

Quick Guide to NAVIGATE Psychopharmacological Treatment

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READ THIS FIRST

Notes about this guide

Thank you for your interest in the NAVIGATE medication treatment model!

What is this guide and how it can help you

- There is a detailed NAVIGATE psychopharmacological treatment manual developed for the RAISE-ETP NIMH-funded study (available at <http://navigateconsultants.org/>)
- The original NAVIGATE psychopharmacological treatment manual is very detailed and was designed to be a reference resource
- RAISE-ETP had a computer decision support program that provided prescribers with much of the information needed to apply NAVIGATE principles of treatment
- After the RAISE-ETP study ended, the computer system was no longer available
- This quick guide is designed to fill partially the knowledge gap from the loss of the NAVIGATE computer system
- This guide also includes new treatment information we learned from the completed RAISE-ETP study and other studies completed after the writing of the NAVIGATE psychopharmacological treatment manual in 2010.
- This guide summarizes the key clinical points for NAVIGATE prescribers
- The guide uses a bullet format as much as possible to make information easily accessible to busy clinicians

- If you are new to NAVIGATE treatment, the guide provides you a quick way to learn the core principles of NAVIGATE treatment
- If you are an experienced NAVIGATE prescriber, this guide can be used as a first-line reference resource
- The NAVIGATE psychopharmacological treatment manual remains the best source for detailed presentation of NAVIGATE treatment principles and the scientific background for NAVIGATE treatment recommendations
- Information about the use of ESPRITO-One and the assessments that will be collected in ESPRITO-One will be added to this guide in the near future

NAVIGATE VERSIONS: This manual covers two versions of NAVIGATE. The first version (labeled standard NAVIGATE in this manual) is the version developed in 2010 for the RAISE-ETP study and subsequently updated to incorporate research findings that have been reported since 2010 and the experiences of clinics providing NAVIGATE outside a research context. The second version of NAVIGATE (Enhanced NAVIGATE) is used by clinics in the ESPRITO network and includes standard NAVIGATE treatment with some additional features. When NAVIGATE without any further qualification is mentioned in this manual, the text is applicable to both versions of NAVIGATE. In the few areas (primarily assessment methods) that differ between the versions, the text will specify either standard NAVIGATE or Enhanced NAVIGATE.

Acknowledgments: The original NAVIGATE medication treatment model was developed by the NAVIGATE Psychopharmacological Treatment Committee. The Committee was chaired by Delbert G. Robinson, M.D. Christoph U. Correll, M.D., Ben Kurian, M.D., Alexander L. Miller, M.D., Ronny Pipes, M.A. and Nina R. Schooler, Ph.D. contributed to the scientific content of the Manual. Patricia Marcy, BSN and Cristina Gomes Gonzalez, CCRP provided administrative support.

A Guide to Finding the Information You Need

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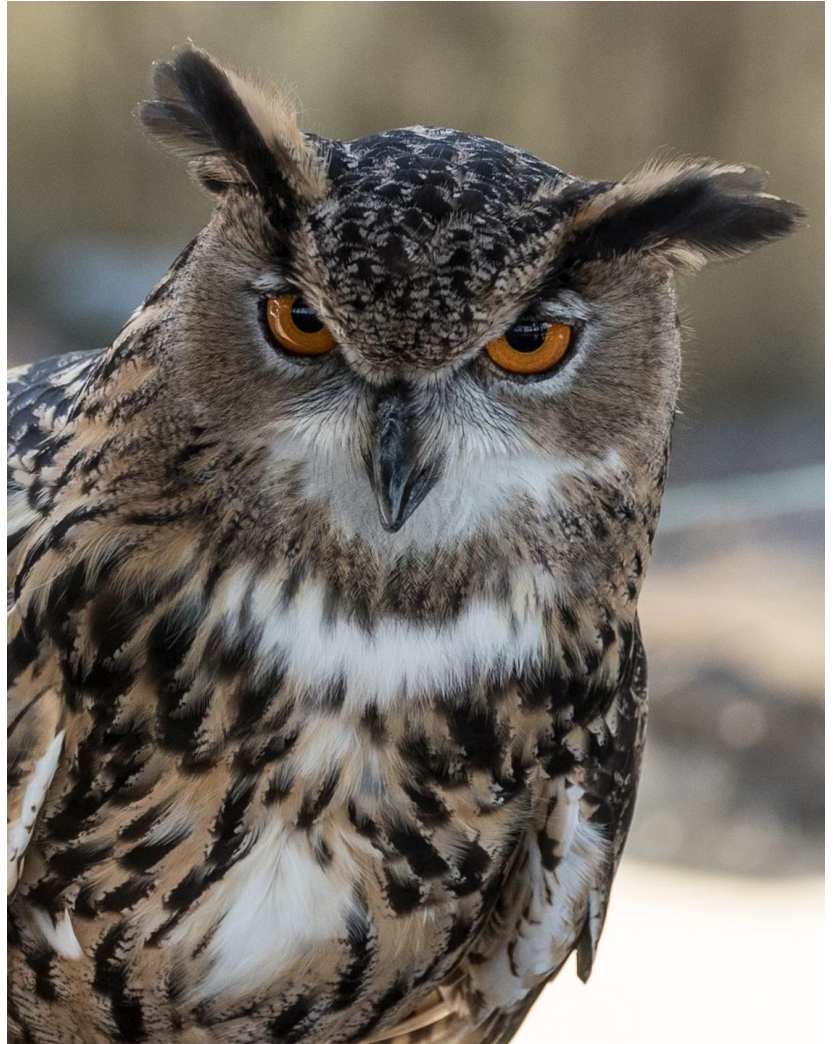
Overview

A. “The Cheat Sheet”

On this page and the next are the overarching principles of NAVIGATE medication treatment. The remaining parts of the manual describe how these principles were developed and how to implement them in clinical practice.

Overall Advice:

- ✓ ALWAYS BE VIGILENT
- ✓ Carefully Monitor for Symptoms, Side Effects and Adherence



B. NAVIGATE Medication Treatment Summary

- Use a measurement-based care approach utilizing the patient self-ratings and your ratings to get the information needed to make the best decisions within a shared decision making process
- Aim for symptom remission, not just improvement
- Choose an antipsychotic with a favorable side effect profile and give for 2 to 4 months, either as an oral or a long acting formulation
- Use doses around half of what is used with multi-episode schizophrenia
- Monitor side effects closely—you will see high rates of side effects
- Monitor closely for medical co-morbidities and follow through with needed medical referrals
- If two different antipsychotics do not work, use clozapine
- Prepare for non-adherence

I. What is NAVIGATE Treatment?

- NAVIGATE is a model of treatment for individuals with a first psychotic episode of a schizophrenia-spectrum disorder
- It is a team based approach
- The team approach spreads the effort to care for the individuals and their families
- First episode individuals and their families often have a lot of issues
- With the team approach, no individual clinician has to deal with all the problems
- Team members bolster each other's efforts
 - E.g. work or education support services can help with maintaining individual engagement

A. NAVIGATE Components

- Medication Treatment and Medical Monitoring
 - Your Role
- Individual Resiliency Training (IRT)
 - Individual Therapy
 - Module-based and manual driven focused on recovery and growth
- Family treatment
 - Involves individual and family
 - Basic psychoeducation
 - Module-based - communication and problem solving
- Supported employment/education
 - Offered to all individuals
 - Goal is return to community functioning- not rehabilitation

B. How Do These Components Work Together?

- There are weekly team meetings that provide the opportunity for team members to share information
- Aspects of the other interventions that relate to the prescriber role
 - Other team members see individuals more frequently than the prescriber so they often can detect symptom return or non-adherence earlier than the prescriber
 - The other team members are trained in the basics of NAVIGATE medication treatment
 - They can provide support for the prescriber recommendations to the individual and to the family
 - As first episode individuals are very susceptible to metabolic side effects, all should receive healthy lifestyle instruction
 - Prescribers can initiate this but IRT and family clinicians can go into this in more depth with individuals and families.
 - IRT has specific modules on:
 - Managing distress and grief
 - Coping with depression and other symptoms
 - Reducing substance abuse/dependence
 - Family Psychoeducation includes education for the individual and family on the disorder and treatment options
 - As part of Supported Education/ Employment, individuals and families sometimes gain more insight into the detrimental effect of symptoms on vocational functioning

First Episode individuals often stop treatment despite best efforts by staff to maintain engagement. With different treatment options available, individuals who stop one

NAVIGATE component may continue with others. This is obviously preferable to dropping out of treatment entirely.

C. What if Patients Need Services Not Provided by NAVIGATE?

NAVIGATE provides a range of services. However, an individual patient may need services beyond those provided by NAVIGATE. In these situations, the treatment model is for the NAVIGATE team to coordinate with the other providers and the patient remains in NAVIGATE treatment while receiving additional services. Part of the coordination includes insuring that the outside services do not contradict NAVIGATE treatment principles and ongoing progress updates between the NAVIGATE and outside program(s).

II. Advantages of NAVIGATE Care Over Standard Care: Results From The RAISE-ETP Study

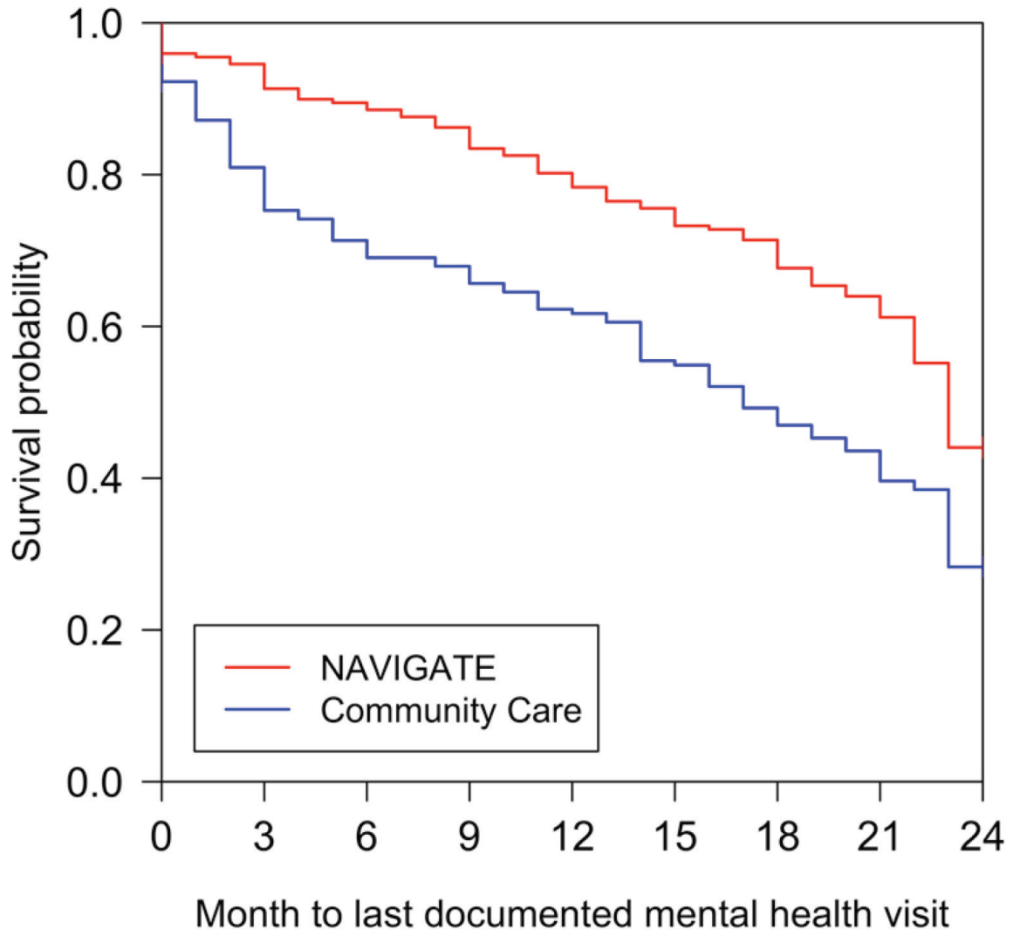
- The RAISE-ETP study compared Navigate with usual care treatment with 404 first episode patients
- We named the usual care treatment “Community Care”.
- In Community Care, clinicians provided whatever treatment they thought was best for each patient
- Patients were recruited from 21 different states in the United States

Over the first 2 years of treatment

- Patients who got Community Care treatment improved as one would expect to happen

but
- Navigate treated patients stayed in treatment longer and had more improvement in overall symptoms, depression and quality of life than patients given Community Care treatment

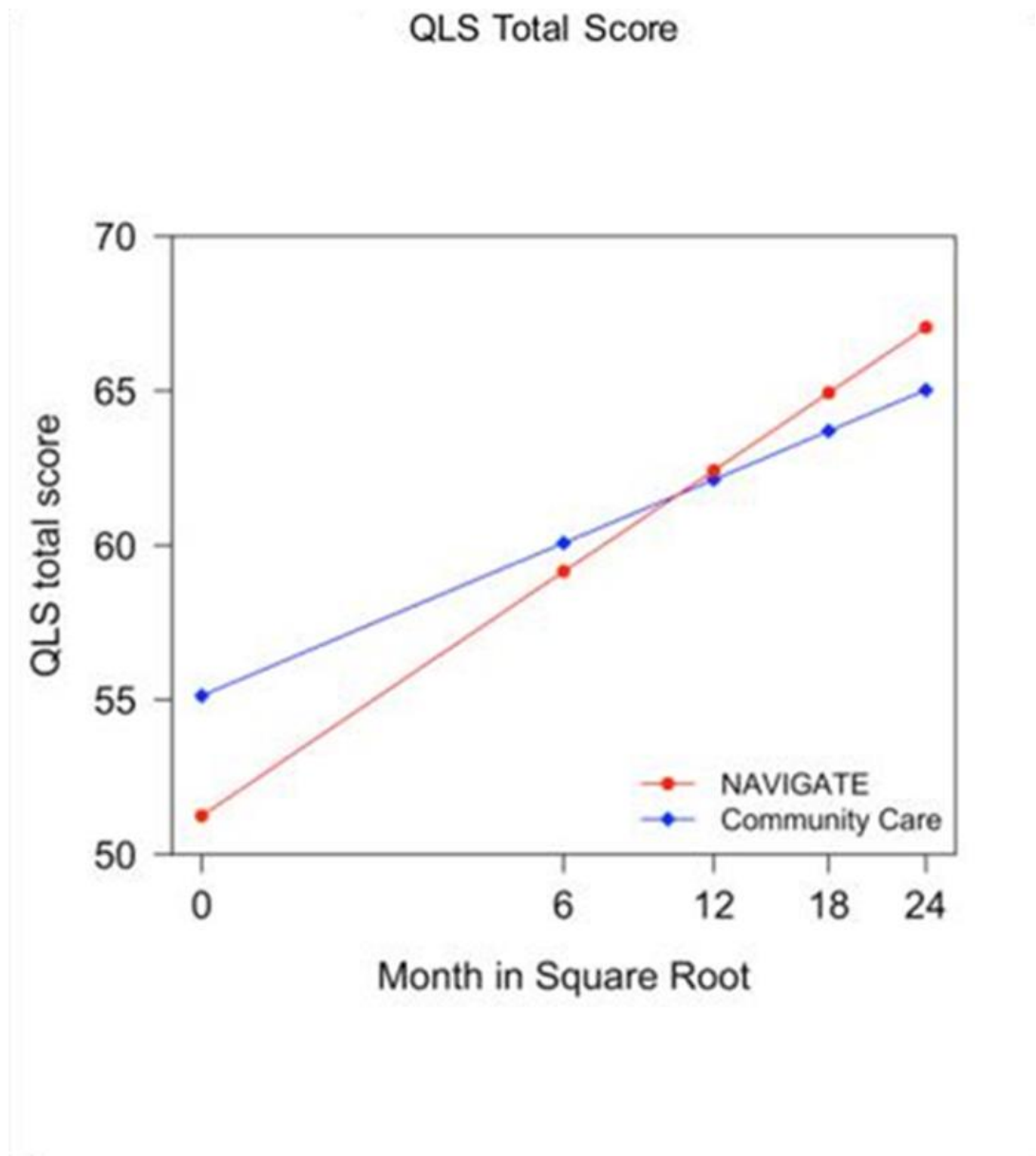
A. NAVIGATE Participants Stayed in Treatment Longer¹:
Time to Last Mental Health Visit (difference between
treatments, $p=0.004$)



B. NAVIGATE Participants Had Better Quality of Life¹:
(treatment by time interaction, $p=0.015$)

Heinrichs-Carpenter
Quality of Life (QLS)
Scale

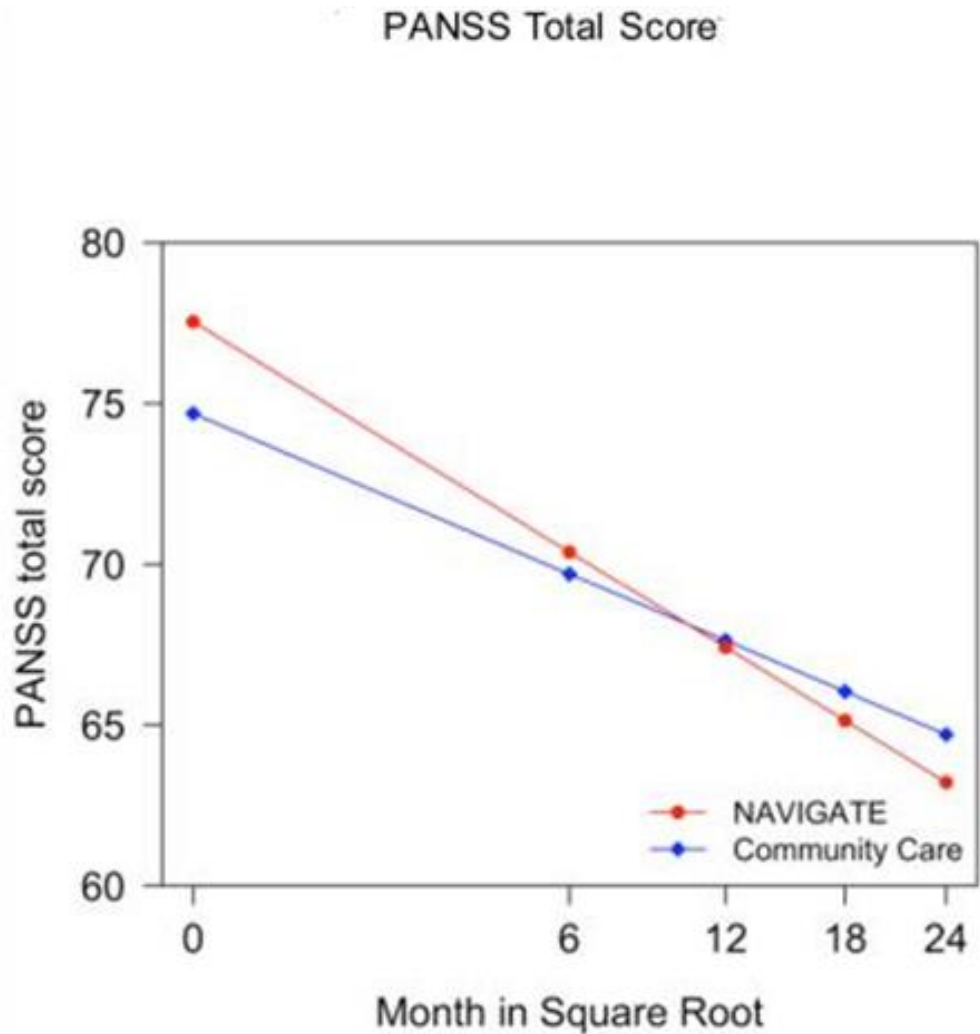
Greater scores
indicate better
quality of life



C. NAVIGATE Participants Had Less Severe Symptoms¹: (treatment by time interaction, p=0.016)

Positive and Negative Syndrome (PANSS) Scale

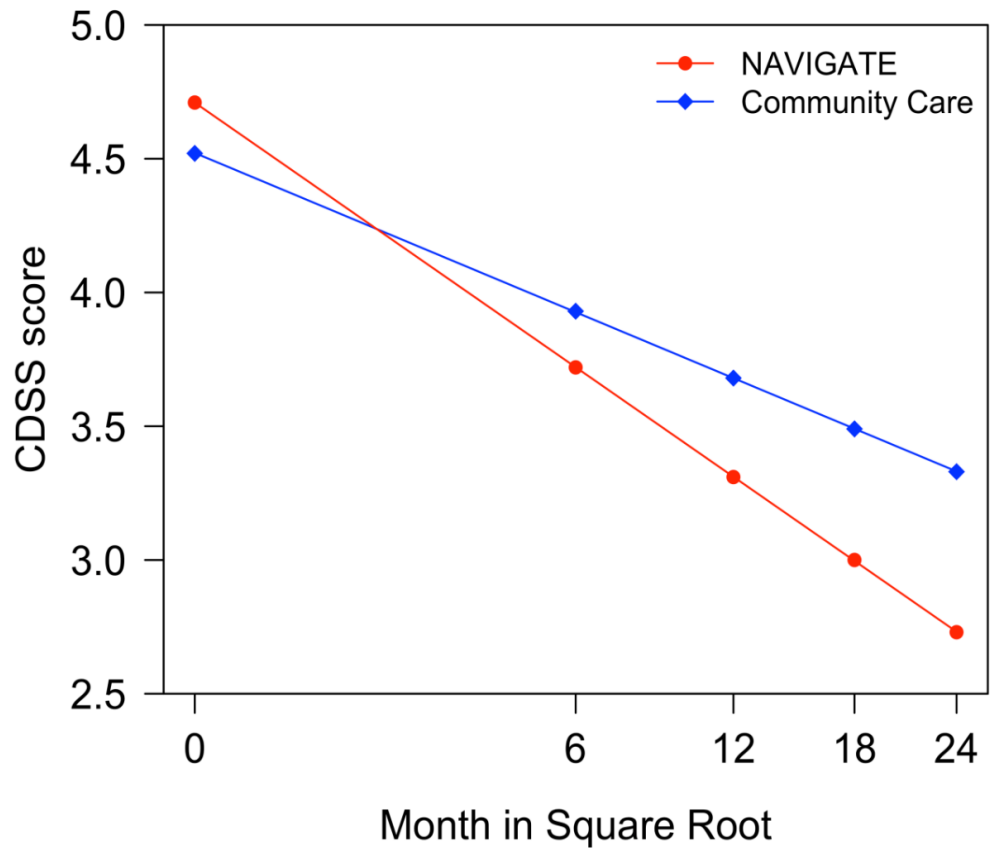
Greater scores indicate more symptoms



D. NAVIGATE Participants Had Less Symptoms of Depression¹: (treatment by time interaction, $p=0.0318$)

Calgary
Depression
Scale for
Schizophrenia
(CDSS)

Greater scores
indicate more
symptoms



E. NAVIGATE Versus Usual Care Prescriptions²

- NAVIGATE patients had more medication visits ($p < 0.001$)
- NAVIGATE Patients Were More Likely To Be Prescribed An Antipsychotic ($p = 0.005$) (All patients had psychotic disorders for which antipsychotic treatment was indicated)
- NAVIGATE Patients Were More Likely To Be Prescribed An Antipsychotic Conforming To First Episode Treatment Principles ($p = 0.037$)
- NAVIGATE Patients Were Less Likely To Be Prescribed An Antidepressant ($p = 0.037$)
 - NAVIGATE does not aim to increase the number of medications prescribed but instead to improve the prescriptions given
 - The NAVIGATE psychosocial interventions include therapies that may improve mood. Thus, NAVIGATE prescribers have additional treatment options beyond simply antidepressants for depressive symptoms.

F. NAVIGATE Participants Had Less Side Effects

- NAVIGATE participants had overall less side effects ($p = 0.0018$) despite being prescribed antipsychotics more often.
- This was a general effect, applicable to most side effect categories

Odds ratios less than 1 indicate that the side effect group occurred less often among NAVIGATE participants than with usual care participants

Side Effect Group	Odds Ratio Between Conditions	95% Confidence Interval of Odds Ratio
Sedation	0.500	0.295, 0.846
Extrapyramidal Symptoms	0.694	0.481, 1.001
Anticholinergic Side Effects	0.582	0.380, 0.892
Increased Appetite or Weight Gain	0.719	0.533, 0.970
Sexual Problems	0.629	0.406, 0.973
Menstrual Problems	0.608	0.274, 1.347

The Scientific Basis for NAVIGATE Treatment



I. Studies Examining Response Rates For Treatment of the Initial Psychotic Episode

Study	N	Antipsychotic (mean dose)	Response Rate
Emsley et al. 1999 ³	183	Risperidone (6.1mg/day)	63% by 6 weeks
		Haloperidol (5.6mg/day)	56%
Lieberman et al. 2003 ⁴	263	Olanzapine (9.1 mg/day)	55% by 12 weeks
		Haloperidol (4.4 mg/day)	46%
Lieberman et al. 2003 ⁵	160	Clozapine (400 mg/day)	81% by 52 weeks
		Chlorpromazine (600 mg/day)	79%
Schooler et al. 2005 ⁶	555	Risperidone (3.3 mg/day)	75% by 12 weeks
		Haloperidol (2.9 mg/day)	78%
Robinson et al 2006 ⁷	112	Olanzapine (11.8 mg/day)	44% by 16 weeks
		Risperidone (3.9 mg/day)	54%
Robinson et al 2015 ⁸	198	Aripiprazole (14.8 mg/day)	63% by 12 weeks
		Risperidone (3.2 mg/day)	57%

A. Key Points From Response Rates to Treatment of the Initial Psychotic Episode Data

- All response rates are high, even using response criteria that are more stringent than those usually used in studies of multi-episode patients
- Doses are low
- The relative advantages/disadvantages of antipsychotics differ between first episode and multi-episode patients

- For example, clozapine and chlorpromazine have the same response rates if used as initial treatments (clozapine is still the treatment of choice for first episode patients who remain symptomatic after trials of other antipsychotics).
- In none of the studies were there significant differences in response rates between the antipsychotics within the trial

B. Treatment Length of an Antipsychotic Medication Trial

- First episode patients may respond to long monotherapy trials of antipsychotics
- The Preventing Morbidity study treated first episode patients with olanzapine or risperidone for 16 weeks
- Cumulative response rates increased steadily every study week until the end of trial
- The cumulative response rate was 40% by week 8; 54% by week 12 and 65% by week 16
- Lack of response after a few weeks of treatment has been demonstrated to predict lack of response to longer trials with multi-episode patients. This may not hold with first episode patients
- In the Preventing Morbidity study, approximately 40% of subjects who had less than a 20% reduction in symptoms by week 4, meet stringent response criteria by week 16 of treatment
- Early antipsychotic switching was also found to not be effective in the Optimize trial (Kahn et al 2018)

C. Side Effects

- As shown in the side effects data from the CAFÉ trial⁹, side effects are frequent despite low medication dosing
- Antipsychotics differ on the side effects they produce
- Choice of initial antipsychotic is often driven by side effect profiles and not efficacy differences
- Even with antipsychotics with “good” side effect profiles, constant monitoring of side effects is crucial

Side Effect Rates from Café Trial

Adverse Event	% experiencing Olanzapine N=133	% experiencing Quetiapine N=134	% experiencing Risperidone N=133	% experiencing All Subjects N=400
Daytime drowsiness	53.4	57.5	49.6	53.5
Weight gain	51.1	40.3	41.4	44.3
Increased sleep hours	33.8	41.8	27.1	34.3
Insomnia	38.4	29.1	33.8	33.8
Menstrual irregularities	31.3	23.8	47.1	33.3
Sex drive	27.8	26.1	27.1	27.0
Akinesia	24.1	24.6	27.1	25.3
Dry mouth	21.8	34.3	15.8	24.0
Akathisia	20.3	18.7	22.6	20.5
Sexual arousal	21.8	16.4	18.1	18.8
Sexual orgasm	16.5	15.7	18.8	17.0
Orthostatic faintness	11.3	19.4	12.8	14.5
Constipation	8.3	11.9	13.5	11.3
Sialorrhea	5.3	6.0	13.5	8.3

D. Weight Gain

- As presented below, first episode patients are very susceptible to weight gain with antipsychotic treatment
- Antipsychotics do differ in their potential to cause weight gain
- However, even with antipsychotics with less propensity to cause weight gain, monitoring of weight and interventions to minimize weight gain are needed

Study	Medication	Weight Gain at 12 Weeks of Treatment
Schooler et al 2005 ⁶	Risperidone	Mean of 10 pounds
Lieberman et al 2003 ⁴	Olanzapine	Mean 16 pounds; 61% gained > 7% of baseline weight
Robinson et al 2006 ⁷	Olanzapine	15.6% of baseline weight
	Risperidone	9.4% of baseline weight
McEvoy et al 2007 ⁹	Olanzapine	35 pounds (baseline wt = 172 lbs)
	Quetiapine	18 pounds (baseline wt = 170 lbs)
	Risperidone	20 pounds (baseline wt = 173 lbs)
Robinson et al 2015 ⁸	Aripiprazole	11.1 pounds
	Risperidone	13.5 pounds

II. Antipsychotic Maintenance Treatment

A. Results from Placebo-Controlled Trials

- There have been several placebo-controlled trials.
- All trials show a substantial advantage of active medication compared with placebo for prevention of relapse.
- The data are primarily from older trials as further trials did not seem warranted given the initial trial results
 - The Chen and colleagues' study¹⁰ used a second generation agent (quetiapine) while the other studies first generation agents
- The reported rates of relapse vary substantially across studies. These differences in relapse rates across studies may be attributable to differences in key aspects of study design (e.g., stability of response before randomization, definition of relapse).

Study	Relapse Rate with Placebo	Relapse Rate with Medication
Kane et al., 1982 ¹¹ (1 year follow-up)	41%	0%
Crow et al., 1986 ¹² (2 year follow-up)	62%	46%
McCreadie, et al. (Scottish Schizophrenia Research Group), 1989 ¹³ (1 year follow-up)	57%	0%
Hogarty and Ulrich, 1998 ¹⁴ (2 year follow-up)	64%	43%
Chen et al. 2010 ¹⁰	79%	41%

B. The Wunderink Study

Despite the evidence for the effectiveness of antipsychotic maintenance treatment to decrease relapse risk among individuals with schizophrenia in general and among specific first-episode populations as presented above, patients and their families may have questions about the Wunderink study.

There are 2 key publications. The first is the randomized trial¹⁵. Remitted first episode patients were randomly assigned to either continue maintenance antipsychotic treatment (N=63) or to antipsychotic discontinuation (N=68) and followed for 18 months. Only 20% of the participants assigned to the discontinuation condition were able to be successfully discontinued. Recurrent symptoms caused another 30% to restart antipsychotic treatment and discontinuation was not feasible at all for the remaining 50%. Relapse rates were twice as high in the discontinuation condition compared with the continuation condition (43% versus 21%).

The second publication¹⁶, a 7 year follow-up of the original study participants, has received much more press even though it is a follow-up study and outcome was determined by assessors who knew the original treatment assignment of the participants. The finding was that 17 of the participants (21.1% of the discontinuation group and 11.8% of the maintenance group) were not taking antipsychotics at the follow-up point.

The evidence is stronger for the Wunderink randomized controlled trial than for the follow-up study.

C. Conclusions About Maintenance Treatment

- Antipsychotic discontinuation during the first years of illness is associated with increased relapse risk
- Some patients do not relapse after antipsychotic discontinuation but the number is small

Until we have a method to determine the small number of patients who can discontinue antipsychotic maintenance, the best strategy is to prescribe continuous antipsychotic maintenance treatment using the lowest effective doses.

D. Beyond the First Relapse

- The primary outcome for most studies of maintenance treatment has been the first relapse following response to treatment of the initial episode.
- The study of Robinson and colleagues¹⁷ provided data showing that most subjects experience multiple relapses during the first years of illness.
 - By 5 years of follow-up, 82% of subjects had experienced one relapse; 78% of subjects who had recovered from their first relapse had a second relapse and 86% of subjects who recovered from their second relapse had a third relapse episode.
 - A survival analysis using medication status as a covariate found a **five times** higher relapse rate for individuals who discontinued medication compared to those who continued medication.

III. Data on Attempts to Find Alternative Medications Other Than Antipsychotics For First Episode Psychosis

NAVIGATE treatment was designed for people experiencing a first episode of a schizophrenia spectrum disorder and thus all NAVIGATE participants meet criteria for treatment with antipsychotic medications.

- The internet has provided patients and their families with previously unavailable access to medical information. Unfortunately, it also provides access to much misinformation.
- We provide data for two issues commonly brought up by patients and families related to alternative treatments

A. Omega-3s as Alternative Treatment

- The Amminger¹⁸ study suggested that omega-3 supplements given to individuals with clinical high risk for developing a psychotic disorder (“prodromal” patients) could prevent conversion to psychosis. Unfortunately, the subsequent large scale NEUROPRO¹⁹ and NAPLS studies found no effect of Omega-3s for preventing conversion.
- Two small scale studies^{20,21} (N=71 and N=50) found more improvement in depression and anxiety symptoms but not positive symptoms with omega-3s versus placebo added to concurrent antipsychotic treatment with first episode patients. This effect may be masked if patients are concurrently taking benzodiazepines.

- Conclusions: We can conclude that omega-3s are NOT a substitute for antipsychotic treatment for first episode psychosis. Whether they have a role as adjuvant treatments is unclear and needs further study.

B. Cannabinoids for the Treatment of Psychosis

- Approximately a third of first episode patients meet lifetime DSM criteria for a marijuana use disorder²² and marijuana use has long been known as a risk factor for relapse among first episode patients (e.g.²³). The increased relapse risk may be due to the direct effects of some cannabinoids inducing psychotic or anxiety symptoms or by marijuana abuse being associated with poor adherence to antipsychotic treatment²⁴ (or a combination of both). The susceptibility to comorbid abuse disorders and the heightened relapse risks with cannabis use should be considered in any evaluation of therapeutic cannabinoids.
- Nevertheless, the cannabinoid system is complex and there are cannabinoid strategies that may (or may not) have therapeutic effects. The current uncertainty of the evidence is reflected in two recent meta-analyses: one²⁵ finding no benefits for the treatment of mental disorders and another²⁶ “encouraging, albeit embryonic” evidence for treatment effects in psychiatric disorders. Further studies are clearly needed to make firm conclusions.

An important point when discussing alternative treatments with patients and their families

- Scientific studies of alternative treatments usually employ formulations that meet stringent standards of preparation both for contents and safety (this is especially the case of studies performed under an IND). “Street” compounds or unregulated products at stores do not have similar standards.

IV. Health Challenges

A. People with Schizophrenia Have Strikingly Shorter Lifespans

- Many studies have found that people with schizophrenia die several decades earlier than the general population
- Typical of these studies, Olfson and colleagues²⁷ studied 1,138, 853 individuals with schizophrenia in the Medicaid program.
 - Those with schizophrenia were more than 3.5 times as likely to die in the follow-up period compared with adults in the general population.
 - On average, the years of potential life lost for each deceased individual were 28.5 years
 - The main causes of early death are cardiovascular disease and pulmonary disease

B. The medical issues driving the excess mortality are often present at initial treatment presentation

Data from the baseline assessments²⁸ in the RAISE-ETP study

Issue	% with Issue at Baseline Assessment	
Obese or Overweight	48.3%	
Smoking Tobacco	50.8%	
Dyslipidemia	56.5%	
Prehypertension	39.9%	
Hypertension	10.0%	
Metabolic Syndrome	13.2%	
Prediabetes	glucose based definition	4.0%
	hemoglobin A1c based definition	15.4%
Diabetes	glucose based definition	3.0%
	hemoglobin A1c based definition	2.9%

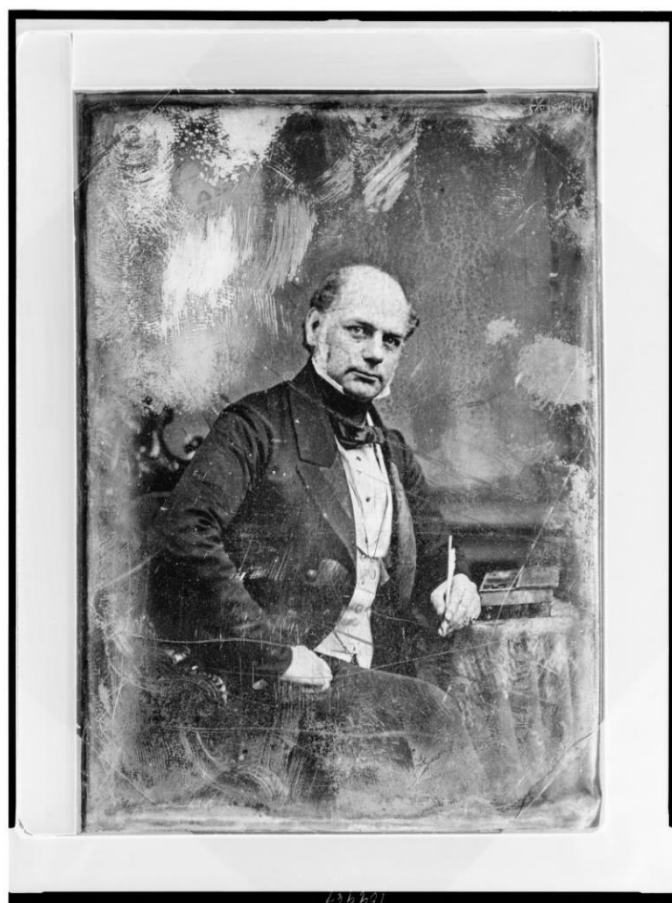
First episode treatment offers the opportunity to identify these issues in their early stages and initiate proper treatment of the factors that long-term lead to premature death

However, the field has been failing to address these problems.

Percent of the RAISE-ETP participants who were receiving medical treatments at baseline.

Medication Type	% receiving
Antihypertensive	3.6%
Antidiabetic	0.8%
Lipid Lowering	0.5%
Smoking Cessation	0.0%

Clinical Issues: Taking Research Findings into the Clinic

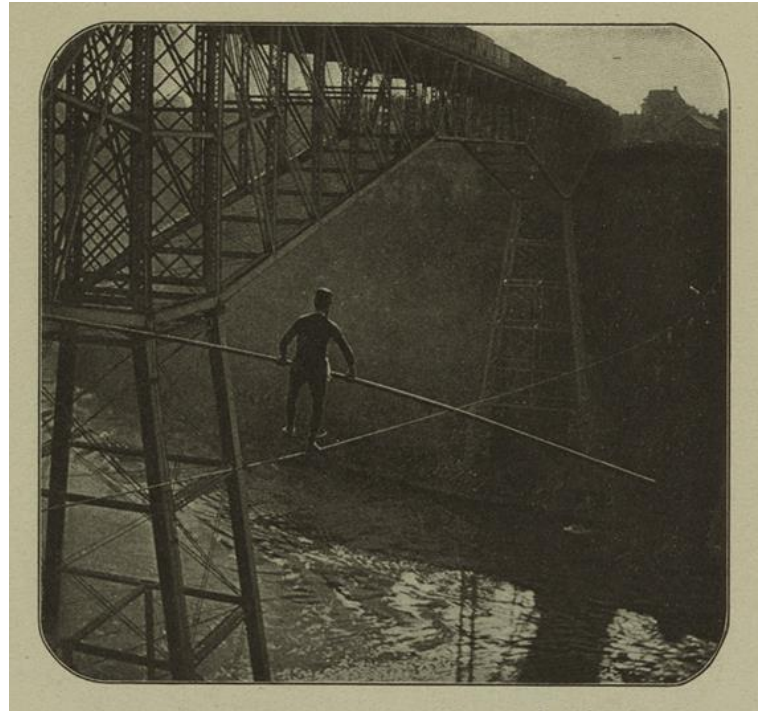


I. The Initial Assessment and Diagnosis

- As every clinician knows, schizophrenia is a common illness.
- However, there are relatively few new cases of schizophrenia each year.
- Unless you have specialized in the treatment of early psychosis, your experiences with individuals with schizophrenia will have been heavily weighted to multi-episode individuals.
- All your accumulated clinical knowledge about how to treat individuals with schizophrenia will be invaluable for treating NAVIGATE individuals.
- In treating any specialized individual group, there are often some clinical areas that require increased emphasis. The following are some clinical tips about treating early phase individuals to supplement your current professional experiences.

A. The Need to Provide Accurate Medical Information

- You have to present accurate medical information, some of which may not be easy for patients and their families to hear/learn
- You want to present this information in a way that they can best understand and use
- These two points sometime are not easy to reconcile, and it may sometimes feel that you are doing a difficult balancing act and that it would be easier to avoid discussions
- Ultimately, you have to use all your clinical skills to get across the accurate information
- For shared decision making we ask patients and their families to make decisions within the evidence base and they cannot do that if they don't



B. The Initial Visit(s) Tasks

Sites vary substantially on the structure within which prescribers can perform initial critical tasks. These tasks include:

- Performing a complete and accurate diagnostic assessment and assessment of current symptom severity
 - Clinical tips provided in the next section
- Determining patient (and in most cases family) understanding psychosis and its treatment
- Determining patient (and in most cases family) goals for treatment
- Orienting the patient (and in most cases family) about the NAVIGATE model for medication prescription and health promotion
- Making initial treatment decisions

C. Clinical Tips on Diagnostic Assessment

- NAVIGATE treatment was designed for individuals with a schizophrenia-spectrum disorders
- NAVIGATE does NOT provide treatments tailored to people with other psychotic disorders
 - People with other psychotic disorders are often best served by other specialty programs
- Prescribers are often the NAVIGATE team member with the most training in diagnosis and thus the team member who often provides the final diagnostic assessment

- Prescribers are also the team member that individuals and families often turn to when wanting to know the individual's diagnosis
- Clinicians are often reluctant to talk to individuals and families about a diagnosis of schizophrenia
 - Clinicians often believe that the diagnosis cannot be made early in the illness course and that the diagnosis is “unstable”
- ***What does research tell us?***
 - The Suffolk County study ²⁹ followed all individuals (a total of 628) in a county in Long Island New York who were admitted for a first psychotic episode. Diagnostic groups followed included schizophrenia-spectrum, bipolar disorder, major depression, substance-induced psychosis and other psychotic disorders.
 - 470 individuals had a 10 year diagnostic assessment
 - Of the 470 individuals, 126 were given a diagnosis of schizophrenia at the baseline visit.
 - At the diagnostic assessment 10 years later, 112 (89%) of the 126 with a baseline diagnosis of schizophrenia continued to have a diagnosis of schizophrenia
 - Overall, 29.6% of individuals had a schizophrenia-spectrum disorder at baseline and this increased to 49.8% at year 10
 - Conclusion: The vast majority of first episode individuals with schizophrenia will continue to have a schizophrenia diagnosis 10 years later. Concerns about a schizophrenia diagnosis being unstable are not supported by the evidence.
- Why might clinicians have concerns about diagnostic stability?

- Over time, a large number of diagnoses for individuals in the Suffolk County study did change. However, for schizophrenia-spectrum disorders (the focus of NAVIGATE treatment), the diagnostic shift was for more people to have a schizophrenia-spectrum disorder over time and for the other disorder diagnoses to become less common. In other words, the diagnostic “instability” was towards a schizophrenia-spectrum disorder diagnosis.
- The Suffolk County study did careful diagnostic assessments. Less careful assessments may not have found the same results.
- This supports doing a careful diagnostic assessment in NAVIGATE treatment.

Obtaining Information for the Initial Diagnostic Assessment

First episode patients often present with a variety of symptoms and you will have little or no prior records. Diagnostic assessments instruments such as the SCID³⁰ or the MINI³¹ can be very valuable for obtaining a comprehensive assessment of the history of symptoms and obtaining the correct diagnosis. The following sections contain suggestions that are applicable whether you use an assessment instrument or a regular clinical interview.

Problem: By definition, early phase individuals have no, or only limited, prior medical records. You will need to be a detective to find out the individuals’ history of illness.

SUGGESTIONS


- Get as much collateral information as possible
 - Families are important sources of information
 - Usually one or more of the parents are the primary informants
 - Siblings frequently are the best informants about substance use

- (Note: while collecting information, you can concurrently assess the knowledge about, and attitudes toward, treatment among the different family members)
- Other NAVIGATE team members may get valuable parts of the individual history
 - This may be discovered during their assessments, e.g., the supported education specialist may find out that poor school functioning is due to severe hallucinations or substance use
- Often the individual is the only source of vital information.
- Some individuals will be forthcoming with their history and for those individuals you can use your standard interview techniques
- ***What if the individual is not being forthcoming?***
- The usual strategy is to find some aspect of the individual's illness that they agree is a problem and use that as an entry point to explore the extent of symptoms. Each individual varies in what they identify as a problem but it usually consists of either:
 - A symptom that the individual experiences as negative (usually this is anxiety or worry, sometimes depression). Exploring what drives these symptoms frequently uncovers psychotic symptoms. For example, anxiety may be a reaction to fears of harm; insomnia to nighttime hallucinations.
 - Problems with role function. First episode individuals usually do not see themselves in a patient role. Their expectations are that they will have a role (school, work) similar to their peers. First episode individuals will frequently respond to discussions of role performance problems. Psychotic symptoms are often elicited when describing performance difficulties (e.g., hallucinations may make it difficult to concentrate in classrooms leading to academic failure).

- Problems with social functioning. Similarly, first episode individuals expect to have the same social interactions as their healthy peers. Discussing problems of social isolation or other social difficulties can be an entry point to exploring psychotic symptoms.

Clinical Characteristics that Influence Assessment

- How long individuals have psychotic symptoms before seeking treatment varies greatly.
 - 24% of individuals in the RAISE-ETP study had durations of untreated psychosis (DUP) of 3 months or less
 - However, the median duration was 74 weeks so many participants had been psychotic for very long periods before getting treatment
 - Both individuals and families can be in denial about the extent of the individual's symptoms
 - One frequently gets only a limited history of symptoms and the extent of symptoms at the first interview. Families and individuals often will need time to fully disclose the extent of symptoms. Be prepared to learn more over the first few months of treatment.

 **TIP!** Dating the onset of symptoms can be especially difficult and the known onset can change over the first months of treatment. Obtaining the time of first social and of first role (education or work) dysfunction often gives good indications of the onset of symptoms.

- For individuals with long DUP, their psychotic symptoms when they finally enter treatment can be very severe

- Be prepared for the assessment of more extreme versions of psychosis, such as bizarre delusions and catatonic features.
- Substance use co-morbidity:
 - 40%-50% of first episode schizophrenia-spectrum individuals met criteria for a past or current DSM-defined substance abuse or dependence disorder (not counting nicotine dependence).
 - In RAISE-ETP, approximately one-third of participants reported recent alcohol use (36.6%) and cannabis use (30.7%), and one half (51.7%) met criteria for any lifetime alcohol or drug use disorder ³².
 - How to tell substance induced psychosis from schizophrenia with substance use?
 - Clinicians sometimes automatically assume that young individuals who present with psychosis and substance use have a drug induced psychosis.
 - An important clinical point is to get a chronology of the psychotic symptoms and of the substance use.
 - For some individuals, you will obtain a clear history of psychotic symptoms predating the substance use.
 - For subjects whose psychotic symptoms started concurrently or after the onset of substance abuse, it is important to determine if there are periods of psychosis in the absence of substance abuse.
 - a) Individuals with early phase schizophrenia and substance use often report that they had a period when they stopped substances all together or drastically cut down the amount of use in an attempt to eliminate their psychotic symptoms, which they attribute to substance use. After a while, individuals realize that their psychotic symptoms persist after stopping their substance abuse. At this point, they usually resume their substance use (and thus are often abusing substances at the time of initial treatment contact).

b) Without obtaining a chronology of substance use and psychotic symptoms, individuals such as these would mistakenly be given solely a diagnosis of substance induced psychosis.

- Individuals may have had brief prior treatment for psychosis that ended when the individual stopped treatment.
 - Always inquire about medication taken versus medication prescribed during prior treatment - they often/usually are different.
- Remember to inquire about the use of over-the-counter or “alternative” medicines.



Often it is useful for the team to review all the diagnostic information they have after an individual has been in the program for a few months. It is a good opportunity to determine if new information has become available that could be incorporated into the diagnosis.

Talking to Individuals and Families about the Individual’s Diagnosis

- The public often has incorrect ideas about psychiatric diagnoses and also often attaches negative connotations to the diagnoses.
 - It is illogical that a diagnosis is stigmatized but logic is not always followed by society
- Clinicians often avoid discussing diagnosis because of this
- Individuals and families can avoid the topic also
 - If individuals and families do not want to discuss diagnosis it is often best to not introduce the issue until they are better prepared for the discussion

- What to do if individuals or families ask about the diagnosis?
- For any medical treatment, questions by individuals and families deserve clear and accurate answers
- In the shared decision making model of NAVIGATE, we ask individuals and families to make decisions within the evidence base
- We cannot ask individuals and families to make decisions within the evidence base if we are not willing to provide them with accurate information about their condition, including the diagnosis
- Tips on the conversation presenting the diagnosis
 - Individuals and families often have incorrect ideas about diagnosis so often the first step is to ask them about what they know about the individual's diagnosis
- This allows assessment of how much the individual and family already know and of areas of incorrect ideas
- Some individuals and families will have a sophisticated understanding and the conversation can develop from that knowledge base
- Often individuals and families lack this background.
- For these individuals, a directed fact-based approach is often useful
- One can start by acknowledging that there is a lot of conflicting information available and that this is sometimes confusing to people
- For your conversation with them, you are going to use the DSM definitions which are the authoritative diagnostic criteria for use in the US

- It is often helpful to have the list of DSM criteria for a diagnosis in the meeting and show how the individual's symptom patterns match each of the criteria listed. This often helps individuals and families understand that a diagnosis is nothing more than patterns of particular symptoms and time frames.
- This requires that individuals be at a level of insight that they can acknowledge that some of their experiences might be symptoms and that their symptoms are distressing or impairing.
 - Individuals who do not have this level of insight may need more time before they can become engaged in discussing diagnosis in a detailed manner.

II. Clinical Tips Concerning Treatment

All your accumulated clinical knowledge about how to treat individuals with schizophrenia will be invaluable for providing NAVIGATE treatment. In treating any specialized individual group, there are often some clinical areas that require increased emphasis. The following are some clinical tips about treating early phase individuals to supplement your current professional experiences.

A. Shared Decision Making and Measurement Based Care

NAVIGATE treatment uses a shared decision making model.

Shared decision-making³³ has been defined as a care delivery process in which practitioners and clients seeking help for disorders collaborate to access relevant information and to enable client-centered selection of health care resources.

How Does NAVIGATE Treatment “Access Relevant Information”

- All NAVIGATE team members need to provide patients and their families the best medical evidence about treatment options
- Education about the results of medical research is often a long-term process with frequent reviews of the evidence base
- The internet has provided patients and their families with previously unavailable access to medical information. Unfortunately, it also provides access to much misinformation.
 - NAVIGATE team members need to actively determine patient and family members’ understanding of medical information and provide correct information in place of inaccurate information

- Besides NAVIGATE provided information, it is often beneficial to suggest that patients and families who want information from the internet to go to the websites of the National Institute of Mental Health or the Food and Drug Administration to receive the latest scientific information from sites that have no commercial interest.

Measurement based care is the systematic administration of scales and their use to drive clinical decision making at the level of the individual patient

- Supports making clinical judgements, does NOT substitute for clinical judgment
- Helps patients become more aware of their clinical status
- Can facilitate patient-provider communication
- Helps to decrease clinical inertia, not changing treatment despite substantial remaining symptoms
- Improves outcomes compared with usual care (reviewed in³⁴)
 - Improvement was found in multiple disorders and across different provider groups (psychotherapists, psychiatrists and primary care providers)

NAVIGATE uses measurement based care to obtain the information about patient problems that then allows selection of the evidence based options that are presented in shared decision making.

What if a patient declines evidence based solutions and thus shared decision making? In this situation, we suggest a harm reduction approach. By this, we mean that the prescriber works with the patient to determine the best options for the patient that are consistent with medical practice.

For example,

- Some patients will ask for prescriptions for medications for which they have no indication (e.g. for a substance of abuse). In this case, NAVIGATE prescribers can continue to provide education about why a medication is not indicated but cannot provide prescriptions for medications that are medically contraindicated.
- Many patients will decline antipsychotic treatment despite the evidence for its use for individuals with schizophrenia-spectrum disorders. In a harm reduction framework, the suggestion is that the patient continue to see the NAVIGATE prescriber for ongoing monitoring and education even when the patient is not taking medications (as long as the patient's symptoms do not meet criteria for intervention as required by the legal and medical requirements of their jurisdiction or best clinical practice). Having ongoing contact increases the chance that if the patient's symptoms become more severe that treatment can be initiated to prevent further illness progression.

B. Patients and Their Families Often Need Support and Time to Achieve an Understanding of the Illness

For most families, having a son or daughter enter treatment for a psychotic episode is a family crisis. Further, most individuals and their families have limited experience with the mental health treatment system.

- Families and individuals usually need support during the process of entering treatment. The IRT and family education components of NAVIGATE are important resources for this.
- Individuals and families often have an unstable view of the illness even after several months of treatment.

- It is important to provide individuals and families with a clear, consistent description of the illness and its treatment.



Important points about treatment usually need to be reviewed multiple times with patients and families. Your team members can provide a lot of this effort.

C. Maintaining Engagement

- Despite presentation of the evidence base for the effectiveness of treatment and the risks from repeated psychotic relapses, many first episode patients will decide to stop treatment, often repeatedly
- For most patients, it is important to include their family in decisions about continuing treatment
- Many families will encourage patients to continue treatment or at least agree to monitoring for relapse
- If patients decide to stop treatment, it is often important that families know that the patient is entering a period of increased relapse risk
- Maintaining engagement is crucial for early detection and management of relapse
- Patients will frequently agree to longitudinal follow-up after medication discontinuation
- Participation in other treatment components such supported employment/education provide another context for patients to maintain contact with the facility and with health care providers

D. Expectations of Outcome of Treatment of the First Psychotic Episode

First episode individuals frequently have a robust positive symptom response to antipsychotic treatment

- 50-60% or more of patients will experience a complete resolution of positive symptoms with their first antipsychotic trial.
- Treatment goals should be high for a young person first starting treatment. For symptom management, the goal is resolution of symptoms, not just improvement in symptoms.

Possibly related to an overall good responsiveness to antipsychotic medication, first episode individuals may respond to long mono-therapy trials of antipsychotics and to lower doses than individuals with chronic psychotic disorders

- Almost all first episode patients will have some degree of symptom improvement relatively quickly after starting an antipsychotic. In this section, “response” is not symptom improvement but instead absence of positive symptoms.
- The Preventing Morbidity study treated first episode individuals with olanzapine or risperidone for 16 weeks. Cumulative response rates increased steadily every study week until the end of trial. The cumulative response rate was 40% by week 8; 54% by week 12 and 65% by week 16.
- Approximately 40% of subjects who had less than a 20% reduction in symptom severity by week 4, meet stringent response criteria by week 16 of treatment.
- In the Optimize trial, first episode patients were initially treated for 4 weeks with amisulpride, a second generation antipsychotic available in many countries but

not in the US. 56% of patients had symptom remission at 4 weeks of treatment. Those who did not were randomly assigned to either continuing amisulpride treatment or switching antipsychotic treatment to olanzapine. Remission rates at 10 weeks for individuals who were not in remission at week 4 were 45% for the amisulpride treated group and 44% for individuals initially treated with amisulpride and then treated with olanzapine.

Clinical Implications:

We lack data about patients who are treated with the same antipsychotic for longer than 16 weeks. Within a time frame of less than 16 weeks, many patients will have remission of psychotic symptoms with antipsychotic monotherapy.

SUGGESTIONS

Some patients will have such persistent severe symptoms that clinically they cannot be safely maintained during a prolonged antipsychotic monotherapy trial so NAVIGATE does not rigidly require continuing long trials. However, most patients will do well on a single antipsychotic if given enough time (and taken as prescribed).

Why avoid early antipsychotic switching or polypharmacy? First episode patients are very vulnerable to antipsychotic side effects and unnecessary switching polypharmacy increases the risk of side effects. First episode patients and families are often ambivalent about antipsychotic treatment and side effects can increase the risk of medication non-adherence. Further, the adherence literature for all of medicine consistently finds that the more complex a medication plan the less likely that the medication will be taken as prescribed (either due to intentional non-adherence or confusion about the proper way to take the medications).

Have a conversation about trial length with patients and family at the beginning of treatment. If they are informed of the time to response data, they are often agreeable to longer trials with the expectation that this may ultimately decrease the number of medications that they need to try. It is important to have the conversation early as they may have been given contradictory information from clinicians who are not familiar with the first episode treatment literature. Further, it is important that the other members of the NAVIGATE team are familiar with this aspect of first episode treatment so that they do not inadvertently give people suggestions that do not apply with a first episode population.

- The recommended NAVIGATE treatment trial duration is a minimum of 8 weeks to establish efficacy (assuming that the patients' symptoms are not so severe that the patient cannot safely be treated for this duration with one medication). Clinicians and individuals may consider longer trials based upon the finding that up to 25% of first episode individuals respond to more lengthy treatment. No data are available for treatment longer than 16 weeks with response defined as in COMPASS, so insufficient trials lasting longer than 16 weeks are not recommended.
- First episode individuals are frequently more sensitive than individuals with multi-episode illness to antipsychotic effects, both in terms of efficacy but also in terms of adverse effects. Antipsychotics doses that are at 50-60% of what is used with multi-episode individuals are often sufficient to obtain a treatment response. Higher doses often are associated with a greater side effect burden.

E. Medication Non-Adherence

Studies across all branches of medicine³⁵ consistently show that around half of patients prescribed medications to take long-term either do not take the medication or take it incorrectly.

SUGGESTIONS

It is important to present adherence enhancement interventions as something that is offered to everyone as having issues taking medications is a common experience, not something unusual

An additional factor with our patient population: Families and individuals usually have no *personal* experience of the negative consequences of treatment discontinuation.

- Young people have difficulty accepting that they have a chronic medical illness, regardless of whether it is psychiatric or of other etiology. Families also often wish to not consider that the individual has a chronic illness.
 - Return to good functioning is often interpreted as meaning that treatment is no longer needed.
 - Substance use and/or stress are frequently cited by individuals and families as the sole cause of the psychotic symptoms and not as factors that exacerbated an underlying disorder.

Key adherence enhancement strategies:

- Clear communication with individuals and their families about the need for maintenance treatment based upon consistent findings from research studies spanning several decades
- Engagement of the entire family in maintaining adherence. Without guidance, families often stop encouraging adherence after the acute crisis of an initial hospitalization subsides.
- Consider having family members supervise medication intake, but also be mindful of the potential power struggles this can cause, especially over long term treatment
- Assessment of adherence at all contacts for individuals taking oral medications

SUGGESTIONS

Don't make the mistake of not assessing adherence when individuals are doing well. Medication adherence may have already become poor, but relapse has not yet occurred.

F. Long-Acting Formulations of Antipsychotics

- Long-acting formulations can be one of the most powerful interventions to support medication adherence but are underutilized in general and specifically with early phase patients.
- Use of long-acting formulations simplifies adherence assessment as it consists solely of knowing if an injection was given.
- Small sample size randomized controlled trials comparing LAI and oral medications with recent onset patients have had mixed results.
 - Weiden and colleagues³⁶ did not find statistically significant adherence differences between 26 patients randomized to LAI risperidone versus 11 patients taking oral antipsychotics.
 - Malla and colleagues³⁷ compared outcomes of 44 patients randomized to LAI risperidone and 41 to oral antipsychotics and found no significant differences between conditions on symptom levels, time to stabilization or time to relapse
 - In contrast, Subotnik and colleagues³⁸ compared 40 patients randomized to LAI risperidone with 43 randomized to oral risperidone and found significant differences in rates of psychotic exacerbation/relapse and need for hospitalization, both outcomes better with LAI risperidone.
- Two large sample size studies with recent onset patients have both shown LAI benefits.

- Schreiner and colleagues³⁹ compared time to relapse over a 2 year timeframe between 376 patients randomized to paliperidone palmitate and 388 patients randomized to oral antipsychotics. Time to relapse was significantly longer for participants randomized to paliperidone palmitate.
- Kane and colleagues^{40,41} compared time to hospitalization over a 2 year timeframe between 234 patients randomized to LAI aripiprazole monohydrate and 255 patients randomized to usual care. Time to hospitalization was significantly longer for the LAI aripiprazole group. 73% of LAI aripiprazole participants did not have a hospitalization versus 58% of usual care participants.

Conclusions

We now have evidence that LAI antipsychotics can improve outcomes for patients with early phase psychosis.

G. Presenting LAI Treatment to Patients with First Episode Psychosis

SUGGESTIONS

There are many incorrect perceptions about LAI medications and prescribers need to be active in presenting an accurate and balanced presentation of LAI medications.

Studies consistently show that patients are often not told about the option of LAI formulations. Without even a discussion of the option of LAI medications patients cannot begin to make informed treatment decisions.

LAI medications are simply a formulation of a medication. However, this simple fact often gets lost in discussions about LAI formulations. The decision about whether to take antipsychotic medications is logically separate from whether to use a LAI formulation but often aspects of whether to take an antipsychotic intrude into discussions about LAI formulations. Try to have a complete discussion and consensus about taking an antipsychotic before discussing LAI formulations. If the decision has been made to take antipsychotic medications, then discussion of LAI formulations is simply about how best to take an antipsychotic.

Medication treatment decisions involve balancing between benefits and negative effects/side effects. Clinicians often start discussions about LAI formulations with negative aspects (e.g. injections) and don't get to the benefit discussion part.

SUGGESTIONS

Start the discussion with an exploration of the benefits that an individual may have using a LAI formulation. If an individual does not perceive any potential benefits from a LAI formulation, there is no need to review negative effects as there is no favorable benefit to negative effect ratio possible. If an individual does perceive possible benefits with a LAI formulation, then the discussion of negative effects follows to come to an overall balance of positive and negative effects.

Potential Benefits To Review

It is critical to determine which (if any) of the potential benefits are of interest to each patient. What may be important for one individual may not be of interest to another.

Some potential benefits to explore with your patients:

- As described above, we now have data showing less relapse risk and risk for hospitalizations with LAIs with early phase patients.
 - A TIP about presenting decreasing relapse risk. Many early phase patients do not relate to the term “relapse” as they have often not had a relapse and often don’t believe that they will experience one. “Staying well” has the same meaning but FEP patients often relate better to this term and it is the term used in the psychosocial NAVIGATE interventions.
- LAIs eliminate the need for patients to keep track of medications and doses—that becomes the responsibility of the clinic
- There often is conflict within families about monitoring medication taking. Patients feel that as adults they should be in charge of their medication taking while family members may be worried about medications not being taken. LAIs can give patients their autonomy while allowing families to feel less need to be vigilant about reminding patients to take their medications.
- Confidentiality—early phase patients often do not want friends and fellow students/co-workers to know that they take medications. With LAIs, the treatment team will know that the patient takes medications but the patient is in total control of who else knows.
- Related to the above, patients are free to go out with friends or go on trips with them without having to plan ahead for having medications available

Common Misperceptions about Potential Negative Aspects

Misperception #1: Loss of control/cannot stop once a LAI is started

- Just like any medication, the patient decides whether they take the medication

- Patients can stop long acting formulations just as they do with oral medication
- As with any medication, before one considers how long to take the medication, the first step is to determine if the medication works. If it doesn't work well, no one expects someone to take the medication over time. If it works well, then one can discuss how long to take it.
- *An important point for many patients is that they can try one injection and then see how it goes. If they like using a LAI they can continue with injections. If they don't like using a LAI, they can stop the LAI.*

Misperception #2: Side Effects are worse on a LAI than an oral medication

- Misawa and colleagues ⁴² did a meta-analysis of adverse events in studies comparing LAI and oral antipsychotics. There were no differences in treatment discontinuation due to adverse events, number of serious adverse events or incidence of an adverse event.

Misperception #3: Stigma/Injections are for sicker or court mandated for treatment patients

- For FEP patients the goal of considering long acting formulations is to keep people well
- People in general need supports for taking medication
- If you wait to talk to patients about long acting formulations until they are experiencing a relapse of symptoms from non-adherence, is it surprising that they think that long acting formulations are for "sicker" people?

Other Issues

Pain/fear of needles

- It is important to acknowledge that no one likes needles
- BUT millions of people get shots around the world
- If the patient acknowledges potential benefits with a long acting formulation but has fear of needles, it is often beneficial to focus the conversation on what supports the patient feels they would need to try an injection
 - *With identified supports, one can determine if the clinic can supply them*
 - *For example, often staff going with the patient to the first injection is a simple but powerful support for patients*

Many agents come in what to patients seem odd dosing strengths. For example, 400 mg for aripiprazole once monthly instead of 15 mg a day for oral

- Understanding pharmacokinetics can be a challenge for patients and their families. Graphics if available often help
- Efficacy and side effects are much more related to blood levels than amount taken

H. The RAISE-ETP NAVIGATE Prescriber Visit Flow

- Patients have vital signs done
- Patients complete self-report of symptoms, side effects, adherence, substance use and preferences about changing or keeping their current medications
 - Standard NAVIGATE uses set questions repeated at each visit
 - Enhanced NAVIGATE uses adaptive methods to assess symptoms—questions asked are modified based upon responses to prior questions

- Prescriber assesses symptoms and side effects guided by patient self-report
- Patient and prescriber review evidence-based treatment possibilities and make treatment decisions

The recommended frequency of visit is at least once monthly. More ill patients often will need visits more frequently.

III. NAVIGATE Medication Selection and Dosing

A. Sequence of Medications

General Principles

- Preference is given to medications with data available from first episode populations
 - This provides the information about dosing and side effect profiles to use in shared decision making about medication choice
- The NAVIGATE shared decision making framework plus the failure of any antipsychotic to demonstrate superior efficacy for initial treatment of psychosis led to the decision to group recommended medications into treatment stages instead of a single medication algorithm.
- Medication grouping criteria included efficacy data with first-episode patients with psychotic disorders and low side effect risk.
- Symptom remission rather than symptom improvement is the treatment goal.
- If satisfactory response is not obtained with a first-line medication (Stage 1) medications are chosen from subsequent stage groups (Stage 2 followed by Stage 3 if needed).

B. How the Antipsychotics Were Grouped into Stages

- The antipsychotics available in the United States with data from contemporary studies with first-episode populations are aripiprazole, chlorpromazine, clozapine, haloperidol, olanzapine, quetiapine, risperidone and ziprasidone.

- First episode treatment guidelines differ but there is general agreement that olanzapine and clozapine should not be first line agents due to their side effect profiles
- Because of concerns about side effects for chlorpromazine, clozapine, haloperidol and for less maintenance treatment efficacy for haloperidol^{6,43}, these medications were also excluded from the stage 1 group
- The first-line (stage 1) consists of the remaining studied agents aripiprazole, quetiapine, risperidone and ziprasidone.
- Note: Paliperidone does not have first episode dosing data but is a metabolite of risperidone so is considered in Stage 1
- Stage 2 agents are the stage 1 agents plus chlorpromazine, haloperidol and olanzapine
- Clozapine is the stage 3 agent.

Consider the use of long-acting formulations of antipsychotics for treatment of patients at all treatment stages.

C. First-Line (Stage 1) Antipsychotics

The table below summarizes key aspects of the first-line antipsychotics. The agents obviously have important properties that are not in the table but this table can be useful for instructing other team members about the agents. It can also be useful as a reminder of areas to review with patients during shared decision making.

Medication	Advantages	Disadvantages
Aripiprazole	Favorable metabolic profile; may have better efficacy for depression and negative symptoms; has long-acting formulations	Higher risk of akathisia
Quetiapine	Sedative effects may be useful in acute treatment	Higher risk for metabolic side effects; sedative effects may not be desirable long term
Risperidone/Paliperidone	Has the most data from first episode studies; has less metabolic effects than quetiapine but more than aripiprazole; has long acting formulations that can last up to 3 months between injections	Causes hyperprolactinemia; no direct paliperidone first episode studies
Ziprasidone	Favorable metabolic profile	BID dosing and need to take with food can be a barrier to patient adherence

What are Reasonable Expectations about How Often First-Line Agents Will Be Used?

- Many factors can affect how often first-line agents are used. Some include:
 - Patient choice
 - Financial limitations on medication choice
 - Patients entering the program already taking medications (discussed in more detail below)
 - A subgroup of patients will not improve sufficiently with first-line agents and other agents will need to be used

- The expectation is NOT that all patients will be on first line agents all the time.

In the first 2 years of the RAISE-ETP study, 51% of ALL prescriptions at NAVIGATE sites were for first-line agents within the suggested dose ranges². This percentage includes prescriptions for non-preferred medications given to patients who enter the program on non-preferred medications, prescriptions for patients who did not improve with first-line medications and all other reasons.

D. What if a Patient Comes to the Program on a Non-Preferred Antipsychotic?

- Your patient and you need to evaluate carefully the potential advantages and disadvantages of switching antipsychotics for that patient and make an informed clinical decision about switching or remaining on the non-preferred antipsychotic. Decisions have to be tailored to each individual. Some usual decision points include:
 - If an antipsychotic that is closely related to one of the first-line antipsychotics is being used (e.g. a dopamine partial agonist other than aripiprazole) the balance between advantages/disadvantages of switching usually favor remaining on the original medication
 - If the antipsychotic is known/can be reasonably inferred from research data to not be optimal for initial treatment (e.g. olanzapine) the balance between advantages and disadvantages of switching is easier to present
 - With newer agents that are not closely related to the first-line agents and that lack first episode data, the balance between switching advantages versus disadvantages will need to be based upon what is known from studies with multi-episode patients and the patient's symptom response and side effect burden
- Some important points for switching versus remaining discussions:

- Switching always has some relapse risk but globally first episode patients are very treatment responsive and all studied antipsychotics have similar efficacy
- It is important to consider both the patient's psychiatric and medical status
- Patients may have good psychiatric symptom control but abnormal metabolic parameters
 - Patients and families will have direct knowledge of the symptom effects and side effects of antipsychotics but will not know laboratory values unless you present these data

E. What if a Patient Comes to the Program on Multiple Medications?

- In RAISE-ETP, many patients came to the program taking medications without a clear history of an indication for some of the medications
- You need to carefully evaluate the indications for all prescribed medications
- Using the fewest number of medications that are needed to achieve the desired results has several advantages
 - It will decrease the risk of side effects
 - Adherence studies consistently show that the more complex a medication regime is, the more likely that it will not be followed as prescribed
- For medications without a clear indication, your patient and you need to evaluate the potential benefits and risk of discontinuing these medications that lack clear indications

F. What if a Patient Does not Respond to an Adequate Trial of a First-Line Antipsychotic?

The first step is to determine if there was an adequate trial

- Some patients will not improve with standard antipsychotics
- However, one always needs to consider non-adherence (including taking medications on an intermittent basis) as the cause of inadequate response
- One long term consideration is that if patients do not respond to two standard antipsychotics, clozapine is indicated. Given clozapine's potential benefits but also its side effect profile, you need to determine which patients might benefit from clozapine and avoid prescribing clozapine to patients who would improve with a standard antipsychotic if taken properly
- If antipsychotic blood levels are available in your clinical situation, is the level inadequate due to non-adherence or rapid metabolism?

If you determine that there was an adequate trial

- As in any situation of a particular patient not achieving the gains typically achieved with a treatment, this is a good time to reconsider the clinical situation
 - Is the diagnosis correct?
 - Are there other factors (e.g. substance misuse) that are impeding improvement?

If a review does not elicit any new clinical factors, you can consider the following next steps

- If a long acting formulation was not used for the initial trial, consider again using a long acting formulation to rule out covert/missed non-adherence as the cause of lack of response
- Having a trial with assured adherence that does not result in sufficient symptom improvement increases confidence in making recommendations about clozapine trials
- Stage 2 treatment includes trying another first-line (Stage 1) antipsychotic or trying one of the second-line (Stage 2) only antipsychotics: chlorpromazine, haloperidol or olanzapine
- Meta-analyses with multi-episode patients suggest that risperidone and olanzapine may have the most symptom efficacy among antipsychotics other than clozapine

G. When to Consider Clozapine

- Clozapine should be considered for patients who have persistent positive symptoms after trials of two antipsychotics
 - Clozapine should be considered at earlier treatment stages for patients with persistent suicidal ideation
- Data on the prevalence of first episode patients with persistent symptoms and of response rates to clozapine for persistent symptoms are limited. The OPTiMiSE trial⁴⁴ included 446 first episode patients and the treatment goal was remission of symptoms. The initial treatment phase consisted of 4 weeks of amisulpride; 56% of patients achieved remission during this

period. The second phase for those who had continued symptoms was 6 weeks of either continued amisulpride or a switch to olanzapine. Seventy-two patients completed phase 2, of whom 40 were not in remission. 5 of these 40 met remission criteria after 12 additional weeks of treatment with clozapine.

- There are no data available specific for first episode patients with persistent positive symptoms after an adequate trial of clozapine
 - Clinicians should base their decisions for these patients on data from studies of patients with treatment-resistant schizophrenia
 - In this context, ECT added to clozapine has shown favorable outcomes in a NIMH-funded study⁴⁵

H. The Most Frequently Chosen Antipsychotics in the RAISE-ETP Study

NAVIGATE Antipsychotic Prescriptions over the 2 Year ETP Trial

	Medication	% of All Antipsychotic Prescriptions
Oral First-Line Antipsychotics	Aripiprazole	22.8%
	Quetiapine	8.3%
	Risperidone/Paliperidone	20.2%
	Ziprasidone	4.7%
Oral Not First-Line Agents	Olanzapine	11.9%
	Clozapine	4.7%
Long Acting Formulations	Any Long Acting Formulation	17.9%
	Paliperidone Palmitate	10.2%

Note: Long acting aripiprazole first became available at the end of ETP. This may account for its low use.

I. Antipsychotic Dosing

- Antipsychotics doses that are at 50-60% of what is used in more chronic patients are often sufficient to obtain a treatment response. Higher doses often are associated with a greater side effect burden

As a guide to usual doses used, the table below presents the mean modal dose for selected oral antipsychotics from the RAISE-ETP study². The doses are from NAVIGATE treatment within the study. Since antipsychotics are often started at low doses that are subsequently titrated upward or are titrated downward during discontinuation, averaging across all prescriptions for an antipsychotic may give a false impression of dosing. Mean modal dose gives a better understanding of usual doses. To calculate mean modal dose, the dose most commonly prescribed for a patient is identified and this is averaged across all patients receiving the medication.

Medication in oral formulation	Mean Modal Dose in total mgs per day	Standard Error
Aripiprazole	11.7947	1.0650
Paliperidone	6.1699	0.4912
Quetiapine	302.35	31.4412
Risperidone	2.8795	0.2233
Ziprasidone	114.65	11.5487
Haloperidol	7.4112	1.4649
Olanzapine	16.0956	1.8331
Clozapine	330.05	51.1483

J. Side Effect Minimization

- Dose reduction is the first line treatment if this is clinically possible
 - The fact that low doses are effective with first episode patients makes this often a feasible option
- If dose reduction is not possible, consider the relative risks and benefits of switching antipsychotics versus adding side effect medications

IV. Treatment For Issues Other Than Psychotic Symptoms

A. Healthy Lifestyles: Diet and Exercise

Our patients and their families often benefit from education and support for proper diet and exercise. Prescribers can present the advantages of proper diet and exercise and support these efforts but the limited time allocated in most clinics for prescriber visits limits the effort that prescribers can devote to these issues, even given their importance. In this situation, all the resources available from the NAVIGATE team should be employed and coordinated. In addition to the NAVIGATE prescribers' effort, NAVIGATE resources include:



IRT includes a Healthy Lifestyles module with 4 topics focused on diet and exercise.

- The first topic provides basic suggestions for making some changes along with developing a plan to make changes
- The second topic helps patients refine and troubleshoot the changes that they want to make.

- Exercise and nutritional recommendations are based upon the National Institute of Diabetes and Digestive and Kidney Diseases suggestions for adolescents⁴⁶. Exercise topics include 1) identify an activity that the patient enjoyed in the past that they would like to try; 2) do a fun physical activity with a friend; 3) do a fun activity outside and 4) plan to be active at least 30-60 minutes a day. Nutritional topics include 1) take it easy on pizza, soda, and sweets; 2) give your body the right fuel; 3) snack smart; and 4) take control.

The IRT Healthy Lifestyles module also has a module on what it means and what it takes to create a healthy habit

B. Treatment of Depressive Symptoms

- Depressive symptoms commonly co-occur with a first episode of schizophrenia.
- Depressive symptoms may be a core part of the acute illness. These symptoms usually resolve with antipsychotic monotherapy as the psychosis remits (see⁴⁷).
- Guidelines for when to initiate adjunctive antidepressant treatment with first episode patients are not available
 - This will be a clinical decision that includes factors such as the severity of the depressive symptoms and response to other interventions
- Since most depressive symptoms will remit with antipsychotic treatment alone, prescription of adjunctive antidepressants for all first episode patients with depressive symptoms is not warranted

- You will need to evaluate the potential for the NAVIGATE psychosocial interventions as treatment options
 - IRT has a module on coping with symptoms and success with school or work goals can enhance patient self-confidence
- Given what is known about antipsychotic treatment with first episode patients (effective dose ranges are low in comparison with those for multi-episode patients; marked side effect sensitivity), consideration of using slow titration and low to moderate antidepressant doses is reasonable in the absence of data

C. Suicide Assessment and Prevention

- The first years of schizophrenia are a time of risk for suicide attempts
- Make sure to look for signs of hopelessness, resignation, or ruminations about falling behind peers or own family expectations
- Make sure to inquire about suicidal thinking or behaviors
 - Again, family members can be a good source of information

D. Laboratory Testing Schedule

- Testing depends upon the patient's medical status
- For patients without a known medical issue, standard lab testing (lipid and glucose metabolism measures at a minimum) occurs when
 - starting a new antipsychotic
 - 3 months after starting the antipsychotic
 - and then annually for patients with no identified abnormalities.

- This schedule is modified (either in frequency or tests needed) if patients develop abnormalities. The schedule is then determined by the medical issue identified

Unfortunately, tests are often ordered but not done. Enlist the NAVIGATE team to help educate patients and families about the rationale for the testing and to provide supports for getting testing

- The IRT and family clinicians can support educational efforts
- Peers and case managers can provide support for patients, especially if testing is done in off-site locations

Similarly, education and support are needed to ensure that patients receive the proper medical follow-up for issues identified by test results

E. Substance Misuse

Studies with first episode populations consistently report high levels of co-morbid substance misuse. In the RAISE-ETP study approximately one-third of participants at study entry reported recent alcohol use (36.6%) and cannabis use (30.7%), and one half (51.7%) met criteria for any lifetime alcohol or drug use disorder²².

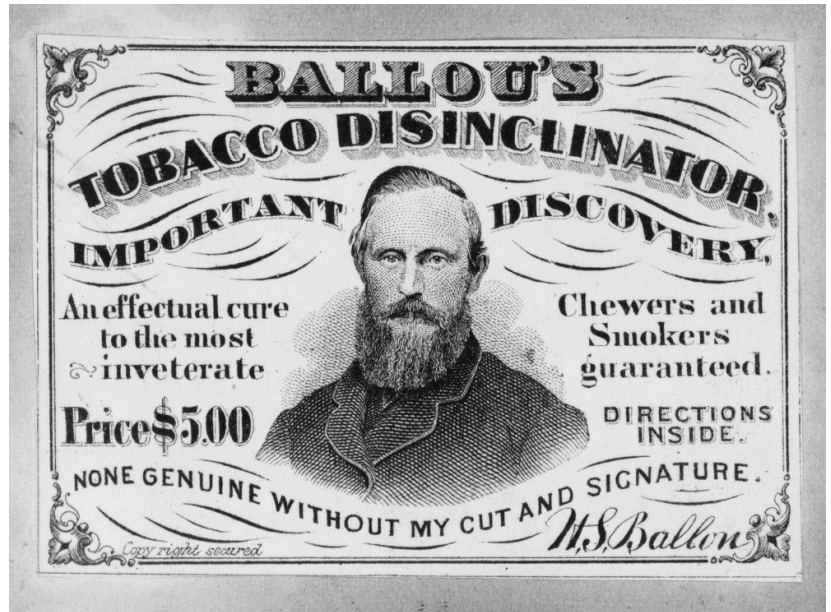
NAVIGATE was designed for use in community facilities across the country. Facilities vary widely in the substance use treatment services available to their patients; this is partially due to local factors and also differences in funding availability across states and other payer mechanisms. As a NAVIGATE prescriber, you will need to determine the best treatment options available within your agency/locality and integrate these into treatment plans.

The psychosocial interventions in NAVIGATE provide some treatment options. These include:

- Education about the relationship between psychosis and substance use is provided to all individuals and family members in the IRT and family educational sessions.
 - Three IRT modules (Assessment and Goal Setting, Education About Psychosis and the Substance Use module) include structured assessment of alcohol, marijuana and other substance use with the CRAFFT⁴⁸, a brief screening instrument validate for use with adolescent populations.
- Individualized treatment using educational, motivational, and cognitive-behavioral strategies is offered via the IRT module on substance use. Specific elements of this treatment include education, goal setting, motivational strategies, behavioral experiments, decision support, skills training, and relapse prevention planning.
- The family manual includes modules on alcohol and drug use and health lifestyles.

F. Tobacco and Nicotine Use

Fortunately, the field has moved beyond Mr. Ballou's intervention and we live in an era that has effective tobacco cessation treatment programs. A recent meta-analysis⁴⁸ of smoking cessation treatment with patients with schizophrenia and bipolar disorders found positive effects compared to placebo at 3 and 6 month time points for varenicline and at 3 months for bupropion.



With effective treatments available, key issues include identifying individuals who are using tobacco products and motivating them to engage in tobacco cessation treatments.

- Rates of tobacco use among young people with psychotic disorders is very high, e.g. 50.8% of RAISE-ETP participants were smoking at the baseline interview.
- Young smokers often use a variety of tobacco products (e.g. small cigars, hookah) and some will be using products but not using cigarettes. Your tobacco and nicotine use assessment should include inquiry about use of all product types, not just cigarettes.
- One of the challenges for motivating young people to engage in tobacco cessation is the perception that they can quit in the future before having tobacco related injury. Designing motivational interventions for young smokers is an area

of active research with positive initial findings for web-based approaches⁴⁹ and use of pictorial/video health warnings⁵⁰.

- The IRT manual includes a tobacco section in the Healthy Lifestyles module to assist with education and motivation for tobacco cessation.
- The family manual Healthy Lifestyle module includes education about the negative effects of using tobacco products.

Note: Our understanding of the dangers of e-cigarettes and if these devices are gateways to other nicotine use or alternatively, in a harm reduction perspective, better than tobacco use for people with psychotic disorders is incomplete at this time and future developments need to be followed closely. These will need to be considered within the context of the Surgeon General's warning about e-cigarette use among the general youth population⁵¹.

The IRT Healthy Lifestyles module includes presentation of current information about e-cigarettes and encourages discussion with patients of e-cigarette use.

V. Assessment Tools

Getting the best
understanding of
your patients'
status



A. Navigate Assessment Strategies

The original NAVIGATE model for the RAISE-ETP study included COMPASS, a NAVIGATE-developed computer clinical decision making tool accessed via a secure web-based platform. COMPASS was designed to facilitate patient-prescriber communication. Participants entered information about symptoms, side effects, treatment preferences, medication adherence and attitudes, and substance use into COMPASS before meeting with prescribers. Vital signs data and laboratory test results were also entered. Using a measurement-based approach, the prescriber's assessments, also entered directly into COMPASS, were modified/informed based upon these prior entered data. Integrating participant treatment priorities and the prescriber's assessments, COMPASS provided suggested guideline treatments.

The COMPASS system was terminated at the end of the RAISE-ETP study. Post RAISE-ETP, NAVIGATE sites used (and continue to use) paper versions of the COMPASS forms. These contain all the questions present in the COMPASS version but lack the interactive aspects (and the decision support provided by COMPASS).

A subsequent version of NAVIGATE used by sites that are part of the ESPRITO network (named Enhanced-NAVIGATE or E-NAVIGATE) uses a newly designed computer system to support assessment. The system includes the same questions to patients about side effects, adherence, substance use and whether a medication change is desired as standard NAVIGATE. Patient self-report procedures differ as an adaptive testing model is used to obtain information about symptom severity.

We first present a discussion of integrating assessment scales into the clinical visit as this is applicable to both the paper version of standard NAVIGATE and E-NAVIGATE. After this section is a review of the standard NAVIGATE and E-NAVIGATE procedures. The relevant forms are included in the Appendix

B. Integrating Assessment Scales into the Clinical Visit

For those who have not routinely used assessment scales in your practice you may have questions about how their use will change your patient visits.

Research has identified some frequent concerns⁵². We present these and some suggested solutions. Before presenting these, an overall point is that the RAISE-ETP study conclusively showed that the NAVIGATE model of medication visits that included assessment scales at each visit was feasible in community settings. Patients completed 3004 self-ratings over the first 2 years; the rate of medication visits in the NAVIGATE treatment condition was approximately twice that of standard care.

Hatfield and Ongles⁵² identified the following frequent concerns about using assessment scales:

1. Some clinicians believe that structured assessments are not useful
 - This is a misperception as research³⁴ has demonstrated better outcomes with measurement based care in multiple disorders and across different provider groups (psychotherapists, psychiatrists and primary care providers)
 - Clinicians sometimes assume that the NAVIGATE assessments were research collection instruments. This also is a misperception. The assessments were instead developed as a support for clinical decision making with first episode patients and are distinct from the research assessments used in RAISE-ETP. The assessments were chosen to cover the minimum amount of information that are needed to determine the clinical status of first episode patients and determine evidence based treatment options
 - The assessments provide several clinical advantages over unstructured care

- At the visit level, the assessments ensure that important domains are always assessed
- Cumulatively, assessments over time provide a useful overview of the trajectory of symptoms and side effects. Everyone has limitations on remembering illness and treatment course long-term. Additional factors with first episode patients and their families can include lack of illness insight and the confusion that can occur when patients and families are coping with the first episode of psychosis. Once symptoms resolve, patients and families sometimes question the need for treatment. Reviewing the results of the assessment scales often provides a quick means to establish the objective course of symptoms and side effects and their relationship with treatments received.
- The NAVIGATE model for patients who decide to stop antipsychotic treatment is for them to continue to see the NAVIGATE prescriber for monitoring visits (as long as this is safe to do). The NAVIGATE visit model with structured assessments provides a framework for monitoring visits. Patients and families often ask what a monitoring visit entails and being able to present that it includes the same procedures as the regular visit facilitates acceptance of the monitoring visits.

2. Practical factors

- Adds to paperwork
- Takes too much time
 - Suggestions for these two concerns are combined as the suggestions cover both. An important point is that the assessments are designed to obtain the clinical information you need. You will be collecting the same information that you would in an unstructured interview but in a systematic way. The assessments substitute for the questions you may have been asking in an

unstructured interview. Being certain to ask questions about all relevant areas can take more time than an unstructured visit that does not include assessment of all the relevant domains. However, the NAVIGATE model can help shorten the time needed to assess some domains compared with unstructured interviews. Examination of the patient self-report data before the visit begins can help you focus your questions during the visit, and this can save time. For example, the patient self-report asks about the 21 most common side effects with antipsychotic treatment of first episode patients. This provides a screen for potential side effects that need inquiry and those that are unlikely to be present.

- Not enough resources
 - Having adequate resources is often an issue in busy clinics. It can be useful to take a proactive stand with clinic administrators from the start of a NAVIGATE program. First episode patients often present with complex problems, they and their families have educational needs and by definition do not have already developed individual treatment programs. They have more service needs than many outpatients and this is appropriate for this patient group. Administrators need to be aware that these extra service needs must be supported if their first episode program is to be successful.

3. Burden to patients

- In fact, patients often perceive assessments as a positive aspect of their treatment.
 - Assessments can help them in their ongoing understand of their progress and of their symptoms
 - It helps to ensure that issues for them are brought to the attention of the prescriber

- The NAVIGATE model of patient self-report followed by the prescriber guiding their questioning based upon the self-report results is a useful communication tool for patients to their prescribers

4. Lack of know-how

5. Lack implementation knowledge

- This guide provides suggestions/information about using measurement in your NAVIGATE visits

6. Unable to interpret scores

- Total scores on an assessment instrument may be hard to translate into clinically meaningful ranges unless you have a lot of experience with the scale. In NAVIGATE we instead focus upon the scores for individual items that drive decision making. Each symptom severity item has a description of what each severity level means in clinical terms. For example, in standard NAVIGATE, severity of symptoms is rated on a 7 point scale. The definition of a level “4” severity for hallucinations is “4. **Moderately Severe:** Experiences daily hallucinations OR some areas of functioning are disrupted by hallucinations”. For positive psychotic symptoms, the treatment target for NAVIGATE is all symptoms at a symptom severity of “3” or less.

A concern not noted by Hatfield and Ongles but frequently mentioned by clinicians who have not done measurement based care is that it will decrease rapport with patients. Some important points to alleviate these concerns:

- Measurement in NAVIGATE is used to provide the data for the shared decision making process. Better information supports better decision making

- The patient self-ratings are a communication tool for patients. It helps them report to you important domains. This is especially relevant for issues like sexual side effects that patients may be reluctant to present.
- The measurements are not the only part of your interview—you and your patients will discuss any additional topics that are not covered in the scales.
- Much of how patients experience the assessments will depend upon you. If you consistently use their self-ratings and your assessments for data collection to support shared decision making, they will perceive the assessments as useful. If they do the self-ratings but you do not use them in the visit, they will have a negative experience
- Many first episode patients have no or little experience with prior treatment. For them, the flow of a NAVIGATE visit is not a new concept as it would be for patients with a lot of experience with unstructured visits.

C. Orienting Patients to the Visit Procedures

- NAVIGATE participants in the RAISE-ETP study quickly acclimated to the NAVIGATE visit flow
- Patients need an orientation for the first visit but usually not to later visits
- Start by describing the visit components and the rationale for each
 - Vital signs are done at each visit to monitor health
 - The questionnaires are designed to make certain that important areas are assessed and that important areas are not missed or not covered
 - Once the questionnaire that the patient completes is finished, you will review it with them. For some items you will ask additional questions to clarify the

patient's responses and you will be keeping notes on a form you have that parallels the structure of the form they complete

- At the end of the visit you and the patient will review all the information collected and use the information to determine jointly the best options for problems identified
- The questionnaires are repeated at each visit in order not to miss important areas and also to document progress
 - It can be useful to acknowledge that this can feel repetitious, but it is the best way we have now to not miss important areas and to document progress
- **An important point to get across:** The questionnaires covers many important areas. However, if there are issues that the patient would like to discuss that are not on the questionnaires, these will be also discussed in the visit.

D. Tips for Those Who Have Not Previously Used Using Assessment Scales in Routine Clinical Care

- You should be able to orient yourself so that when you do assessments that you maintain eye contact with the patient.
 - Have your computer or clipboard to the side so that you can make your ratings while maintaining eye contact with the patient
 - If needed, you may need to move your office furniture to facilitate the interview
- You will be implementing a new clinical skill.
 - The first times that you do a new skill/procedure you will not be as proficient as you will be after you have done the procedure many times
 - Don't get discouraged if the first few assessments seem difficult or take more time than you expect—you will get more comfortable and faster over time.

- If possible, it can be helpful to do a practice interview with a team member playing a patient before doing an actual patient interview
- Allocate more time for the first interviews
- You will need to modify your clinical interview. The scales assess the key data that are needed to make treatment decisions. Use scale questions to substitute for the clinical questions that you normally ask that cover the same domains. For example, the first question on the patient self-report questionnaire is “How have you been doing in the last month? Have you had problems keeping up with what you need to do for work, home, school or friends?” If the patient says yes to the question, they write in the problems that they have been having. Instead of asking open ended questions to determine a chief complaint, you can instead start the interview by acknowledging the problems the patient identified and asking focused questions about these.
- The NAVIGATE prescribers were able to do their routine patient visits in a 30 minute time allotment so the model is feasible from a time perspective in community settings
- **When should assessment scale be done?** Assessments should be done monthly and at each additional visit that includes making clinical decisions (e.g. extra visits due to patients having severe symptoms). Assessments are designed to obtain the information for making clinical decisions, so they are not needed for visits that do not involve clinical decisions (e.g. visits to complete insurance or other forms).

The Standard NAVIGATE Patient Self-Report Questionnaire

The questionnaire in its entirety is included in the appendix

Notes about the questionnaire

- The format is a set of questions with parallel yes/no answers. The sentences associated with yes and no responses are the same as possible with the insertion “not” in the sentence describing the no response. This format may seem odd but it was chosen as a format that is understandable by people with very limited education (as some of our patients with early onset illness have).
- Examples of the format are provided below:

Question	Answers
<p>How have you been doing in the last month? Have you had problems keeping up with what you need to do for work, home, school or friends?</p>	<p>_____ Yes, I have had problems</p> <p>If Yes what are they: _____</p> <p>_____ No, I haven't had any problems</p>
<p>1 Since your last visit, have you been feeling depressed, sad, or down?</p>	<p>_____ Yes, I have felt depressed, sad or down</p> <p>_____ No, I have not felt depressed, sad or down</p>
<p>2 Since your last visit, have you been feeling anxious, worried or nervous?</p>	<p>_____ Yes, I have been feeling anxious, worried or nervous</p> <p>_____ No, I have not been feeling anxious, worried or nervous</p>

- The first section of the self-report covers symptoms (other than psychotic symptoms)
- The next section side effects
- The next adherence and attitudes toward medications
- The next tobacco and substance use

The last question is “Between now and your next visit, do you think we should keep your medication the same or consider changing the medications?” and the possible responses are “Consider changing” or “Stay the Same”. This question gives prescribes a quick overview of the patient’s overall assessment of their medications.

The Standard NAVIGATE Clinician Rating Form

The form in its entirety is included in the appendix

Notes about the form

- The form is designed for you to rate your best evidence for the severity/presence of symptom and side effect domains
 - Often your assessment will agree with the patient self-report but sometimes differ
 - For example, patients often misinterpret co-occurring medical issues as side effects
- The items assessed on the clinician form have the same order as the items on the patient self-report form.
 - The order of questions was developed with feedback from patients who had experience with rating scales. Thus, the order works for most visits. If a patient wants to discuss areas in a different order, follow the order that best fits the situation. Using a different order takes longer as you have to flip between sections so it is best to not change the order routinely.
- An example of the format for the first question is below.

1. Depressed Mood

Sadness, grief, or discouragement (do not rate emotional indifference or empty mood here - only mood which is associated with a painful, sorrowful feeling).

Individual endorsed depressed mood on self-report:

You said on the questionnaire that you have been feeling depressed, sad, or down.

Tell me about what you have been experiencing. How often did it happen? Does it come and go? How long does it last? How bad is the feeling? (Can you stand it?)

Individual did not endorse depressed mood on self-report:

You said on the questionnaire that you have not had any problems recently feeling depressed, sad, or down.

Any problems not being interested in things you usually enjoy? (If yes, probe for the presence of depressed mood).

Rating

0 = **Not reported/symptom not present**

1 = **Very Mild:** occasionally feels sad or “down”; of questionable clinical significance

2 = **Mild:** occasionally feels moderately depressed or often feels sad or “down”

3 = **Moderate:** occasionally feels very depressed or often feels moderately depressed

4 = **Moderately Severe:** often feels very depressed

5 = **Severe:** feels very depressed most of the time

6 = **Very Severe:** constant extremely painful feelings of depression

Unable to assess (e.g. subject uncooperative or incoherent)

- The item to rate is depressed mood. The item definition appears directly below the item name

- Below that in italic type are suggested probe questions. Probe questions are suggested questions that are asked across visits. This ensures that each item is asked consistently across visits.
- Two sets of probe questions are provided for the symptom items that come before the psychotic symptom items. One set is based upon the patient responding yes to the corresponding item on their self-report questionnaire and the other based upon the patient responding no to the item.
- Usually the patient self-report response and the clarifying responses to the probe questions will be enough for you to assess whether a symptom is present and if it is how severe it is. If these issues remain unclear, please ask any additional questions you need to establish symptom presence and if applicable severity.
- The presence/severity of a symptom is then rated on a 7 point scale. Descriptions of each severity level (called “anchors”) are provided. The anchors use 2 dimensions to describe a severity level, how long a symptom lasts and how severe it is when it occurs. Usually these dimensions increase in a parallel manner (e.g. more severe symptoms usually also are more likely to be present for longer periods of time) and the anchors reflect this. Anchors can only describe general situations. If following the anchors would result in an inaccurate severity level rating, rate instead on a continuum of the severity levels. An example of such a situation is a symptom that lasted only a very short time but was very severe and influenced the patient’s behavior substantially.
- Positive symptoms items 7 through 10 (Suspiciousness, Unusual Thought Content, Hallucinations and Conceptual Disorganization) and negative symptom items 11 (Avolition/Apathy) and 12 (Asociality/Low Social Drive) do not have corresponding questions on the patient self-report form. Therefore, there are only one group of probe questions for these items.

- Item 13 assesses medication adherence. This is the clinician's best estimate based upon the patient self-report of adherence and subsequent questioning. It is often useful to ask about adherence during periods of high risk of nonadherence that have been identified in previous patient visits. For example, weekends are high risk periods for many patients as they may be around friends who they do not want to know that the patient takes medications.
- Item 14 is assessment of elbow rigidity. It was chosen as a screen for EPS-- patients with Parkinsonism usually have some degree of elbow rigidity and assessing elbow rigidity can be done quickly. If elbow rigidity is present, further evaluation of EPS is warranted.
- Similar to the use of item 14 as a screening question, item 16 is an evaluation of oral facial movements. Oral facial movements are present in patients with tardive dyskinesia and can be assessed quickly. If present, a full examination for tardive dyskinesia is warranted.
- The patient self-report answers are particularly useful for completing the side effect section. Patients sometimes over endorse the self-report questions about side effects due to somatic preoccupation/worries about health. Further, for use as a screen for side effects, patients are asked to report issues regardless of the cause (e.g. medical issue, side effect). For your assessment of potential side effects, the usual strategy is to assume that a side effect is not present if the patient reports that the medical issue is not present on the self-report form and focus your questioning on the medical items that were reported on the self-report form. An exception to this strategy occurs if you are prescribing a new medication/dose of a medication with a high risk of a particular side effect.
- Along with the severity rating for each side effect, the side effect items include a check box to indicate that a medical issue is present but not related to medication

treatment. This is provided as an aid to remember in future visits that a medical issue that may be a side effect is caused by another factor such as concurrent medical illnesses.

- The remaining sections cover substance misuse

Using the data you have collected

- The data are the basis for determining the best evidence-based practices for consideration in a visit
- It is helpful to enter the data (or a subset of key data elements) into a file such as a spreadsheet
 - These longitudinal data can be useful for reviewing clinical progress with patients and family members
 - The longitudinal data can also be useful from a programmatic perspective to document effects of the program to clinic administrators and stakeholders such as governmental agencies or payers

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Appendix

Standard NAVIGATE Patient Self-Report Questionnaire Clinician Rating Form

Self-Report Questionnaire

Date: _____

Thank you for participating in our program.

As part of the program, you can help us learn how you are doing by answering the following questions. The questions should take only a few minutes to complete. Your prescriber will get the completed form for your visit with him/her and he/she will review your answers with you. This is a good way to get an overview of how you are.

On the left side of the page are the questions. On the right side of the page please check the answer to the question. If you have any questions about the form, please let us know and we can help.

Question	Answer
<p>How have you been doing in the last month? Have you had problems keeping up with what you need to do for work, home, school or friends?</p>	<p><input type="checkbox"/> Yes, I have had problems If Yes what are they: _____ _____ <input type="checkbox"/> No, I haven't had any problems</p>
<p>1 Since your last visit, have you been feeling depressed, sad, or down?</p>	<p><input type="checkbox"/> Yes, I have felt depressed, sad or down <input type="checkbox"/> No, I have not felt depressed, sad or down</p>
<p>2 Since your last visit, have you been feeling anxious, worried or nervous?</p>	<p><input type="checkbox"/> Yes, I have been feeling anxious, worried or nervous <input type="checkbox"/> No, I have not been feeling anxious, worried or nervous</p>
<p>3 Since your last visit, have you been thinking about death or have you had any feelings that you would be better off dead?</p>	<p><input type="checkbox"/> Yes, I have been thinking about death or I have felt that I would be better off dead <input type="checkbox"/> No, I have not been thinking about death and I have not had any feelings that I would be better off dead</p>
<p>4 Since your last visit, have you been feeling particularly good?</p>	<p><input type="checkbox"/> Yes, I have been feeling particularly good <input type="checkbox"/> No, I have not been feeling particularly good</p>

<p>5 Since your last visit, have you been feeling annoyed, angry, or resentful (whether you showed it or not)?</p>	<p><input type="checkbox"/> Yes, I have been feeling annoyed, angry or resentful</p> <p><input type="checkbox"/> No, I have not been feeling annoyed, angry or resentful</p>
<p>6 Since your last visit, did you do anything that could have gotten you in trouble?</p>	<p><input type="checkbox"/> Yes, I have done something that could have gotten me in trouble</p> <p><input type="checkbox"/> No, I have not done anything that could have gotten me into trouble</p>
<p>Since your last visit, please let us know if you have experienced any of the following. Please tell us about your experience whether you think that it was because of a medical problem, a medication side effect or other causes.</p>	
<p>7 Have you felt dizzy or faint?</p>	<p><input type="checkbox"/> Yes, I have felt dizzy or faint</p> <p><input type="checkbox"/> No, I have not felt dizzy or faint</p>
<p>8 Have you had blurred vision?</p>	<p><input type="checkbox"/> Yes, I have had blurred vision</p> <p><input type="checkbox"/> No, I have not had any blurred vision</p>
<p>9 Have you had dry mouth?</p>	<p><input type="checkbox"/> Yes, I have had dry mouth</p> <p><input type="checkbox"/> No, I have not had dry mouth</p>
<p>10 Have you had too much saliva in your mouth or had drooling?</p>	<p><input type="checkbox"/> Yes, I have had too much saliva or have had drooling</p> <p><input type="checkbox"/> No, I have not had too much saliva and I have not had any drooling</p>
<p>11 Have you felt nauseous?</p>	<p><input type="checkbox"/> Yes, I have felt nauseous</p> <p><input type="checkbox"/> No, I have not had any nausea</p>
<p>12 Have you been constipated?</p>	<p><input type="checkbox"/> Yes, I have had constipation</p> <p><input type="checkbox"/> No, I have not had any constipation</p>
<p>13 Has your appetite for food been increased?</p>	<p><input type="checkbox"/> Yes, my appetite for food has been increased</p> <p><input type="checkbox"/> No, my appetite for food has not been increased</p>
<p>14 Have you gained weight?</p>	<p><input type="checkbox"/> Yes, my weight has gone up</p> <p><input type="checkbox"/> No, my weight has not gone up</p>

<p>15 Have you lost weight?</p>	<p><input type="checkbox"/> Yes, I have lost weight</p> <p><input type="checkbox"/> No, I have not lost weight</p>
<p>16 Have you felt restless or like you can't stay still?</p>	<p><input type="checkbox"/> Yes, I have felt restless or have had difficulty staying still</p> <p><input type="checkbox"/> No, I have not felt restless and I have not had any difficulty staying still</p>
<p>17 Any shaking of your hands, legs or other muscles?</p>	<p><input type="checkbox"/> Yes, I have had shaking of my hands, legs or other muscles</p> <p><input type="checkbox"/> No, I have not had any shaking</p>
<p>18 Any problems walking or moving or any problems feeling stiff or rigid?</p>	<p><input type="checkbox"/> Yes, I had problems walking or moving or have had problems feeling stiff</p> <p><input type="checkbox"/> No, I have not had any problems walking and I have not had any feelings of being stiff</p>
<p>19 Have your felt tired or fatigued?</p>	<p><input type="checkbox"/> Yes, I have felt tired or fatigued</p> <p><input type="checkbox"/> No, I have not felt tired or fatigued</p>
<p>20 Have you felt drowsy during the day?</p>	<p><input type="checkbox"/> Yes, I have felt drowsy during the daytime</p> <p><input type="checkbox"/> No, I have not felt drowsy during the daytime</p>
<p>21 Have you been sleeping too much at night?</p>	<p><input type="checkbox"/> Yes, I sleep too many hours a night</p> <p><input type="checkbox"/> No, I do not sleep too much at night</p>
<p>22 Have you been sleeping too little or had problems sleeping at night?</p>	<p><input type="checkbox"/> Yes, I sleep too little or have had problems sleeping at night</p> <p><input type="checkbox"/> No, I do not have any problems sleeping</p>
<p>23 Any decrease in your interest in sex?</p>	<p><input type="checkbox"/> Yes, my interest in sex is low</p> <p><input type="checkbox"/> No, my interest in sex is fine</p>
<p>24 Any other problems with sex?</p>	<p><input type="checkbox"/> Yes, I have problems with sex</p> <p><input type="checkbox"/> No, I do not have any problems with sex</p>

<p>25 Any problems with your breasts such as swelling or discharge?</p>	<p><input type="checkbox"/> Yes, I have had problems with my breasts</p> <p><input type="checkbox"/> No, I did not have any problems with my breasts</p>
<p>26 For women, any problems with your period?</p>	<p><input type="checkbox"/> Yes, I have had problems with my period</p> <p><input type="checkbox"/> No, I did not have any problems with my period</p>
<p>27 Are there other medical or side effect problems you wish to discuss with your prescriber?</p>	<p><input type="checkbox"/> Yes, I have these problems (please list):</p> <p><input type="checkbox"/> No, I don't have any other medical or side effect problems</p>
<p>Next, please let us know some information about your medications</p>	
<p>28 Since your last visit, how many days have you not taken your medication?</p>	<p>Number of days not taking medication <input type="text"/></p> <p>(if you have not missed any medication, please put 0 for number of days)</p>
<p>29 Have you had trouble remembering to take your medication?</p>	<p><input type="checkbox"/> Yes, I have trouble remembering to take the medication</p> <p><input type="checkbox"/> No, I do not have trouble remembering to take the medication</p>
<p>30 Do you find the number of medicines or the times when you are supposed to take them confusing or burdensome?</p>	<p><input type="checkbox"/> Yes, the way I am supposed to take the medication is confusing or is burdensome to do</p> <p><input type="checkbox"/> No, the way I am supposed to take the medication is clear and is not a problem</p>
<p>31 Are you afraid of the medication?</p>	<p><input type="checkbox"/> Yes, I am afraid of the medication</p> <p><input type="checkbox"/> No, I am not afraid of the medication</p>
<p>32 Do you think that you have an illness that requires taking medication?</p>	<p><input type="checkbox"/> Yes, I have an illness that requires that I take medication</p> <p><input type="checkbox"/> No, I do not have an illness that requires that I take medication</p>

<p>33 Do you think that other people would think poorly of you if they knew that you take medication?</p>	<p><input type="checkbox"/> Yes, taking medication might make other people think poorly of me</p> <p><input type="checkbox"/> No, taking medication would not make people think poorly of me</p>
<p>Some final questions</p>	
<p>34 On average, how many cigarettes do you smoke per day?</p>	<p>Number of cigarettes I smoke per day <input type="text"/></p> <p>(if you do not smoke cigarettes, please put 0 for number of cigarettes smoked)</p>
<p>35 Since your last visit, did you drink any alcohol?</p>	<p><input type="checkbox"/> Yes, I have used alcohol</p> <p><input type="checkbox"/> No, I have not used any alcohol</p>
<p>36 Since your last visit, have you used any marijuana?</p>	<p><input type="checkbox"/> Yes, I have used marijuana</p> <p><input type="checkbox"/> No, I have not used any marijuana</p>
<p>37 Since your last visit, have you used any street drugs (other than marijuana)?</p>	<p><input type="checkbox"/> Yes, I have used street drugs other than marijuana.</p> <p><input type="checkbox"/> No, I have only used marijuana</p> <p><input type="checkbox"/> No, I have not used any street drugs including marijuana</p>
<p>38 Between now and your next visit, do you think we should keep your medication the same or consider changing the medications?</p>	<p><input type="checkbox"/> Consider changing</p> <p><input type="checkbox"/> Stay the Same</p>

Thank you for completing the form.

Standard NAVIGATE Clinician Rating Form

1. Depressed Mood

Sadness, grief, or discouragement (do not rate emotional indifference or empty mood here - only mood which is associated with a painful, sorrowful feeling).

Individual endorsed depressed mood on self-report:

You said on the questionnaire that you have been feeling depressed, sad, or down.

Tell me about what you have been experiencing. How often did it happen? Does it come and go? How long does it last? How bad is the feeling? (Can you stand it?)

Individual did not endorse depressed mood on self-report:

You said on the questionnaire that you have not had any problems recently feeling depressed, sad, or down.

Any problems not being interested in things you usually enjoy? (If yes, probe for the presence of depressed mood).

Rating

0 = **Not present**

1 = **Very Mild:** occasionally feels sad or "down"; of questionable clinical significance

2 = **Mild:** occasionally feels moderately depressed or often feels sad or "down"

3 = **Moderate:** occasionally feels very depressed or often feels moderately depressed

4 = **Moderately Severe:** often feels very depressed

5 = **Severe:** feels very depressed most of the time

6 = **Very Severe:** constant extremely painful feelings of depression

Unable to assess (e.g. subject uncooperative or incoherent)

2. Anxiety / Worry

Subjective experience of worry, apprehension; over-concern for present or future. Anxiety/fear from a psychotic symptom should be rated (e.g. the subject feels anxious because of a belief that he/she is about to be killed).

Individual endorsed anxious mood on self-report:

You said on the questionnaire that you have been feeling anxious, worried or nervous.

Tell me about what you have been experiencing. What are some things you worry about or that make your nervous? How often did it happen? Does it come and go? How bad is the feeling?

Individual did not endorse anxious mood on self-report:

Would you say that you have usually been calm and relaxed recently?

Rating

0 = **Not present**

1 = **Very Mild:** occasionally feels a little anxious; of questionable clinical significance

2 = **Mild:** occasionally feels moderately anxious or often feels a little anxious or worried

3 = **Moderate:** occasionally feels very anxious or often feels moderately anxious

4 = **Moderately Severe:** often feels very anxious or worried

5 = **Severe:** feels very anxious or worried most of the time

6 = **Very Severe:** individual is continually preoccupied with severe anxiety

Unable to assess (e.g. subject uncooperative or incoherent)

3. Suicidal Ideation / Behavior

The subject reports a passive death wish, thoughts of suicide, or engages in suicidal behavior (do not include self-injurious behavior without suicidal intent).

Individual endorsed thoughts about death on self-report:

You said on the questionnaire that you have been thinking about death or that you would be better off dead.

Tell me about what you have been thinking. How often do you think about death? Have you thought about hurting yourself? (Have you thought of any ways to hurt yourself?) (Do these thoughts upset you?) (Any times when you have tried to hurt yourself since our last visit?)

Individual did not endorse thoughts about death on self-report:

You said on the questionnaire that you have not had any thoughts since your last visit about death or being better off dead. Is that correct?

Rating

- 0 = **Not present**
 - 1 = **Very Mild:** occasional thoughts of dying, "I'd be better off dead" or "I wish I were dead"
 - 2 = **Mild:** frequent thoughts of dying or occasional thoughts of killing self, without a plan or method
 - 3 = **Moderate:** often thinks of suicide or has thought of a specific method
 - 4 = **Moderately Severe:** has mentally rehearsed a specific method of suicide or has made a suicide attempt with questionable intent to die (e.g. takes aspirins and then tells family)
 - 5 = **Severe:** has made preparations for a potentially lethal suicide attempt (e.g. acquires a gun and bullets for an attempt)
 - 6 = **Very Severe:** has made a suicide attempt with definite intent to die
- Unable to assess (e.g. subject uncooperative or incoherent)

4. Elevated / Expansive Mood

elevation of mood (mood unusually good, cheerful, high or expansive)

Individual endorsed feeling particularly good on self-report

On the questionnaire, you said that you have been feeling particularly good. Were you just in a good mood or was it something more than that? Was this different from your normal self? (Did you feel on top of the world?)

Individual did not endorse feeling particularly good on self-report

On the questionnaire, you said that you have not been feeling particularly good. Is that correct? Any times recently when people have thought that you were not your usual self?

Rating

0 = **Not present**

1 = **Very Mild:** questionable; more cheerful than most people in his/her circumstances but of only possible clinical significance

2 = **Mild:** brief elevated/expansive mood but only somewhat out of proportion to the circumstances.

3 = **Moderate:** brief/occasional elevation of mood which is clearly out of proportion to the circumstances

4 = **Moderately Severe:** sustained/frequent elevation of mood which is clearly out of proportion to the circumstances

5 = **Severe:** mood is euphoric most of the time

6 = **Very Severe:** sustained elation; "everything is wonderful" almost all of the time

Unable to assess (e.g. subject uncooperative or incoherent)

5. Hostility / Anger / Irritability / Aggressiveness

anger, verbal and non-verbal expressions of anger and resentment including a belligerent attitude, sarcasm, abusive language, and assaultive or threatening behavior.

Individual endorsed feeling annoyed, angry or resentful

On the questionnaire, you said that you had been feeling annoyed, angry or resentful. Tell me how you have been feeling. Have other people done things to make you mad?

(Could other people tell that you were angry?)

(Have you done anything about your anger [for example, shout at people])?

Individual did not endorse feeling annoyed, angry or resentful

On the questionnaire, you said that you have not been feeling annoyed, angry or resentful. Have other people done things that could have make you mad?

Rating

- 0 = **Not present**
 - 1 = **Very Mild:** occasional irritability of doubtful clinical significance
 - 2 = **Mild:** occasionally feels angry or mild or indirect expressions of anger, e.g. sarcasm, disrespect or hostile gestures
 - 3 = **Moderate:** frequently feels angry, frequent irritability or occasional direct expression of anger, e.g. yelling at others
 - 4 = **Moderately Severe:** often feels very angry, often yells at others or occasionally threatens to harm others
 - 5 = **Severe:** has acted on his anger by becoming physically abusive on one or two occasions or makes frequent threats to harm others or is very angry most of the time
 - 6 = **Very Severe:** has been physically aggressive and/or required intervention to prevent assaultiveness on several occasions; or any serious assaultive act.
- Unable to assess (e.g. subject uncooperative or incoherent)

6. Impulsive Behavior

Doing things at the spur of the moment without thinking, planning, or considering the consequences. Do not rate general poor judgement (e.g. not taking medication, drug abuse) unless there is a short term impulsive quality to the act.

Individual endorsed doing something that could have gotten themselves in trouble

On the questionnaire you said that you had done something recently that could have gotten you in trouble. Can you tell me the circumstances?

Did you do anything reckless? For example, spending too much money? Did anything sexual that was unusual or reckless for you?

Individual did not endorse doing something that could have gotten themselves in trouble

On the questionnaire you said that you had not done anything recently that could have gotten you in trouble. Have you recently done anything reckless?

Rating

- 0 = **Not present**
 - 1 = **Very Mild:** one instance of impulsive behavior which is of doubtful clinical significance
 - 2 = **Mild:** occasional impulsive acts, e.g. making phone calls at odd hours
 - 3 = **Moderate:** occasional impulsive acts with some potential negative consequence, e.g. leaving work abruptly; changing plans without thinking
 - 4 = **Moderately Severe:** impulsive acts with definite negative consequences, e.g. overspending on non-essentials; repeated reckless sexual behavior
 - 5 = **Severe:** impulsive acts with direct negative consequences, e.g. spends entire income on nonessentials without regard for basic needs
 - 6 = **Very Severe:** impulsive behavior which is potentially life threatening, e.g. jumps from dangerous height (without suicidal intent) or criminal behavior, e.g. impulsive robbery
- Unable to assess (e.g. subject uncooperative or incoherent)

7. Suspiciousness

Expressed or apparent belief that other persons have acted maliciously or with discriminatory intent. Include persecution by supernatural or other nonhuman agencies (e.g., the devil). Note: Ratings of “3” or above should also be rated under Unusual Thought Content.

Do you ever feel uncomfortable in public? Does it seem as though others are watching you?

Are you concerned about anyone's intentions toward you?

Is anyone going out of their way to give you a hard time, or trying to hurt you? Do you feel in any danger?

[If individual reports any persecutory ideas/delusions, ask the following]:

How often have you been concerned that [use individual's description]? Have you told anyone about these experiences?

Rating

0 = **Not Present**

1 = **Very Mild:** Seems on guard. Reluctant to respond to some “personal” questions. Reports being overly self-conscious in public.

2 = **Mild:** Describes incidents in which others have harmed or wanted to harm him/her that sound plausible. Individual feels as if others are watching, laughing, or criticizing him/her in public, but this occurs only occasionally or rarely. Little or no preoccupation.

3 = **Moderate:** Says others are talking about him/her maliciously, have negative intentions, or may harm him/her. Beyond the likelihood of plausibility, but not delusional. Incidents of suspected persecution occur occasionally (less than once per week) with some preoccupation.

4 = **Moderately Severe:** Same as 4, but incidents occur frequently such as more than once a week. Individual is moderately preoccupied with ideas of persecution OR individual reports persecutory forces.

6 = **Extremely Severe:** Same as 6, but the beliefs are delusions expressed with much doubt (e.g. partial delusion).

5 = **Severe:** Delusional -- speaks of Mafia plots, the FBI, or others poisoning his/her food, persecution by supernatural bizarre or more preoccupying. Individual tends to disclose or act on persecutory delusions.

Unable to assess (e.g. subject uncooperative or incoherent)

8. Unusual Thought Content

Unusual, odd, strange or bizarre thought content. Rate the degree of unusualness, not the degree of disorganization of speech. Delusions are patently absurd, clearly false or bizarre ideas that are expressed with full conviction. Consider the individual to have full conviction if he/she has acted as though the delusional belief were true. Ideas of reference/persecution can be differentiated from delusions in that ideas are expressed with much doubt and contain more elements of reality. Include thought insertion, withdrawal and broadcast. Include grandiose, somatic and persecutory delusions even if rated elsewhere. Note: If Suspiciousness is rated "6" or "7" due to delusions, then Unusual Thought Content must be rated a "4" or above.

Have you been receiving any special messages from people or from the way things are arranged around you? Have you seen any references to yourself on TV or in the newspapers? Can anyone read your mind? Do you have a special relationship with God?

Is anything like electricity, X-rays, or radio waves affecting you? Are thoughts put into your head that are not your own? Have you felt that you were under the control of another person or force? [If individual reports any odd ideas/delusions, ask the following]: How often do you think about [use individual's description]? Have you told anyone about these experiences? How do you explain the things that have been happening [specify]?

Rating

0 = **Not Present**

1 = **Very Mild:** Ideas of reference (people may stare or may laugh at him), ideas of persecution (people may mistreat him). Unusual beliefs in psychic powers, spirits, UFOs, or unrealistic beliefs in one's own abilities. Not strongly held. Some doubt.

2 = **Mild:** Same as 2, but degree of reality distortion is more severe as indicated by highly unusual ideas or greater conviction. Content may be typical of delusions (even bizarre), but without full conviction. The delusion does not seem to have fully formed, but is considered as one possible explanation for an unusual experience.

3 = **Moderate:** Delusion present but no preoccupation or functional impairment. May be an encapsulated delusion or a firmly endorsed absurd belief about past delusional circumstances.

4 = **Moderately Severe:** Full delusion(s) present with some preoccupation OR some areas of functioning disrupted by delusional thinking.

5 = **Severe:** Full delusion(s) present with much preoccupation OR many areas of functioning are disrupted by delusional thinking.

6 = **Extremely Severe:** Full delusions present with almost total preoccupation OR most areas of functioning are disrupted by delusional thinking.

Unable to assess (e.g. subject uncooperative or incoherent)

9. Hallucinations

Reports of perceptual experiences in the absence of relevant external stimuli. When rating degree to which functioning is disrupted by hallucinations, include preoccupation with the content and experience of the hallucinations, as well as functioning disrupted by acting out on the hallucinatory content (e.g., engaging in deviant behavior due to command hallucinations). Include "thoughts aloud" ("gedankenlautwerden") or pseudohallucinations (e.g., hears a voice inside head) if a voice quality is present.

Do you ever seem to hear your name being called? Have you heard any sounds or people talking to you or about you when there has been nobody around? [If hears voices]: What does the voice/voices say? Did it have a voice quality? Do you ever have visions or see things that others do not see? What about smell — odors that others do not smell? [If the individual reports hallucinations, ask the following]: Have these experiences interfered with your ability to perform your usual activities/work? How do you explain them? How often do they occur?

Rating	0 = Not Present
	1 = Very Mild: While resting or going to sleep, sees visions, smells odors, or hears voices, sounds or whispers in the absence of external stimulation, but no impairment in functioning.
	2 = Mild: While in a clear state of consciousness, hears a voice calling the subject's name, experiences non-verbal auditory hallucinations (e.g., sounds or whispers), formless visual hallucinations, or has sensory experiences in the presence of a modality-relevant stimulus (e.g., visual illusions) infrequently (e.g., 1-2 times per week) and with no functional impairment.
	3 = Moderate: Occasional verbal, visual, gustatory, olfactory, or tactile hallucinations with no functional impairment OR non-verbal auditory hallucinations/visual illusions more than infrequently or with impairment.
	4 = Moderately Severe: Experiences daily hallucinations OR some areas of functioning are disrupted by hallucinations.
	5 = Severe: Experiences verbal or visual hallucinations several times a day OR many areas of functioning are disrupted by these hallucinations.
	6 = Extremely Severe: Persistent verbal or visual hallucinations throughout the day OR most areas of functioning are disrupted by these hallucinations.
<input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)	

10. Conceptual Disorganization

Degree to which speech is confused, disconnected, vague or disorganized. Rate tangentiality, circumstantiality, sudden topic shifts, incoherence, derailment, blocking, neologisms, and other speech disorders. Do not rate content of speech.

Rating

- 0 = **Not Present**
 - 1 = **Very Mild:** Peculiar use of words or rambling but speech is comprehensible.
 - 2 = **Mild:** Speech a bit hard to understand or make sense of due to tangentiality, circumstantiality, or sudden topic shifts.
 - 3 = **Moderate:** Speech difficult to understand due to tangentiality, circumstantiality, idiosyncratic speech, or topic shifts on many occasions OR 1-2 instances of incoherent phrases.
 - 4 = **Moderately Severe:** Speech difficult to understand due to circumstantiality, tangentiality, neologisms, blocking, or topic shifts most of the time OR 3-5 instances of incoherent phrases.
 - 5 = **Severe:** Speech is incomprehensible due to severe impairments most of the time. Many PSRS items cannot be rated by self-report alone.
 - 6 = **Extremely Severe:** Speech is incomprehensible throughout interview.
- Unable to assess (e.g. subject uncooperative or incoherent)

11. Avolition /Apathy

Avolition manifests itself as a characteristic lack of energy, drive, and interest. Consider degree of passivity in pursuing goal-directed activities. Factor in the range of activities available to the subject (e.g. individual hospitalization often substantially limits the range of activities available to individuals)

During the past week, how have you been spending your time?

Rating

- 0 = **Not present**
- 1 = **Very Mild:** questionable decrease in time spent in goal-directed activities.
- 2 = **Mild:** spends less time in goal-directed activities than is appropriate for situation and age.
- 3 = **Moderate:** initiates activities at times but does not follow through.
- 4 = **Moderately Severe:** rarely initiates activity but will passively engage with encouragement

	<p>5 = Severe: almost never initiates activities; requires assistance to accomplish basic activities.</p> <p>6 = Very Severe: does not initiate or persist in any goal-directed activity even with outside assistance</p> <p><input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)</p>
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12. Asociality / Low Social Drive

The subject pursues little or no social interaction, and tends to spend much of the time alone or non-interactively.

Some people are very outgoing and like to always be around people; they are “the life of the party”. Other people are very reserved and like to have a lot of time alone. What type of person are you? (Are you more reserved or more outgoing?)

What types of things have you done with people during the past week?

Tell me about your friends?

Have you had a chance to see or speak with them lately?

(If an individual) How about people on the ward?

What types of things do you do with them?

Rating	<p>0 = Not present</p> <p>1 = Very Mild: questionable;</p> <p>2 = Mild: slow to initiate social interactions but usually responds to overtures by others.</p> <p>3 = Moderate: rarely initiates social interactions; sometimes responds to overtures by others.</p> <p>4 = Moderately Severe: does not initiate but sometimes responds to overtures by others; little social interaction outside close family members.</p> <p>5 = Severe: never initiates and rarely encourages conversations or activities; avoids being with others unless prodded, may have contacts with family.</p> <p>6 = Very Severe: avoids being with others (even family members) whenever possible, extreme social isolation.</p> <p><input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)</p>
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13. Adherence

Based upon responses by individual on questionnaire:

If individual said that they had not missed any medication days on the questionnaire: On the questionnaire you said that you had not missed any days taking your medication. Were there any times when you were too busy to take the medication or didn't have it available for you to take? (What about weekends?)

If individual said that they had missed some medication days on the questionnaire: On the questionnaire you said that since your last visit you had missed _____ days taking your medication. When did that occur? What were the circumstances? Any other days when you were too busy to take the medication or didn't have it available? What about weekends? When did you last need to get your medication refilled?

Based upon all available information, the longest continuous time in days since the last visit when the subject did not take medication:

14. EPS

Rate Elbow Rigidity for all subjects

Examiner separately bends at right angles and extends and flexes each elbow joint, with the subject's biceps observed and simultaneously palpated. The resistance to this procedure is rated.

Rating

- 0 = Normal
- 1 = Slight stiffness and resistance
- 2 = Moderate stiffness and resistance
- 3 = Marked rigidity with difficulty in passive movement
- 4 = Extreme stiffness and rigidity with almost a frozen joint
- Unable to assess (e.g. subject uncooperative or incoherent)

EPS part 2

Check here _____ if other signs of EPS (e.g. diminished arm swing, postural instability, cog wheeling, tremor, akinesia) are present based upon individual report or exam.

15. Akathisia

Subject is observed for restlessness. If restlessness is noted, ask: "Do you feel restless or jittery inside; is it difficult to sit still?" Subjective response is not necessary for scoring but subject report can help make the assessment.

Rating

- 0 = No restlessness reported or observed
 - 1 = Mild restlessness observed; e.g., occasional jiggling of the foot occurs when subject is seated
 - 2 = Moderate restlessness observed; e.g., on several occasions, jiggles foot, crosses and uncrosses legs or twists a part of the body
 - 3 = Restlessness is frequently observed; e.g., the foot or legs moving most of the time
 - 4 = Restlessness persistently observed; e.g., subject cannot sit still, may get up and walk
- Unable to assess (e.g. subject uncooperative or incoherent)

16. Dyskinetic Movement Ratings

Rate highest severity observed. Rate movements that occur upon activation one less than those observed spontaneously.

Individuals with Tardive Dyskinesia almost always have oral-facial movements as the sole or one of the muscle groups involved. Please assess for the presence of these involuntary movements.

Muscles of Facial Expression (e.g. movements of forehead, eyebrows periorbital area, cheeks, including frowning blinking, smiling, grimacing) **or Lips and Perioral Area** (e.g., puckering, pouting, smacking) **or Jaw** (e.g. biting, clenching, chewing, mouth opening, lateral movement) **or Tongue** (darting in and out of mouth, choreoathetoid movements of tongue).

Rating

- 0 = None
 - 1 = Minimal, may be extreme normal
 - 2 = Mild
 - 3 = Moderate
 - 4 = Severe
- Unable to assess (e.g. subject uncooperative or incoherent)

Side Effects

<p>Feel dizzy or faint</p>	<p>0 = Side effect/medical issue not present</p> <p><input type="checkbox"/> Not related to treatment – <u>medical issue present but not related to medication treatment</u> (e.g. intercurrent illness)</p> <p>If side effect or medical issue is present, rate severity:</p> <p>1 = Minimal, may be extreme of normal</p> <p>2 = Mild</p> <p>3 = Moderate</p> <p>4 = Severe</p> <p><input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)</p>
<p>Blurred vision</p>	<p>0 = Side effect/medical issue not present</p> <p><input type="checkbox"/> Not related to treatment – <u>medical issue present but not related to medication treatment</u> (e.g. intercurrent illness)</p> <p>If side effect or medical issue is present, rate severity:</p> <p>1 = Minimal, may be extreme of normal</p> <p>2 = Mild</p> <p>3 = Moderate</p> <p>4 = Severe</p> <p><input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)</p>
<p>Dry mouth</p>	<p>0 = Side effect/medical issue not present</p> <p><input type="checkbox"/> Not related to treatment – <u>medical issue present but not related to medication treatment</u> (e.g. intercurrent illness)</p> <p>If side effect or medical issue is present, rate severity:</p> <p>1 = Minimal, may be extreme of normal</p>

	<p>2 = Mild</p> <p>3 = Moderate</p> <p>4 = Severe</p> <p><input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)</p>
Having too much saliva or drooling	<p>0 = Side effect/medical issue not present</p> <p><input type="checkbox"/> Not related to treatment – <u>medical issue present but not related to medication treatment</u> (e.g. intercurrent illness)</p> <p>If side effect or medical issue is present, rate severity:</p> <p>1 = Minimal, may be extreme of normal</p> <p>2 = Mild</p> <p>3 = Moderate</p> <p>4 = Severe</p> <p><input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)</p>
Nausea	<p>0 = Side effect/medical issue not present</p> <p><input type="checkbox"/> Not related to treatment – <u>medical issue present but not related to medication treatment</u> (e.g. intercurrent illness)</p> <p>If side effect or medical issue is present, rate severity:</p> <p>1 = Minimal, may be extreme of normal</p> <p>2 = Mild</p> <p>3 = Moderate</p> <p>4 = Severe</p> <p><input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)</p>
Constipation	<p>0 = Side effect/medical issue not present</p>

	<p><input type="checkbox"/> Not related to treatment – <u>medical issue present but not related to medication treatment</u> (e.g. intercurrent illness)</p> <p>If side effect or medical issue is present, rate severity:</p> <p>1 = Minimal, may be extreme of normal</p> <p>2 = Mild</p> <p>3 = Moderate</p> <p>4 = Severe</p> <p><input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)</p>
Increased appetite for food	<p>0 = Side effect/medical issue not present</p> <p><input type="checkbox"/> Not related to treatment – <u>medical issue present but not related to medication treatment</u> (e.g. intercurrent illness)</p> <p>If side effect or medical issue is present, rate severity:</p> <p>1 = Minimal, may be extreme of normal</p> <p>2 = Mild</p> <p>3 = Moderate</p> <p>4 = Severe</p> <p><input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)</p>
Weight gain	<p>0 = Side effect/medical issue not present</p> <p><input type="checkbox"/> Not related to treatment – <u>medical issue present but not related to medication treatment</u> (e.g. intercurrent illness)</p> <p>If side effect or medical issue is present, rate severity:</p> <p>1 = Minimal, may be extreme of normal</p> <p>2 = Mild</p> <p>3 = Moderate</p> <p>4 = Severe</p>

	<input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)
Weight loss	<p>0 = Side effect/medical issue not present</p> <input type="checkbox"/> Not related to treatment – <u>medical issue present but not related to medication treatment</u> (e.g. intercurrent illness) <p>If side effect or medical issue is present, rate severity:</p> <p>1 = Minimal, may be extreme of normal</p> <p>2 = Mild</p> <p>3 = Moderate</p> <p>4 = Severe</p> <input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)
Feeling tired or fatigued	<p>0 = Side effect/medical issue not present</p> <input type="checkbox"/> Not related to treatment – <u>medical issue present but not related to medication treatment</u> (e.g. intercurrent illness) <p>If side effect or medical issue is present, rate severity:</p> <p>1 = Minimal, may be extreme of normal</p> <p>2 = Mild</p> <p>3 = Moderate</p> <p>4 = Severe</p> <input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)
Daytime sedation	<p>0 = Side effect/medical issue not present</p> <input type="checkbox"/> Not related to treatment – <u>medical issue present but not related to medication treatment</u> (e.g. intercurrent illness) <p>If side effect or medical issue is present, rate severity:</p> <p>1 = Minimal, may be extreme of normal</p>

	<p>2 = Mild</p> <p>3 = Moderate</p> <p>4 = Severe</p> <p><input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)</p>
Hypersomnia	<p>0 = Side effect/medical issue not present</p> <p><input type="checkbox"/> Not related to treatment – <u>medical issue present but not related to medication treatment</u> (e.g. intercurrent illness)</p> <p>If side effect or medical issue is present, rate severity:</p> <p>1 = Minimal, may be extreme of normal</p> <p>2 = Mild</p> <p>3 = Moderate</p> <p>4 = Severe</p> <p><input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)</p>
Insomnia	<p>0 = Side effect/medical issue not present</p> <p><input type="checkbox"/> Not related to treatment – <u>medical issue present but not related to medication treatment</u> (e.g. intercurrent illness)</p> <p>If side effect or medical issue is present, rate severity:</p> <p>1 = Minimal, may be extreme of normal</p> <p>2 = Mild</p> <p>3 = Moderate</p> <p>4 = Severe</p> <p><input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)</p>
Low libido	<p>0 = Side effect/medical issue not present</p>

	<p><input type="checkbox"/> Not related to treatment – <u>medical issue present but not related to medication treatment</u> (e.g. intercurrent illness)</p> <p>If side effect or medical issue is present, rate severity:</p> <p>1 = Minimal, may be extreme of normal</p> <p>2 = Mild</p> <p>3 = Moderate</p> <p>4 = Severe</p> <p><input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)</p>
Other problems with sex	<p>0 = Side effect/medical issue not present</p> <p><input type="checkbox"/> Not related to treatment – <u>medical issue present but not related to medication treatment</u> (e.g. intercurrent illness)</p> <p>If side effect or medical issue is present, rate severity:</p> <p>1 = Minimal, may be extreme of normal</p> <p>2 = Mild</p> <p>3 = Moderate</p> <p>4 = Severe</p> <p><input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)</p>
Breast enlargement or discharge	<p>0 = Side effect/medical issue not present</p> <p><input type="checkbox"/> Not related to treatment – <u>medical issue present but not related to medication treatment</u> (e.g. intercurrent illness)</p> <p>If side effect or medical issue is present, rate severity:</p> <p>1 = Minimal, may be extreme of normal</p> <p>2 = Mild</p> <p>3 = Moderate</p> <p>4 = Severe</p>

	<input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)
Irregular menstruation or amenorrhea	<p>0 = Side effect/medical issue not present</p> <input type="checkbox"/> Not related to treatment – <u>medical issue present but not related to medication treatment</u> (e.g. intercurrent illness) <p>If side effect or medical issue is present, rate severity:</p> <p>1 = Minimal, may be extreme of normal</p> <p>2 = Mild</p> <p>3 = Moderate</p> <p>4 = Severe</p> <input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)
Other reported side effects (list):	<p>0 = Side effect/medical issue not present</p> <input type="checkbox"/> Not related to treatment – <u>medical issue present but not related to medication treatment</u> (e.g. intercurrent illness) <p>If side effect or medical issue is present, rate severity:</p> <p>1 = Minimal, may be extreme of normal</p> <p>2 = Mild</p> <p>3 = Moderate</p> <p>4 = Severe</p> <input type="checkbox"/> Unable to assess (e.g. subject uncooperative or incoherent)

Substance Use Assessment

Note: The assessment of substance use is frequently compromised by individual denial. Impairments in social functioning or intermittent symptom exacerbations may be clues to possible substance use and should be followed up in supplement to the suggested probe questions below.

Severity of alcohol, marijuana and other substances is assessed separately. This may be challenging for some individuals as combinations of substance use, particularly alcohol and marijuana, are common.

ALCOHOL SECTION

1) If the subject endorsed using alcohol currently on self report:

Since our last visit, how often have you been drinking any alcohol?

What have you been drinking (beer, wine, mixed drinks, etc.)? How many drinks did you have?

Did you drink with other people or alone? If with others, then ask: With who?

Have you had any hang overs the next day or feel sick in any way after drinking?

If yes, ask if they missed work, school, their program or other activities due to alcohol use.

2) If the subject denied using alcohol on self report:

For subjects who do not drink by history and deny current use on self report, rate alcohol use now.

For subjects who do drink alcohol but deny current use on self-report:

When was the last time you drank any alcohol?

If drank since last visit, use probes above for subjects who used alcohol since the last visit

3) For subjects who did not answer self-report questions:

Since our last visit, how often have you been drinking any alcohol? If response is that they did not drink: When was the last time you drank any alcohol?

For subjects with some indication of alcohol use since last visit,

What have you been drinking (beer, wine, mixed drink, etc.)? How many drinks did you have?

Did you drink with other people or alone? If with others, then ask: With who?

Have you had any hang overs the next day or feel sick in any way after drinking?

If yes, ask if they missed work, school or their program.

Alcohol use Severity

0 = none

1 = use without impairment: drinks but no immediate social or medical impairment

2 = use with impairment: e.g. becomes grossly intoxicated; alcohol use or withdrawal compromises school, work or social functioning; alcohol use or withdrawal exacerbates symptoms (e.g. gets depressed when drinking)

MARIJUANA

1) If the subject endorsed using marijuana on self report:

Since our last visit, how often have you smoked pot or weed?

Did you use mostly with other people or when you were alone? If with others, then ask: With who?

How much did you use (bowl, joint, blunt, etc.)?

Approximately how many days did you use since our last visit?

After you used, did you feel sick or abnormal in any way? What about the next day?

If yes, ask if they missed work, school or their program.

2) If the subject denied using marijuana on self report:

For subjects who do not use marijuana by history and deny current use on self-report, rate marijuana use now.

For subjects who do use marijuana but deny current use of self-report:

When was the last time you smoked pot or weed?

If used marijuana since last visit, use probes above

3) For subjects who did not answer questions about marijuana on self-report

Since our last visit, how often have you smoked pot or weed?

(If no, When was the last time you did?)

If used marijuana since last visit:

Did you use mostly with other people or when you were alone? If with others, then ask: With who?

How much did you use (bowl, joint, blunt, etc.)?

Approximately how many days did you use since our last visit?

After you used, did you feel sick or abnormal in any way? What about the next day?

If yes, ask if they missed work, school or their program.

Marijuana use Severity

0 = none

1 = occasional use without impairment: e.g. uses marijuana a few days a month and has no immediate social or medical impairment

2 = frequent use without impairment: e.g. uses marijuana several or more days a week but has no immediate social or medical impairment

3 = use with impairment: e.g. becomes grossly intoxicated; marijuana use compromises school, work or social functioning; marijuana use exacerbates symptoms (e.g. gets paranoid when using)

DRUG USE OTHER THAN MARIJUANA AND ALCOHOL

1) If the subject endorsed using other drugs currently on self report:

Since our last visit, how often have you used any other street drugs?

If yes, continue, if response is no, go to next question. (If no, you might want to ask When was the last time you did?)

Did you use mostly with other people or when you were alone? If with others, then ask: With who?

How much did you use?

Approximately how many days did you use since our last visit?

After you used, did you feel sick or abnormal in any way? What about the next day?

If yes, ask if they missed work, school or their program.

Type of drug(s) used (e.g. sedatives, hallucinogens): _____

2) If the subject denied using other drugs on self-report:

For subjects who do not use other drugs by history and deny current use on self-report, rate other drug use now.

For subjects who do use other drugs but deny current use of self-report:

When was the last time you used street drugs?

If used other street drugs, use probes above

3) For subjects who did not answer questions about other drug use on self report

Since our last visit, how often have you used any other street drugs?

If yes, continue, if response is no, go to next question. (If no, you might want to ask When was the last time you did?)

Did you use mostly with other people or when you were alone? If with others, then ask: With who?

How much did you use?

Approximately how many days did you use since our last visit?

After you used, did you feel sick or abnormal in any way? What about the next day?

If yes, ask if they missed work, school or their program.

Other Drug Use Severity (rate overall severity of use separate from use of alcohol or marijuana)

0 = none

1 = occasional use without impairment: e.g. uses drug(s) a few days a month and has no immediate social or medical impairment

2 = frequent use without impairment: e.g. uses drug(s) several or more days a week but has no immediate social or medical impairment

3 = use with impairment: e.g. becomes grossly intoxicated; drug use compromises school, work or social functioning; drug use exacerbates symptoms (e.g. gets paranoid when using)

TOBACCO USE

The patient currently smokes _____ cigarettes per day.