

Johnson & Johnson



CHALLENGES IN ACHIEVING FUNCTIONAL RECOVERY AMONG SCHIZOPHRENIC PATIENTS IN THE APAC REGION

The critical role of long-acting injectable antipsychotics and community support

January 2025

Supported by:  vista health

CONTENTS PAGE

1.	INTRODUCTION	3
2.	LAIS USE RESULTS IN FAVOURABLE PATIENT OUTCOMES, ULTIMATELY LEADING TO FUNCTIONAL RECOVERY	7
3.	INSUFFICIENT LAI RECOMMENDATION IN GUIDELINES AND SUBOPTIMAL USE OF LAIS IMPEDE THE ACHIEVEMENT OF FUNCTION RECOVERY	9
4.	STIGMA AND DISCRIMINATION HINDER PATIENT ACCESS TO CARE	11
5.	CALL TO ACTION	13
6.	REFERENCES	14

1. INTRODUCTION

1.1. Schizophrenia in the Asia-Pacific region

Schizophrenia is a serious mental health condition affecting patients, caregivers and societies at large¹. Globally, the prevalence of schizophrenia has increased gradually by 7% between 2016 and 2021, affecting over 23 million individuals in 2021. Within the Southeast Asia region, it impacts 2.2 million individuals, resulting in a Disability-Adjusted Life Year (DALY) loss of 1.4 million years (*Figure 1*)^{2,3}.

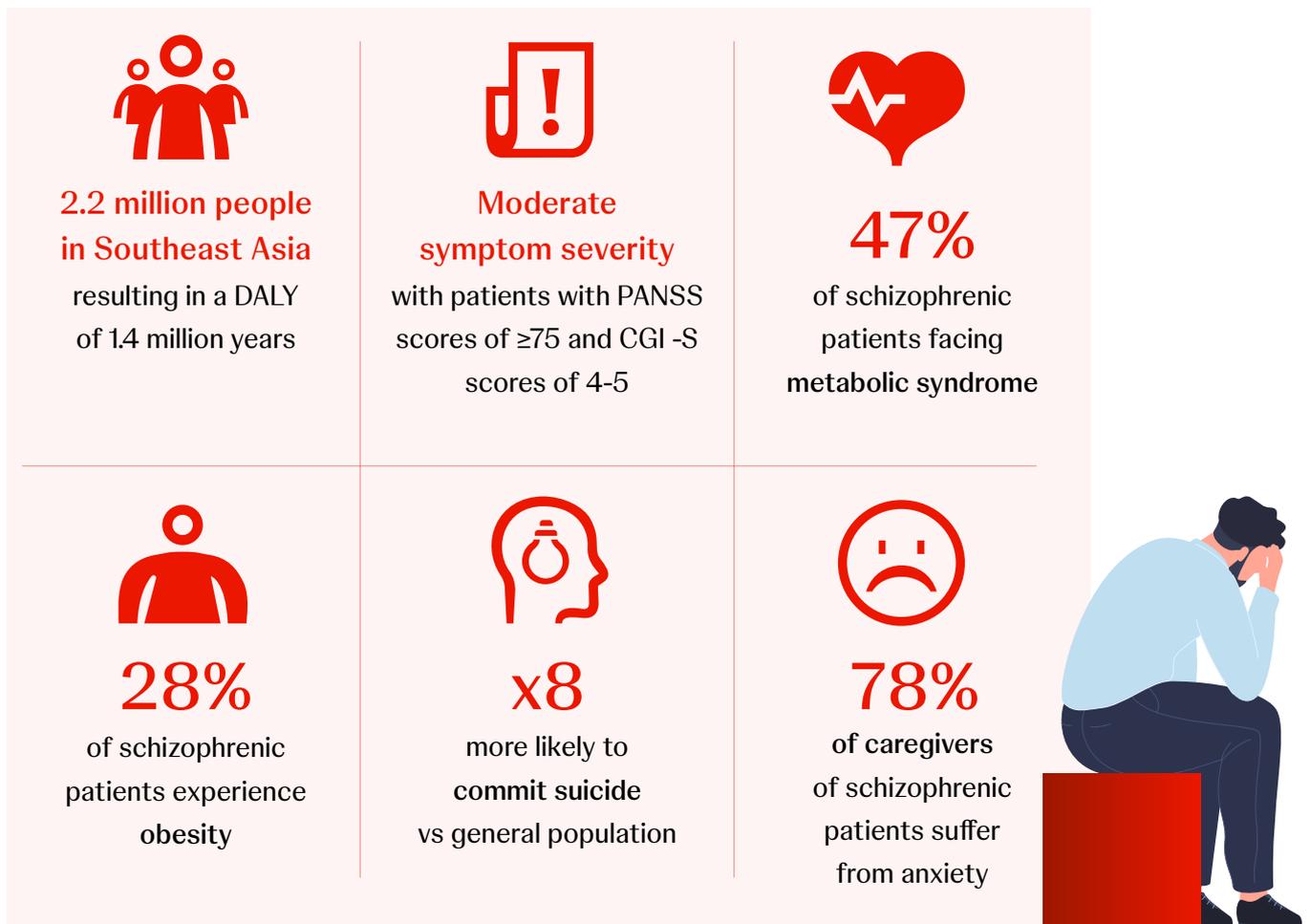


Figure 1 - Burden faced by schizophrenic patients in the APAC region

Patients with schizophrenia and their caregivers face a significant disease burden. While individuals with schizophrenia experience moderate symptom severity, as measured by a Positive and Negative Syndrome Scale (PANSS) score of ≥ 75 and a Clinical Global Impression-Severity (CGI-S) score of 4-5, 47% of patients face metabolic syndrome and 28% are obese⁴.

The economic burden of schizophrenia includes both direct and indirect economic costs, with direct costs also including medical and non-medical costs (*Figure 2*)⁵⁻⁷. In Japan, outpatient care for schizophrenia can cost up to USD 9,000 annually⁵. In Malaysia, schizophrenia accounts for 0.04% of the national gross domestic product (GDP), resulting in a government expenditure of USD 100 million in direct medical, non-medical, and indirect costs⁸. However, the true extent of this burden may be under reported due to the limited number of studies focusing on non-medical costs.

Schizophrenia imposes significant economic burden on patients

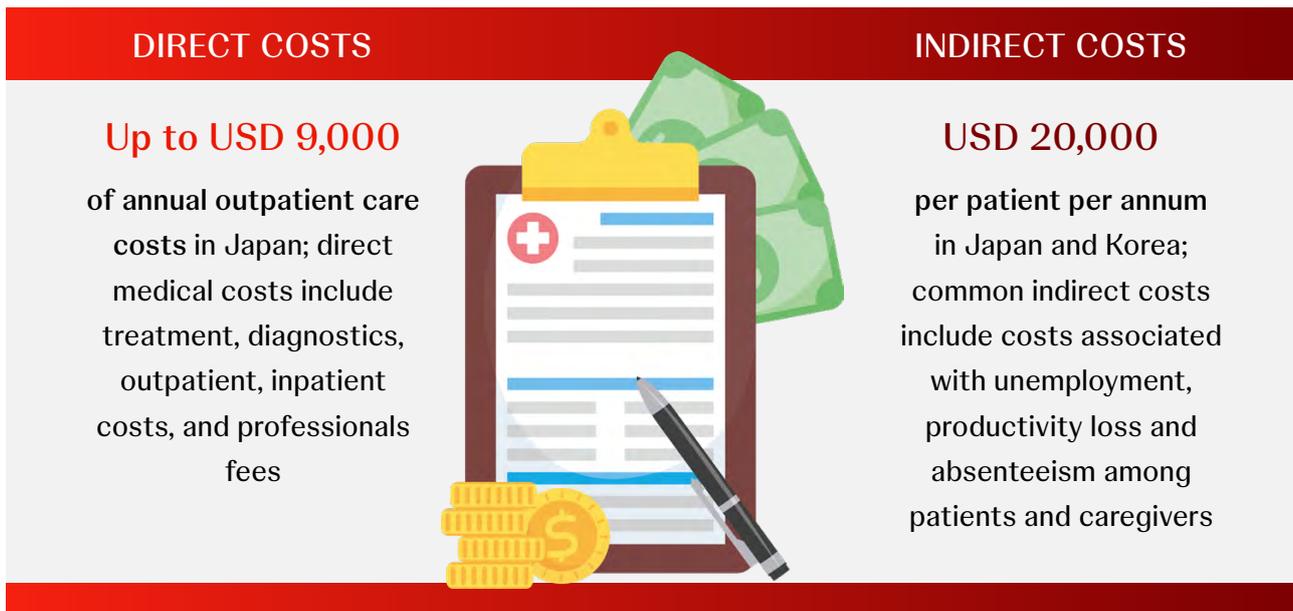


Figure 2 - Economic burden of schizophrenia

Schizophrenia also poses substantial consequences on the mental health and behaviour of patients and their caregivers. Schizophrenic patients are 8 times more likely to commit suicide and nearly half (~50%) experience agitation^{9,10}.

Caregivers also bear a heavy burden; many have to alter their employment, often taking monthly leaves or switching to part-time employment to fulfil caregiving responsibilities. Furthermore, around 78% of caregivers reportedly suffer from anxiety¹¹.

Without proper care management, schizophrenic patients display elevated rates of criminal behaviour, placing a significant burden on society. For instance, patients in South Korea are found to be twice as likely to engage in drug-related crimes, five times more likely to commit murder and six times more likely to commit arson compared to the general population (*Figure 3*)¹². Similarly, in Thailand, approximately 7.7% of schizophrenic patients exhibit violent or aggressive behaviour¹³, while in rural China, the rate of criminal activity among schizophrenic patients is reported at 10%¹⁴. These societal issues are closely associated with high levels of illness symptoms¹⁴, highlighting the critical need for effective symptom control.

Schizophrenic patients may engage in elevated rates of criminal behaviours



Figure 3 - Burden of schizophrenia on society

Despite the substantial burden on patients, caregivers, and society, support for individuals with schizophrenia remains inadequate, underscoring the importance of expanding resources and improving treatment options.

1.2. Comprehensive schizophrenia treatment combines antipsychotics and psychosocial interventions to achieve functional recovery

The goal of schizophrenia treatment is to achieve symptomatic remission and improve overall quality of life, ultimately leading to functional recovery^{15,16}. Functional recovery is the ability of a person with stabilised symptoms to live independently and without relapse for an extended period, while actively engaging in work, social activities and independent living^{15,16}.

Functional recovery is critical because it represents not only the absence of symptoms but also the restoration of a person's ability to lead a productive, independent, and fulfilling life as part of society.

Schizophrenia treatment typically involves a combination of pharmacological therapy, psychosocial interventions and supportive care¹⁵. Pharmacological therapy involves the use of antipsychotic medication, with second-generation (atypical) antipsychotics (SGAs) being more commonly prescribed as first-line treatment compared to first-generation (typical) antipsychotics (FGAs)^{15,17}. Second-generation and first-generation antipsychotics are available in both oral and long-acting injectable (LAI) formulations. Antipsychotic treatments, both oral and LAI formulations, reduce symptom severity¹⁸⁻³⁸ and improve the personal and social performances of schizophrenic patients^{22,27-29,39}. The oral formulations of antipsychotic treatments are commonly considered the initial treatment option⁴⁰⁻⁴⁵.

Psychosocial interventions, including cognitive-behavioural therapy, family therapy, and social skills training, are essential in improving communication, reducing relapse, and enhancing daily functioning¹⁵. Additionally, supportive care services, such as rehabilitation programmes, employment assistance, and community support groups, are important to reduce stigma and discrimination among patients, reintegrate schizophrenic patients into society and improve their quality of life significantly¹⁵.



2. LAIS USE RESULTS IN FAVOURABLE PATIENT OUTCOMES, ULTIMATELY LEADING TO FUNCTIONAL RECOVERY

Poor adherence to treatment is a significant challenge among individuals with schizophrenia, often resulting in relapses and hospital readmissions^{46,47}. This hinders patients' progress towards achieving symptomatic remission and functional recovery. Studies indicate that lack of treatment adherence is associated with an over 7-fold increase in the risk of hospitalisation for schizophrenic patients⁴⁸.

2.1. Long-acting injectable (LAI) formulations of antipsychotics enhance treatment adherence and patient functional recovery, resulting in alleviated economic burden on patients and society

LAI offer a promising alternative to daily oral medications for schizophrenia, requiring less frequent administration – typically every 2 to 4 weeks, and more recently every 3 or 6 months (*Figure 4 in page 8*). This reduced dosing frequency enhances medication adherence^{24,25,30,31,34} and improve patient outcomes⁴⁹.

Research suggests that switching from oral antipsychotics to LAIs can lead to higher rates of remission and low relapse rates^{19,34,37}, with many patients reporting improvements in symptom severity^{26,33,37,50,51}. Additionally, LAIs have been linked to greater patient satisfaction regarding medication^{26,37,51}. Reduced relapse rates and better symptom management through LAIs also help lessen the burden on caregivers and the healthcare system, allowing for more sustainable care delivery.

Furthermore, studies indicate that LAI treatment contributes to significant improvements in patients' psychosocial functioning^{25,26,37,50,52}, including a reduction in disturbing and aggressive behaviours of approximately 40%⁵⁰, increased employment rates³⁷, and improved quality of life measures, which encompasses subjective well-being, cognitive function, and social functioning^{53,54}. With fewer episodes of disruptive behaviours, public safety is improved, and individuals with schizophrenia can be reintegrated more effectively into the workforce and community. The accelerated functional recovery associated with LAIs may also reduce productivity losses to the economy, estimated at around USD 20,000 per patient per annum in developed countries like Japan and Korea^{5,55}.



The improvement in symptoms among schizophrenic patients receiving LAIs has led to reduced hospitalisation days – up to 6-fold in some studies^{37,51,56–59} – and reduced hospital admissions and emergency room visits^{56–59}. The reduction in hospitalisation, emergency interventions, and long-term care needs contributes to more efficient healthcare resource allocation, lowering the overall cost burden to healthcare systems and allowing reallocation of resources.

Cost-effectiveness studies conducted in the Philippines, Hong Kong, and Japan highlight the financial advantages of increased LAI use^{59–61}. For instance, Kasahara-Kiritani et al. (2020)⁶⁰ estimated that the budgetary impact of providing an additional 10% of patients with LAI each year will create net savings of JPY 36.5 billion over 5 years. This was mainly due to a reduction in hospitalisation costs.

Key benefits of LAIs

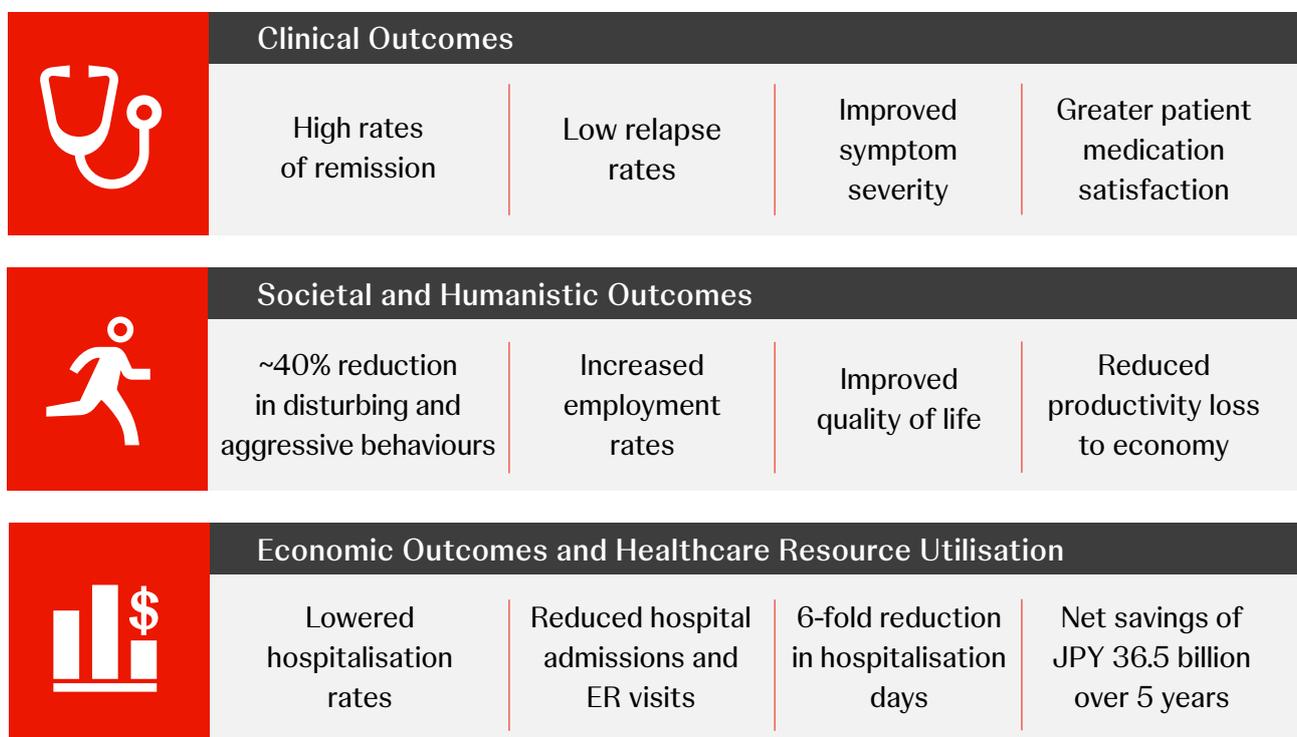


Figure 4 - Benefits of LAI treatment

2.2. Longer formulations of LAIs amplify improvements in patient outcomes

The advantages of LAIs are further enhanced in formulations with longer dosing intervals. Studies indicate that switching from monthly LAIs to those administered every three months can yield greater improvements in symptom severity^{62,63} and remission rates¹⁹, along with additional reductions in hospital admissions and emergency room visits¹⁹. These longer-acting formulations have also been shown to result in significant improvements in psychosocial functioning^{19,62}.

A study in China revealed that longer-acting injection formulations are more cost-effective compared to their shorter-acting counterparts, underscoring the potential for both clinical and economic benefits in managing schizophrenia with longer-acting options⁶⁴.

3. INSUFFICIENT LAI RECOMMENDATION IN GUIDELINES AND SUBOPTIMAL USE OF LAIS IMPEDE THE ACHIEVEMENT OF FUNCTIONAL RECOVERY

Limited access to LAIs for all schizophrenic patients, along with patients' reluctance to accept LAI treatment, impede progress towards achieving symptomatic remission and functional recovery.

3.1. Guidelines in the region typically recommend the use of depot antipsychotics or LAI for non-adherent patients, rather than as a standard option for all individuals with schizophrenia

Clinical guidelines in Southeast Asia, and the Asian region at large, have not yet been updated to recommend LAI as an early treatment option for all patients, including those with first-episode schizophrenia. Currently, the use of LAIs is often restricted to the maintenance phase and is typically reserved as a second- or third-line treatment for non-adherent patients with acute schizophrenia^{65–67} or those unresponsive to oral antipsychotics^{40–45}. This is despite existing evidence indicating that early use of LAIs can reduce hospital stays, lower emergency room visits, and generate cost savings⁵⁹. As a result, oral antipsychotics continue to be widely prescribed, with a high prescription rate of approximately 72%^{68,69}.

However, an exception is the 2021 consensus statement by the Taiwanese Society of Biological Psychiatry and Neuropsychopharmacology (TSBPN)⁴⁴, which recommended that LAIs be offered as a treatment option for all patients, including those with first-episode schizophrenia, and can be initiated both during an acute episode and after stabilisation.

3.2. LAI usage among patients lags due to stigma, fear, and high costs of injections



Based on a study conducted among psychiatrists in 2019, only 9% of patients were prescribed LAI in Japan and China, compared to 47% in France and Spain and 22% in the US, reflecting a notable gap in the adoption of LAIs in the region⁷⁰. Common barriers to LAI use reportedly include fear/dislike of injections, high costs associated with injections and social stigma faced by patients^{69,70}.

Fear of injections is a common factor limiting LAI adoption. In a cross-sectional study conducted in Beijing in 2021, LAI prescriptions accounted for only 2.4%, with over 68% of patients unwilling to accept LAI treatment⁴⁹. Concerns about pain, discomfort, and potential complications associated with injections contribute to patients' hesitation, which may be substantial, especially among patients with limited exposure to or knowledge about injectable treatments.

Financial constraints also limit the uptake of LAIs. The cost of injectable antipsychotics is often higher than that of oral medications, making them less accessible for many patients. For instance, a study conducted in China in 2022, LAI medication costed twice that of oral treatment⁵⁷.

Besides financial barriers and fear of injections, schizophrenic patients also face stigma in some regions, where injectable treatments are associated with severe illness⁷¹. This perception can deter patients from choosing LAIs, or treatment in general, as the stigma may intensify feelings of shame or reinforce negative stereotypes associated with schizophrenia⁷¹.



4. STIGMA AND DISCRIMINATION HINDER PATIENT ACCESS TO CARE

In Asia, 80% of psychiatric patients report experiencing discrimination and reported that the burden extends to their family members⁷²⁻⁷⁴.



The stigma surrounding schizophrenia in Asia is driven by cultural and social factors. In many Asian countries, mental illness is sometimes perceived as a moral failing or a family disgrace⁷¹. These cultural beliefs can result in people viewing schizophrenia as shameful or embarrassing, reinforcing stigma⁷¹. Limited public awareness and mental health education may also exacerbate this issue. Without widespread initiatives to inform the public, misinformation about causes and symptoms persists, leading to widespread misconceptions^{75,76}.

Furthermore, sensationalised portrayals of schizophrenia in media, often associating it with violence or erratic behaviour, reinforce negative stereotypes. This creates fear and misunderstanding among the public, especially in places where mental health awareness is limited⁷⁷. Additionally, outdated or limited mental health policies can lead to inadequate support systems and a lack of protective laws for people with schizophrenia, leaving many without the care or legal protections they need⁷⁸.

The resulting impact of stigma discourages schizophrenic patients from seeking or adhering to treatment⁷⁹. These individuals may perceive seeking treatment as a sign of personal weakness, which sustains a belief system that discourages them from pursuing necessary care⁷⁹.

As a case in point, while approximately 1 in 7 individuals live with a mental health condition in the Southeast Asian region, up to 90% of patients do not receive timely care in some countries⁸⁰.

As such, addressing stigma and creating a safe, empowering environment is crucial to promote timely care-seeking behaviour, treatment adherence, and support recovery among patients. When designing such intervention programmes, the needs of caregivers should also be considered as they play critical roles in patient care, providing support throughout the extended treatment and recovery process to help schizophrenic patients achieve symptomatic remission and functional recovery.

4.1. Progress in combating stigma and discrimination against mental health conditions, including schizophrenia, in Asia

Recent years have seen progress in combating stigma and discrimination against mental health conditions, including schizophrenia, through advocacy efforts and the implementation of community-based interventions aimed at reducing stigma and discrimination.

Several countries in the region, such as Thailand, the Philippines, and Singapore, have integrated mental health services into their national public health service system. In Thailand, community mental health (CMH) services are integrated into the public health service system throughout the Ministry of Public Health administrative infrastructure, from villages to regions⁸¹.



Thailand⁸¹⁻⁸²

2019

Community mental health (CMH) services are integrated into the public health service system throughout the Ministry of Public Health administrative infrastructure, from villages to regions

- » New mental health legislation was signed into law

2020

- » New publication of a mental health plan⁸²

- » National initiatives to raise public awareness and reduce stigma are also being implemented⁸²



Philippines⁸³

2018

Signed into law the Mental Health Act (Republic Act no. 11036), which establishes a comprehensive framework for optimal mental healthcare

- » The law mandates the provision of psychiatric, psychosocial, and neurological services in hospitals and basic mental health services in community settings
- » It includes measures to protect patient's rights, such as the right to freedom from discrimination



Singapore⁸⁴⁻⁸⁶

2022

Singapore's National Council of Social Service launched the Beyond the Label (BTL) Collective, aimed at raising public awareness and acceptance of individuals with mental health conditions

2023

Singapore's Inter-agency Taskforce on Mental Health and Well-being initiated the National Mental Health and Well-being Strategy

- » Seeks to enhance the mental health ecosystem
- » Encourage individuals with mental health needs to seek help without facing stigma

However, there are still rooms for improvement. In Vietnam, while access to mental health services has improved over the years, the country lacks a comprehensive mental health policy or legislation. Mental health services are not fully integrated into primary care, and there is inadequate government support for community caregivers, who are responsible for the majority of care for individuals with mental disorders^{87,88}.

5. CALL TO ACTION

To support functional recovery in individuals with schizophrenia, HCPs, policymakers, and payers should act decisively by ensuring access to LAIs and advancing anti-discrimination initiatives.

We propose three key actions targeted for the APAC region:

5.1



Review and update clinical guidelines to align with updated evidence

- a. Local and regional policymakers can leverage international data to update and ensure clinical guidelines are aligned with updated evidence
- b. Payers can use international data to guide evidence-based decisions in the absence of local data and expand LAI reimbursement coverage for all individuals with schizophrenia
- c. Healthcare providers and patient associations can advocate to expand LAI use to all schizophrenic patients in acute and maintenance phases in the guidelines

5.2



Promote the use of LAIs and longer-injection formulations to achieve functional recovery

- a. Healthcare providers can offer diverse treatment options, including longer-injection formulations, tailored to patients' needs
- b. Healthcare providers can educate patients and caregivers on injection procedures using videos or hands-on demonstrations to reduce reluctance towards injections

5.3



Empower mental health patients and caregivers to promote timely care-seeking behaviour and support recovery

- a. Policymakers and patient associations should drive anti-discrimination campaigns and educate caregivers to better support mental health patients
- b. Policymakers should uphold mental health patients' rights to discrimination-free communities and ensure access to affordable and inclusive mental health services
- c. Healthcare providers can advocate for navigation services, with resources such as financial aid options and personalised support services, to simplify patient and caregiver journeys

In conclusion, schizophrenia is a serious mental health condition affecting patients, caregivers, and society. Reducing this burden demands collective actions from all stakeholders. By ensuring access to proper treatment and fostering a stigma-free environment, we can enhance patient outcomes, reduce caregiver burden, and ease economic strain on both the family and society.

6. REFERENCES

1. Schizophrenia. National Institute of Mental Health (2024).
2. World Health Organization (WHO). Schizophrenia. <https://www.who.int/news-room/fact-sheets/detail/schizophrenia> (2022).
3. Institute of Health Metrics and Evaluation (IHME). Global Health Data Exchange (GHDx). <https://vizhub.healthdata.org/gbd-results/?params=gbd-api-2021-public/a6eb04433e31ada7738e54365090>.
4. Said, M. A. et al. Metabolic syndrome and cardiovascular risk among patients with schizophrenia receiving antipsychotics in Malaysia. *Singapore Med J* 53, 801–807 (2012).
5. Sado, M. et al. The cost of schizophrenia in Japan. *NDT* 787 (2013) doi:10.2147/NDT.S41632.
6. Teoh, S. L. et al. The economic burden of schizophrenia in Malaysia. *NDT Volume 13*, 1979–1987 (2017).
7. de Silva, J., Hanwella, R. & de Silva, V. A. Direct and indirect cost of schizophrenia in outpatients treated in a tertiary care psychiatry unit. *Ceylon Med J* 57, 14–18 (2012).
8. Chaiyakunapruk, N. et al. Global economic burden of schizophrenia: a systematic review. *NDT* 357 (2016) doi:10.2147/NDT.S96649.
9. Yeh, S.-T., Ng, Y.-Y. & Wu, S.-C. Association of psychiatric and physical illnesses with suicide in older adults in Taiwan. *Journal of Affective Disorders* 264, 425–429 (2020).
10. Mi, W. et al. Prevalence and risk factors of agitation in newly hospitalized schizophrenia patients in China: An observational survey. *Psychiatry Research* 253, 401–406 (2017).
11. Wan, K. & Wong, M. M. C. Stress and burden faced by family caregivers of people with schizophrenia and early psychosis in Hong Kong. *Internal Medicine Journal* 49, 9–15 (2019).
12. Kim, A. M. Crimes by people with schizophrenia in Korea: comparison with the general population. *BMC Psychiatry* 19, 377 (2019).
13. Maneeton, N., Maneeton, B., Jaiyen, N., Woottlik, P. & Khemawichanurat, W. Prevalence of Aggressive or Violent Behaviour in Thai Patients with Schizophrenia: a Cross-Sectional Study. *East Asian Arch Psychiatry* 29, 87–90 (2019).
14. Ran, M.-S. et al. Criminal behavior among persons with schizophrenia in rural China. *Schizophrenia Research* 122, 213–218 (2010).
15. Patel, K. R., Cherian, J., Gohil, K. & Atkinson, D. Schizophrenia: Overview and Treatment Options. *P T* 39, 638–645 (2014).
16. Ponce-Correa, F., Caqueo-Urizar, A., Berrios, R. & Escobar-Soler, C. Defining recovery in schizophrenia: A review of outcome studies. *Psychiatry Research* 322, 115134 (2023).
17. Sim, K. et al. High-dose antipsychotic use in schizophrenia: a comparison between the 2001 and 2004 Research on East Asia Psychotropic Prescription (REAP) studies. *Br J Clin Pharmacol* 67, 110–117 (2009).
18. Cheng, Z. et al. Rates and predictors of one-year antipsychotic treatment discontinuation in first-episode schizophrenia: Results from an open-label, randomized, “real world” clinical trial. *Psychiatry Research* 273, 631–640 (2019).
19. Chung, Y.-C., Yang, Y. K., Sulaiman, A. H., Bergmans, P. & Tan, W. Asian Subgroup Analysis of the REMISSIO Study: A Long-Term Efficacy and Safety Study of Paliperidone Palmitate 3-month Formulation in Patients with Stable Schizophrenia in a Naturalistic Clinical Setting. *Clin Psychopharmacol Neurosci* 20, 427–439 (2022).
20. Huang, M. et al. A randomized, 13-week study assessing the efficacy and metabolic effects of paliperidone palmitate injection and olanzapine in first-episode schizophrenia patients. *Progress in Neuro-Psychopharmacology and Biological Psychiatry* 81, 122–130 (2018).
21. Ishigooka, J. et al. Efficacy and safety of aripiprazole once-monthly in Asian patients with schizophrenia: A multicenter, randomized, double-blind, non-inferiority study versus oral aripiprazole. *Schizophrenia Research* 161, 421–428 (2015).
22. Ishigooka, J. et al. Discontinuation and remission rates and social functioning in patients with schizophrenia receiving second-generation antipsychotics: 52-week evaluation of JUMPS, a randomized, open-label study. *Psychiatry Clin Neurosci* 76, 22–31 (2022).
23. Iyo, M., Akiyoshi, H., Sekine, D., Shibasaki, Y. & Mamiya, N. An exploratory database study of factors influencing the continuation of brexpiprazole treatment (prescription) in patients with schizophrenia using information from psychiatric electronic medical records processed with natural language processing. *Schizophrenia Research* 255, 122–131 (2023).
24. Joo, S. W. et al. Continuation of schizophrenia treatment with three long-acting injectable antipsychotics in South Korea: A nationwide population-based study. *European Neuropsychopharmacology* 29, 1051–1060 (2019).
25. Kim, S. et al. Effects of Long-Acting Injectable Paliperidone Palmitate on Clinical and Functional Outcomes in Patients With Schizophrenia Based on Illness Duration. *J. Clin. Psychiatry* 82, (2021).
26. Kwon, J. S. et al. Satisfaction of immediate or delayed switch to paliperidone palmitate in patients unsatisfied with current oral atypical antipsychotics: International Clinical Psychopharmacology 30, 320–328 (2015).
27. Lee, J.-S. et al. Dose Pattern and Effectiveness of Paliperidone Extended-Release Tablets in Patients With Schizophrenia. *Clinical Neuropharmacology* 34, 186–190 (2011).
28. Li, H., Rui, Q., Ning, X., Xu, H. & Gu, N. A comparative study of paliperidone palmitate and risperidone long-acting injectable therapy in schizophrenia. *Progress in Neuro-Psychopharmacology and Biological Psychiatry* 35, 1002–1008 (2011).
29. i, X., Ye, C., Zhang, W., Jia, M. & Wang, G. Factors Associated with Symptom Stabilization that Allow for Successful Transition from Once-Monthly Paliperidone Palmitate to Three-Monthly Paliperidone Palmitate: A Post Hoc Analysis Examined Clinical Characteristics in Chinese Patients with Schizophrenia. *CNS Drugs* 38, 55–65 (2024).
30. Lin, C.-H., Chen, F.-C., Chan, H.-Y. & Hsu, C.-C. Time to Rehospitalization in Patients With Schizophrenia Receiving Long-Acting Injectable Antipsychotics or Oral Antipsychotics. *International Journal of Neuropsychopharmacology* 22, 541–547 (2019).
31. Lin, C.-H. et al. Treatment Retention Rates of 3-monthly Paliperidone Palmitate and Risk Factors Associated with Discontinuation: A Population-based Cohort Study. *Clin Psychopharmacol Neurosci* 21, 544–558 (2023).
32. Si, T. et al. Pharmacokinetics and tolerability of paliperidone palmitate injection in Chinese subjects: PALIPERIDONE PALMITATE PHARMACOKINETICS. *Hum. Psychopharmacol Clin Exp* 29, 203–210 (2014).
33. Si, T. et al. A Subgroup Analysis of Chinese Patients Switched to Paliperidone Palmitate One-Month Injectable by Prior Oral Antipsychotic Treatment. *Pharmacopsychiatry* 49, 32–41 (2015).
34. Si, T. et al. Impact of paliperidone palmitate one-month formulation on relapse prevention in patients with schizophrenia: A post-hoc analysis of a one-year, open-label study stratified by medication adherence. *J Psychopharmacol* 32, 691–701 (2018).
35. Takahashi, N. et al. Randomized, placebo-controlled, double-blind study assessing the efficacy and safety of paliperidone palmitate in Asian patients with schizophrenia. *NDT* 1889 (2013) doi:10.2147/NDT.S54051.
36. Yoshimura, B. et al. Incidence and predictors of acute akathisia in severely ill patients with first-episode schizophrenia treated with aripiprazole or risperidone: secondary analysis of an observational study. *Psychopharmacology* 236, 723–730 (2019).
37. Zhang, F. et al. Efficacy, safety, and impact on hospitalizations of paliperidone palmitate in recent-onset schizophrenia. *NDT* 657 (2015) doi:10.2147/NDT.S77778.
38. Zhang, Y. & Dai, G. Efficacy and metabolic influence of paliperidone ER, aripiprazole and ziprasidone to patients with first-episode schizophrenia through 52 weeks follow-up in China. *Human Psychopharmacology* 27, 605–614 (2012).
39. Zheng, Y. et al. Psychotic Symptoms and Attitudes toward Medication Mediate the Effect of Insight on Personal-Social Functions in Patients with Schizophrenia: One-Year Randomized Controlled Trial and Follow-Up. *Psychopathology* 51, 167–176 (2018).
40. Psychosis and Schizophrenia in Adults: Prevention and Management. (NICE, London, 2014).
41. The American Psychiatric Association Practice Guideline for the Treatment of Patients with Schizophrenia. (American Psychiatric Association, Washington, DC, 2021).
42. Grover, S. et al. Stigma experienced by caregivers of patients with severe mental disorders: A nationwide multicentric study. *Int J Soc Psychiatry* 63, 407–417 (2017).
43. Galletly, C. et al. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the management of schizophrenia and related disorders. *Aust N Z J Psychiatry* 50, 410–472 (2016).

44. Yang, K.-C. et al. Evidence-Based Expert Consensus Regarding Long-Acting Injectable Antipsychotics for Schizophrenia from the Taiwanese Society of Biological Psychiatry and Neuropsychopharmacology (TSBPN). *CNS Drugs* 35, 893–905 (2021).
45. Verma, S. et al. Ministry of Health clinical practice guidelines: schizophrenia. *Singapore Med J* 52, 521–525; quiz 526 (2011).
46. Wang, H. et al. Persistence With and Adherence to Paliperidone Palmitate Once-Monthly Injection for Schizophrenia Treatment in China and Japan. *J. Clin. Psychiatry* 83, (2021).
47. Wei, Y. et al. Association of Long-Acting Injectable Antipsychotics and Oral Antipsychotics With Disease Relapse, Health Care Use, and Adverse Events Among People With Schizophrenia. *JAMA Netw Open* 5, e2224163 (2022).
48. Dilokthornsakul, P., Thooputra, T., Patanaprteeep, O., Kongsakon, R. & Chaikunapruk, N. Effects of medication adherence on hospitalizations and healthcare costs in patients with schizophrenia in Thailand. *SAGE Open Medicine* 4, 2050312116637026 (2016).
49. Zhu, J. et al. Attitudes and Willingness to Accept Long-Acting Injections for Patients With Schizophrenia in Beijing: A Cross-Sectional Investigation Based on Samples From the Communities. *Front. Public Health* 9, 770276 (2021).
50. Turkoz, I., Li, H. & Zhang, F. Efficacy and safety of once-monthly injection of paliperidone palmitate in hospitalized Asian patients with acute exacerbated schizophrenia: an open-label, prospective, noncomparative study. *NDT* 15 (2015) doi:10.2147/NDT.S83651.
51. Tang, T.-C. et al. Long-term safety, efficacy, treatment satisfaction, and impact on healthcare service use of paliperidone palmitate one-month intramuscular formulation in patients with recent-onset schizophrenia in Taiwan: A subgroup analysis of an Asia-Pacific, 18-month, phase 3b study. *Taiwan J Psychiatry* 33, 198 (2019).
52. Si, T. et al. Efficacy and safety of flexibly dosed paliperidone palmitate in Chinese patients with acute schizophrenia: an open-label, single-arm, prospective, interventional study. *NDT* 11, 1483–1492 (2015).
53. Takekita, Y. et al. Cognitive function and risperidone long-acting injection vs. paliperidone palmitate in schizophrenia: a 6-month, open-label, randomized, pilot trial. *BMC Psychiatry* 16, 172 (2016).
54. Koshikawa, Y. et al. The Comparative Effects of Risperidone Long-Acting Injection and Paliperidone Palmitate on Social Functioning in Schizophrenia: A 6-Month, Open-Label, Randomized Controlled Pilot Trial. *Neuropsychobiology* 73, 35–42 (2016).
55. Chang, S. M. et al. Economic Burden of Schizophrenia in South Korea. *J Korean Med Sci* 23, 167 (2008).
56. Wu, D. B.-C. et al. Cost analysis of risperidone long-acting injection in the treatment of schizophrenia and schizoaffective disorders in Hong Kong: An approach using generalised estimating equations. *Psychiatry Research* 210, 745–750 (2013).
57. Liu, J. et al. A health economics study of long-acting injectable once-monthly paliperidone palmitate in schizophrenia: a one-year mirror-image study in China. *BMC Psychiatry* 22, 95 (2022).
58. Chan, C. T., Verma, S., Subramaniam, M., Abdin, E. & Tay, J. Effectiveness of Paliperidone Palmitate in Reducing Acute Psychiatric Service Use for Patients Suffering from Psychosis—A Retrospective Mirror-Image Study. *IJERPH* 20, 3403 (2023).
59. Choon, J. W. Y. et al. Real-world evidence of improved healthcare utilization in patients with schizophrenia or schizoaffective disorder after early treatment of paliperidone palmitate once-monthly treatment in Hong Kong. *Journal of Medical Economics* 22, 273–279 (2019).
60. Kasahara-Kiritani, M., Chaturvedi, A., Inagaki, A., Wakamatsu, A. & Jung, W. Budget impact analysis of long acting injection for schizophrenia in Japan. *Journal of Medical Economics* 23, 848–855 (2020).
61. Eduardo C., J. et al. The Community Mental Health Program in Calabarzon: Preliminary report from an internal program review of an innovative service integration initiative for schizophrenia. *Philippine Journal of Health Research and Development* 25, 69–74 (2021).
62. Oh, J. et al. Effects of Long-acting Injectable 3-Monthly Paliperidone Palmitate on the Clinical and Social Performance of Patients with Schizophrenia. *Clin Psychopharmacol Neurosci* 21, 126–134 (2023).
63. Savitz, A. J. et al. Efficacy and safety of paliperidone palmitate three-monthly formulation in East Asian patients with schizophrenia: subgroup analysis of a global, randomized, double-blind, Phase III, noninferiority study. *Neuropsychiatr Dis Treat* 13, 2193–2207 (2017).
64. Luo, R., Lu, H. & Li, H. Cost-utility analysis of using paliperidone palmitate in schizophrenia in China. *Front. Pharmacol.* 14, (2023).
65. The Philippine National Formulary. DOH Philippines (2024).
66. Formulari Ubat KKM (FUKKM). MOH Malaysia (2024).
67. List of Subsidised Drugs. MOH Singapore (2024).
68. Barnes, T. R. E., Shingleton-Smith, A. & Paton, C. Antipsychotic long-acting injections: Prescribing practice in the UK. *Br J Psychiatry* 195, s37–s42 (2009).
69. Lin, S.-K. & Chung, A.-N. T213. TREND OF LONG-ACTING INJECTABLE ANTIPSYCHOTICS USE IN ASIA: FINDINGS FROM REAP ANTIPSYCHOTIC STUDIES. *Schizophrenia Bulletin* 46, S313–S314 (2020).
70. Keenan, A. et al. Patient-psychiatrist discordance and drivers of prescribing long-acting injectable antipsychotics for schizophrenia management in the real-world: a point-in-time survey. *BMC Psychiatry* 22, 187 (2022).
71. Lauber, C. & Rössler, W. Stigma towards people with mental illness in developing countries in Asia. *International Review of Psychiatry* 19, 157–178 (2007).
72. Wang, N. X., Xu, F. Z. & Shi, Q. C. A survey of residents' awareness and attitude towards mental illness in Zhejiang province. *Zhejiang J. Prev. Med* 13, 14–21 (2005).
73. Wang, H. Q., Ren, Z. B., Guo, C. Y. & Wang, N. X. Research progress of stigma in patients with schizophrenia. *Zhejiang J. Prev. Med* 24, 18–21 (2012).
74. Zhang, Z. et al. Overview of Stigma against Psychiatric Illnesses and Advancements of Anti-Stigma Activities in Six Asian Societies. *IJERPH* 17, 280 (2019).
75. Murthy, M. K. S., Dasgupta, M. & Chaturvedi, S. K. Mental Health Literacy in Rural India. in *Mental Health and Illness in the Rural World* (ed. Chaturvedi, S. K.) 273–284 (Springer, Singapore, 2020). doi:10.1007/978-981-10-2345-3_34.
76. Hanafiah, A. N. & Van Bortel, T. A qualitative exploration of the perspectives of mental health professionals on stigma and discrimination of mental illness in Malaysia. *International Journal of Mental Health Systems* 9, (2015).
77. Stuart, H. Media portrayal of mental illness and its treatments: what effect does it have on people with mental illness? *CNS Drugs* 20, 99–106 (2006).
78. World Health Organization (WHO). Mental health action plan 2013 - 2020. <https://www.who.int/publications/i/item/9789241506021>.
79. Tsang, H. W., Fung, K. M. & Chung, R. C. Self-stigma and stages of change as predictors of treatment adherence of individuals with schizophrenia. *Psychiatry Research* 180, 10–15 (2010).
80. Yang, C. 1 in 7 in Southeast Asia live with a mental health condition, treatment gap in some countries is 'huge': WHO official. *CNA* (2023).
81. Community Mental health: Thailand Country Report 2008. Department of Mental Health, MOPH (2008).
82. World Health Organization (WHO). Mental Health Atlas 2020: Thailand. (2020).
83. ally, J., Samaniego, R. M. & Tully, J. Mental health legislation in the Philippines: Philippine Mental Health Act. *BJPsych Int* 16, 65–67 (2019).
84. Over 55,000 individuals supported by Beyond the Label Collective since last year. *NCSS* (2023).
85. Beyond the Label: A Mental Health Anti-Stigma Movement. *NCSS* (2024).
86. Ministry of Health Singapore (MOH). National Mental Health and Well-being Strategy 2023: A Multi-Agency Report. (2023).
87. Vuong, D. A., Van Ginneken, E., Morris, J., Ha, S. T. & Busse, R. Mental health in Vietnam: Burden of disease and availability of services. *Asian Journal of Psychiatry* 4, 65–70 (2011).
88. Nguyen, T., Tran, T., Tran, H., Tran, T. & Fisher, J. Challenges in Integrating Mental Health into Primary Care in Vietnam. in *Innovations in Global Mental Health* (ed. Okpaku, S.) 1–21 (Springer International Publishing, Cham, 2019). doi:10.1007/978-3-319-70134-9_74-1.

Johnson & Johnson

At Johnson & Johnson, we believe good health is the foundation of vibrant lives, thriving communities and forward progress. That is why for more than 135 years, we have aimed to keep people well at every age and every stage of life. Today we are committed to using our reach and size for good. We strive to improve access and affordability, create healthier communities, and put a healthy mind, body and environment within reach of everyone, everywhere.

For more information, visit: <https://www.jnj.com/>



Vista Health is the leading life sciences advisory in the Asia-Pacific region. Vista Health offers strategic consulting and tech enabled solutions across all corners of health care, building lasting partnerships with payers, providers, patients, and industry.

For more information, visit: <https://vista.health/>