PsychU
Improving mental health care... together

A Foundational Approach to the Treatment of Schizophrenia

Noel Gardner, MD
Adjunct Professor of Psychiatry,
University of Utah School of Medicine
Medical Director and Executive Director,
The Polizzi Clinic
Salt Lake City, UT

Michael Measom, MD
Medical Director, Assertive Community Treatment (ACT) team, Volunteers of America
Medical Director, New Roads Behavioral Health
Salt Lake City, UT

Otsuka Pharmaceutical Development and Commercialization, Inc.

Lundbeck, LLC

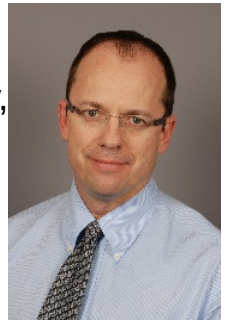
January 2016 MRC2.CORP.D.00089

Noel Gardner, MD

Position: Dr. Gardner is currently engaged in the clinical and forensic practice of psychiatry in Salt Lake City, Utah. He is also the Medical Director and Executive Director of the Polizzi Clinic, a privately-funded, non-profit free clinic that provides mental health care to severely mentally ill indigent and uninsured children, adolescents, and adults in Salt Lake City. He is Adjunct Professor of Psychiatry and Adjunct Professor of Family and Preventive Medicine at the University of Utah School of Medicine, where he served as Chief of Consultation-Liaison Psychiatry from 1988–2002.

Education: Dr. Gardner received a Master of Divinity degree from Andrews University in Berrien Springs, Michigan in 1978 and his MD from Loma Linda University in California in 1984. He completed his residency training in Psychiatry at the UCLA Neuropsychiatric Institute in 1988.

Michael Measom, MD



Position: Dr. Measom in the Medical Director of an ACT (assertive community treatment) program, a residential program for young adults and of a private practice with a focus on Addiction Psychiatry, both in Salt Lake City, UT. He is board certified in general psychiatry, addiction psychiatry and addiction medicine.

Education: Dr. Measom received a Doctorate in Medicine from University of Utah. He completed his Residency in Psychiatry at the University of Wisconsin-Madison and then completed a Fellowship in Addiction Psychiatry at The Medical University of South Carolina.

This program is paid for by Otsuka Pharmaceutical Development and Commercialization, Inc. and Lundbeck, LLC. The speakers are paid contractors of Otsuka Pharmaceutical Development and Commercialization, Inc.

PsychU Virtual Forum Rules of Engagement:

Otsuka Pharmaceutical Development and Commercialization, Inc. (OPDC) and Lundbeck, LLC. have entered into collaboration with Open Minds, LLC. to explore new ways of bringing/increasing awareness around serious mental illness.

OPDC/Lundbeck's interaction with Open Minds is through PsychU, an online, non-branded portal dedicated to providing information and resources on important disease state and care delivery topics related to mental illness. One of the methods employed for the sharing of information will be the hosting of virtual fora. Virtual fora conducted by OPDC/Lundbeck are based on the following parameters:

When conducting medical dialogue, whether by presentation or debate, OPDC/Lundbeck and/or its paid consultants aim to provide the viewer with information that is accurate, not misleading, scientifically rigorous, and does not promote OPDC/Lundbeck products.

OPDC/Lundbeck and/or their paid consultants do not expect to be able to answer every question or comment during a PsychU Virtual Forum; however, they will do their best to address important topics and themes that arise.

OPDC/Lundbeck and/or their paid consultants are not able to provide clinical advice or answer questions relating to specific patient's condition.

Otsuka and Lundbeck employees and contractors should not participate in this program (e.g., submit questions or comments) unless they have received express approval to do so from Otsuka Legal Affairs.

OPDC and Lundbeck operate in a highly regulated and scrutinized industry. Therefore, we may not be able to discuss every issue or topic that you are interested in, but we will do our best to communicate openly and directly. The lack of response to certain questions or comments should not be taken as an agreement with the view posed or an admission of any kind.

Why Are We Here?

- Because schizophrenia is a devastating disease.
- Because we must intervene earlier and more effectively.
- Because we must prevent the toxicity of recurrent relapses.
- Because we can make more effective treatment decisions.
- Because effective treatment requires optimal collaboration with our patients.

PsychU™
Improving mental health care... together

SCHIZOPHRENIA:

An Illness With Deep and Wide-ranging Impact

Schizophrenia Is Common, Affecting Millions Globally, Domestically

Prevalence* (millions) of Selected Condition by WHO Region, 2004[1]

Condition	The Americas	World
Asthma	53.3	234.9
Diabetes	46.4	220.5
Depressive disorders (unipolar)	22.7	151.2
Osteoarthritis	22.3	151.4
Epilepsy	8.6	40.0
Alzheimer and other dementias	5.0	24.2
Stroke survivors	4.8	30.7
Rheumatoid arthritis	4.6	23.7
Bipolar affective disorder	4.1	29.5
Schizophrenia	3.9	26.3
HIV infection	2.8	31.4
Parkinson's disease	1.2	5.2
Tuberculosis	0.5	13.9

*Prevalence is the proportion of a population who have (or had) a specific characteristic in a given time period—in medicine, typically an illness, a condition, or a risk factor.[2]
WHO, World Health Organization; HIV, human immunodeficiency virus.

1. Part 3. Disease incidence, prevalence and disability. In: The Global Burden of Disease. 2004 Update. World Health Organization (WHO) Web site. http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf. Accessed March 24, 2015.
2. What is prevalence? National Institute of Mental Health (NIMH) Web site. http://www.nimh.nih.gov/health/statistics/prevalence/index.shtml. Accessed March 4, 2015.

Schizophrenia Is Costly: Economic and Societal Burden

- Three categories of costs
  - **Direct costs:** payments are made for services; largest portions are inpatient and long-term care[2]
  - **Indirect costs:** lost productivity or disability[2]
  - **Intangible costs:** unquantifiable (eg, impaired QoL through pain, depression, impact on comorbidities)[2,3]
- Total economic burden in the US (2013): $155.7 billion[1]
- Failed treatment increases costs in all 3 categories[2]

QoL, quality of life.

1. Data on file. HEOR-001.
2. Knapp M, et al. *Schizophrenia Bull*. 2004;30(2):279-293.
3. Lehman AF et al; on behalf of the Work Group on Schizophrenia. *Practice Guideline for the Treatment of Patients with Schizophrenia*. Second Edition. 2010. American Psychiatric Association PsychiatryOnline® Web site. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/schizophrenia.pdf. Accessed February 4, 2015.

Schizophrenia Is Catastrophic: Onset Occurs at a Critical Point in Life and Often Causes Profound Disability

- The onset of schizophrenia occurs at critical time in development (ie, late teens and 20s), causing
  - Disruption in education, career, and family formation[1]
  - Relapse and recurrences, which are associated with progressive functional decline[2]
  - Brain atrophy, which may be associated with relapses[3]
- Schizophrenia can cause profound disability in many patients[4]
- Third most disabling condition (after quadriplegia and dementia, and ahead of paraplegia and blindness)[5]

1. Schizophrenia. WHO Web site. http://www.who.int/mental_health/management/schizophrenia/en/. Accessed February 10, 2015.
2. Ascher-Svanum H, et al. *J Clin Psychiatry*. 2006;67(3):453-460.
3. Andreasen NC, Liu D, et al. *Am J Psychiatry*. 2013;170(6):609-615.
4. About Schizophrenia. Schizophrenia and Related Disorders Alliance of America (SARDAA) Web site. http://www.sardaa.org/resources/about-schizophrenia/. Accessed February 6, 2015.
5. Ustün TB, et al. *Lancet*. 1999;354(9173):111-115.

PsychU™
Improving mental health care... together

DISCUSSION

PsychU
Improving mental health care... together

Schizophrenia: 3 Important Perspectives

Descriptive/Phenomenologic[1,2]

- Observing behavior and describing symptoms
- *DSM-5* criteria

Focus: Symptomatology

Biomedical/Pathophysiologic[3]

- Genetic and epigenetic models
- Disrupted functional connectivity models
- Aberrant signaling and neurotransmission

Focus: Proposed underlying disease mechanisms*

Social and Experiential/Existential[4]

- What living with schizophrenia means for the patient and family
- Impact† of the illness on individuals, families, and society

Focus: Patient and family experience and process

*The exact cause of schizophrenia is unknown.[3]

†Impact could include human development, social and occupational potential, and the physical, relational, emotional, financial, and spiritual well-being of individuals, family, and society.[4]

DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.

1. Phenomenology in perspective? Is there schizophrenia? Schizophrenia Bull. http://schizophreniabulletin.oxfordjournals.org/content/1/2/11.full.pdf. Accessed February 15, 2015.
2. Clinician-related Dimensions of Psychosis Symptom Severity. American Psychiatric Association Web Site. http://www.psychiatry.org/file%20library/practice/dsm/dsm-5/clinicianrateddimensionsofpsychosissymptomseverity.pdf. Accessed February 4, 2015.
3. Patel KR, et al. *P&T*. 2014;39(9):638-645.
4. Frese FJ, et al. *Schizophrenia Bull*. 2009;35(2):370-380.

Schizophrenia: Neurodevelopment Model and Trajectories of Illness

The Stages of Schizophrenia[1,*]

	Stage I/ Presymptomatic risk <12 years	Stage II/ Prepsychotic prodrome 12-18 years	Stage III/ Acute psychosis 18-24 years	Stage IV/ Chronic illness >24 years
Features	• Genetic vulnerability • Environmental exposure	• Cognitive, behavioral, and social deficits • Seeking help	• Abnormal thought behavior • Relapsing-remitting course	• Loss of function • Medical complications • Incarceration
Diagnosis	• Genetic sequence • Family history	• SIPS • Cognitive assessment • Imaging	• Clinical interview • Loss of insight	• Clinical interview • Loss of function
Disability†	• None/mild cognitive deficit	• Change in school and social function	• Acute loss of function • Acute family distress	• Chronic disability • Unemployment • Homelessness
Intervention	• Unknown	• Cognitive training? • Polyunsaturated fatty acids? • Family support?	• Medication • Psychosocial interventions	• Medication • Psychosocial interventions • Rehabilitation services

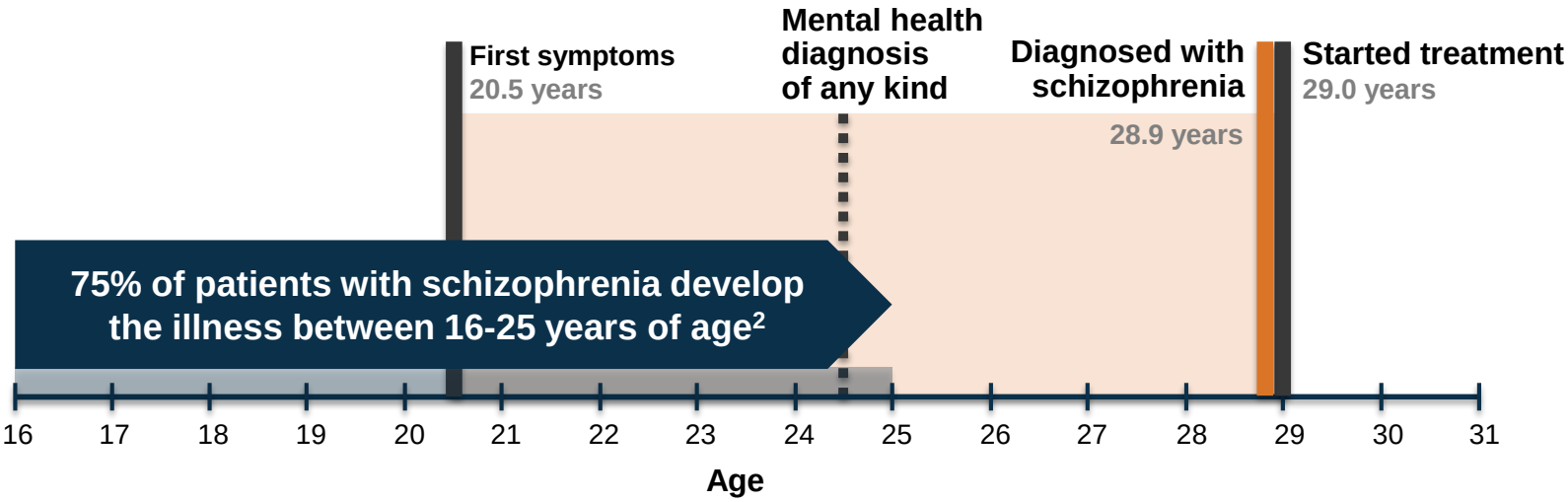
Psychosis of late adolescence may be viewed not as the onset, but rather the late stage of the disorder.[1]

*Note: As the syndrome of schizophrenia is likely heterogeneous, this course of illness cannot be applied to all patients with schizophrenia.[2]
†The PAS is a rating scale, developed for use in a research setting, and can be used to evaluate the degree of achievement of developmental goals at each of several periods of a patient's life prior to the onset of schizophrenia. The PAS may be useful in identifying patients likely to become chronically hospitalized or at high risk for readmission, and may also predict patients with brain abnormalities on a CT scan.[3]
CT, computerized tomography; PAS, Premorbid Adjustment Scale; SIPS, Structured Interview for Prodromal Syndromes.

1. Insel T. *Nature*. 2010;468:187-193.
2. Lehman AF et al; on behalf of the Work Group on Schizophrenia. Practice Guideline for the Treatment of Patients with Schizophrenia. Second Edition. 2010. American Psychiatric Association PsychiatryOnline® Web site. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/schizophrenia.pdf. Accessed February 4, 2015.
3. Cannon-Spoor HE, et al. *Schizophr Bull*. 1982;8(3):470-484.

Schizophrenia From the Perspective of Patients and their Families[1]

There is an average delay of 8.5 years between the onset of symptoms and the beginning of treatment for schizophrenia[1]



Based on a 2008 survey of 250 patients with schizophrenia and 250 caregivers conducted by Harris Interactive for NAMI.[1]

NAMI, National Alliance on Mental Health.

1. Schizophrenia: Public Attitudes, Personal Needs. Views from People Living with Schizophrenia, Caregivers, and the General Public Analysis and Recommendations. June 10, 2008. NAMI, The National Alliance on Mental Illness Web site. http://www2.nami.org/SchizophreniaSurvey/SchizeExecSummary.pdf. Accessed February 8, 2015.
2. About Schizophrenia. Schizophrenia and Related Disorders Alliance of America (SARDAA) Web site. http://www.sardaa.org/resources/about-schizophrenia/. Accessed February 6, 2015.

Treatment of Schizophrenia: Service Priorities of Patients, Providers, and Family Members

- The mean rankings given to the 9 services by patients with schizophrenia/consumers and caregivers/family members were virtually identical
- Providers ranked programs that teach self-care skills as less important than did other stakeholders, whereas they ranked case management services and psychoeducation programs as more important

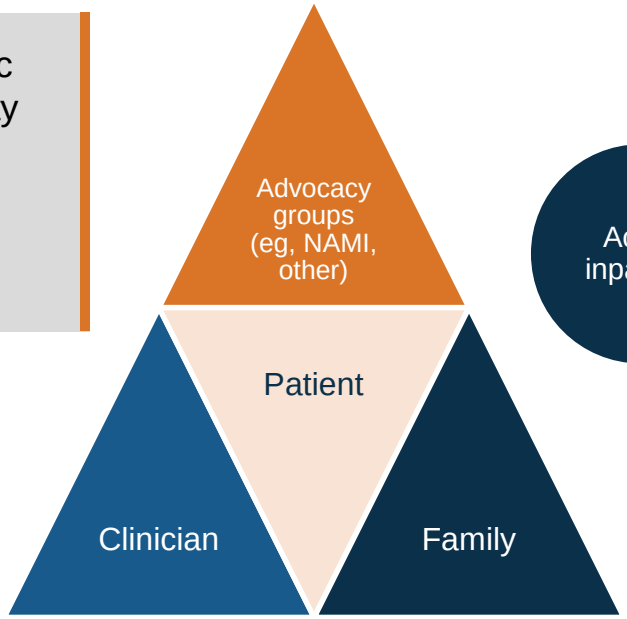
Service
Regular appointments with a doctor who prescribes and manages your medications
Classes or information about your mental disorder, its symptoms, and treatment
Information or education for your family members about your mental disorder, its symptoms, and treatment
Programs or classes to help improve your skills in taking care of yourself, such as managing money, shopping, and keeping a schedule
Groups or programs that help you improve your social life or family life
Programs to help you find and keep a job
Regular appointments with a doctor who manages your physical health problems
Programs or groups to help you cut down on or stop drinking alcohol or using drugs
A case manager to help you get the benefits and services you need and help you make appointments and keep them

Participants are instructed to put the 9 services (printed on cards) in order of importance to them, starting with the most important and working down to the least important. Once the domains had been ranked, participants are asked to state the magnitude of the differences in importance between the domains (magnitude estimation).

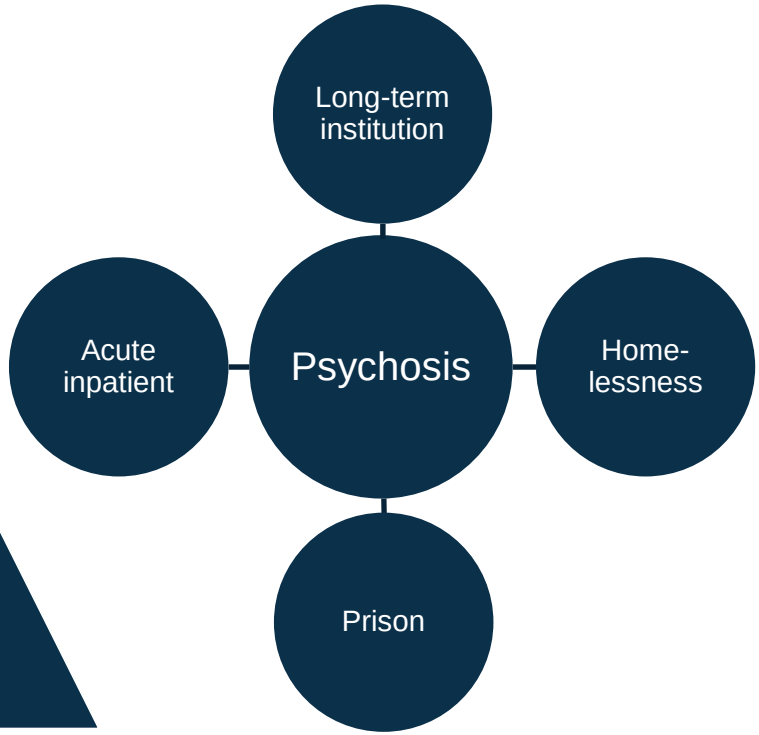
1. Fischer EP, et al. Priorities of consumers, providers, and family members in the treatment of schizophrenia. *Psychiat Serv*. 2002;53(6):724-729.

Potentially Successful Treatment Is Patient-centric

Optimal psychopharmacologic treatment depends on a quality therapeutic alliance, and a quality therapeutic alliance depends on optimal pharmacologic treatment.[1,2]



Successful Treatment[2]



Failed Treatment[3]

NAMI, National Alliance on Mental Illness.

1. Rossi G, et al. *BMC Psychiatry*. 2012;12:122.
2. Lehman AF et al; on behalf of the Work Group on Schizophrenia. Practice Guideline for the Treatment of Patients with Schizophrenia. Second Edition. 2010. American Psychiatric Association PsychiatryOnline® Web site. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/schizophrenia.pdf. Accessed February 4, 2015.
3. Insel T. *Nature*. 2010;468:187-193.

PsychU™
Improving mental health care... together

DISCUSSION

PsychU
Improving mental health care... together

A Large Majority of Patients in a First Episode of Psychosis Respond to Antipsychotic Medications—But They Also Relapse

87%

OF YOUNG PEOPLE

IN A FIRST EPISODE OF PSYCHOSIS WILL RESPOND TO ANTIPSYCHOTIC MEDICATION[1,*,†]

FOR MANY FIRST-EPISODE PATIENTS, TREATMENT CONSISTS OF HOSPITALIZATION AND MEDICATION[2]

AFTER INITIAL ONSET OF **SCHIZOPHRENIA,**

>80%

OF PATIENTS IN A STUDY (N=104)

EXPERIENCED THEIR SECOND PSYCHOTIC EPISODE WITHIN

5 YEARS[3]

PATIENTS WHO RECOVERED FROM A

1ST RELAPSE

ALSO HAD HIGH

2ND AND 3RD

RATES OF RELAPSE[3]

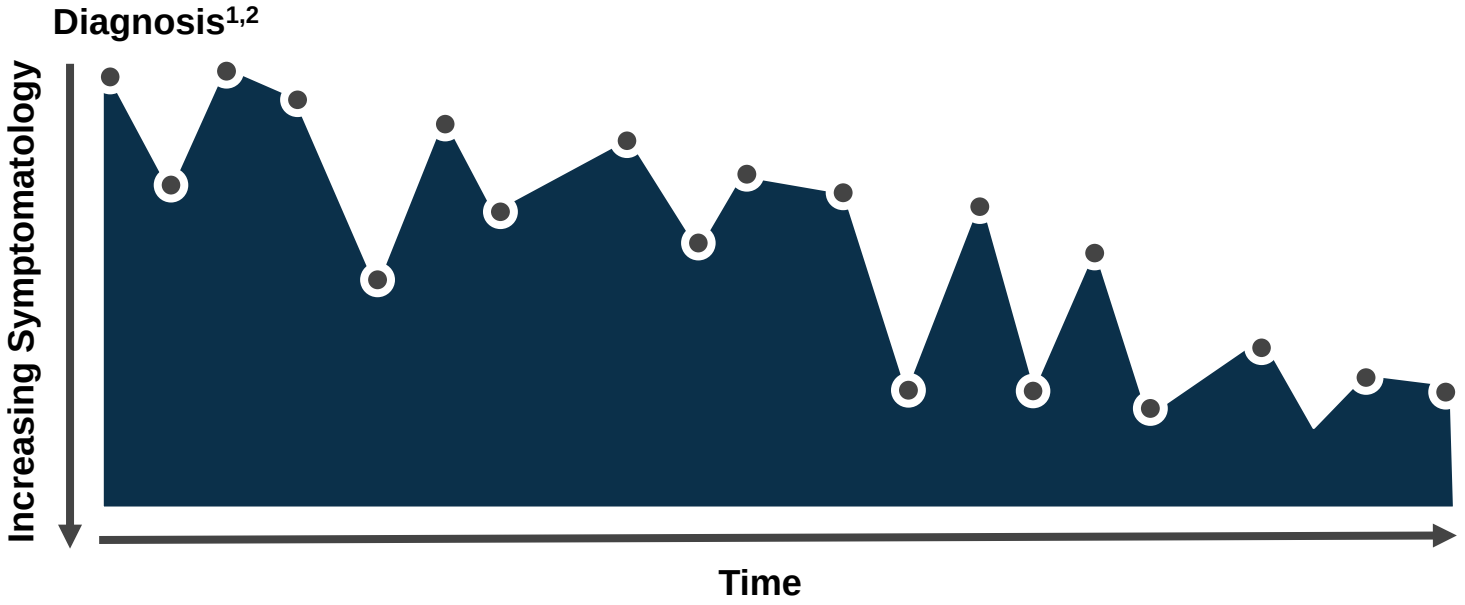
*Data from a study of 118 patients.[1]

†Treatment response was operationally defined as a CGI rating of "much" or "very much" improved and a rating of 3 (mild) or less on all of the following SADS-C+ PDI items: severity of delusions, severity of hallucinations, impaired understandability, derailment, illogical thinking, and bizarre behavior. To be classified as responders, patients had to sustain this level of improvement for 8 consecutive weeks; treatment response was dated from the time response criteria were first met, ie, the beginning of this 8-week period.[1]

CGI, Clinical Global Impression; SADS-C+ PDI, Schedule for Affective Disorders and Schizophrenia Change Version with Psychosis and Disorganization Items rating scale.

1. Robinson DG, et al. *Am J Psychiatry*. 1999;156:544-549.
2. Lehman AF et al; on behalf of the Work Group on Schizophrenia. Practice Guideline for the Treatment of Patients with Schizophrenia. Second Edition. 2010. American Psychiatric Association PsychiatryOnline® Web site. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/schizophrenia.pdf. Accessed February 4, 2015.
3. Robinson D, et al. *Arch Gen Psychiatry*. 1999;56(3):241-247.

The Majority of Patients With Schizophrenia Experience Recurring Relapses



Note: This is a theoretical pattern only and is not based on an actual patient.

1. Harvey PD, Davidson M. In: Davis KL et al., eds. *Neuropsychopharmacology: The Fifth Generation of Progress.* Philadelphia, PA: Lippincott Williams & Wilkins; 2002:641-655.
2. Lieberman JA, et al. *Biol Psychiatry*. 2001;50(11):884-897.

PsychU™
Improving mental health care... together

SCHIZOPHRENIA:

Preventing Relapse and Avoiding Medication Gaps

PsychU
Improving mental health care... together

Foundational Treatment: Early, Uninterrupted, and Continuous Treatment

WHAT'S THE SINGLE LARGEST PREDICTOR OF RELAPSE RISK IN SCHIZOPHRENIA?

PATIENTS DISCONTINUING THEIR MEDICATION

WHAT'S THE MOST IMPORTANT MODIFIABLE RISK FACTOR IN THE DEVELOPMENT OF TREATMENT RESISTANCE IN SCHIZOPHRENIA?

PROLONGED AND RECURRENT RELAPSE

1. Kane JM. J Clin Psychiatry. 2006;67(suppl 5):9-14.

Relapse in Schizophrenia: Some Potential Causes

- Possible medication-related causes of relapse in schizophrenia

Patient no longer responds to medication

Patient stops taking medication

1. Lehman AF, et al. American Psychiatric Association. *Practice Guideline for the Treatment of Patients With Schizophrenia*. 2nd ed. 2004:1-184.

Patient Nonadherence: Potential Causes

- There are a variety of reasons why a patient with schizophrenia may become nonadherent, including

Poor insight about their illness[1,2]

Lack of support from their family and friends/ family and caregiver conflict[1,5]

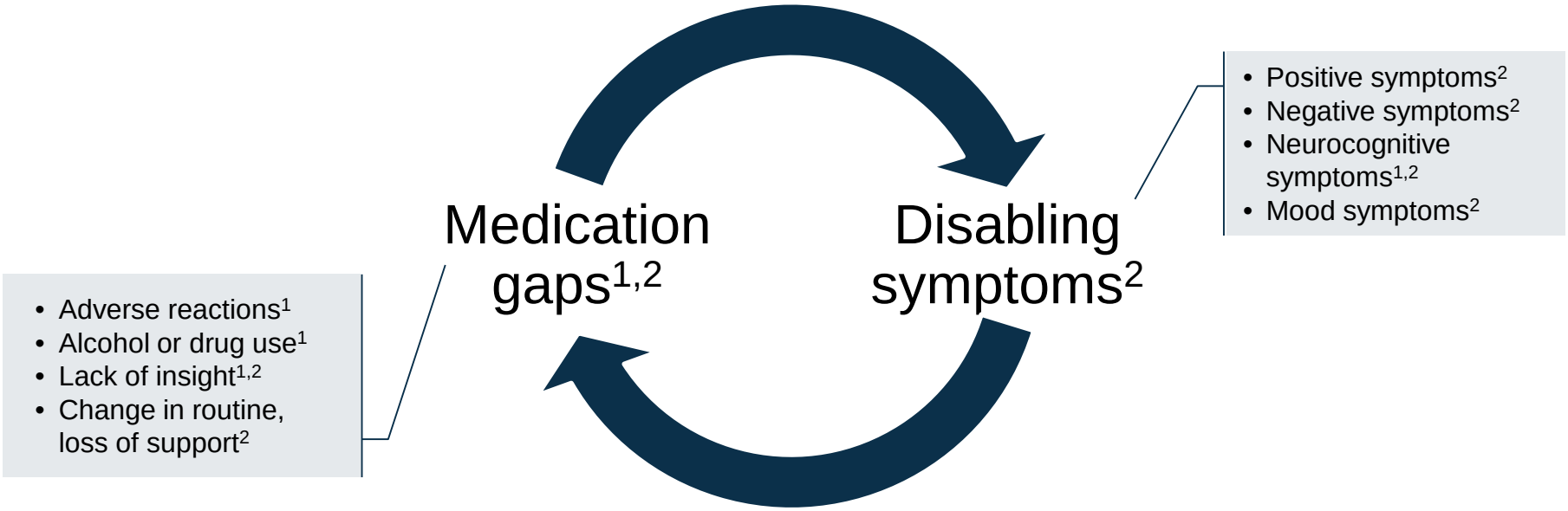
Treatment-related adverse reactions[3]

Stigma[1]

Complicated medication regimens[1,4]

1. Hudson TJ, et al. *J Clin Psychiatry*. 2004;65(2):211-216.
2. Lacro JP, et al. *J Clin Psychiatry*. 2002;63(10):892-909.
3. Perkins DO. *J Clin Psychiatry*. 2002;63(12):1121-1128.
4. Pfeiffer PN, et al. *Psychiatr Serv*. 2008;59(10):1207-1210.
5. Kane JM, et al. *J Clin Epi*. 2013;66:S37-S41. 6.

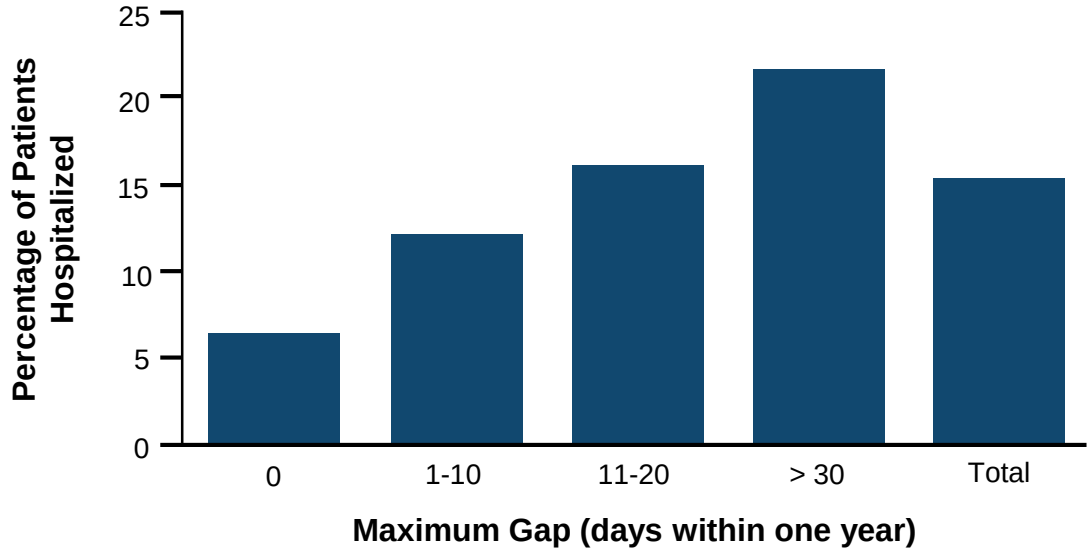
Schizophrenia:
Disease Pathology Increases Medication Gap Likelihood



1. Zhornitsky S, Stip E. *Schizophr Res Treatment*. 2012:407171.
2. Higashi K, et al. *Ther Adv Psychopharmacol*. 2013;3(4):200-218.

Treatment Gaps: What Happens When Patients Miss Doses?

Percentage of Patients With Schizophrenia Who Were Rehospitalized, by Maximum Gap in Therapy[1]



"For a person with schizophrenia, being without antipsychotic medication for as few as ten days over the course of a year has a profound effect on the likelihood of hospitalization."[2]

All pairwise comparisons were significant at $P<0.005$.
Data from a retrospective pharmacy refill and medical claims review of 4325 outpatients with schizophrenia.

1. Weiden PJ, et al. *Psychiatric Services* 2004;55(8): 888-891.
2. Keith SJ. *Psychiatric Services*. 2004;55(8):857.

Patient Nonadherence: Potential Effects

Compared with adherent patients with schizophrenia, nonadherent patients were

>10 TIMES
MORE LIKELY TO HAVE A PSYCHOTIC RELAPSE[1,*]

2.4 TIMES
MORE LIKELY TO BE HOSPITALIZED,
AND ONCE HOSPITALIZED, HAD LONGER LENGTH OF STAYS[3,‡]

85% OF PHYSICIANS IDENTIFIED **NONADHERENCE** AS THE MAIN CAUSE OF RELAPSE AMONG THEIR PATIENTS[2,†]

Adherence issues, including treatment discontinuation and partial adherence, appear to be common during the early[§] stages of schizophrenia and have important effects on course and outcome.[4]

*Study included 50 Norwegian patients with recent onset schizophrenia, schizoaffective or schizophreniform disorders. Patients were clinically stable at study entry and had <2 years duration of psychotic symptoms.[1]
[†]Results of a survey of 330 Spanish psychiatrists on their perceptions of adherence behavior among their patients.[2,4]
[‡]Cohort study which linked pharmacy and utilization data for 67,709 veterans with schizophrenia.[3]
[§]Early has typically been defined as 2-5 years following diagnosis.[5-7]

1. Morken G, et al. *BMC Psychiatry*. 2008, 8:32.
2. Giner J, et al. *Eur Neuropsychopharmacol*. 2004;14(suppl 3):s266.
3. Valenstein M, et al. *Med Care*. 2002;40(8):630-639.
4. Masand PS, et al. *Prim Care Companion J Clin Psychiatry*. 2009;11(4):147-154.
5. Heres S, et al. *European Psychiatry*. 2014;29(suppl 2):1409-1413.
6. Harvey PD, Davidson M. Schizophrenia: course over the lifetime. In: *Neuropsychopharmacology: The Fifth Generation of Progress*. Eds. Davis KL, Charney D, Coyle JT, Nemeroff. C Lippincott, Williams and Wilkins: Philadelphia, 2002.
7. Nicholl D, et al. *Curr Med Res Opin*. 2010;26(4):943-955.

PsychU™
Improving mental health care... together

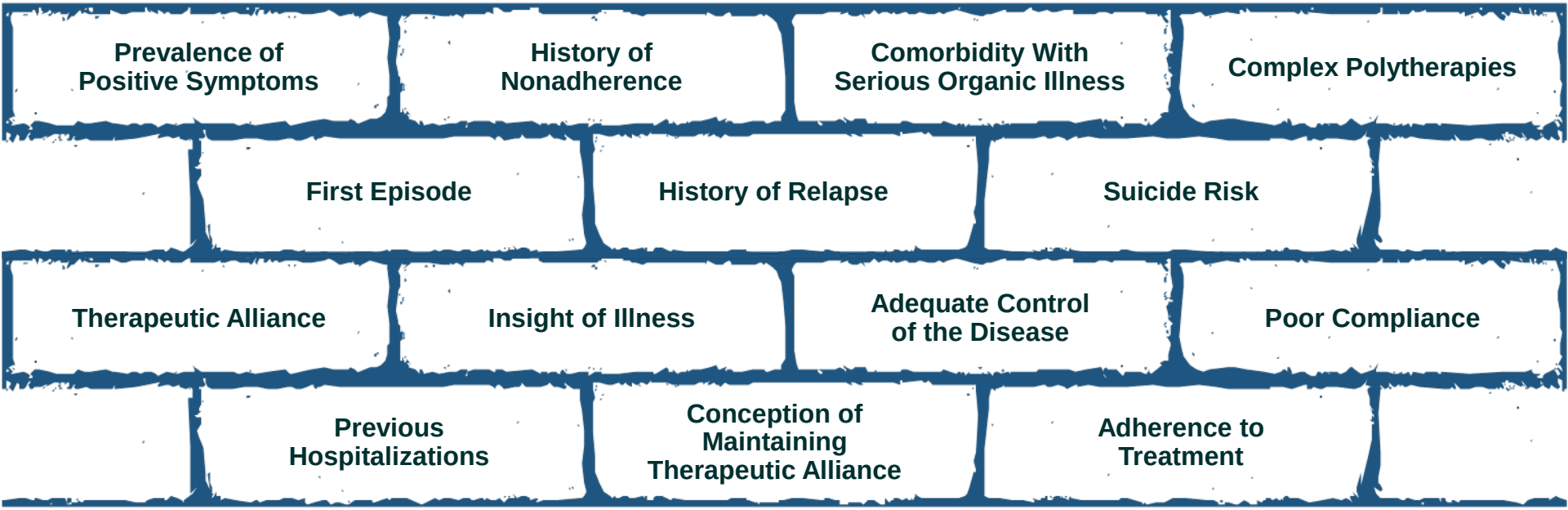
DISCUSSION

PsychU
Improving mental health care... together

AIMING HIGH:

What Does Optimal Schizophrenia Treatment Look Like?

Schizophrenia Treatment Decisions: Numerous Factors For Consideration by Prescribing Clinicians, Patients, and Caregivers



1. Rossi G, et al. *BMC Psychiatry*. 2012;12:122. http://www.biomedcentral.com/1471-244X/12/122.

Schizophrenia: Treatment Considerations

Therapeutic Class	Important Considerations
FGAs (typical antipsychotics)	• Have fewer metabolic adverse reactions (eg, weight gain, hyperlipidemia, and diabetes mellitus) than SGAs • Are associated with more EPS vs SGAs
SGAs (atypical antipsychotics)	• Usually preferred over FGAs because they are associated with fewer EPS • Have metabolic adverse reactions (eg, weight gain, hyperlipidemia, and diabetes mellitus), which may contribute to CV mortality observed in patients with schizophrenia
LAI antipsychotic agents	• Prior to starting an LAI, a brief trial should be conducted with the oral counterpart of the LAI to determine tolerability
Augmentation therapy (with ECT or a mood stabilizer)	• Used only in patients with an inadequate response to prior therapy • Augmentation agents are rarely effective for schizophrenia symptoms when given individually • Responders usually improve rapidly • If symptoms are not improved, agent should be discontinued
Combination therapy (2 antipsychotics)	• Used only in patients with an inadequate response to prior therapy • Concurrent administration of an FGA + SGA or 2 different SGAs • May increase risk of serious adverse reactions • Also may increase risk of drug interactions, nonadherence, and medication errors

CV, cardiovascular; ECT, electroconvulsive therapy; EPS, extrapyramidal symptoms; FGAs, first-generation antipsychotics; LAI, long-acting injectableS; SGAs, second-generation antipsychotics.

1. Patel KR, et al. *P&T.* 2014;39(9):638-645.

Oral Formulations: Potential Advantages and Disadvantages

POTENTIAL ADVANTAGES	POTENTIAL DISADVANTAGES
Specific Patient Attributes	**Specific Patient Attributes**
• Ease of administration [1] • Flexibility[2] • Short duration of action/side effects likely to cease with treatment termination[2-5]	• Daily administration; patients need to make the daily decision to take their medication for schizophrenia[10] • Patients need to remember to take a pill daily for schizophrenia[6] • Higher potential for medication to be taken incorrectly or misused[2,6]
Fewer Logistical Issues for Patient and/or Clinician	**Clinical Insight and Established Touchpoints Are Reduced**
• Reduced requirements for patients to get to regular appointments to receive their medications[1,2] • For the prescribing clinician, no infrastructure is needed for medication delivery or removal[6]	• Adherence status is not known[6] • Little to no knowledge of when an antipsychotic dose is missed; attempts at appropriate intervention(s) are hindered/more difficult or can't be made at all[8] • Inability to distinguish a relapse due to inadequate response to pharmacotherapy from a relapse due to other factors[3,6,11] • More frequent dosing is required[6,10]
Efficacy and Other Related Parameters	**Pharmacokinetic Challenges**
• Effective/steady-state plasma concentrations are achieved more quickly[2,7,8] • Extensive clinical and safety data history[9] • Availability of numerous generic options[9]	• Influenced by first-pass metabolism[6,12] • Fluctuations in peak and overall plasma levels[6] • Short duration of action[6,13]

Not all treatments or medications will carry these disadvantages.

1. Long-acting Injectable Antipsychotics Fact Sheet. National Alliance on Mental Illness (NAMI). May 2013. http://www2.nami.org/factsheets/LAI_factsheet.pdf. Accessed February 12, 2014.
2. Burton N. *Psychiatry (Second edition)*. Wiley-Blackwell; 2010.
3. Agid O, et al. *Exp Opin Pharmacother*. 2010;11(13):2301-2307.
4. Kane JM, et al. Eur Neuropsychopharmacol. 1998;8(1):55-66.
5. Nasrallah HA. Acta Psychiatr Scand. 20007;115(4):260-267.
6. Bera RB. *J Clin Psychiatry*. 2014;75(suppl 2):30-33.
7. Citrome L. *Expert Opin Pharmacother*. 2012;13:1545-1573.
8. Brissos S, et al. *Ther Adv Psychopharmacol*. 2014;4:198-219.
9. Albright B. *Behav Healthcare*. 2011;1-4.
10. Kane JM. The Potential Advantages of Long-Acting Injectable Antipsychotics. Psychiatry Advisor. August 14, 2014. http://www.psychiatryadvisor.com/the-potential-advantages-of-long-acting-injectable-antipsychotics/article/366232/. Accessed February 16, 2015.
11. Velligan DI, et al. *J Clin Psychiatry*. 2009;70(suppl 4):1-46.
12. Zhornitsky S, Stip E. *Schizophr Res Treat*. 2012;2012: Article ID: 407171.
13. Patel MX, David AS. *Adv Psychiatr Treat*. 2005;11(3):203-2135.

LAIs: Potential Advantages and Disadvantages

POTENTIAL ADVANTAGES	POTENTIAL DISADVANTAGES
Specific Patient Attributes	**Specific Patient Attributes**
• Patients do not need to make the daily decision to take their medication for schizophrenia[1] • Patients no longer needs to remember to take a pill daily for schizophrenia[2] • Lower potential for medication to be taken incorrectly[2]	• The idea of getting any kind of injection at the doctor's office may bring up hesitant feelings[7] – Some patients may feel it takes away their rights – Others may perceive that receiving an injection is physically uncomfortable • Pain at injection site[3] • Side effects may persist beyond treatment termination[4,8,9]
Opportunity for Clinical Insight and Established Touchpoints	**Logistical Issues for Patient and/or Clinician**
• Adherence status is known[2] • Knowledge of when an antipsychotic dose is missed, which allows for an attempt at appropriate intervention(s)[3] • Ability to distinguish a relapse due to inadequate response to pharmacotherapy from a relapse due to other factors[2,4,5] • Less frequent dosing is required[1]	• Some patients may have difficulty getting to regular appointments to receive their medications by injection[7] • Lack of infrastructure for the delivery and removal of injectables[2]
Pharmacokinetic Profile	**Dosing-Related Challenges**
• Avoidance of first-pass metabolism[2] • Fluctuations in peak and overall plasma levels are minimized[2] • Uninterrupted medication coverage for up to 30 days at a time[2,6]	• Oral antipsychotic supplementation may be needed, which adds to the complexity of the titration process[3] • Requires longer time to achieve steady-state plasma concentrations[3] • Slow dose titration[3]

Not all treatments or medications will carry these disadvantages.
LAIs, long acting injectables.

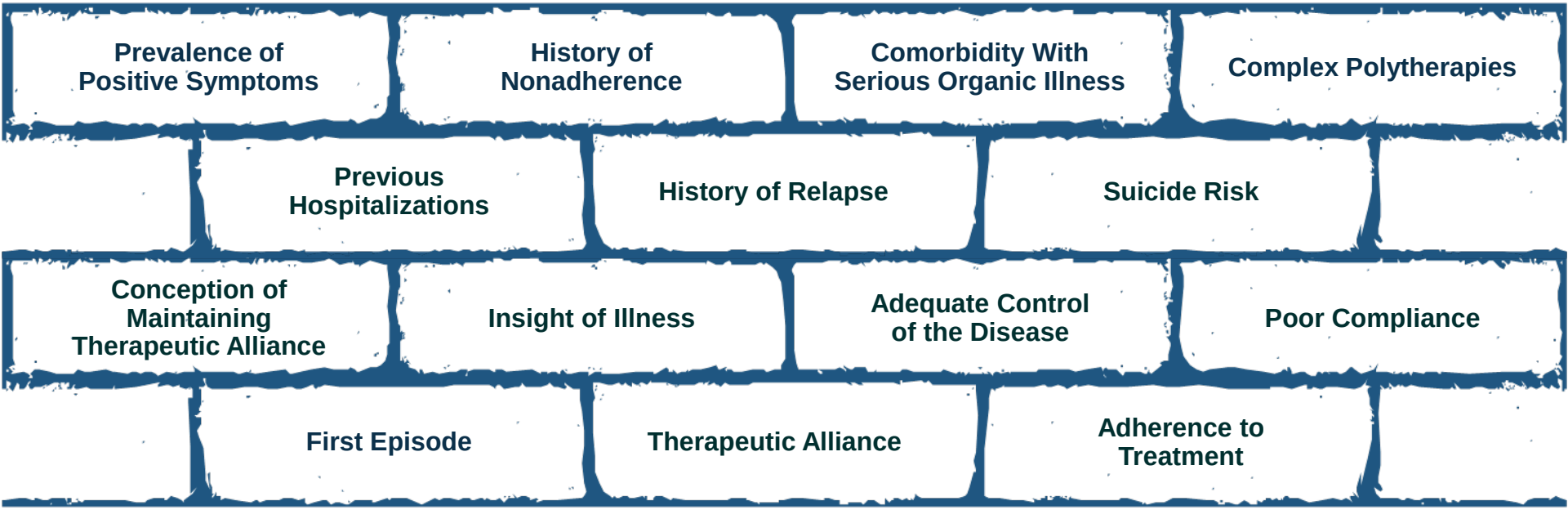
1. Kane JM. The Potential Advantages of Long-Acting Injectable Antipsychotics. Psychiatry Advisor. August 14, 2014. http://www.psychiatryadvisor.com/the-potential-advantages-of-long-acting-injectable-antipsychotics/article/366232/. Accessed February 16, 2015.
2. Bera RB. *J Clin Psychiatry*. 2014;75(suppl 2):30-33.
3. Brissos S, et al. *Ther Adv Psychopharmacol*. 2014;4:198-219.
4. Agid O, et al. *Exp Opin Pharmacother*. 2010;11(13):2301-2307.
5. Velligan DI, et al. *J Clin Psychiatry*. 2009;70(suppl 4):1-46.
6. Patel MX, David AS. *Adv Psychiatr Treat*. 2005;11(3):203-2135.
7. Long-acting Injectable Antipsychotics Fact Sheet. National Alliance on Mental Illness (NAMI). May 2013. http://www2.nami.org/factsheets/LAI_factsheet.pdf. Accessed February 12, 2014.
8. Kane JM, et al. *Eur Neuropsychopharmacol*. 1998;8(1):55-66.
9. Nasrallah HA. *Acta Psychiatr Scand*. 20007;115(4):260-267.

PsychU™
Improving mental health care... together

DISCUSSION

PsychU
Improving mental health care... together

Schizophrenia Treatment Decisions: Numerous Factors Require Prioritizing an Optimal Foundation from the First Episode



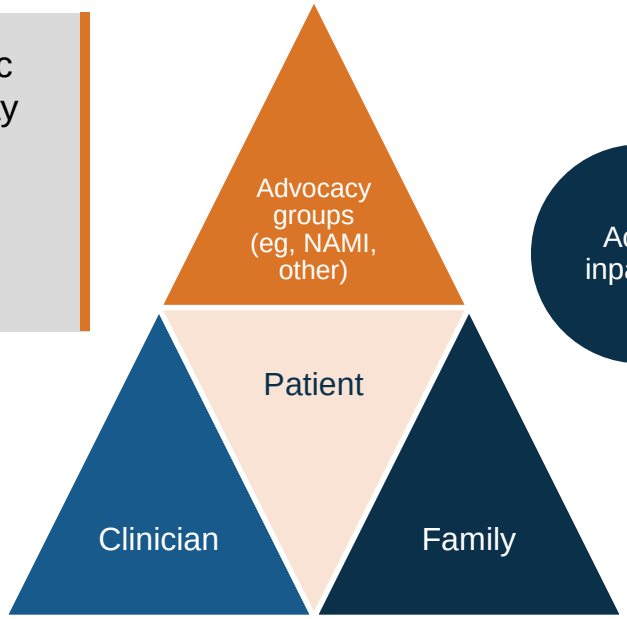
1. Rossi G, et al. *BMC Psychiatry*. 2012;12:122. http://www.biomedcentral.com/1471-244X/12/122.

PsychU™
Improving mental health care... together

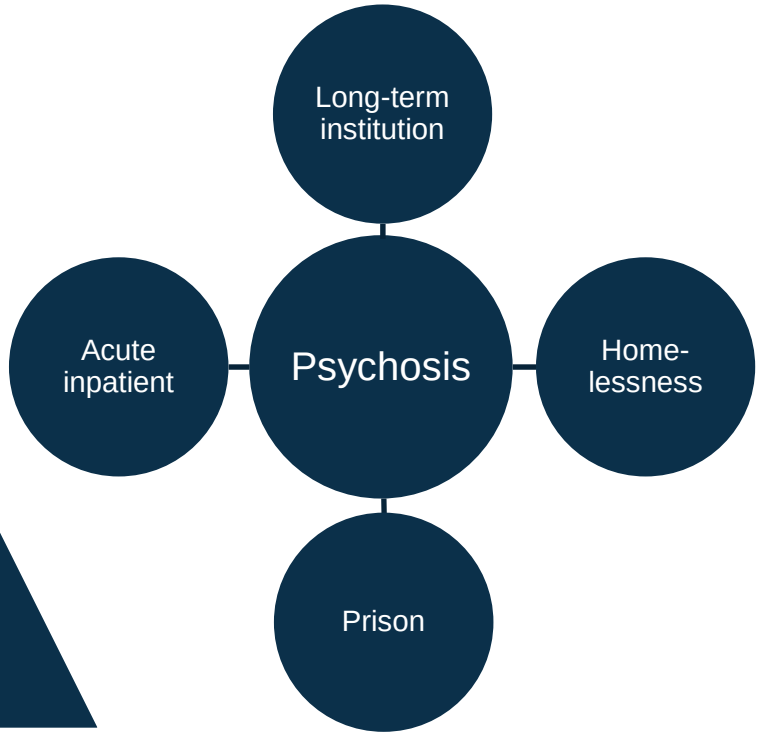
DISCUSSION

Potentially Successful Treatment Is Patient-centric

Optimal psychopharmacologic treatment depends on a quality therapeutic alliance, and a quality therapeutic alliance depends on optimal pharmacologic treatment.[1,2]



Successful Treatment[2]



Failed Treatment[3]

1. Rossi G, et al. *BMC Psy*chiatry. 2012;12:122.
2. Lehman AF et al; on behalf of the Work Group on Schizophrenia. Practice Guideline for the Treatment of Patients with Schizophrenia. Second Edition. 2010. American Psychiatric Association PsychiatryOnline® Web site. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/schizophrenia.pdf. Accessed February 4, 2015.
3. Insel T. *Nature*. 2010;468:187-193.

Summary: Minimizing Relapse Risk In Schizophrenia With Maintenance Medication

- Most patients with schizophrenia have a very high risk of relapse in the absence of antipsychotic treatment
- HCPs should discuss the risks of relapse versus the long-term potential risks of maintenance treatment with the prescribed antipsychotic with the patient
- Educating the patient and family members about the importance of avoiding gaps in treatment, advising them on the importance of working with their provider on finding medication they can commit to without interruptions, and encouraging the patient to attend outpatient visits on a regular basis are warranted.
- Indefinite maintenance antipsychotic medication is recommended for patients who have had multiple prior episodes or 2 episodes within 5 years

HCPs, healthcare professionals.

1. Lehman AF et al; on behalf of the Work Group on Schizophrenia. Practice Guideline for the Treatment of Patients with Schizophrenia. Second Edition. 2010. American Psychiatric Association PsychiatryOnline® Web site. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/schizophrenia.pdf. Accessed February 4, 2015.

Key Takeaways

PsychU™
Improving mental health care... together

QUESTIONS

PsychU
Improving mental health care... together

PsychU™
Improving mental health care... together

CLOSING