Uganda, Vietnam, and Ethiopia, where treatment affordability played a major role (13, 20, 51,59).
- Community-based and psychosocial interventions, including cognitive remediation and supported employment, showed favorable cost-effectiveness profiles compared with treatment-as-usual models, particularly for patients with cognitive impairments (20, 91).
- Analyses adopting a societal perspective, including indirect costs such as productivity loss and caregiver time, more frequently identified interventions as cost-effective or cost-saving, compared with payer-only perspectives (54, 59, 82, 83, 88, 90, 91).
- Short time horizons (mostly 1 year) and healthcare payer perspectives were common analytical choices, limiting the assessment of long-term and societal cost offsets, such as productivity gains and caregiver burden (31, 34, 52, 66).
- Across studies, relapse frequency, medication adherence, hospitalization rates, and drug acquisition costs were the main drivers of ICER variability and uncertainty.
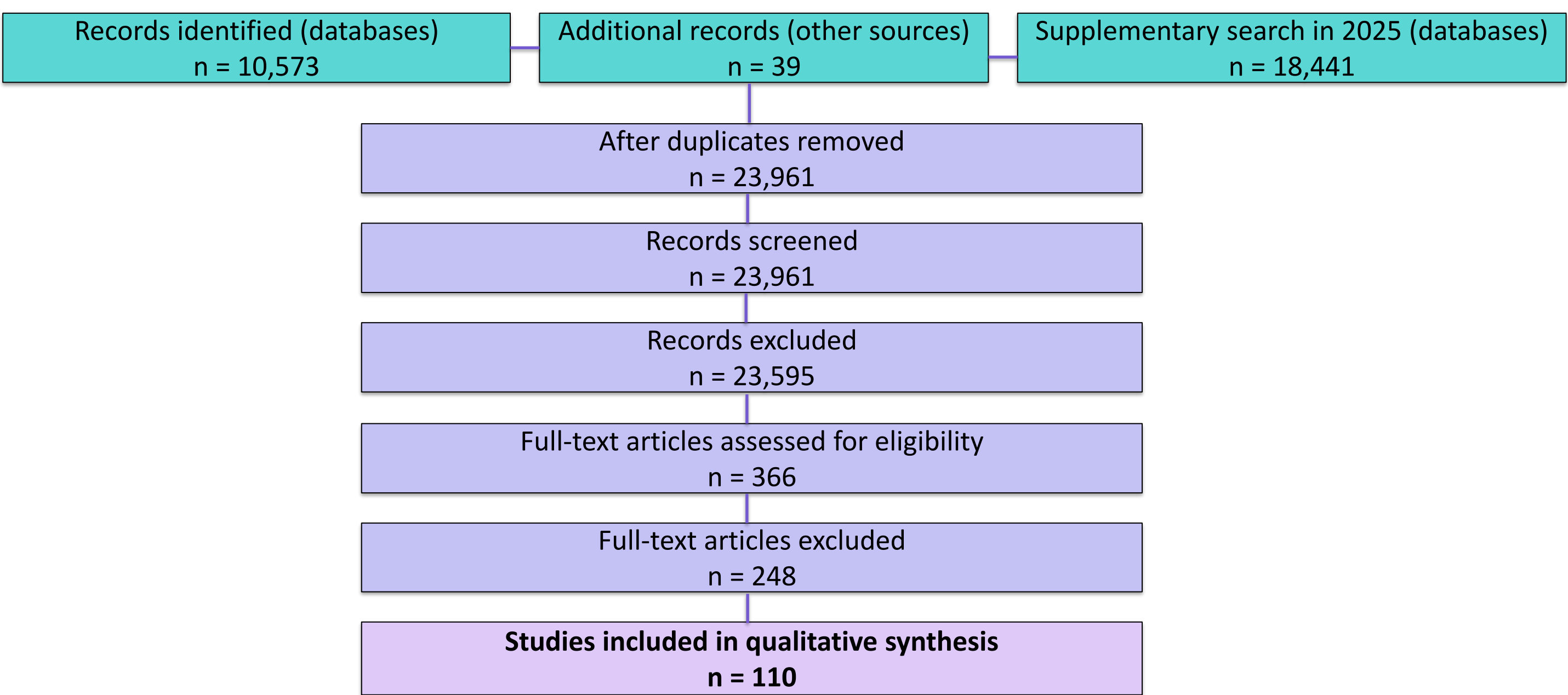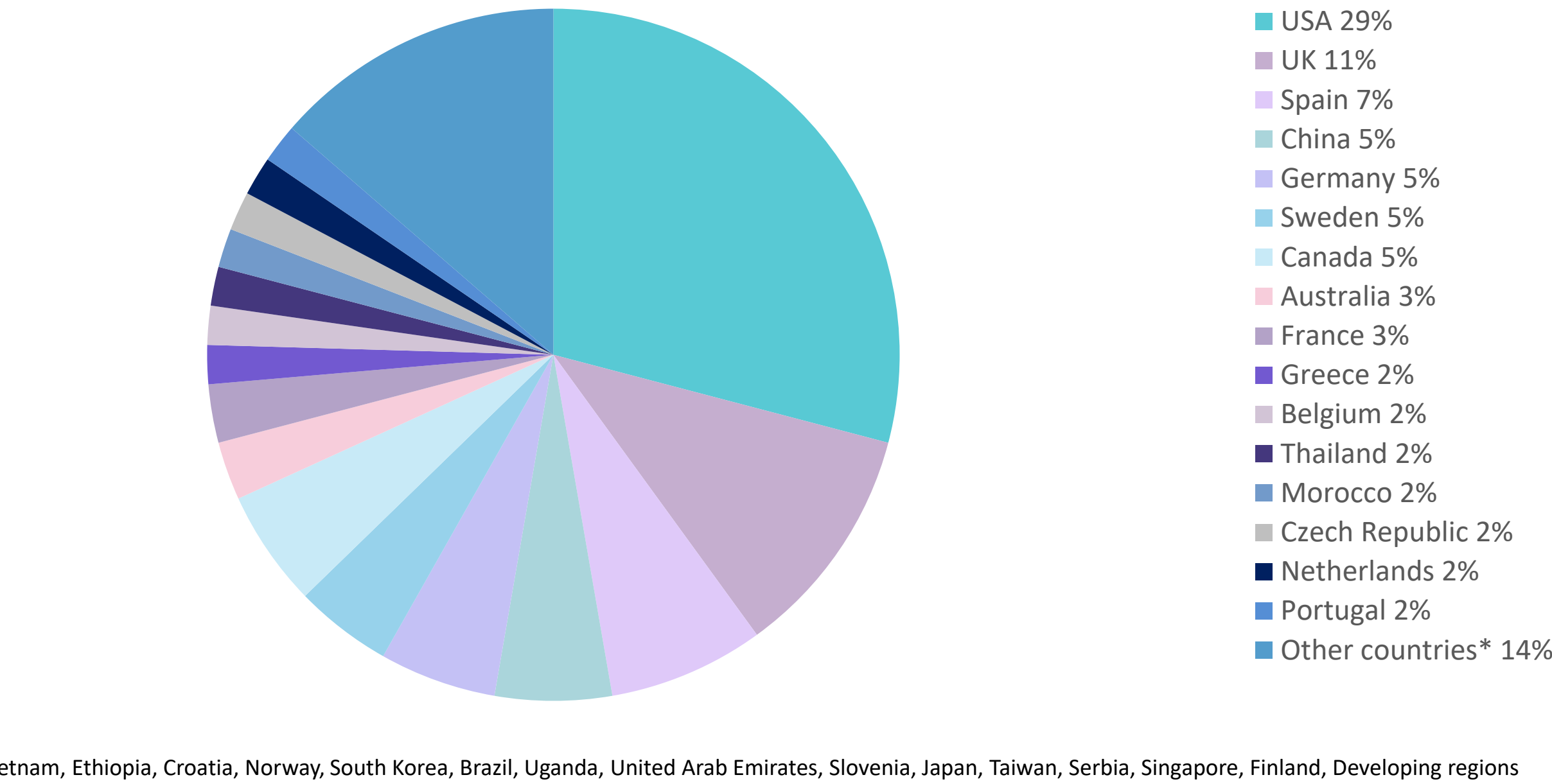
Figure 1. PRISMA flow diagram

Figure 2. Distribution of studies by region

USA 29%, UK 11%, Spain 7%, China 5%, Germany 5%, Sweden 5%, Canada 5%, Australia 3%, France 3%, Greece 2%, Belgium 2%, Thailand 2%, Morocco 2%, Czech Republic 2%, Netherlands 2%, Portugal 2%, Other countries* 14%

*Vietnam, Ethiopia, Croatia, Norway, South Korea, Brazil, Uganda, United Arab Emirates, Slovenia, Japan, Taiwan, Serbia, Singapore, Finland, Developing regions
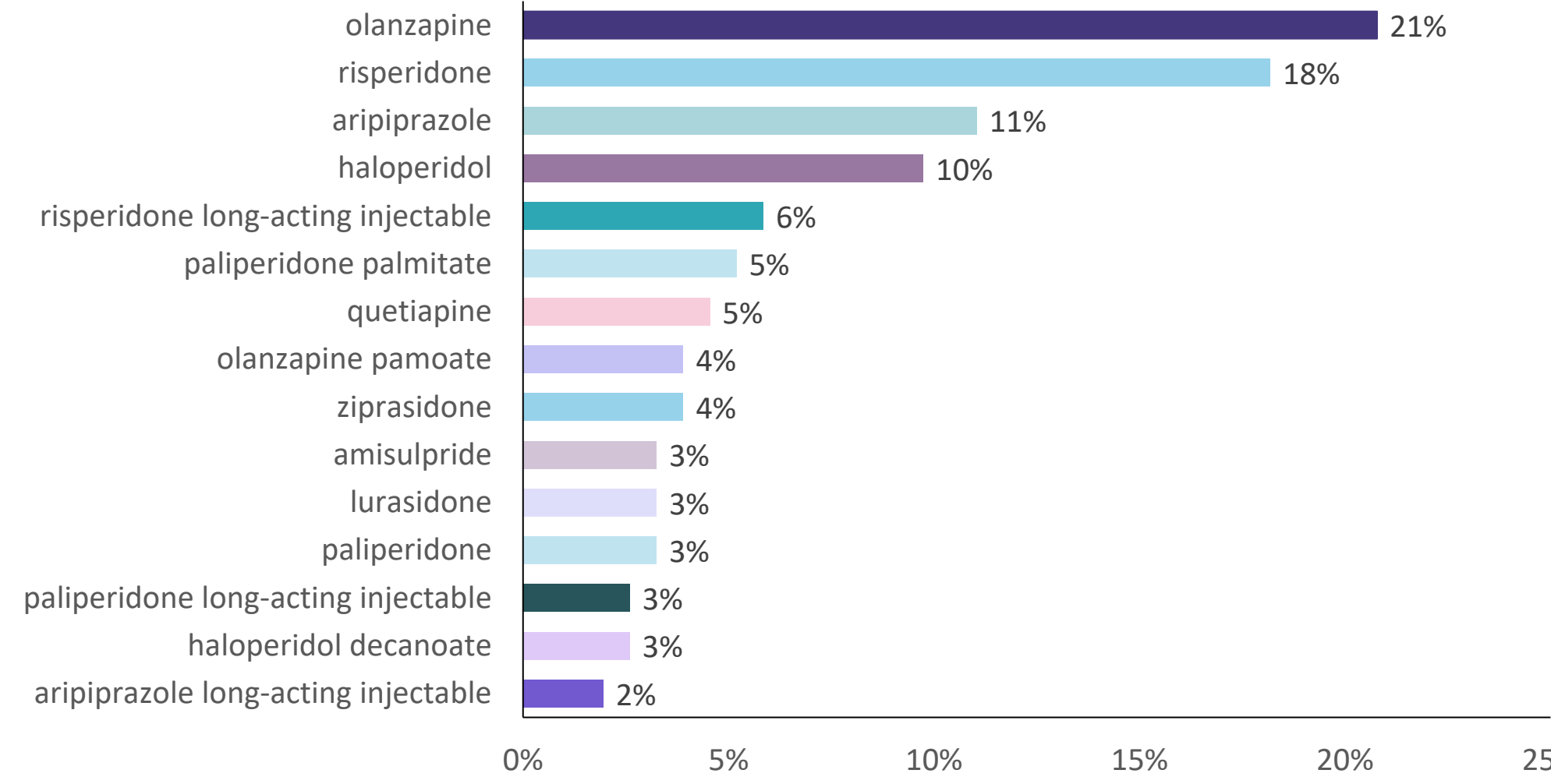
Figure 3. Studied treatments

Treatment	%
olanzapine	21%
risperidone	18%
aripiprazole	11%
haloperidol	10%
risperidone long-acting injectable	6%
paliperidone palmitate	5%
quetiapine	5%
olanzapine pamoate	4%
ziprasidone	4%
amisulpride	3%
lurasidone	3%
paliperidone	3%
paliperidone long-acting injectable	3%
haloperidol decanoate	3%
aripiprazole long-acting injectable	2%

Table 1. Summary of Study Characteristics

Characteristic group	Overall (N=110)	Antipsychotic (N=93)	Community and other interventions (N=17)
Time horizon			
< 1 Year	4	1	3
1-5 years	83	72	11
10-20 years	8	7	1
lifetime	7	7	0
Unreported	8	6	2
Perspective			
Healthcare/Payer	85	77	8
Societal	6	4	2
Both (healthcare/social)	7	3	4
Unreported	12	9	3
Type of economic evaluation			
CEA	92	78	14
CUA	12	11	1
CBA	1	0	1
CMA/Cost-comparison	3	2	1
Other	2	2	0
Outcome metrics			
QALY	59	57	2
DALY	5	4	1
LY	2	2	0
Other	44	31	13
Unreported	3	2	1

CEA, Cost-effectiveness analysis; CBA, Cost-benefit analysis; CMA, Cost-minimization analysis ; CUA, Cost-utility analysis; DALY, Disability-Adjusted Life Year; LY, Life Years; QALY, Quality-Adjusted Life Year.

Conclusions

Economic evaluations consistently highlight LAI antipsychotics and clozapine as cost-effective options, driven by relapse prevention and improved adherence. However, their ability to inform decision-making remains constrained by methodological heterogeneity, short time horizons, and restricted perspectives. The scarcity of real-world and societal data further limits comparability and policy relevance. Broader, standardized, and context-adapted approaches are needed to strengthen the validity and impact of future analyses.

References: 1. Lin, C., Zhang, X. & Jin, H. The Societal Cost of Schizophrenia: An Updated Systematic Review of Cost-of-Illness Studies. PharmacoEconomics 41, 139–153 (2023). 2. Wang J., Shi F, Guan X, et al. A Systematic Review of Methods and Study Quality of Economic Evaluations for the Treatment of Schizophrenia. Front Public Health. 2021 Oct 20;9:689115. 3. Knapp M. Cost-effectiveness in the treatment of schizophrenia. Eur J Psychiatry. 1996;11(3):137-41. doi: 10.1016/0924-9338(96)81479-0. 4. Pennington, M., McCrone, P. The Cost of Relapse in Schizophrenia. PharmacoEconomics 35, 921–936 (2017). 5. Sobieva A, Bhbai S, Arsai S, et al. Socioeconomic burden of schizophrenia: a targeted literature review of types of costs and associated drivers across 10 countries. [truncated bibliography]