The Pharmacologic Treatment of Schizophrenia: Status Report

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Disclosures

I have an interest in relation with one or more organizations that could be perceived as a possible conflict of interest in the context of this presentation. The relationships for the past 5 years are summarized:

Interest	Name of organization
Grants	Lundbeck, Otsuka, Janssen, Sunovion
Shares	HealthRhythms (private/stock options), LB Pharmaceuticals, Inc. (public), North Shore Therapeutics (private/stock), Vanguard Research Group (private); NW Pharmatech (private/stock options), Saladax (private/stock options), Reviva (stock options); Terran (private/stock options), Intracellular Therapies (public)
Paid positions, honoraria and advisory boards	AbbVie, Alkermes, Boehringer-Ingelheim, Bristol Meyer-Squibb, Cerevel, Click Therapeutics, Dainippon Sumitomo, H. Lundbeck, HealthRhythms, HLS Therapeutics, Intracellular Therapies, Janssen Pharmaceutical, Johnson & Johnson, LB Pharmaceuticals, Mapi, Maplight, Merck, Minerva, Neurocrine, Newron, Novartis, NW PharmaTech, Otsuka, Saladax, Sunovion, Teva, Terran, UpToDate

Learning Objectives

1. To bring the audience up to date on the data regarding a new class of medicines-the muscarinic agonists.

2. To review data on the underutilization of evidenced based treatments and discuss potential reasons for this problem.

Limitations of Current Treatments of Schizophrenia

>80% do not achieve full recovery

>35% are resistant to current treatment

>80% experience disruptive adverse effects

>50% have difficulty adhering to current medications

>50% experience clinically significant negative symptoms

>80% experience cognitive dysfunction

Rationale for Utilizing Cholinergic Treatment for Schizophrenia

Excessive presynaptic DA release leads to increased levels of DA in specific striatal regions

Blocking DA receptors is a post synaptic solution for a presynaptic problem affecting multiple uninvolved brain regions

Muscarinic receptor activation can modulate dopamine release in key brain regions, better addressing the core dysfunction

This dopamine modulation can be achieved without producing weight gain, extrapyramidal side effects, sedation or prolactin elevation

Potential cholinergic adverse effects require management

Pipeline of Muscarinic Antipsychotics

Xanomeline and trospium chloride was FDA approved in September 2024

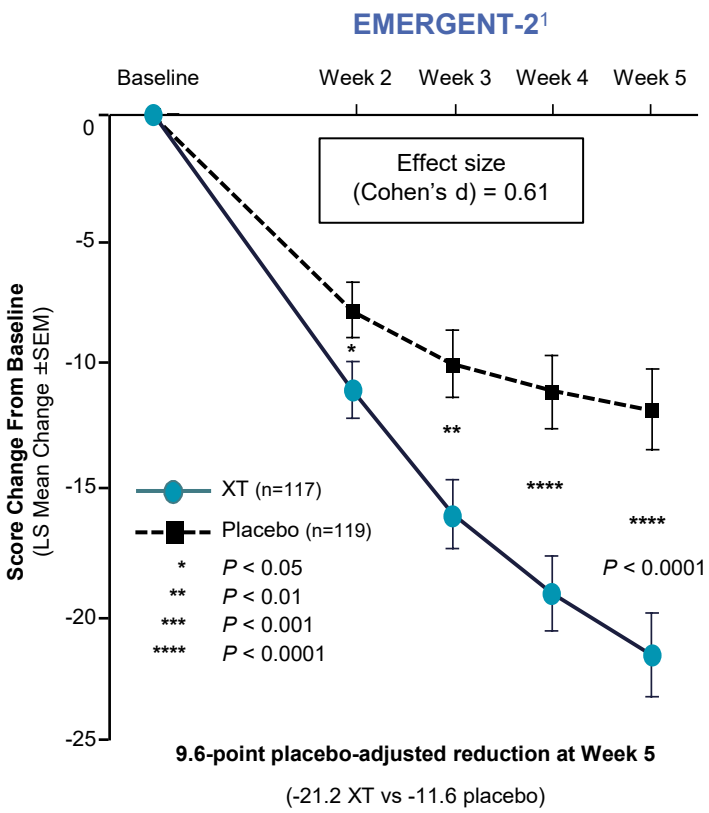
Emraclidine showed promise in phase 1b but failed in phase 2

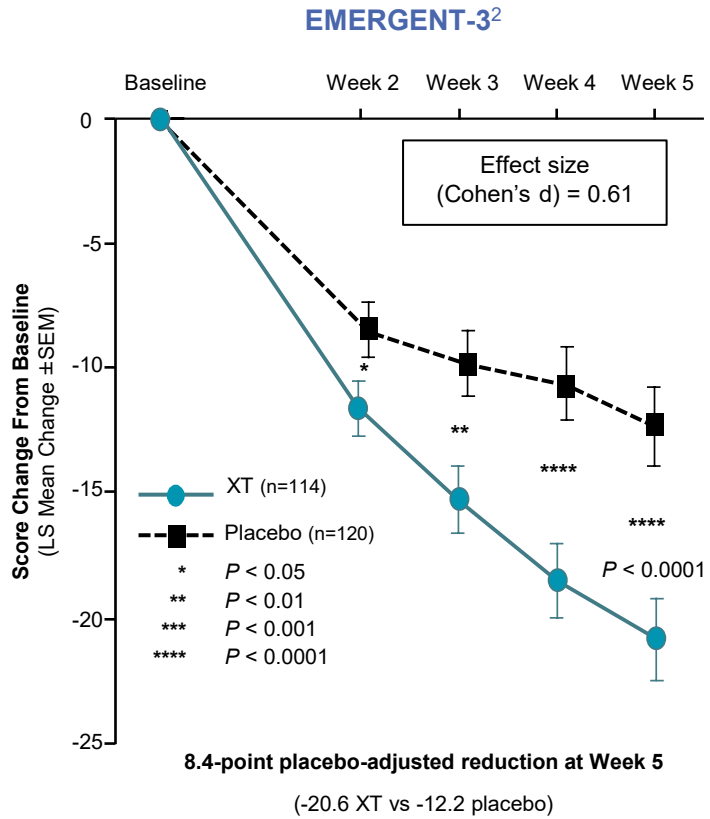
ML-007 is currently undergoing phase 2 clinical trials

NBI-1117568 is currently in phase 1

KAUL I, ET AL. LANCET. 2024;403(10422):160-170.

Main Result of EMERGENT Phase 3 Trials

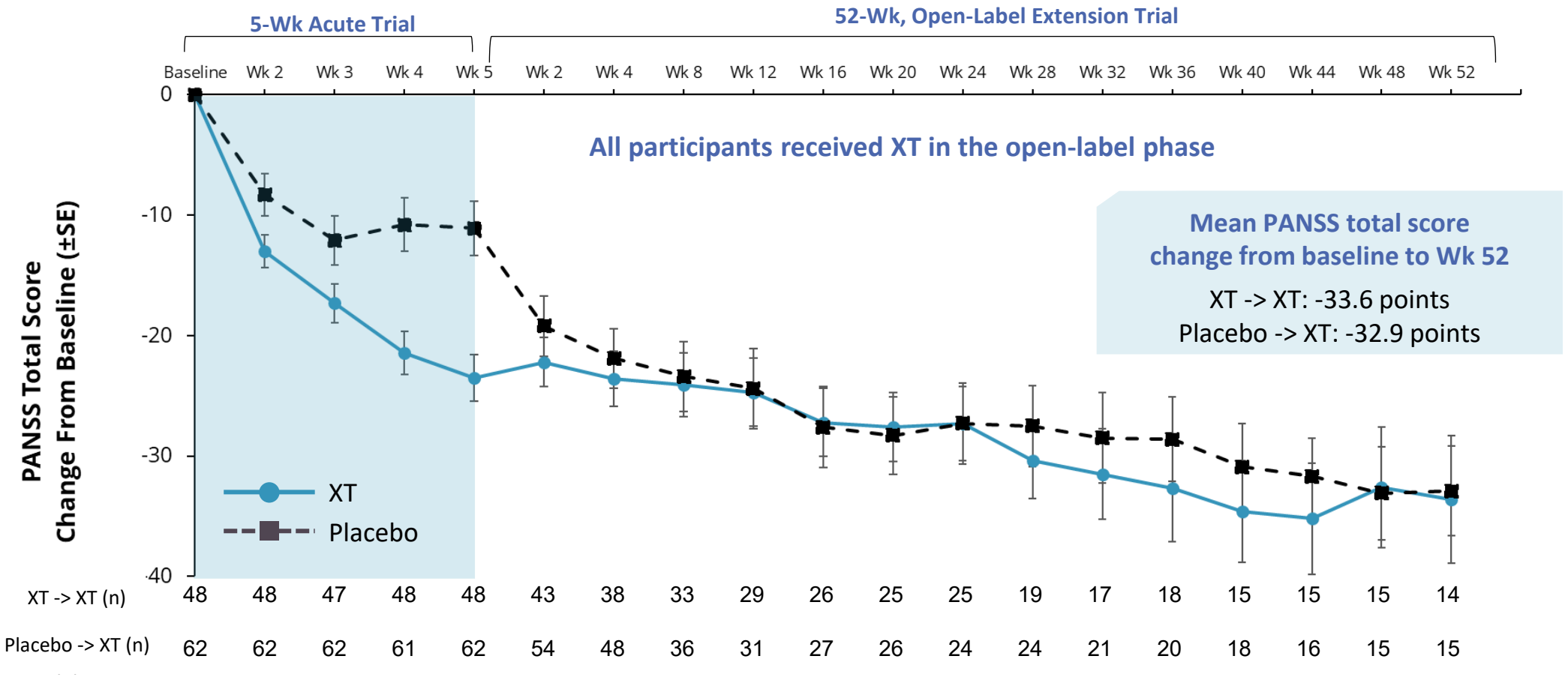




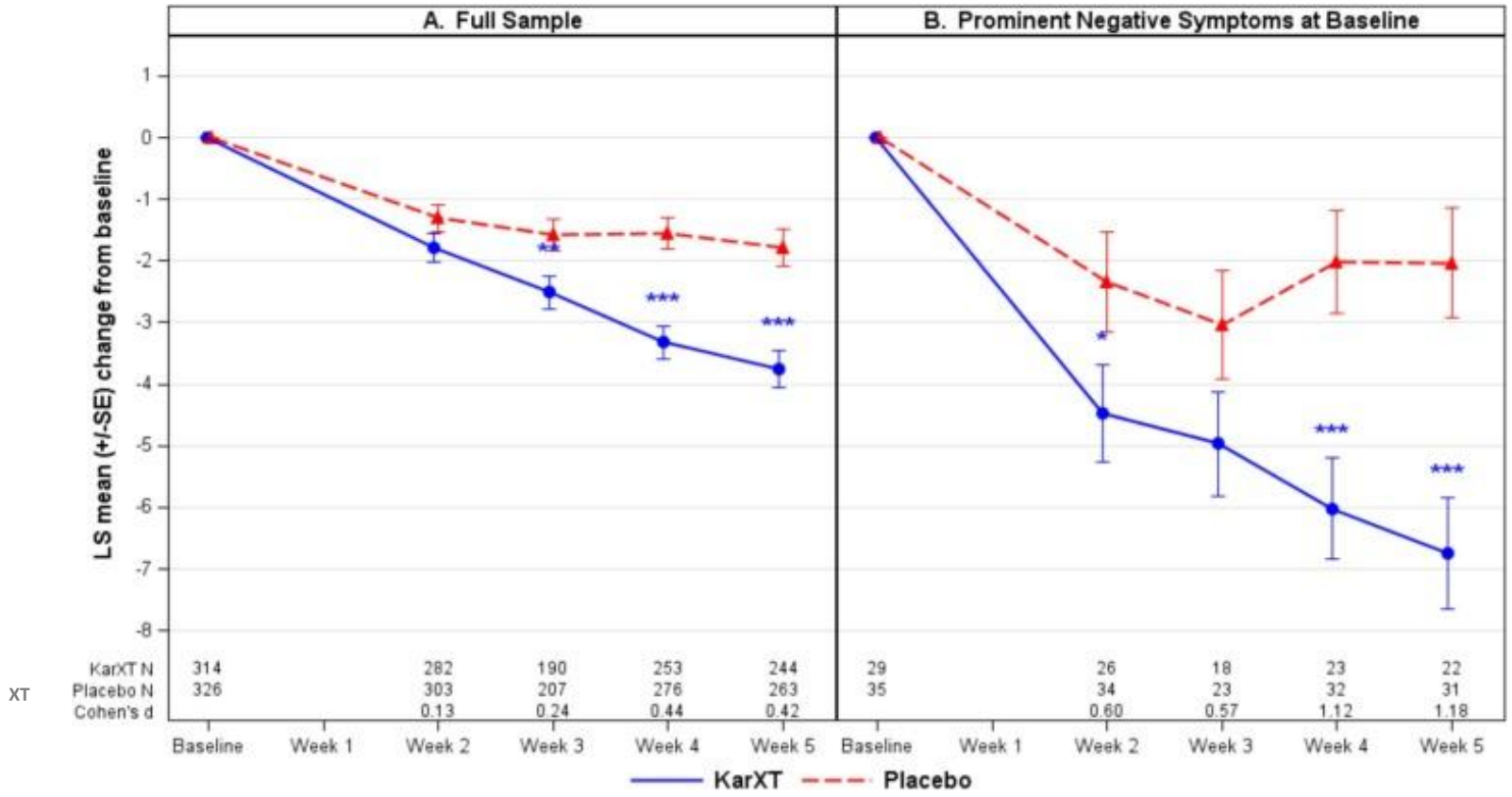
1. KAUL I, ET AL. LANCET. 2024;403(10422):160-170.
2. BRANNAN SK, ET AL. N ENGL J MED. 2021;384:717-726.

Long-Term Change in PANSS Total Score

EMERGENT-4: Subjects were rolled over from EMERGENT 1, 2 and 3, ***and*** retitrated during the first week



Main Result of EMERGENT Phase 3 Trials: Negative Symptoms



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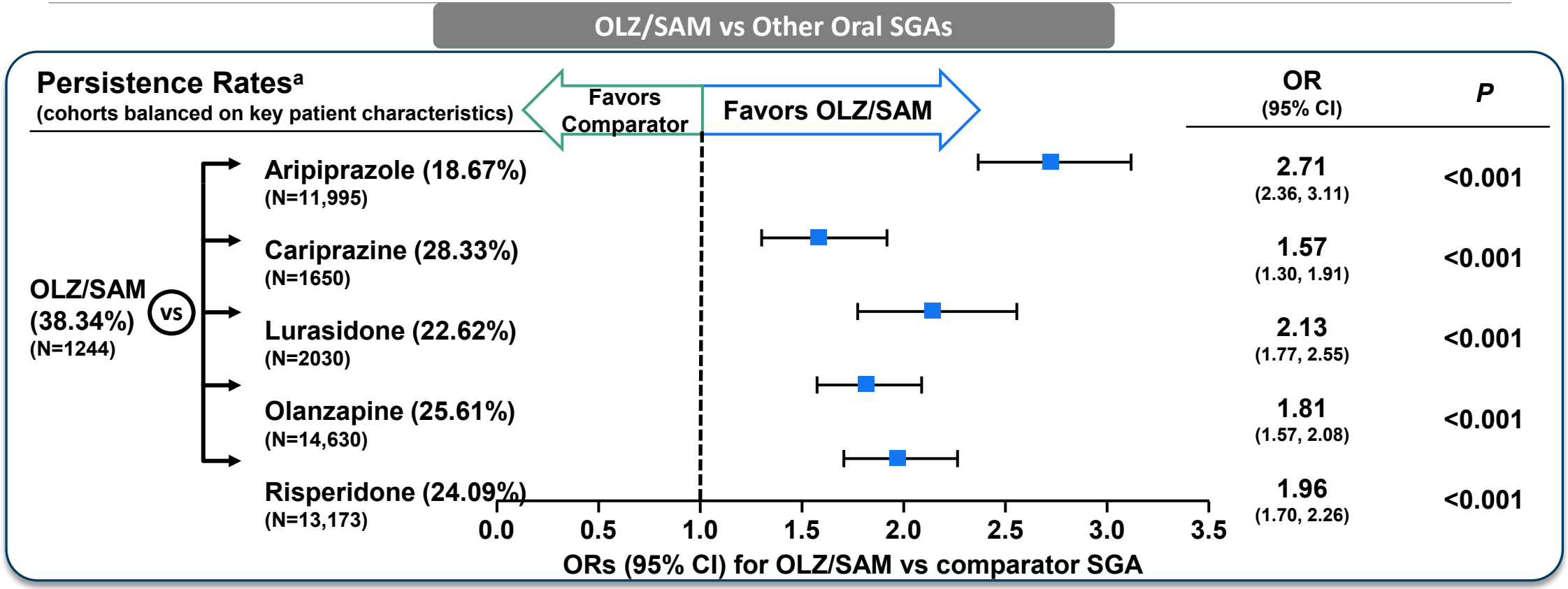
OLZ/SAM Resulted in Significantly Higher Persistence Compared to Other Oral SGAs in Patients With Schizophrenia



Persistence rate measured as proportion of patients who remain on index treatment for entire 12-month follow-up period.

[a]Given lower sample sizes for brexpiprazole (persistence rate, 28.98%; N=421) and lumateperone (persistence rate, 2.84%; N=423), data are descriptive only and not compared with OLZ/SAM. OLZ/SAM, combination olanzapine and samidorphan; OR, odds ratio; SGA, second-generation antipsychotic.

Antipsychotic Efficacy and Safety of LB-102 in the Treatment of Adults With Acute Schizophrenia: A Randomized Clinical Trial

Study Population:
- Total N=359 participants randomized (ITT & safety populations).
- Mean age 39.1 (SD 9.3) years; 80.8% male.
- Baseline PANSS total score ≈94 across groups.

Efficacy - Primary Endpoint (PANSS Total Score Change from Baseline at Week 4):
- Trial met primary endpoint: LB-102 50mg and 75mg significantly superior to placebo.

Mean (SE) change:
- Placebo: -9.3 (1.08)
- LB-102 50mg: -14.3 (1.10); P < .001; Hedges g = 0.61
- LB-102 75mg: -14.0 (1.11); P = .002; Hedges g = 0.41
- LB-102 100mg: -16.1 (1.91); Nominal P = .002; Hedges g = 0.83

Safety (Treatment-Emergent Adverse Events - TEAEs):
Overall TEAE incidence:
- Placebo: 56% (n=60)
- LB-102 50mg: 69% (n=74)
- LB-102 75mg: 57% (n=62)
- LB-102 100mg: 75% (n=27)

TEAEs leading to withdrawal: 10 participants (PBO: 2; 50mg: 2; 75mg: 3; 100mg: 3).
Serious TEAEs: 5 participants (PBO: 2 [incl. 1 death]; LB-102 arms: 1 each).

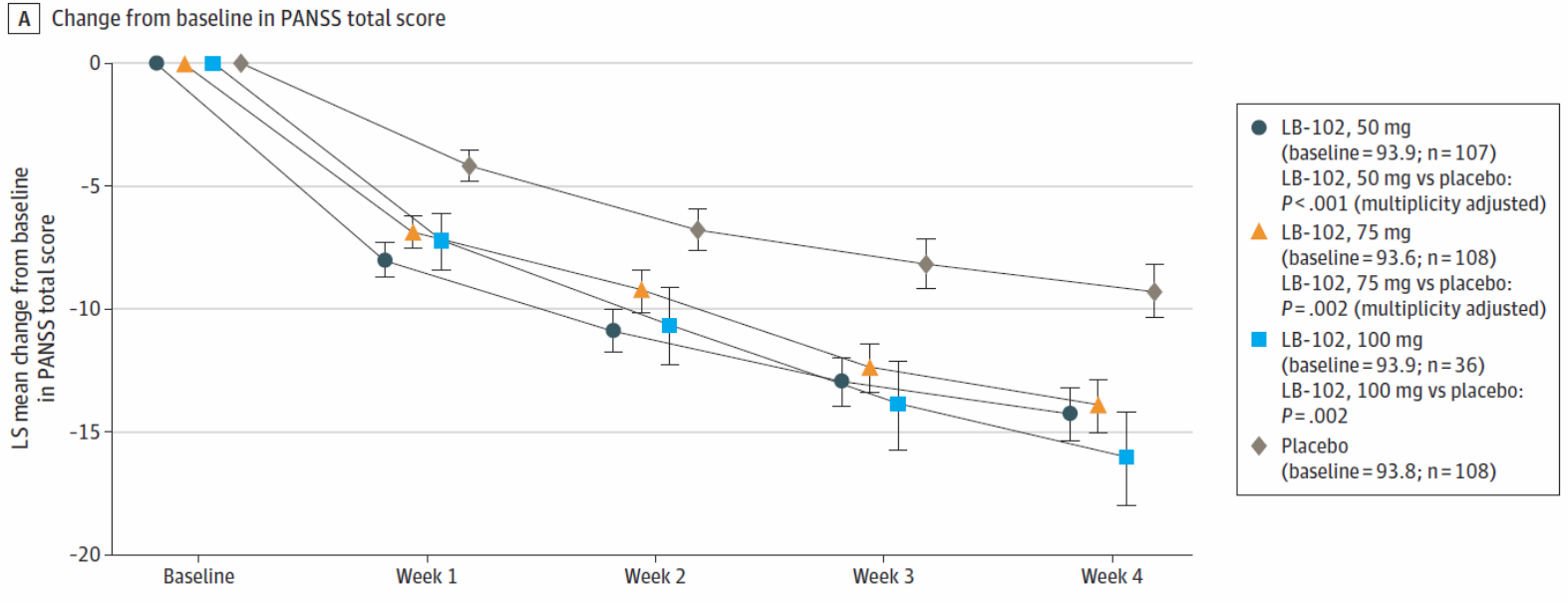
JAMA PSYCHIATRY. 2026 APR 22:E260428. DOI: 10.1001/JAMAPSYCHIATRY.2026.0428. ONLINE AHEAD OF PRINT.

Antipsychotic Efficacy and Safety of LB-102 in the Treatment of Adults With Acute Schizophrenia

A Randomized Clinical Trial

Anna Eramo, MD; Christoph U. Correll, MD; David P. Walling, PhD; Rishi Kakar, MD; Niccolo Bassani, PhD; Leslie Callahan, MS; Baker P. Lee, MBA; Zachary Prensky; Andrew R. Vaino, PhD; John M. Kane, MD

Figure 2. Line Graph and Bar Charts Depicting Efficacy Outcomes



Participants were randomized (3:3:3:1) to oral once-daily placebo, LB-102 50mg, 75mg, or 100mg.

Change from baseline over time in Positive and Negative Syndrome Scale (PANSS) total score; Results from the analysis of the primary end point for LB-102 50mg and 75mg were adjusted for multiplicity using a standard Hochberg procedure. Error bars show SE.

JAMA PSYCHIATRY. 2026 APR 22:E260428. DOI: 10.1001/JAMAPSYCHIATRY.2026.0428. ONLINE AHEAD OF PRINT.

Comparative effectiveness of antipsychotic treatment strategies for relapse prevention in first-episode schizophrenia in Finland: a population-based cohort study

Compared with continuing the same treatment strategy used before the first relapse, **switching to clozapine was associated with the lowest risk of second relapse compared with continuing any non-clozapine oral antipsychotic monotherapy** (aHR 0·66, 95% CI 0·49–0·89; relapse rate 73·2% with oral non-clozapine antipsychotic monotherapy continuation vs 57·1% with switch to clozapine). **Switching to another non-clozapine oral antipsychotic monotherapy** (0·99, 0·76–1·28) **was approximately as unhelpful in preventing the next relapse as switching to antipsychotic non-use** (1·07, 0·80–1·42).

Study Population: N=3000 individuals with first psychosis relapse (1996-2017).

- Mean age: 30.0 years (SD 7.6); 35.6% women.
- Ethnicity data unavailable.

Relapse Rate: 71.7% experienced a second relapse within 2 years.

Baseline Treatment (prior to 1st relapse):

- 45.5% were not using antipsychotics.
- 32.4% were on non-clozapine oral antipsychotic monotherapy.

Treatment Effectiveness Post-First Relapse:

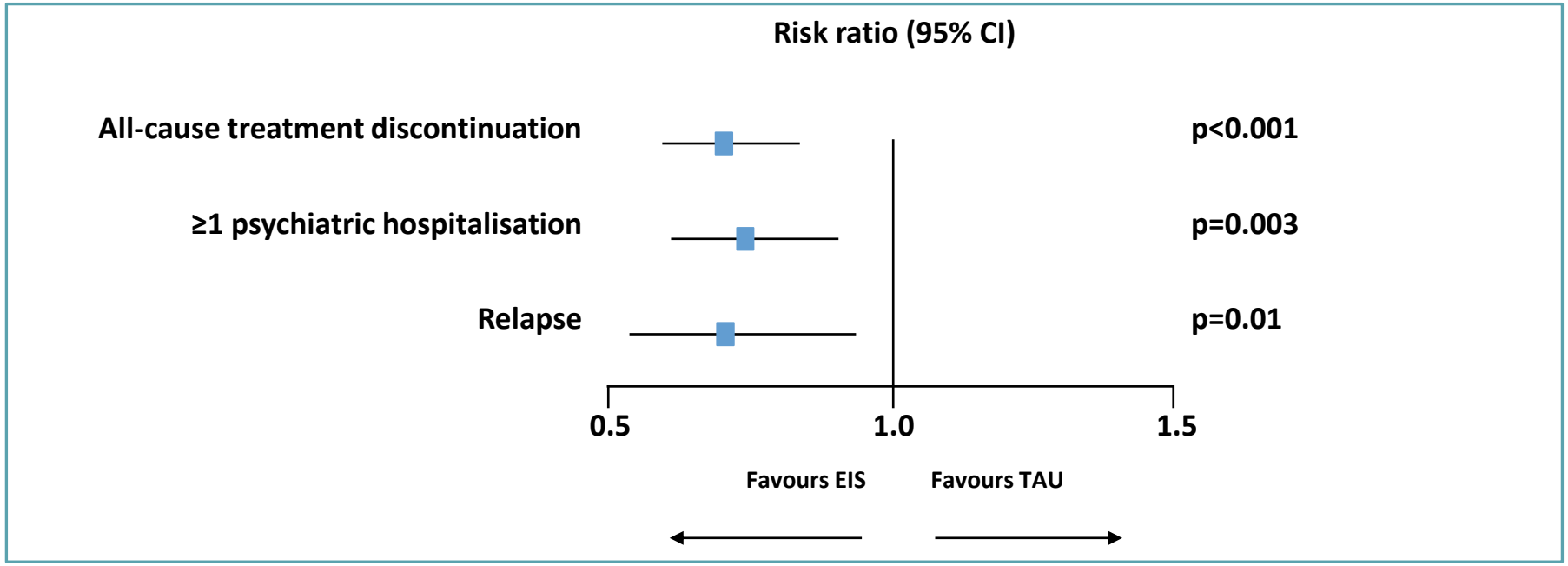
- **Switching to clozapine** significantly reduced second relapse risk:
  - aHR 0.66 (95% CI 0.49–0.89) compared to continuing non-clozapine oral monotherapy.
  - Relapse rate: 57.1% (clozapine switch) vs. 73.2% (non-clozapine oral monotherapy continuation).
- **Other treatment strategies showed no significant benefit** (compared to continuing prior treatment strategy):
  - Switching to another non-clozapine oral antipsychotic: aHR 0.99 (95% CI 0.76–1.28).
  - Switching to antipsychotic non-use: aHR 1.07 (95% CI 0.80–1.42).

TAIPALE, H. ET. AL. LANCET PSYCH 2026 12, 122-130

Comparative effectiveness of antipsychotic treatment strategies for relapse prevention in first-episode schizophrenia in Finland: a population-based cohort study

“In patients with first-episode schizophrenia having their first psychosis relapse despite use of non-clozapine oral antipsychotics, continuation with the same antipsychotic modality or switch to another non-clozapine oral antipsychotic did not show evidence of being beneficial in relapse prevention, suggesting that clozapine should be started instead. This finding, together with existing knowledge of decreased risk of mortality associated with clozapine, challenges current treatment guidelines that recommend clozapine as a third-line treatment, resulting in treatment practices characterised by long delays to clozapine initiation.”

Comparison of early-intervention services vs. treatment as usual for early-phase psychosis



The risk of ≥1 psychiatric hospitalisation in 10 studies among 2,105 patients was significantly lower with EIS than TAU (32.3% vs 42.4%; RR 0.74 [95% CI: 0.61, 0.90], p=0.003; NNT 10.1 [95% CI: 6.4, 23.9], p=0.001)

CI=confidence interval; EIS=early-intervention services; NNT=number-needed-to-treat; RR=relative risk; TAU=treatment as usual

Recovery in Remitted First-Episode Psychosis at 7 Years of Follow-up of an Early Dose Reduction/Discontinuation or Maintenance Treatment **Strategy** Long-term Follow-up of a 2-Year Randomized Clinical Trial

Results

The DR patients experienced twice the recovery rate of the MT patients (40.4% vs 17.6%). Logistic regression showed an odds ratio of 3.49 (*P* = .01). Better DR recovery rates were related to higher functional remission rates in the DR group but were not related to symptomatic remission rates.

Conclusions and Relevance

Dose reduction/discontinuation of antipsychotics during the early stages of remitted FEP shows superior long-term recovery rates compared with the rates achieved with MT. To our knowledge, this is the first study showing long-term gains of an early-course DR strategy in patients with remitted FEP. Additional studies are necessary before these results are incorporated into general practice.

The mean antipsychotic dose (daily dose in haloperidol-equivalent milligrams) in patients originally receiving DR (2.20 [2.27] mg) remained significantly lower during the last 2 years of follow-up compared with the dose in patients who were receiving MT (mean, 3.60 [4.01] mg; $t_{101} = -2.18$; $P = .03$).

DR, Dose Reduction
MT, Maintenance Treatment

WUNDERINK, L. ET. AL. JAMA PSYCHIATRY. 2013;70(9):913–920.

Antipsychotic dose reduction and discontinuation versus maintenance treatment in people with schizophrenia and other recurrent psychotic disorders in England (the RADAR trial): an open, parallel-group, randomised controlled trial

Summary of Key Findings

- This study examined **antipsychotic dose reduction versus maintenance dosing** in a randomized controlled trial.

Participants

- **253 randomly allocated** (from 4,157 screened)
- Demographics: 66% men, 32% women, 1% transgender
- Mean age: 46 years (SD 12, range 22–79)
- Ethnicity: 67% White, 21% Black, 6% Asian, 5% other

Dose Reduction Achieved

- **Reduction group**: Median dose reduction of **67%** at any point during the trial, **33%** at 24 months
- **Maintenance group**: Zero reduction at both timepoints

Primary Outcome (Social Functioning)

- At 24 months, **no significant difference** in Social Functioning Scale scores between groups (β 0.19, 95% CI –1.94 to 2.33; **p = 0.86**)
- Follow-up data obtained for 90/126 (reduction) and 94/127 (maintenance)

Safety Concerns

- **More serious adverse events in the reduction group**: 93 events (affecting 49 individuals) vs. 64 events (affecting 29 individuals) in the maintenance group
- The majority of serious adverse events were **admissions for mental health relapse**

Interpretation

- While dose reduction did **not improve social functioning**, it was associated with a **higher burden of serious adverse events**, predominantly psychiatric relapses. This suggests that substantial antipsychotic dose reduction, while not detrimental to social functioning on average, carries meaningful risks related to relapse that must be weighed carefully in clinical decision-making.

MONCRIEFF, J. ET. AL. LANCET PSYCHIATRY 2023;10: 848–59

Early Dose Reduction or Discontinuation vs Maintenance Antipsychotics After First Psychotic Episode Remission:
A Randomized Clinical Trial

A total of 347 patients (241 male [69.5%]; mean [SD] age, 27.9 [8.7] years) were included, with 168 randomized to early DRD and 179 to maintenance. **WHODAS-2 showed no time × condition interaction.** In the first year, DRD was associated with higher risk of relapse (odds ratio, 2.84; 95% CI, 1.08 to 7.66; *P* = .04) and lower quality of life (β = −3.31; 95% CI, −6.34 to −0.29; *P* = .03). At 3 years (β = 3.61; 95% CI, 0.28 to 6.95; *P* = .03) and 4 years (β = 6.13; 95% CI, 2.03 to 10.22; *P* = .003), a nonlinear effect of time occurred, showing significantly better GAF for patients in the DRD condition, with a similar trend for PANSS at 4 years (*P* for trend = .06).

Although SAEs and adverse effects were similar between groups, 3 confirmed deaths by suicide occurred in the DRD group, against 1 death by suicide in the maintenance group.

Table 1. Baseline Characteristics of Participants and Nonparticipants and of DR and MT Participants

Characteristic	No. (%)		Statistic	*P* Value	Strategy, No. (%)		Statistic	*P* Value
	Participants (n = 103)	Nonparticipants (n = 25)			DR (n = 52)	MT (n = 51)		
DUP, mean (SD) [median], d[a]	1.51 (1.10) [1.49]	1.39 (1.17) [1.49]	$t_{126} = -0.48$	.63	1.45 (1.13) [1.49]	1.56 (1.08) [1.78]	$t_{101} = -0.50$	.62
Age at onset of psychosis, mean (SD), y	25.83 (6.87)	24.93 (5.84)	$t_{126} = -0.60$	.55	26.26 (6.79)	25.39 (6.99)	$t_{101} = 0.64$	.52
Regular job for ≥16 h/wk[b]	45 (45)	12 (48)	Pearson $\chi^2 = 0.07$	.79	27 (54.0)	18 (36.0)	Pearson $\chi^2 = 3.27$	.07
Living alone	37 (35.9)	9 (36)	Pearson $\chi^2 = 0.00$	.99	19 (36.5)	18 (35.3)	Pearson $\chi^2 = 0.02$	.89
Dependence or abuse								
Alcohol	22 (21.4)	2 (8.0)	Pearson $\chi^2 = 2.36$	.12	13 (25.0)	9 (17.6)	Pearson $\chi^2 = 0.83$	.36
Cannabis	26 (25.2)	5 (20)	Pearson $\chi^2 = 0.30$	.58	14 (26.9)	12 (23.5)	Pearson $\chi^2 = 0.16$	.69
Any	37 (35.9)	8 (32.0)	Pearson $\chi^2 = 0.14$	.71	22 (42.3)	15 (29.4)	Pearson $\chi^2 = 1.86$	.17
Schizophrenia	45 (43.7)	13 (52.0)	Pearson $\chi^2 = 3.80$	.58	19 (36.5)	26 (51.0)	Pearson $\chi^2 = 7.05$	.22
Schizophreniform disorder	26 (25.2)	3 (12.0)			14 (26.9)	12 (23.5)		
Schizoaffective disorder	6 (5.8)	1 (4.0)			4 (7.7)	2 (3.9)		
Delusional disorder	12 (11.7)	5 (20.0)			8 (15.4)	4 (7.8)		
Brief psychotic disorder	3 (2.9)	0			0	3 (5.9)		
Psychotic disorder, NOS	11 (10.7)	3 (12.0)			7 (13.5)	4 (7.8)		
PANSS subscale mean (SD)								
Positive	10.28 (3.08)	10.44 (2.43)	$t_{126} = 0.24$	.81	9.79 (2.96)	10.78 (3.15)	$t_{101} = -1.66$	.10
Negative	13.50 (5.14)	14.12 (4.89)	$t_{126} = 0.62$	.53	12.87 (4,80)	13.96 (5.51)	$t_{101} = -1.08$	.28
General	25.85 (6.53)	26.24 (6.78)	$t_{126} = 0.29$	.77	25.27 (6.44)	26.45 (6.62)	$t_{101} = -0.92$	.36
Total score, mean (SD)								
GSDS	8.46 (4.19)	8.56 (4.64)	$t_{126} = 0.11$	.91	8.48 (4.10)	8.43 (4.33)	$t_{101} = 0.06$	.95
WHOQoL	91.48 (11.50)	93.08 (15.18)	$t_{125} = 0.58$	.56	90.42 (11.21)	92.55 (11.79)	$t_{101} = -0.94$	.35

Abbreviations: DR, dose reduction strategy; DUP, duration of untreated psychosis; GSDS, Groningen Social Disability Schedule; MT, maintenance treatment; NOS, not otherwise specified; PANSS, Positive and Negative Syndrome Scale; WHOQoL, World Health Organization Quality of Life scale.

[a] DUP days were log transformed because of the skewed distribution.

[b] Three cases missing in follow-up sample: 2 in the DR group and 1 in MT group.

Risk of relapse during tapering of antipsychotic medication after a first psychotic episode: association with D2 receptor affinity but not with tapering speed

Key Findings: Relapse Risk During Antipsychotic Tapering

- **45.8% of participants (N=104)** experienced relapse during follow-up after tapering
- **Tapering speed did not predict** relapse risk (logistic regression)
- **D2 receptor affinity** of the antipsychotic was a **more important predictor** of relapse than tapering speed
- Patients on **high D2 affinity antipsychotics** had approximately **2× higher relapse risk** compared to users of other antipsychotic types
- **Clinical implication:** Patients using strong D2 antagonists after first-episode psychosis remission require **enhanced monitoring** during tapering

Mortality in people with schizophrenia: a systematic review and meta-analysis of relative risk and aggravating or attenuating factors

Consistent and long-term use of SGAs, SGA LAIs and, if indicated, clozapine in patients with schizophrenia across all stages of illness can **reduce the mortality risk**, as antipsychotics are protective compared to non-use of antipsychotics against many kinds of mortality, including that due to cardio-cerebrovascular disease. This finding indicates that **even antipsychotics with elevated cardiometabolic adverse effects, such as clozapine, can reduce overall mortality**, which is not counterbalanced by larger but supported by reduced cardiometabolic-related mortality.

Data from this meta-analysis point to the responsibility of reducing mortality risk by screening for and optimizing the management of physical as well as psychiatric comorbidities, and by earlier use of LAIs and, if indicated, clozapine in individuals with schizophrenia. This information should be considered by treatment guidelines and incorporated into actionable policies by health care administrators.

CORRELL, C. U., ET AL. (2022). *WORLD PSYCHIATRY*, *21*(2), 248-271.

20-year follow-up study of physical morbidity and mortality in relationship to antipsychotic treatment in a nationwide cohort of 62,250 patients with schizophrenia (FIN20)

The most beneficial mortality outcome was associated with use of clozapine in terms of all-cause (aHR=0.39, 95% CI: 0.36-0.43), cardiovascular (aHR=0.55, 95% CI: 0.47-0.64) and suicide mortality (aHR=0.21, 95% CI: 0.15-0.29). The cumulative mortality rates during maximum follow-up of 20 years were 46.2% for no antipsychotic use, 25.7% for any antipsychotic use, and 15.6% for clozapine use.

These data suggest that long-term antipsychotic use does not increase severe physical morbidity leading to hospitalization, and is associated with substantially decreased mortality, especially among patients treated with clozapine.

TAIPALE, H. ET AL. WORLD PSYCHIATRY 2020 FEB;19(1):61-68.

Effectiveness of Antipsychotic Use for Reducing Risk of Work Disability: Results From a Within-Subject Analysis of a Swedish National Cohort of 21,551 Patients with First-Episode Nonaffective Psychosis

Objective: The authors sought to determine whether antipsychotic use, compared with nonuse, is associated with lower work disability in first-episode nonaffective psychosis, and if so, for how long.

Methods: A within-subject design was used to study the risk of sickness absence or disability pension during antipsychotic use compared with nonuse during a maximum of 11 years of follow-up (2006–2016) in a Swedish nationwide cohort of patients with first-episode nonaffective psychosis (N=21,551; age range, 16–45 years). The within-subject analyses were conducted with stratified Cox regression models, adjusted for time-varying factors, using each individual as her or his own control to eliminate selection bias. The primary outcome was work disability (sickness absence or disability pension).

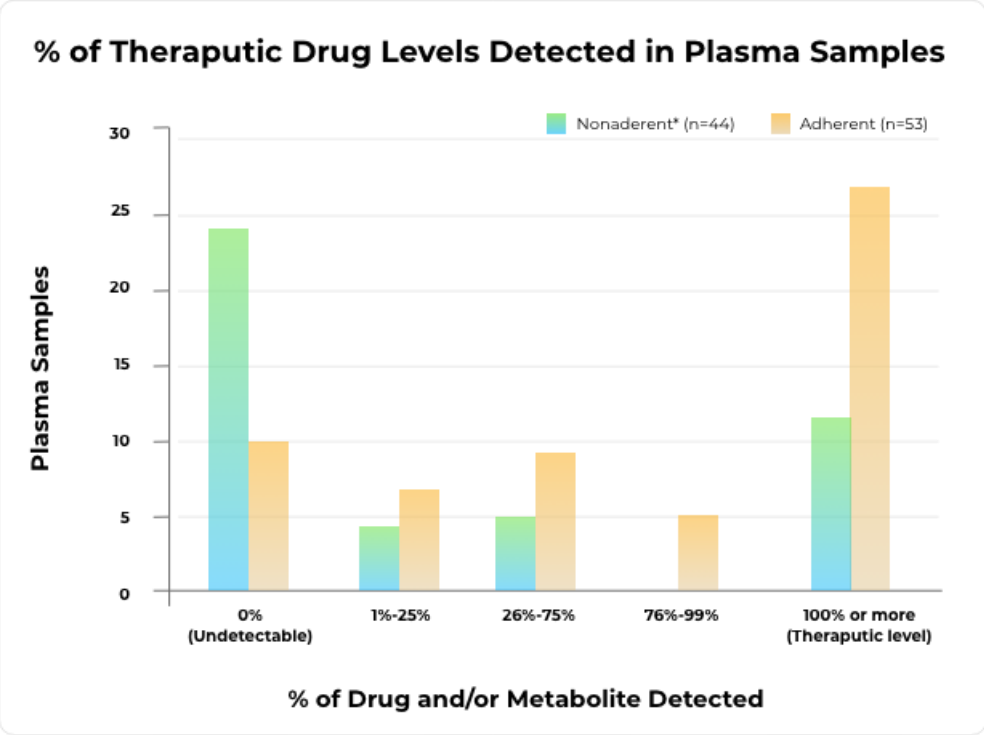
Results: Overall, 45.9% of first-episode patients had work disability during the median length of follow-up of 4.8 years. The risk of work disability was lower during use compared with nonuse of any antipsychotic (adjusted hazard ratio [aHR]=0.65, 95% CI=0.59–0.72). The lowest adjusted hazard ratios emerged for long-acting injectable antipsychotics (aHR=0.46, 95% CI=0.34–0.62), oral aripiprazole (aHR=0.68, 95% CI=0.56–0.82), and oral olanzapine (aHR=0.68, 95% CI=0.59–0.78). Long-acting injectables were associated with lower risk than olanzapine, the most commonly used oral antipsychotic (aHR=0.68, 95% CI=0.50–0.94). Adjusted hazard ratios were similar during the periods of <2 years, 2–5 years, and >5 years since diagnosis.

Conclusions: Among individuals with first-episode nonaffective psychosis, antipsychotic treatment (with long-acting injectables in particular) was associated with about 30%–50% lower risk of work disability compared with nonuse of antipsychotics in the same individuals, which held true beyond 5 years after first diagnosis. These findings are informative regarding the important topic of early discontinuation of antipsychotic treatment after a first episode of nonaffective psychosis, but they need replication.

Am J Psychiatry 2022; 179:938–946; doi: 10.1176/appi.ajp.21121189

This study on first-episode non-affective psychosis patients found that **antipsychotic treatment was associated with a significantly lower risk of work disability compared to nonuse**. Specifically, **long-acting injectable antipsychotics showed the greatest reduction (30-50%) in work disability**, with this beneficial effect sustained for over five years since diagnosis.

Indirect Measures of Adherence are Often Inaccurate



Study comparing clinician assessment of adherence and plasma levels in 97 patients presenting to ED. Adherence typically based on patient self-report or report of individuals involved in patient's care.*

Nearly 20% of patients (10 of 53) assessed as adherent had undetectable plasma levels (0%)

25% of patients (11 of 44) assessed as nonadherent had therapeutic levels (≥100%)

ED, emergency department.
*As assessed by ED psychiatrist.

Acta Psychiatr Scand 2018: 137: 39–46

DOI: 10.1111/acps.12825

ACTA PSYCHIATRICA SCANDINAVICA

Antipsychotic plasma levels in the assessment of poor treatment response in schizophrenia

McCutcheon R, Beck K, D'Ambrosio E, Donocik J, Gobjila C, Jauhar S, Kaar S, Pillinger T, Reis Marques T, Rogdaki M, Howes OD. Antipsychotic plasma levels in the assessment of poor treatment response in schizophrenia.

Objective: Treatment resistance is a challenge for the management of schizophrenia. It is not always clear whether inadequate response is secondary to medication ineffectiveness, as opposed to medication underexposure due to non-adherence or pharmacokinetic factors. We investigated the prevalence of subtherapeutic antipsychotic plasma levels in patients identified as treatment-resistant by their treating clinician.

Method: Between January 2012 and April 2017, antipsychotic plasma levels were measured in 99 individuals provisionally diagnosed with treatment-resistant schizophrenia by their treating clinicians, but not prescribed clozapine. Patients were followed up to determine whether they were subsequently admitted to hospital.

Results: Thirty-five per cent of plasma levels were subtherapeutic, and of these, 34% were undetectable. Black ethnicity ($P = 0.006$) and lower dose ($P < 0.001$) were significantly associated with subtherapeutic/undetectable plasma levels. Individuals with subtherapeutic/undetectable levels were significantly more likely to be admitted to hospital ($P = 0.02$).

Conclusion: A significant proportion of patients considered treatment-resistant have subtherapeutic antipsychotic plasma levels, and this is associated with subsequent admission. The presence of subtherapeutic plasma levels may suggest a need to address adherence or pharmacokinetic factors as opposed to commencing clozapine treatment. While antipsychotic levels are not recommended for the routine adjustment of dosing, they may assist with the assessment of potential treatment resistance in schizophrenia.

R. McCutcheon[1,2,3,4], K. Beck[1,2,3], E. D'Ambrosio[1,4], J. Donocik[1,2,3,4], C. Gobjila[1,4], S. Jauhar[1,2,3,4], S. Kaar[1,2,3,4], T. Pillinger[1,2,3,4], T. Reis Marques[1,2,3,4], M. Rogdaki[1,2,3,4], O. D. Howes[1,2,3,4]

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Key words: adherence; compliance; therapeutic drug monitoring; treatment-resistant; psychosis

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Accepted for publication September 28, 2017

Long-acting injectable versus oral antipsychotics for the maintenance treatment of schizophrenia: a systematic review and comparative meta-analysis of randomised, cohort, and pre–post studies

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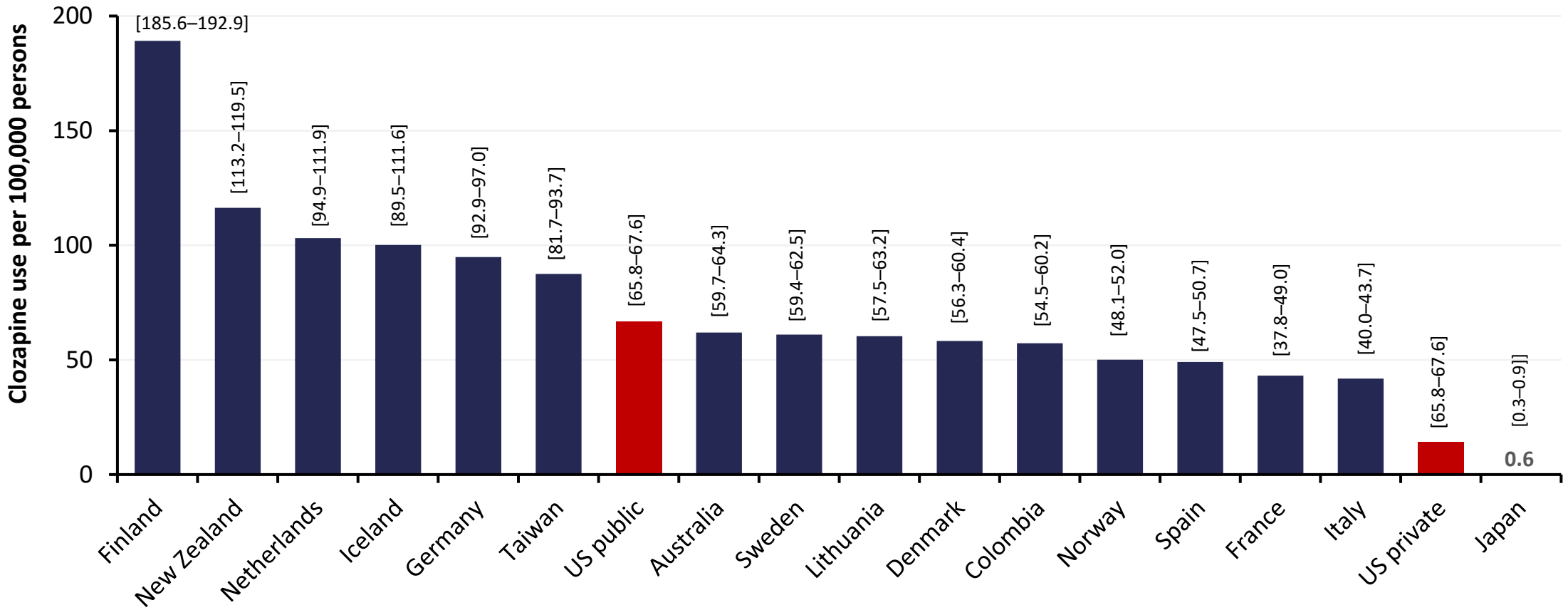
LAIs were associated with a lower risk of hospitalization or relapse than oral antipsychotics in each of the three study designs *(RCTs: 29 studies, 7833 patients, RR 0·88 [95% CI 0·79–0·99], p=0·033; cohort studies: 44 studies, 106136 patients, RR 0·92 [0·88–0·98], p=0·0044; pre–post studies: 28 studies, 17876 patients, RR 0·44 [0·39–0·51], p<0·0001). This association was maintained across the study designs when we reversed the preferential order to risk of relapse over hospitalization, and in individual analysis of hospitalization risk.*

Interpretation

Although study designs have strengths and weaknesses, including potential low quality of observational studies, we consistently identified significant benefit with LAIs versus oral antipsychotics in preventing hospitalisation or relapse, in settings ranging from restricted research (RCTs) to real-word application (cohort and pre–post studies). **Our findings suggest that increased clinical use of LAIs could improve outcomes in schizophrenia.**

LANCET PSYCHIATRY 2021 8:387–404

The US Lags Behind in Clozapine Use



Implementation Science: Data From EPINET

Hub number	Number with medication data at any point	Number (%) taking clozapine at any point	Number (%) taking a LAI at any point
1	714	62 (8.7%)	157 (22%)
2	960	28 (2.9%)	191 (19.9%)
3	152	3 (2%)	12 (7.9%)
4	346	31 (9%)	66 (19.1%)
5	577	10 (1.7%)	128 (22.2%)
6	942	43 (4.6%)	353 (37.5%)
7	381	34 (8.9%)	19 (5%)
8	1252	86 (6.9%)	335 (26.8%)

KANE, J.M., ET. AL., UNDER REVIEW