長效針應用
Benefit of Early Use of LAI
Strategy to Manage Relapses in Early Stage Schizophrenia

八里療養院社區精神科
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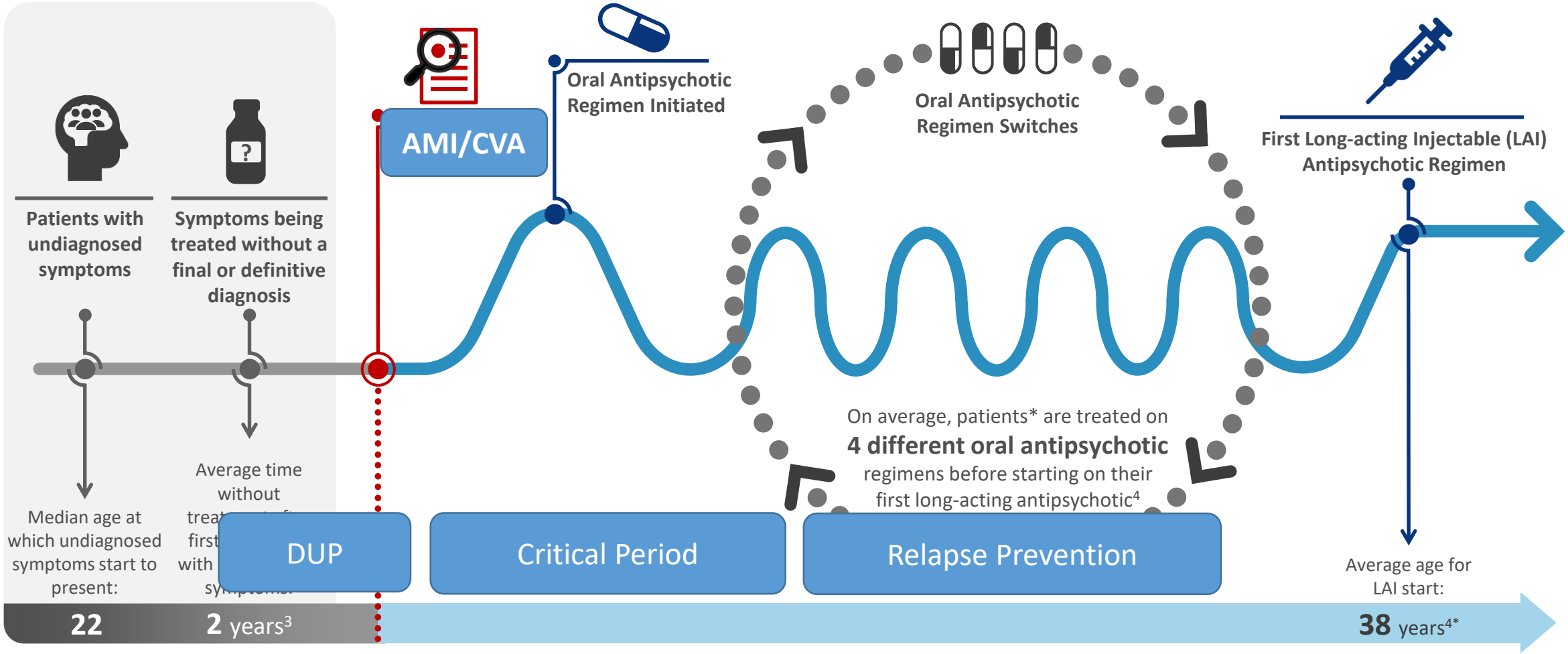
Good value Great hope
區域教學醫院-精神專科醫院

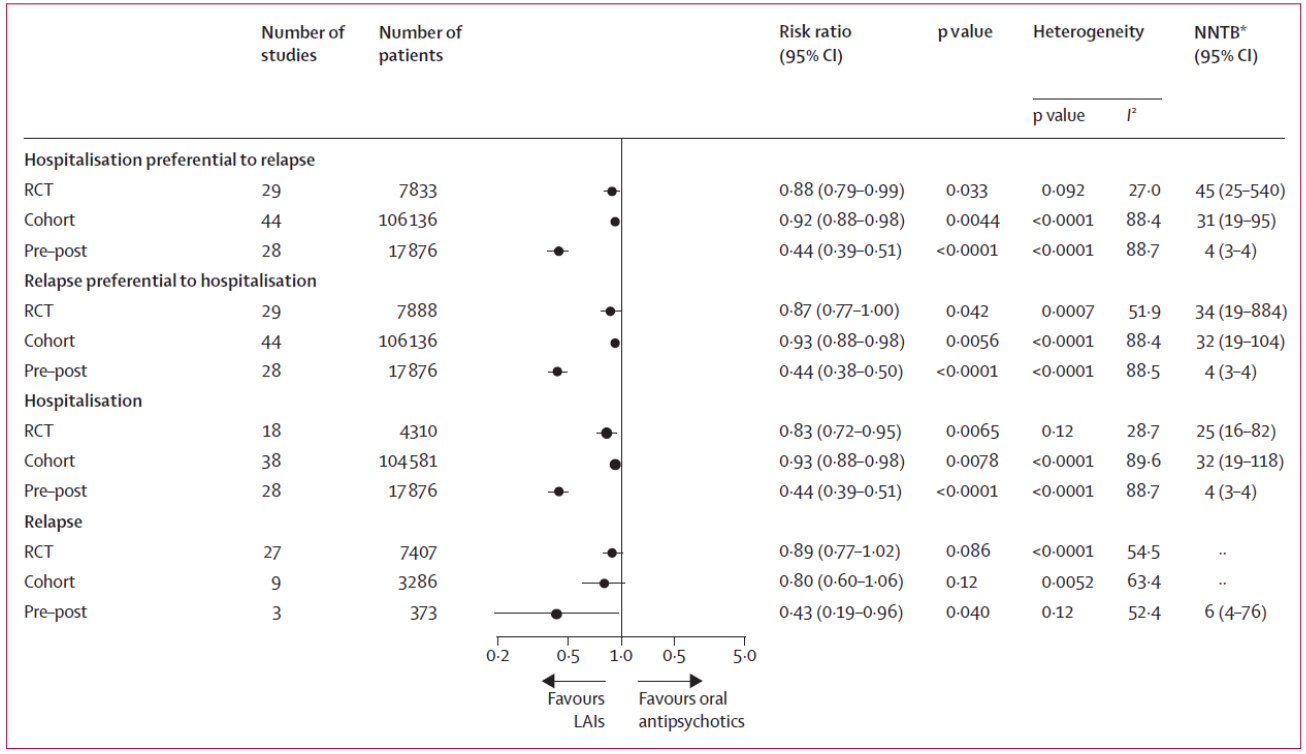
Treatment journey of schizophrenia patients *



*From Janssen-sponsored market research, a total of 620 patient charts were collected from 161 healthcare providers (HCPs) from August 22 through September 12, 2016. Key screening criteria included: Must have seen at least 30 individual patients with schizophrenia in the past 3 months, must have treated at least one patient with one of the 10 specified antipsychotics in the past 3 months, should have been in practice for a minimum of 2 and a maximum of 35 years.

Systematic review and meta-analysis

- Comparative benefits of LAIs versus oral antipsychotics in **RCT/Cohort/Pre-post studies**
- LAIs were associated with a lower risk of hospitalization or relapse than OAP
- Significant benefit with LAIs versus OAP in preventing hospitalization or relapse



	Number of studies	Number of patients	Risk ratio (95% CI)	p value	Heterogeneity p value	Heterogeneity I^2	NNTB* (95% CI)
Hospitalisation preferential to relapse							
RCT	29	7833	0·88 (0·79–0·99)	0·033	0·092	27·0	45 (25–540)
Cohort	44	106136	0·92 (0·88–0·98)	0·0044	<0·0001	88·4	31 (19–95)
Pre–post	28	17876	0·44 (0·39–0·51)	<0·0001	<0·0001	88·7	4 (3–4)
Relapse preferential to hospitalisation							
RCT	29	7888	0·87 (0·77–1·00)	0·042	0·0007	51·9	34 (19–884)
Cohort	44	106136	0·93 (0·88–0·98)	0·0056	<0·0001	88·4	32 (19–104)
Pre–post	28	17876	0·44 (0·38–0·50)	<0·0001	<0·0001	88·5	4 (3–4)
Hospitalisation							
RCT	18	4310	0·83 (0·72–0·95)	0·0065	0·12	28·7	25 (16–82)
Cohort	38	104581	0·93 (0·88–0·98)	0·0078	<0·0001	89·6	32 (19–118)
Pre–post	28	17876	0·44 (0·39–0·51)	<0·0001	<0·0001	88·7	4 (3–4)
Relapse							
RCT	27	7407	0·89 (0·77–1·02)	0·086	<0·0001	54·5	..
Cohort	9	3286	0·80 (0·60–1·06)	0·12	0·0052	63·4	..
Pre–post	3	373	0·43 (0·19–0·96)	0·040	0·12	52·4	6 (4–76)

Figure 3: **Forest plot for summary outcomes related to hospitalisation or relapse with LAIs versus oral antipsychotics**
Studies without available data on hospitalisation or relapse were excluded from relevant analyses. LAI=long-acting injectable antipsychotic. NNTB=number needed to treat for an additional beneficial outcome. RCT=randomised controlled trial. *NNTB was calculated when the RR for that comparison was statistically significant (p<0·05).

Kishimoto T, Hagi K, Kurokawa S, Kane JM, Correll CU. Lancet Psychiatry. 2021;8(5):387-404

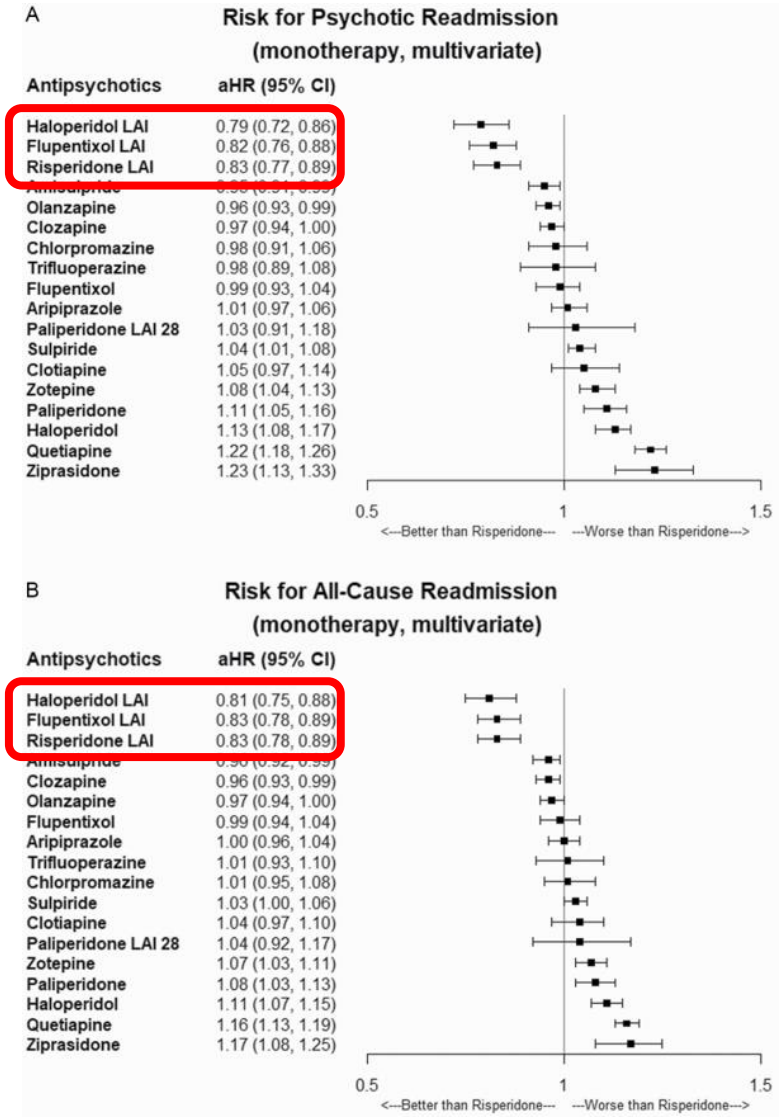
Real-world effectiveness of LAI in TAIWAN

JOURNAL ARTICLE

Comparative Effectiveness of Antipsychotics in Preventing Readmission for First-Admission Schizophrenia Patients in National Cohorts From 2001 to 2017 in Taiwan FREE

Yi-Hsuan Lin, Chi-Shin Wu, Chen-Chung Liu, Po-Hsiu Kuo, Hung-Yu Chan, Wei J Chen

Schizophrenia Bulletin, Volume 48, Issue 4, July 2022, Pages 785–794,
https://doi.org/10.1093/schbul/sbac046
Published: 15 May 2022



- 首次住院的思覺失調症病人，出院後若接受長效針劑型的抗精神病藥物治療，相較於口服抗精神病藥物，可以降低**15-20%**的再住院率。
- 目前**不到25%**的病人，在出院的一年內會接受長效針劑的治療。

N=75,986

早期精神病分期之定義

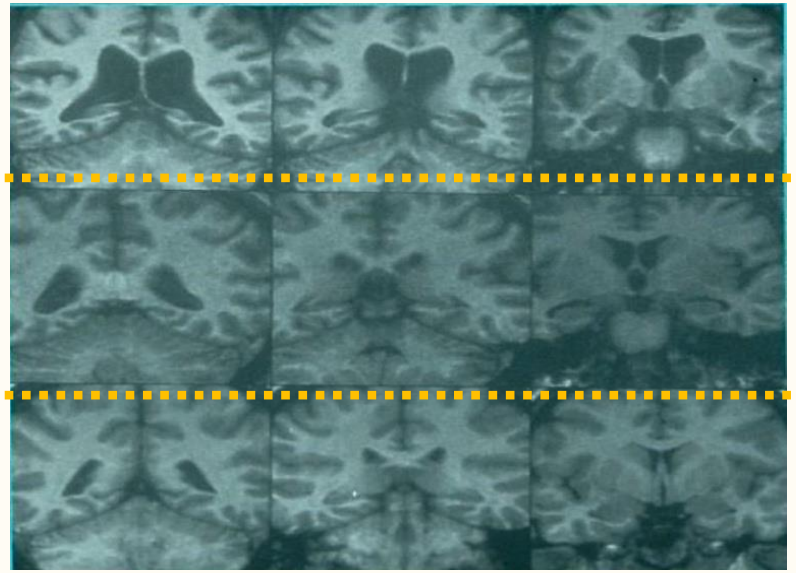
ref:發展我國精神醫療早期介入及長效針劑臨床指引, 2022

臨床分期	定義
0	增加精神病風險(一等親當中有思覺失調症患者) 無症狀
1a	**具精神病風險狀態(At-Risk Mental State, ARMS)** 輕微或非特異的精神病症狀，包含認知缺損 輕微功能變化或下降
1b	**精神病之超高風險群 (Ultra-High Risk, UHR)** 中度但未達診斷閾值的精神病症狀，伴隨中度認知功能改變及功能下降或慢性功能不佳
2	**首次發作精神病(first episode psychosis, FEP)**：達到診斷精神病之閾值，伴隨中度到重度的症狀、認知功能缺損及功能下降 (整體功能評估分數(GAF) 30-50分) 包含急性及早期恢復期
3a	未完全從首次發作精神病中緩解
3b	復發或再發之精神病經治療後穩定，但功能、殘餘症狀或認知比首次發作緩解時下降
3c	多次復發伴隨臨床症狀惡化及受疾病影響程度增加
4	由症狀、認知及失能狀況評估為嚴重、持續或未緩解之疾病

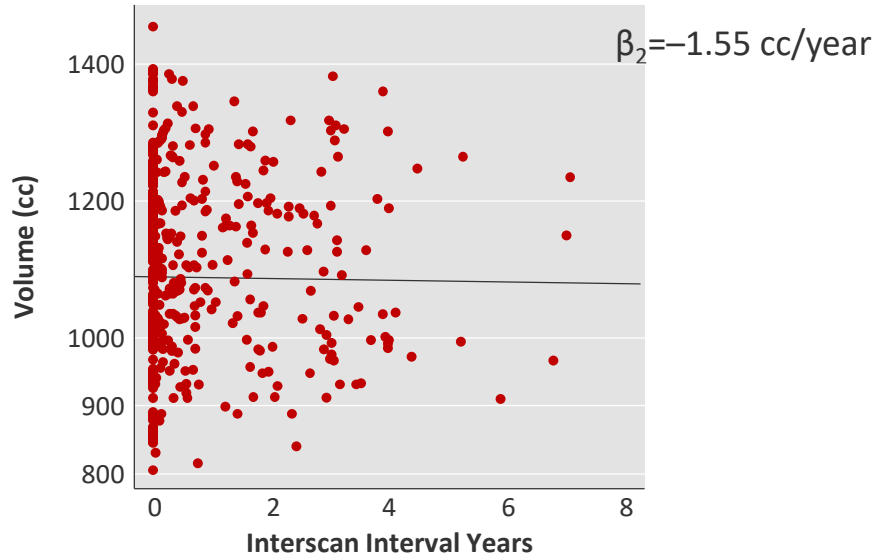
Progressive brain change over multiple relapse in FES

- **Duration of relapses & antipsychotic treatment intensity** were related to significant decreases in both general and regional brain measures

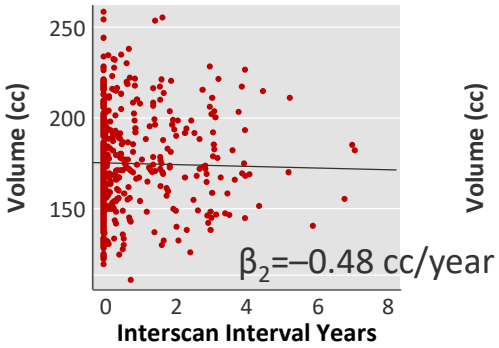
Brain MRI imaging change[1]



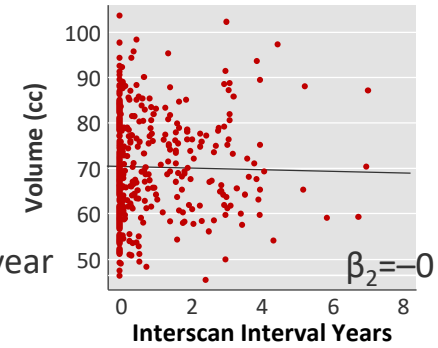
Total Brain Volume Change (N=202)[2]



Frontal lobe white matter*



Temporal lobe white matter*

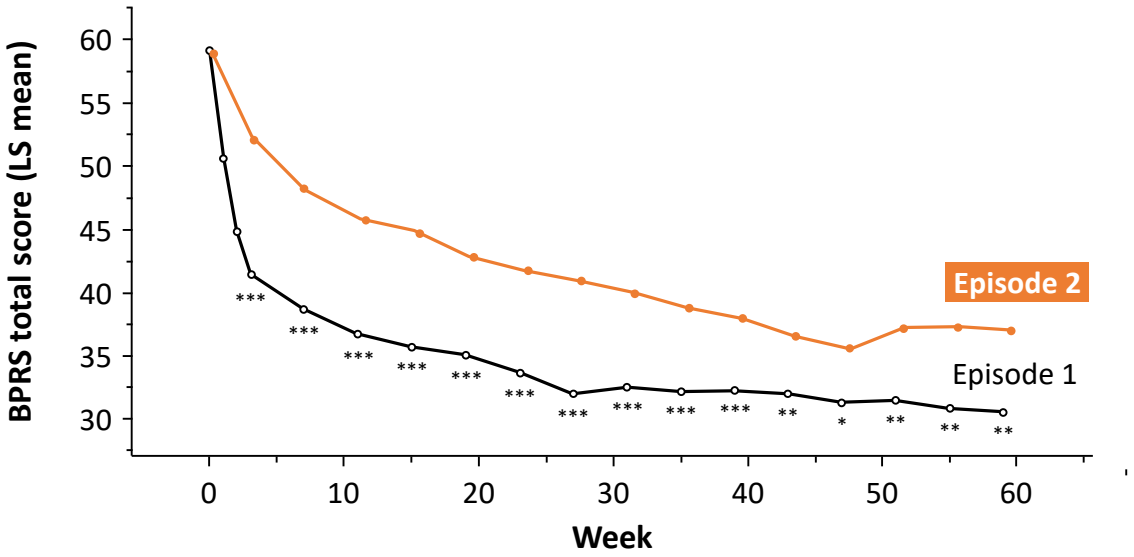


*Note: 202 patients who had at least two structural MRI scans and were followed for at least 5 years

1. Adapted from Dr Henry Nasrallah speaks expert sharing
2. Andreasen N. et al., Am J Psychiatry. 2013 Jun 1;170(6):689

Increased number of relapses might result in poorer treatment responses and prolong recovery process[1]

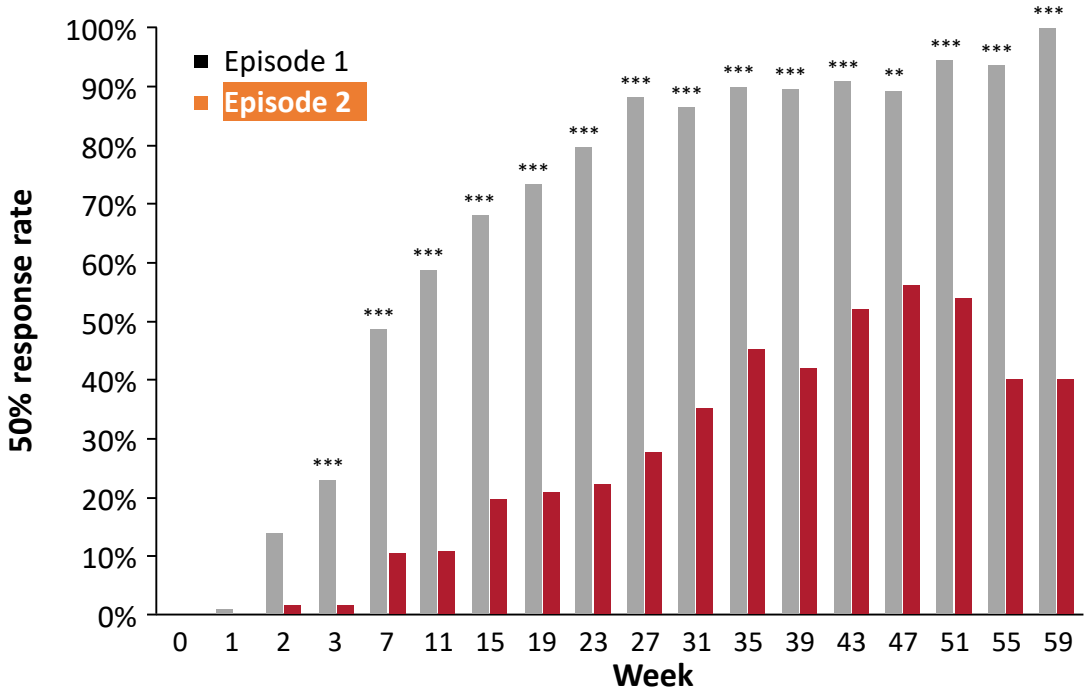
- **Changes in BPRS total scores over time in first vs. second episodes (N = 130)**



(Episode 1)	130	126	115	102	97	90	79	68	59	50	39	34	28	19	16	11
(Episode 2)	129	127	125	120	117	105	94	90	82	44	31	23	16	13	10	10

The mixed-model analysis revealed a significant interaction between episode and time (F = 13.8, df = 15, 2242, P < 0.001). ***P < 0.001, **P < 0.01, *P < 0.05. BPRS brief psychiatric rating scale.

- **Changes in 50% response§ rates over time in first vs. second episodes (N = 130)**



§: The proportions of patients achieving ≥50% reduction in the BPRS total scores over time in first vs. second episodes (N = 130). The generalized estimating equation analysis revealed a significant interaction between episode and time (F = 105.0, P < 0.001). ***P < 0.001, **P < 0.01

*Included patients with a diagnosis of first-episode schizophrenia or schizoaffective disorder who met the following criteria: (1) referral to the FEP Program between 2003 and 2013; (2) treatment with an oral second-generation antipsychotic according to a standardized treatment algorithm; (3) positive symptom remission; (4) subsequent relapse (i.e., second episode) in association with non-adherence; and (5) reintroduction of antipsychotic treatment with the same agent used to achieve response in the first episode.

**BPRS: 18-item brief psychiatric rating scale; § 50% response was defined as ≥50% reduction in the BPRS total scores.

1. Takeuchi H, et al., Neuropsychopharmacology. 2019 May; 44(6): 1036–1042

Relapses potentially may lead to brain damages and cause cognitive decline and functional impairment[1,2]

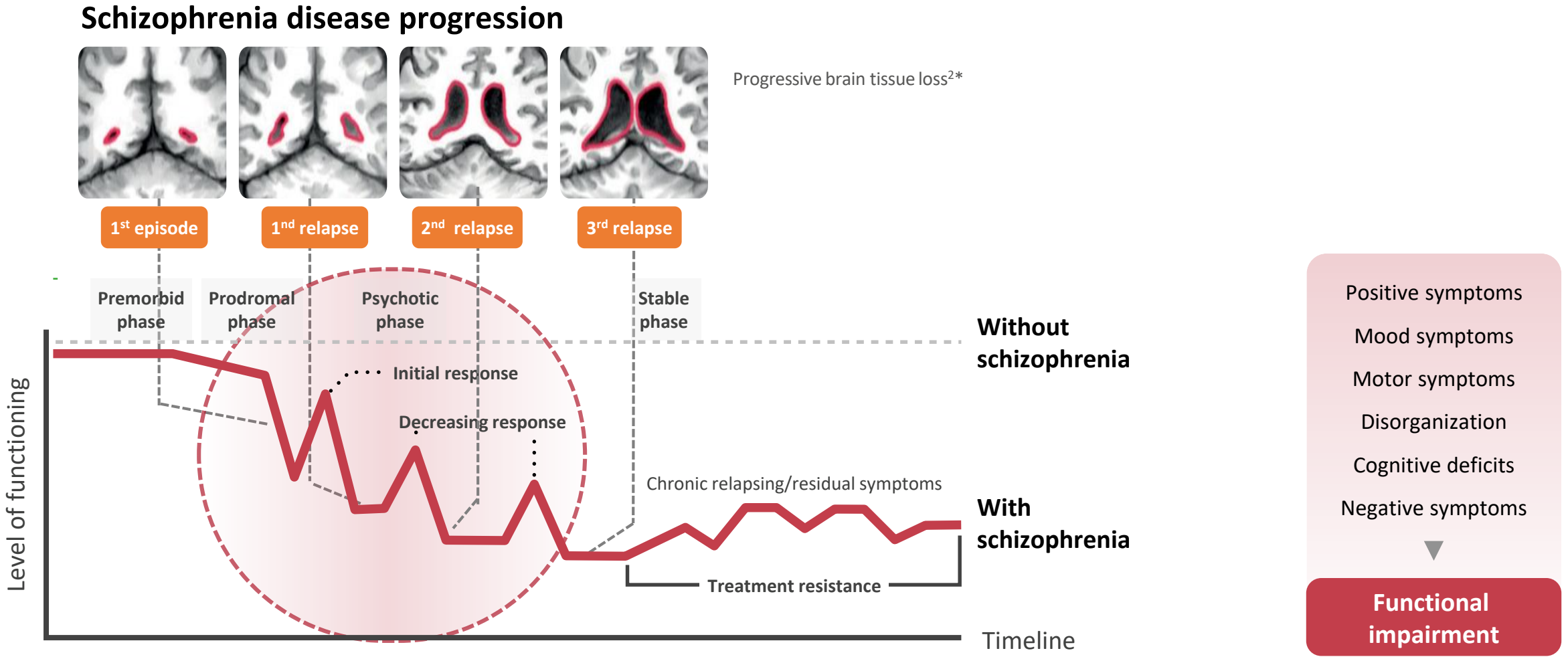
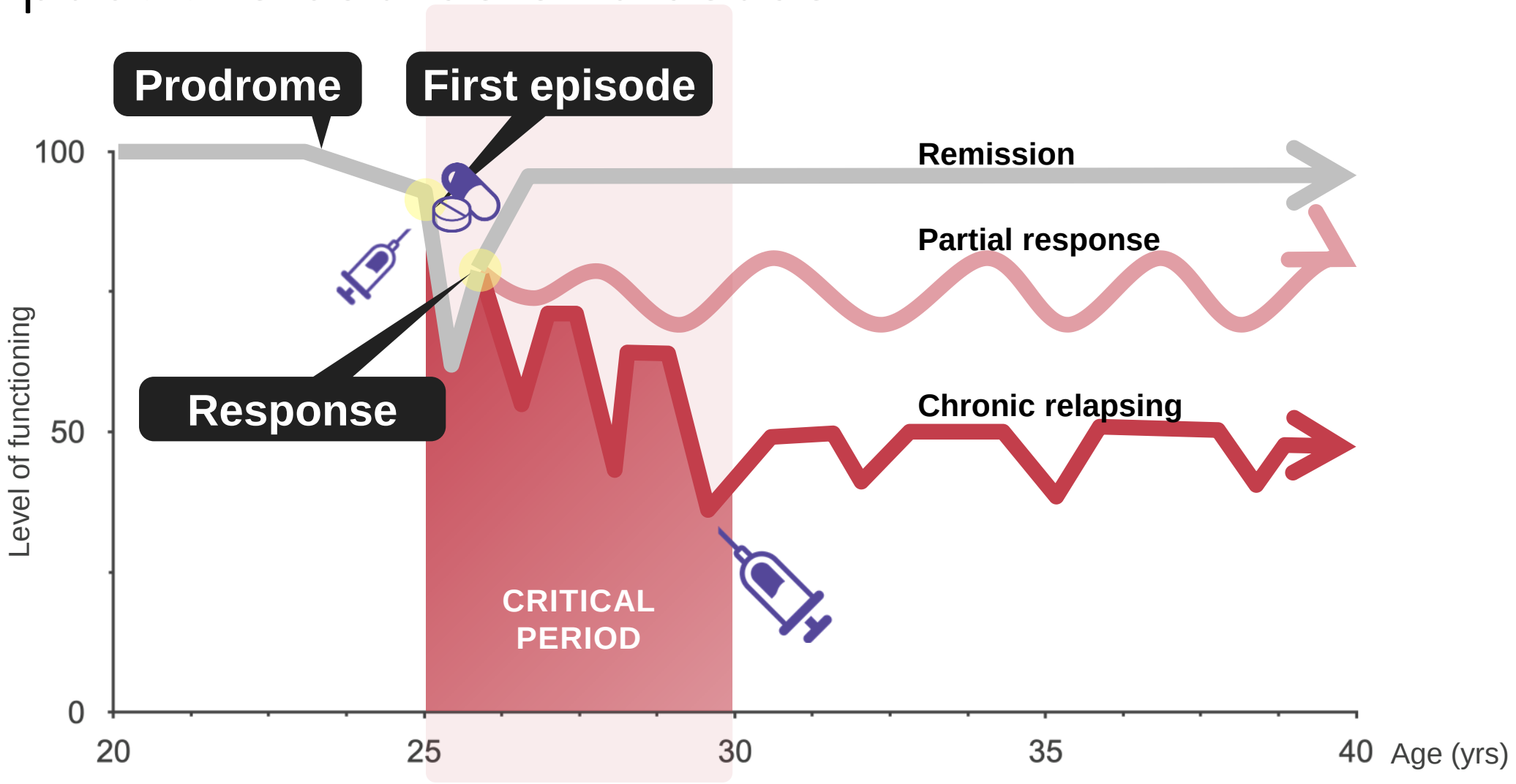


Figure adapted from Gardner & Nasrallah 2015.

1. Tandon R et al. Schizophr Res 2009; 110(1–3): 1–23;
2. Gardner KN & Nasrallah HA. Current Psychiatry 2015;14(7):33, 38–45, e3.

Early treatment intervention from 1st Episode could impact the course of disease[1,2]



Adapted from: Lieberman JA, et al. Biol Psychiatry. 2001;50(11):884-897

Reference: 1. Lieberman JA, et al. Biol Psychiatry. 2001;50(11):884-897 2.Birchwood M et al. Br J Psychiatry 1998;172 (S 33):53-9.

Risk factors for relapse following treatment for first episode psychosis[1]

Significative Risk Factors	Risk (OR)
Nonadherence to Treatment	4x
Persistent Substance Use Disorder	3x
Caregivers' Excessive Criticism	2.3x
Poor Premorbid Adjustment	2.2x

- Risk (2.2x) persists even after controlling for confounding factors
- Risk persists even in groups with high adherence to treatment

- But not other components of Expressed Emotion.
- Social support is associated with reduced risks of relapse

N=29 studies

HOW CAN WE IMPROVE ADHERENCE TO ANTIPSYCHOTIC TREATMENT ?

1. Adapted from Álvarez-Jiménez M et al. Schizophrenia Research 2012;139:116-128

Discontinuation of the initial antipsychotic is a major concern in the course of treating FEP

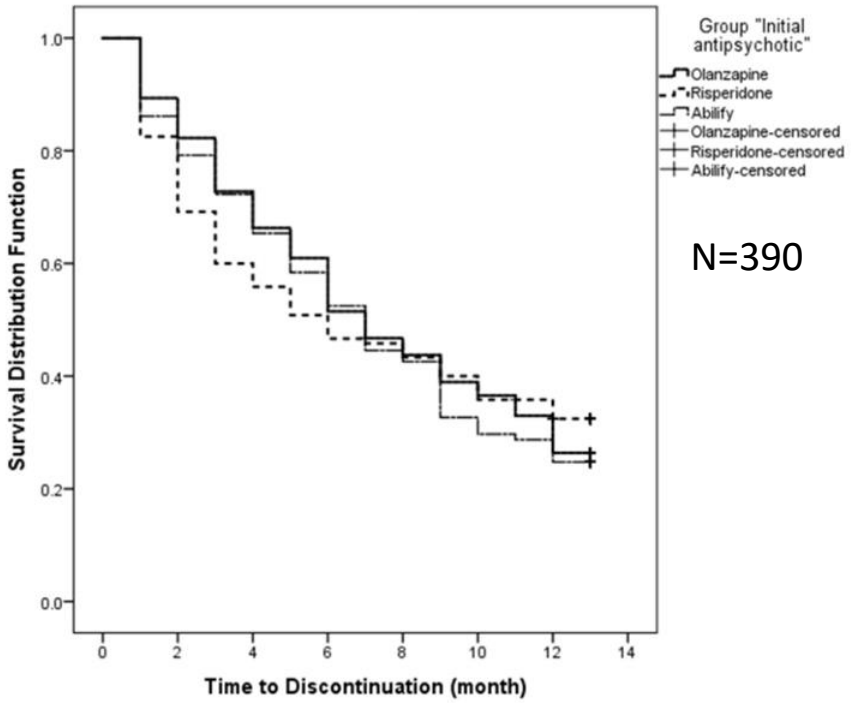


Fig. 1. Kaplan-Meier estimated survival curves by antipsychotic.

N=390

- Rate of discontinuation of the first antipsychotic was **72%,** between the 3 investigated antipsychotics (olanzapine (73%), risperidone (68%) and aripiprazole (75%))
- Mean time to discontinuation was 7.2 (4.6) months and was not different among the three antipsychotics

or

Mustafa S, Joober R, Lepage M, Iyer S, Shah J, Malla A. Predictors of 'all-cause discontinuation' of initial oral antipsychotic medication in first episode psychosis. Schizophr Res. 2018 Nov;201:287-293. doi: 10.1016/j.schres.2018.04.027. Epub 2018 Apr 26. PMID: 29706449.

The Journal of Clinical Psychiatry
CELEBRATING 85 YEARS

ORIGINAL RESEARCH

Long-term Outcomes of Early Use of Long-Acting Injectable Antipsychotics in Schizophrenia

Su-Chen Fang, PhD[a]; Cheng-Yi Huang, MD[b]; and Yu-Hsuan Joni Shao, PhD[c,d,*]

Published: June 1, 2022

Early stage group (LAIs within 3 years of OAP initiation):

- The hazard ratios for all- and natural-cause mortalities were **0.49** and **0.30**, respectively in the 13-yr study up.
- A marked decrease of risks of re-hospitalization, psychiatric hospitalization, and psychiatric ER visits.

Use of LAIs in the late stage of treatment did not decrease the risk of relapse or mortality.

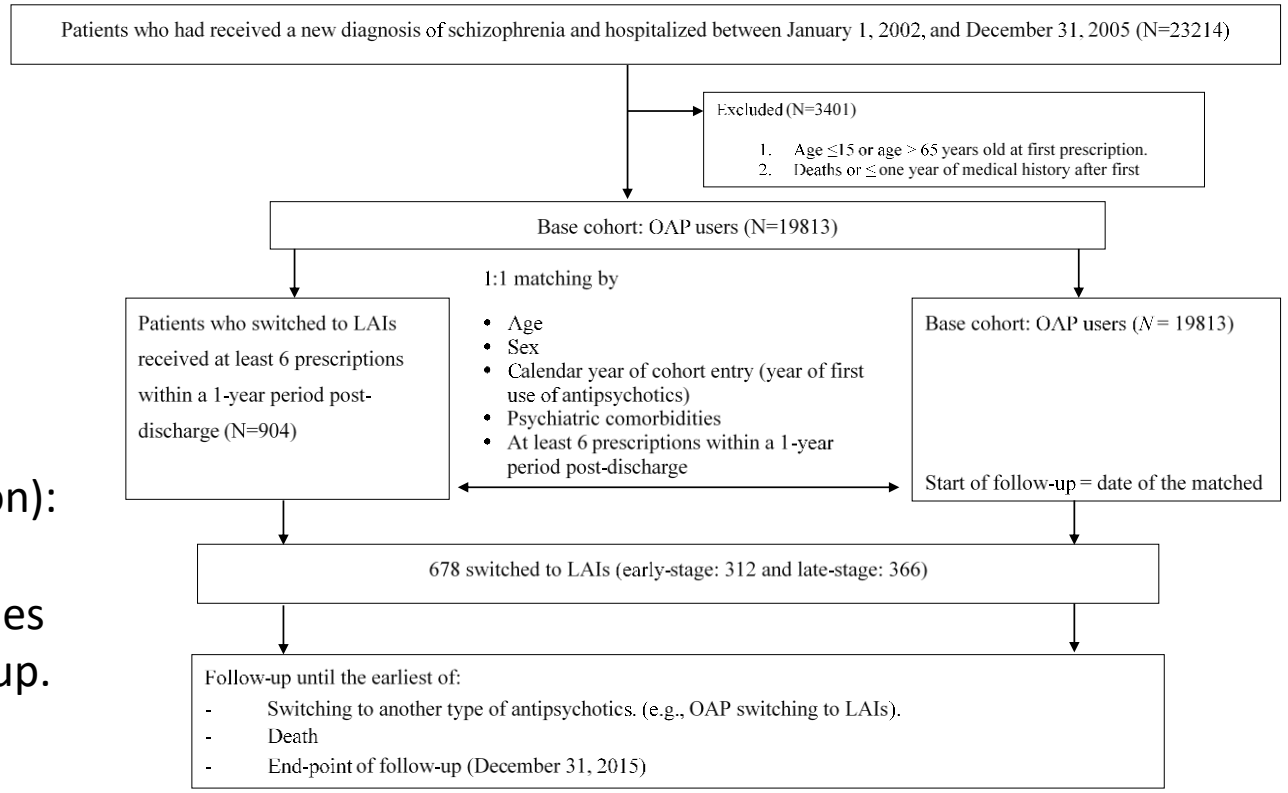


Figure 1 Flowchart showing the study cohorts.

Role of LAI in the early phase of schizophrenia

This Issue | Views 1,744 | Citations 0 | Altmetric 15

Invited Commentary | Psychiatry

July 28, 2022

Improving Outcomes in Schizophrenia—A Case for Initiation of Long-Acting Antipsychotics in Early-Phase Illness

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JAMA Netw Open. 2022;5(7):e2224172. doi:10.1001/jamanetworkopen.2022.24172

Efficacy

- Emerging evidence supports the initiation of LAIs within the early phase of illness to alter the disease trajectory.[2,3,4]

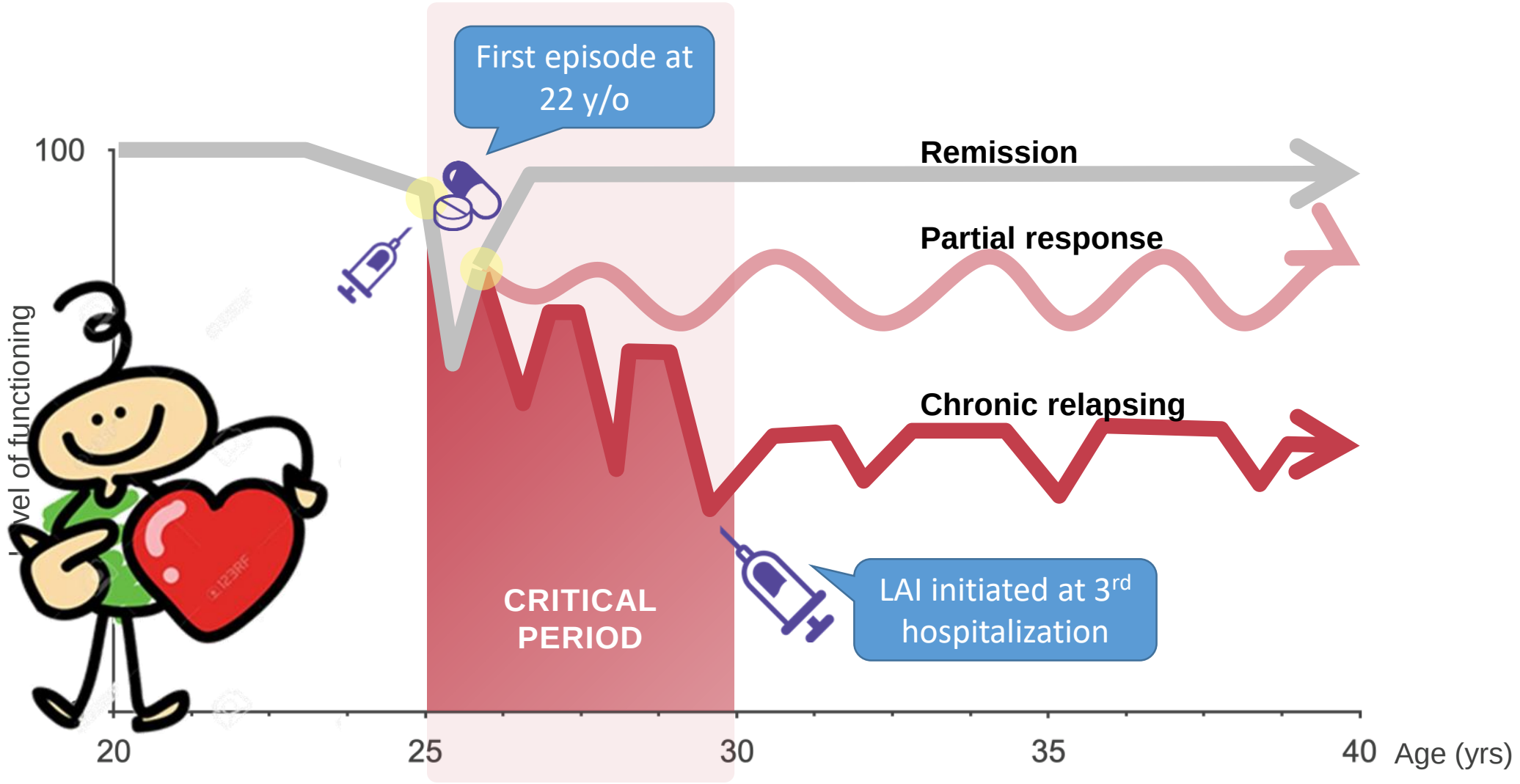
Safety

- A lower risk of EPS and fewer hospitalizations for CV diseases and for somatic disorders during LAI treatment compared with OA treatment.[2]

A critical need for research in populations with a FEP to explore the use of LAI as a **first-line treatment**, regardless of the perceived level of adherence to an OA.[1]

1. Gouse BM, Brown HE. JAMA Netw Open. 2022;5(7):e2224172.
2. Wei Y, Yan VKC, Kang W, et al. JAMA Netw Open. 2022;5(7):e2224163.
3. Kishimoto T, Hagi K, Kurokawa S, Kane JM, Correll CU. Lancet Psychiatry. 2021;8(5):387-404.
4. Huang CY, Fang SC, Shao YJ. JAMA Netw Open. 2021;4(5):e218810.

What if we had initiated LAI earlier in Mr. H case?



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Reference: 1. Lieberman JA, et al. Biol Psychiatry. 2001;50(11):884-897 2.Birchwood M et al. Br J Psychiatry 1998;172 (S 33):53-9.

報告結束
恭請指教

Bali is a good place to work, to relax, to retreat, to be treated, doing research and study……

具精神病風險狀態 / At-Risk Mental State

- 常出現在年齡介於14至35歲之間，可能會出現持續且逐漸惡化的主觀經驗及某些看得出來的行為變化。
- 此段時期的個案和對照組相比，已開始有神經生理和腦部結構變化，但詳細的神經病理機轉仍未完全明朗。
- ARMS/UHR的個案，一年內有兩成、兩年內累積到近三成被診斷為精神病
- 發病前的階段開始介入有好處，因為症狀相對較輕、個案現實感尚不致有嚴重的缺損，有機會於此時提供衛教，避免更大的壓力讓情況惡化、而教導對疾病的認識與警覺、也較容易建立良好的治療關係
- ARMS的個案一般建議要持續接受追蹤，並且觀察是否有其他共存之精神疾病，如焦慮症或者憂鬱症等
- 並非所有ARMS的病人皆會發展成為精神疾病，因此並不建議過早使用抗精神病藥物治療

首次發作精神病 / First Episode Psychosis

- 首次發作精神病為病史中第一次出現明顯的精神病症狀的時期
- 定義為有一周以上達到精神病診斷閾值、持續的妄想、幻覺、混亂言談行為等正性症狀
- FEP是包含思覺失調症、類思覺失調症或情感性思覺失調症、短暫性精神病、妄想症等不同診斷的第一次發作的統稱
- FEP有三成為first episode schizophrenia (FES)，而在一至兩年後增加至五成診斷為思覺失調症

ref1:Liu CC, Lai MC, Liu CM, Chiu YN, Hsieh MH, Hwang TJ, Chien YL, Chen WJ, Hua MS, Hsiung PC et al: Follow-up of subjects with suspected pre-psychotic state in Taiwan. Schizophr Res 2011, 126(1-3):65-70.
2. Fusar-Poli P, Cappucciati M, Rutigliano G, Heslin M, Stahl D, Brittenden Z, Caverzasi E, McGuire P, Carpenter WT: Diagnostic Stability of ICD/DSM First Episode Psychosis Diagnoses: Meta-analysis. Schizophr Bull 2016, 42(6):1395-1406.