

The Association between Patterns of Cannabis Use, Symptomatic and Functional Outcomes, and Early Intervention Services in First Episode Psychosis Patients: Results from a Cluster Randomized Controlled Trial

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Disclosure

- All my clothes were made by my son, J. Mueser
- Bespoke Hand Tailored Suits and Shirts, with stores in New York City:



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Substance Use in First Episode Psychosis (FEP)

- Cannabis and alcohol most commonly used substances
- Poorly recognized and often missed
 - Effects of use and misuse may be disguised by florid psychotic symptoms
 - Reduced motivation related to substance use may appear to be negative symptoms
- Psychomimetic effects of cannabis use especially concerning
- Cannabis use in adolescence predicts subsequent onset of schizophrenia (multiple national cohort studies)
- Cannabis use related to earlier onset of psychosis and precipitation of relapses in FEP
- More broadly, substance use related to worse outcomes in schizophrenia

Current Use at Treatment Entry

24-61%

Report
cannabis use



28-46%

Report
alcohol use



Lifetime Substance Use Disorders in Early Psychosis

28-58%

Cannabis use
disorder

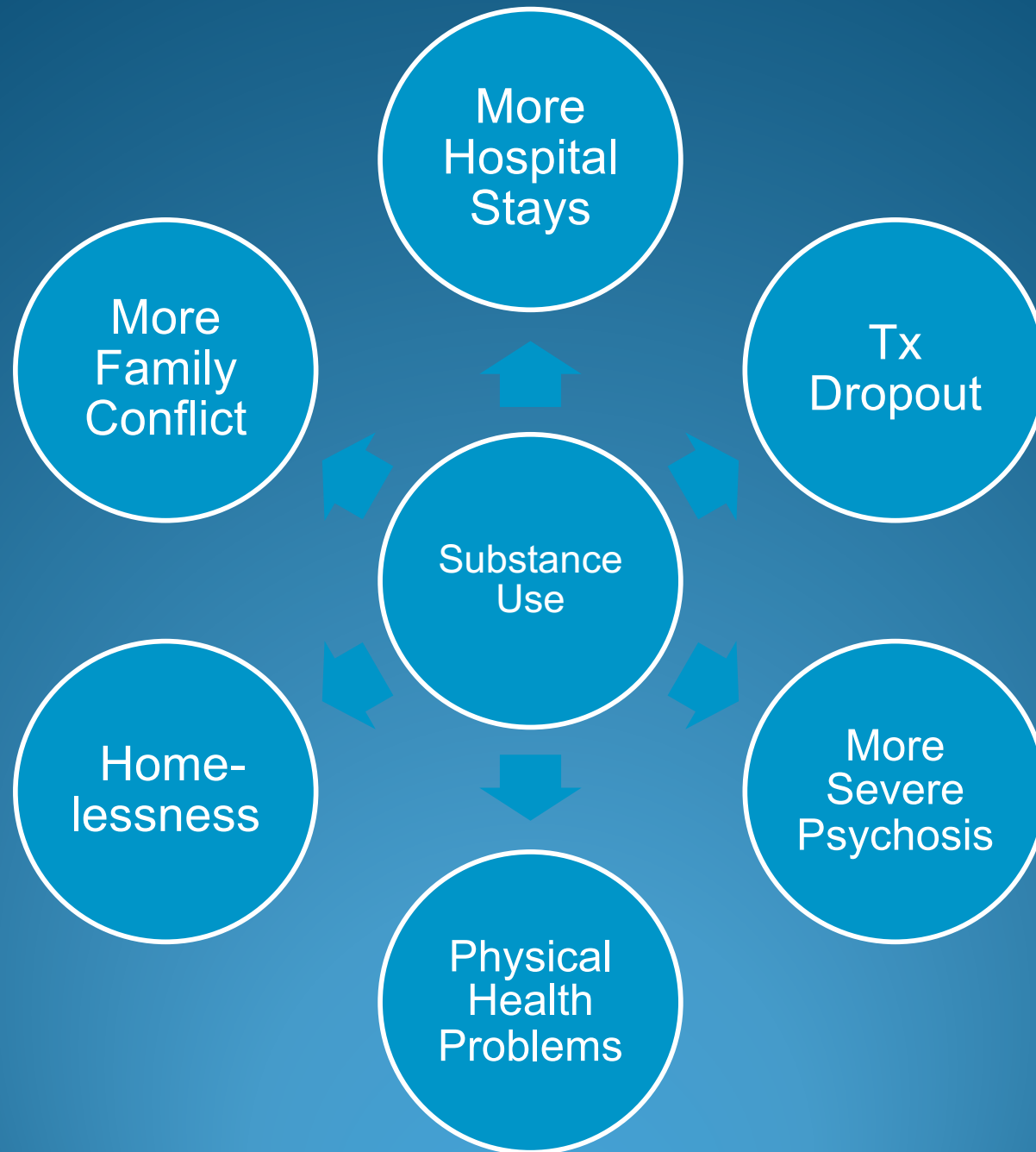


20-53%

Alcohol use
disorder



Archie et al., 2007; Cather et al., 2018; Dixon et al., 2015; Green et al., 2004;
Gonzalez-Pinto et al., 2011; Sara et al., 2014; Shinn et al., 2015



Motives for Substance Use

- Coping
 - Depression, anxiety, psychosis
 - Sleep difficulties
 - Cravings
 - Boredom
- Social
 - Conformity
 - Acceptance
- Pleasure
 - Relax
 - Have fun
 - Get high / alter perceptions

Questions About Cannabis Use in FEP

- Previous research suggests some clients stop using cannabis following entry into early intervention services (EIS) for FEP, but how many?
- Most studies of comprehensive EIS programs do not report changes in cannabis use following entry into treatment, but few controlled studies
- Are there different patterns of cannabis use among persons with FEP following entry into EIS?
- Are different patterns of cannabis use in FEP stable over time?
- Does cannabis use influence the course of symptomatic or functional outcomes in people entering EIS?
- Does cannabis use interact with the effects of comprehensive EIS (compared to usual treatment) on the symptomatic or functional trajectories of FEP clients?
- These questions addressed in large cluster RCT conducted in US comparing EIS (NAVIGATE program) with usual Community Care (CC)

Recovery After Initial Schizophrenia Episode – Early Treatment Program (RAISE-ETP) Evaluated the NAVIGATE Program for FEP

The logo for the RAISE program, featuring the word "RAISE" in a bold, sans-serif font. The letter "1" is replaced by a blue number "1".

A Research Project of the NIMH

Early Treatment Program

(Kane et al., 2015, 2016; Mueser et al., 2015)

NAVIGATE Treatment Team and Interventions

- Director (Team Leader, usually provided *Family Psychoeducation* program)
- Prescriber (provided *Individualized Medication Management*)
- Vocational specialist (provided *Supported Employment & Education* program)
- 2 MA level clinicians (provided *Individual Resiliency Training*; usually also provided *case management*)
- Sometimes separate case manager on team
- Team members were NOT on team full time, and usually had other clinical responsibilities

Core Competencies of the NAVIGATE Team Members

- Shared decision-making
- Strengths and resiliency focus
- Motivational enhancement skills
- Psychoeducational skills
- Cognitive-behavioral skills
- Collaboration with community supports

Inclusion Criteria

- Age 15-40
- SCID confirmed diagnosis:
 - Schizophrenia
 - Schizophreniform disorder
 - Schizoaffective disorder
 - Brief Psychotic disorder
 - Psychosis NOS
- No more than 6 months lifetime antipsychotic medication treatment
- First episode of psychosis
- Lifetime substance use disorders (SUD) assessed by SCID at baseline but no exclusion for SUD

Research Design

- NAVIGATE program vs. usual Community Care (CC)
- Cluster/site randomization: 34 sites
- Treated for minimum of two-years in NAVIGATE program
- Remote assessment of clinical outcomes every 6 months for 2 years
- Self-report monthly assessments

Project Sites



ETP Study Outcomes

- Primary outcome measure: Quality of Life Scale
 - Primary hypothesis
 - NAVIGATE intervention will improve Quality of Life significantly compared to Community Care
- Other measured outcomes
 - Symptoms (PANSS, Calgary Depression Scale)
 - Service utilization and substance use (assessed monthly throughout 2-year study)
 - Cost
 - Prevention of relapse
 - Recovery

Demographics of Clients

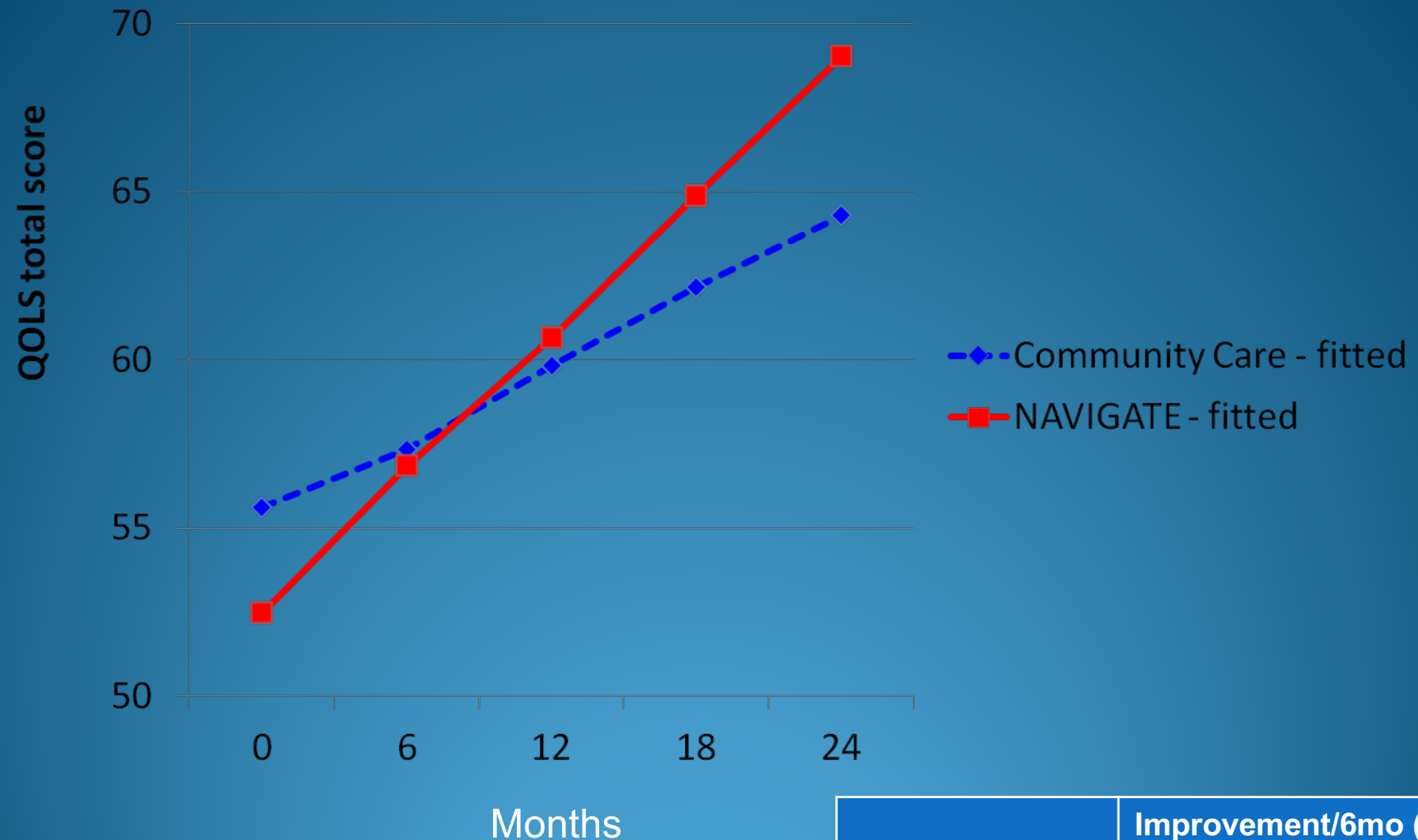
	Total Sample = 404
<i>Age and Gender</i>	
Age (mean)	23.6%
Males (%)	73%
<i>Race</i>	
White (%)	54%
African American (%)	37%
Other (%)	8%
<i>Community Population</i>	
Rural (%)	25%
Urban (%)	50%
<i>Prior Hospitalization (%)</i>	78%

Major 2-Year Study Findings

- Compared to usual Community Care (CC), participants in NAVIGATE program improved more in:
 - Psychosocial functioning and quality of life (QLS)
 - Overall severity of symptoms (PANSS)
 - Severity of depression (CDSS)
 - Involvement in work or school
- Participants in NAVIGATE remained in treatment longer than CC
- No treatment group differences in substance use outcomes for any substances

Quality of Life Scale Fitted Model

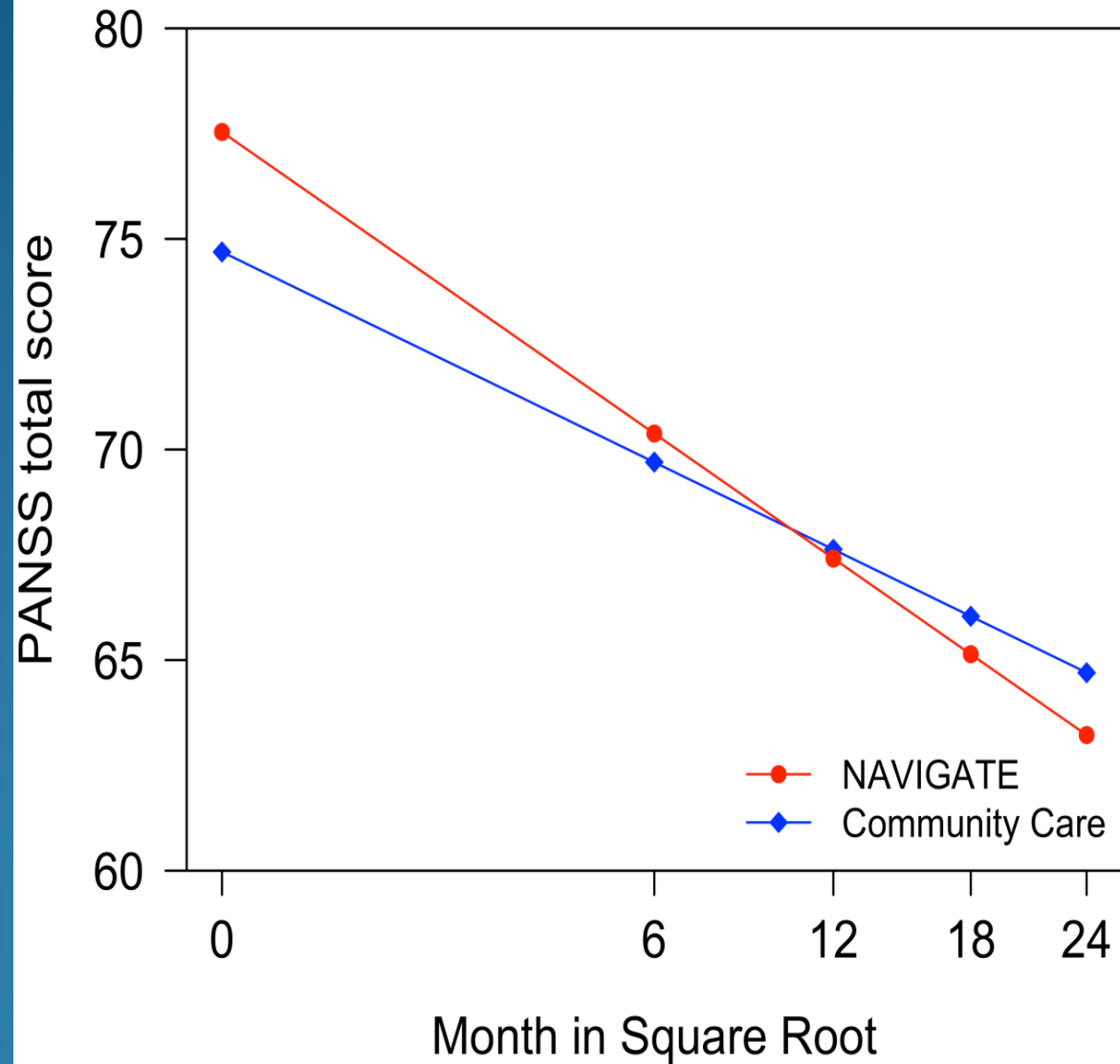
Group by time interaction ($p = 0.046$)



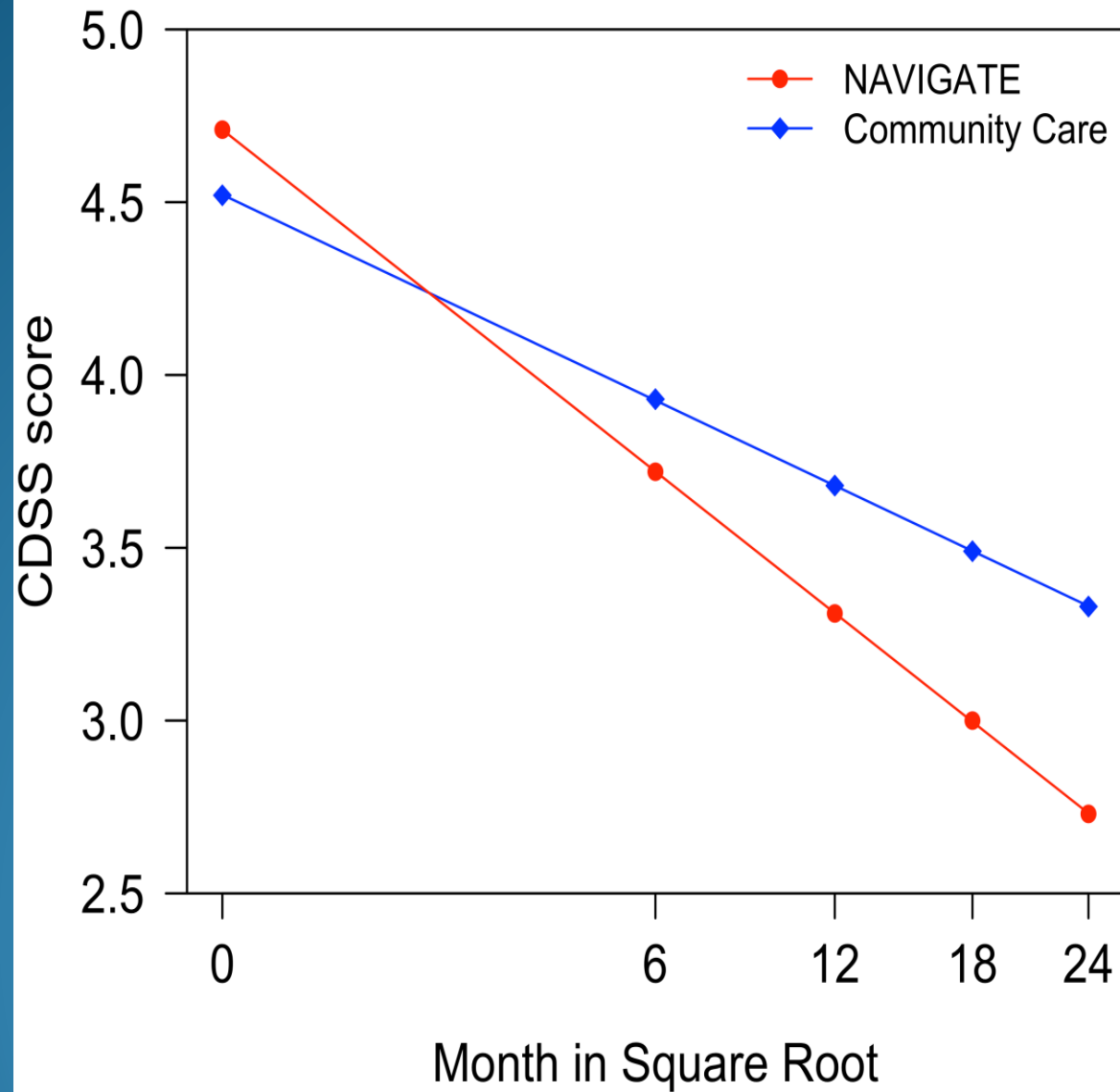
Cohen's $d = 0.257$

	Improvement/6mo (SE)
Community Care	2.359 (0.473)
NAVIGATE	3.565 (0.379)
Difference	1.206 (0.606)

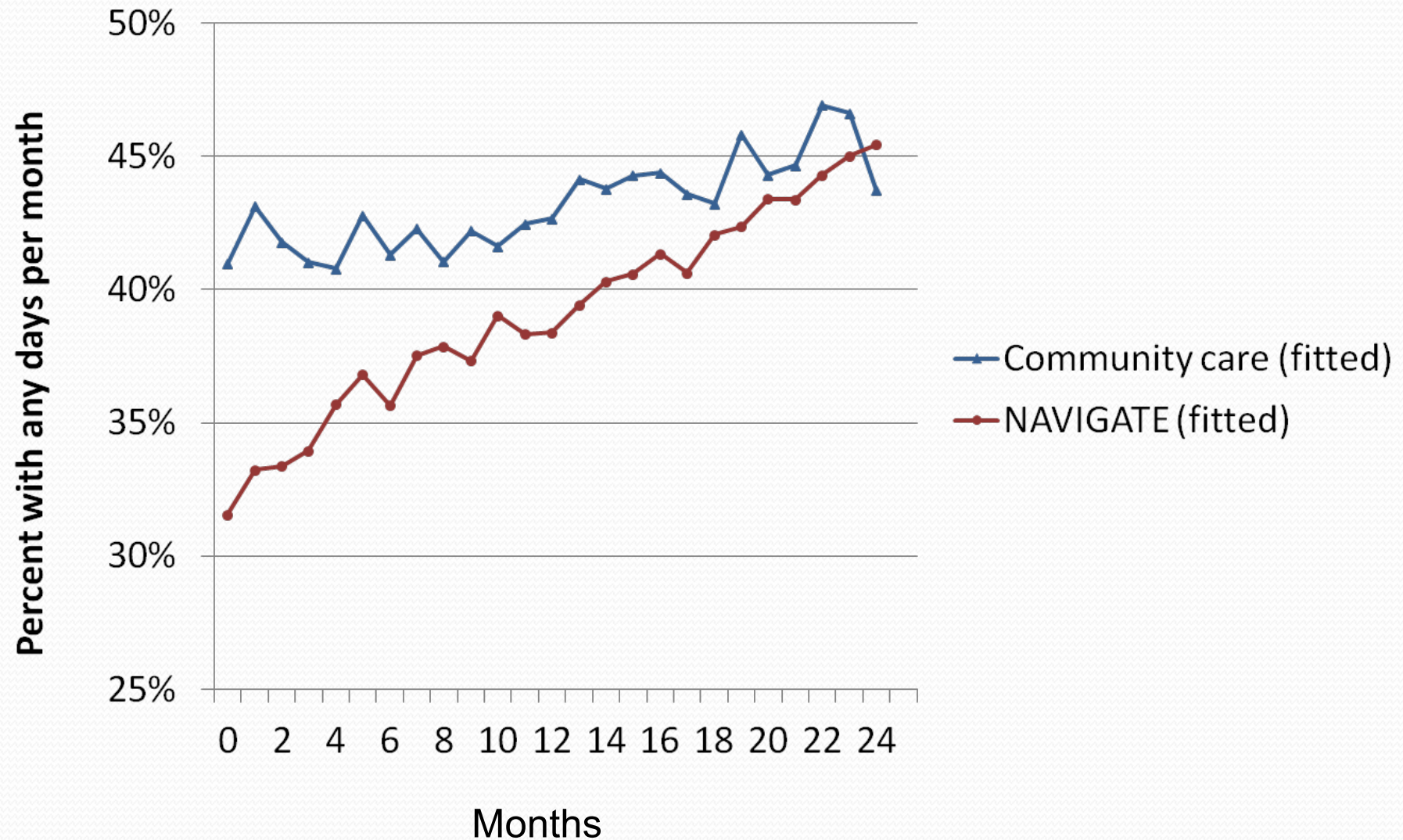
PANSS Total Score ($p < 0.02$)



CDSS Score ($p < 0.04$)



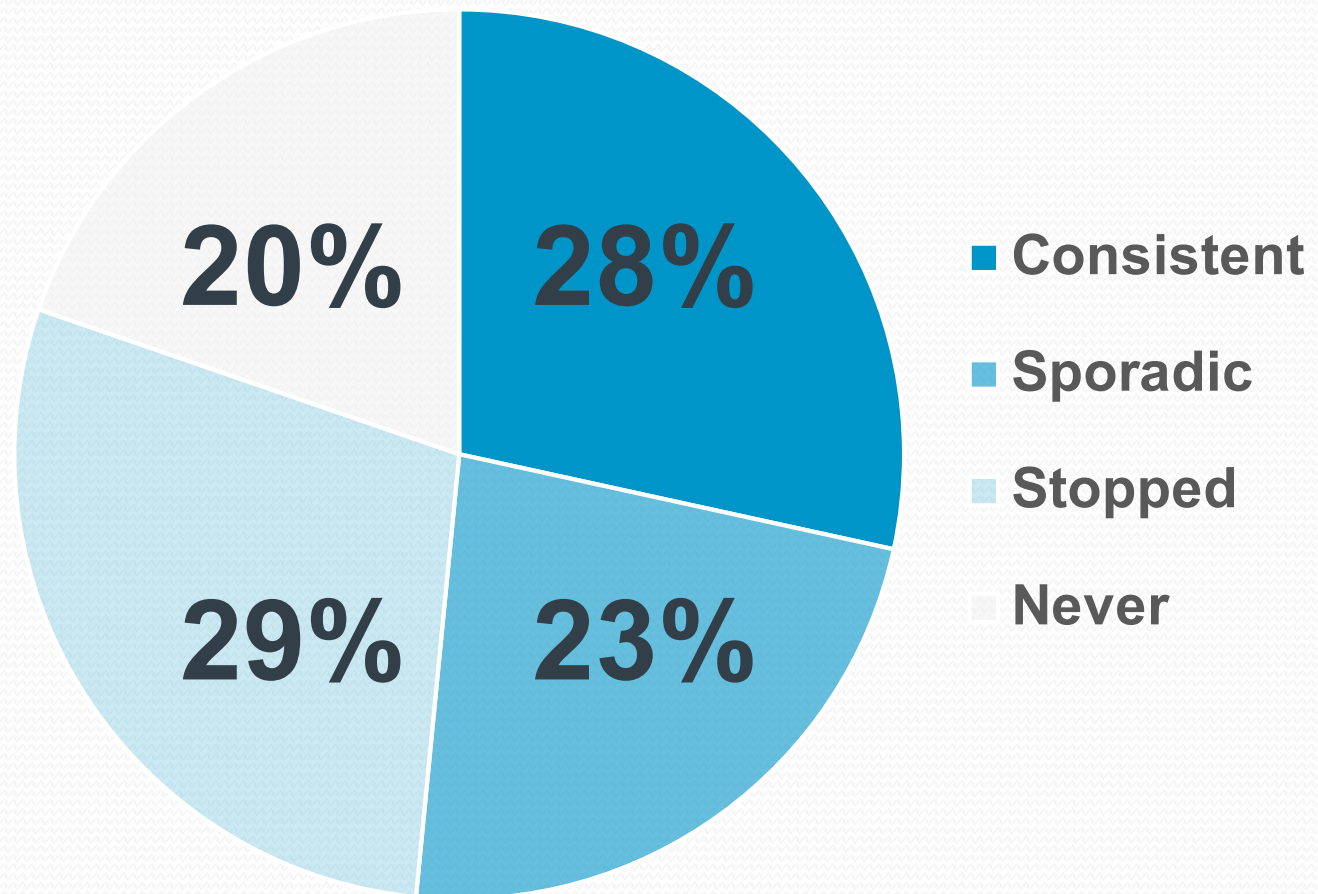
Percent With Any Work or School Days per Month (Group by Time interaction: $p=0.044$)



Cannabis Subgroups Based Past Use and Use Over Year 1 (N = 334)

- *Consistent users*: Used prior to study and used ≥ 3 months in first year
- *Sporadic users*: Used prior to study and used 1-2 months in first year
- *Stopped users*: Used prior to study but did not use in first year
- *Never users*: Never used prior to study or in first year
- *New users*: Never used prior to study and began using in first year [None reported in sample]

Cannabis Patterns During First Year of RAISE-ETP Study (N=334)

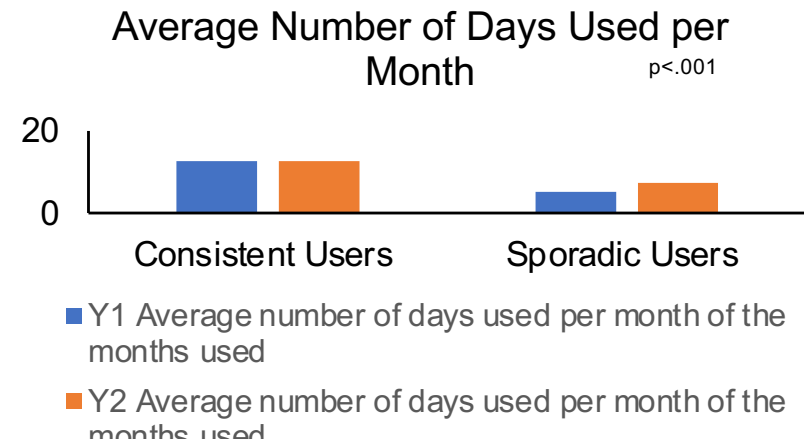
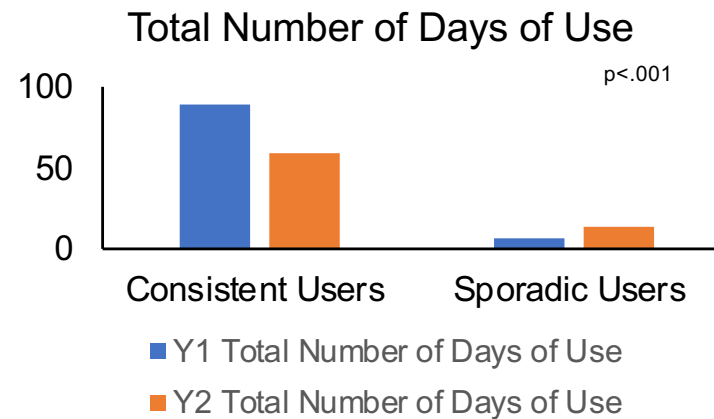
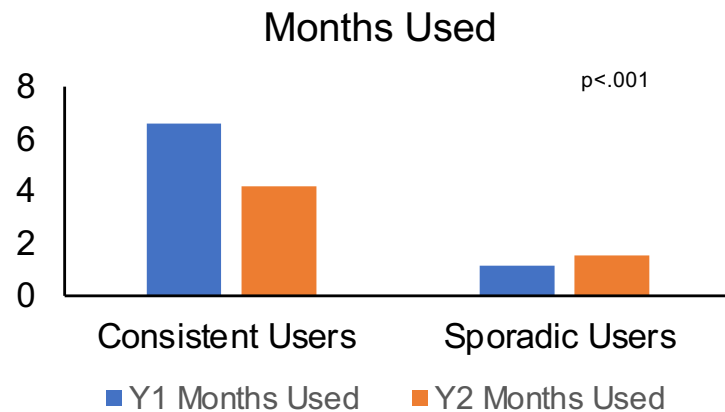


Wright et al., in press

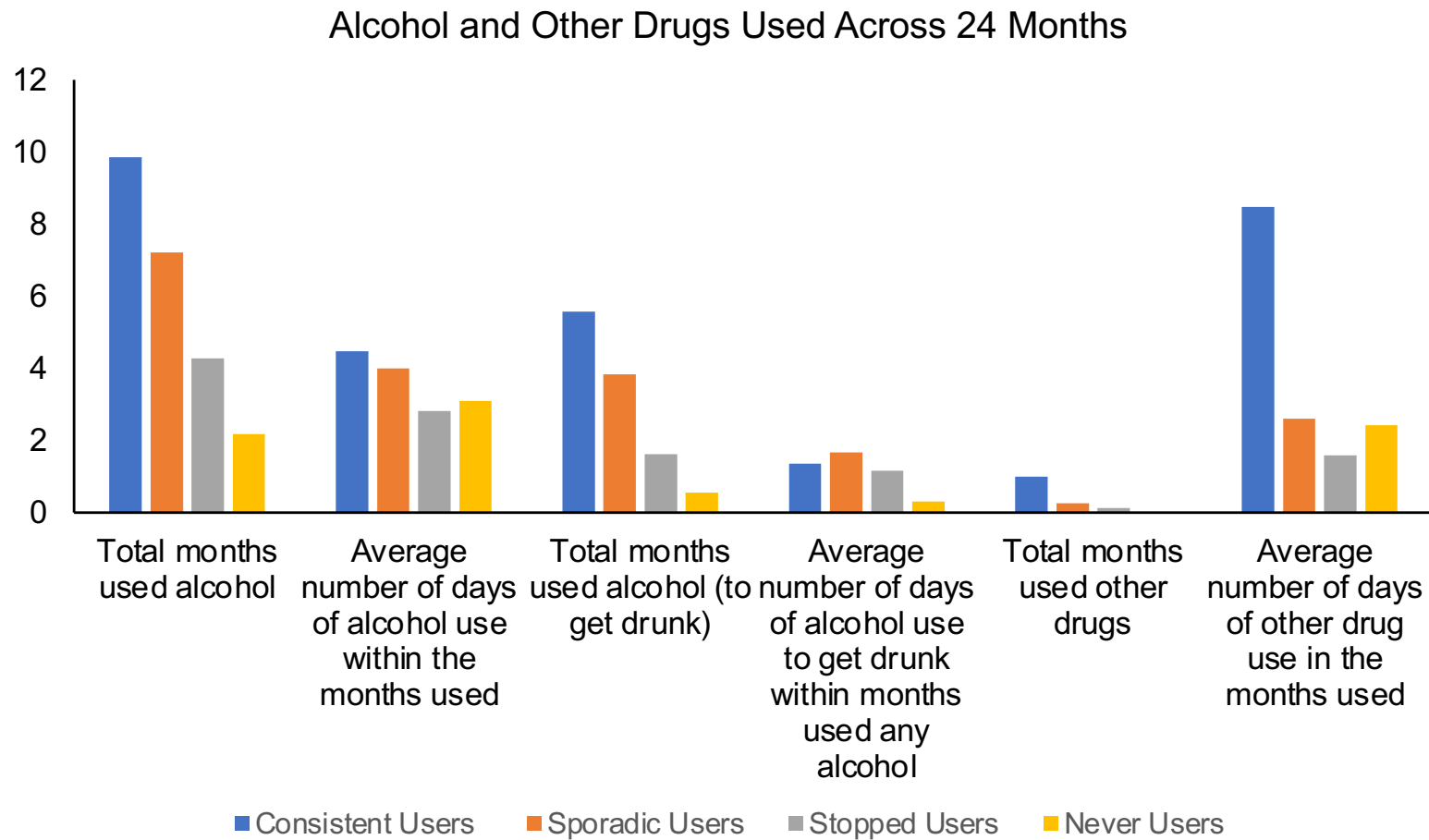
Stability and Validity of Cannabis Subgroups

- Year 1 classifications stable with Year 2 classification (Kappa = 0.71)
- Concurrent validity supported by differences between the 4 groups over 2 years in:
 - Cannabis use
 - Alcohol use
 - Other drugs used
- Concurrent validity also supported by differences between consistent, sporadic, and stopped users in lifetime cannabis use disorder at baseline

COMPARISONS OF THE CONSISTENT AND SPORADIC GROUPS IN CANNABIS USE



MONTHS OF ALCOHOL AND OTHER DRUGS USED ACROSS 24 MONTHS (EXCLUDING BASELINE) FOR CANNABIS USE GROUPS, AND AVERAGE NUMBER OF DAYS OF USE WITHIN MONTHS SUBSTANCE WAS USED



Other Differences Between Cannabis Subgroups

- Stopped users were older than other three groups
- Consistent users had earlier age of first hospitalization
- Consistent and sporadic users had worse instrumental (work and school) functioning at baseline than stopped users and never users
- Sporadic users had worse depression at baseline than other three groups

DEMOGRAPHIC AND BASELINE CLINICAL VARIABLES FOR FOUR CANNABIS USE GROUPS AND DIFFERENCE TESTS

	Consistent Users (1) (n=95)	Sporadic Users (2) (n=77)	Stopped Users (3) (n=96)	Never Users (4) (n=66)	χ^2	df, N	p value	Adjusted standardized residuals / Tukey posthoc test
Gender (% male)	84%	75%	75%	59%	13.02	3, 334	.005	1>exp count* 4<exp count*
Age	22.5 (4.7)	22.3 (3.6)	24.7 (5.3)	23.7 (6.5)	4.17	3, 333	.006	1<3*, 2<3*
Age at first hospitalization	20.4 (5.0)	20.6 (3.9)	21.9 (5.0)	22.9 (5.8)	3.41	3, 256	.02	1<4*
QLS instrumental	4.76 (6.11)	3.92 (4.96)	6.76 (7.22)	8.18 (7.59)	6.54	3, 332	<.001	1<4**, 2<3*, 2<4***
CDSS total	4.09 (3.75)	5.73 (4.54)	4.11 (3.91)	3.86 (3.75)	3.57	3, 332	.01	1<2*, 2>3*,>4*

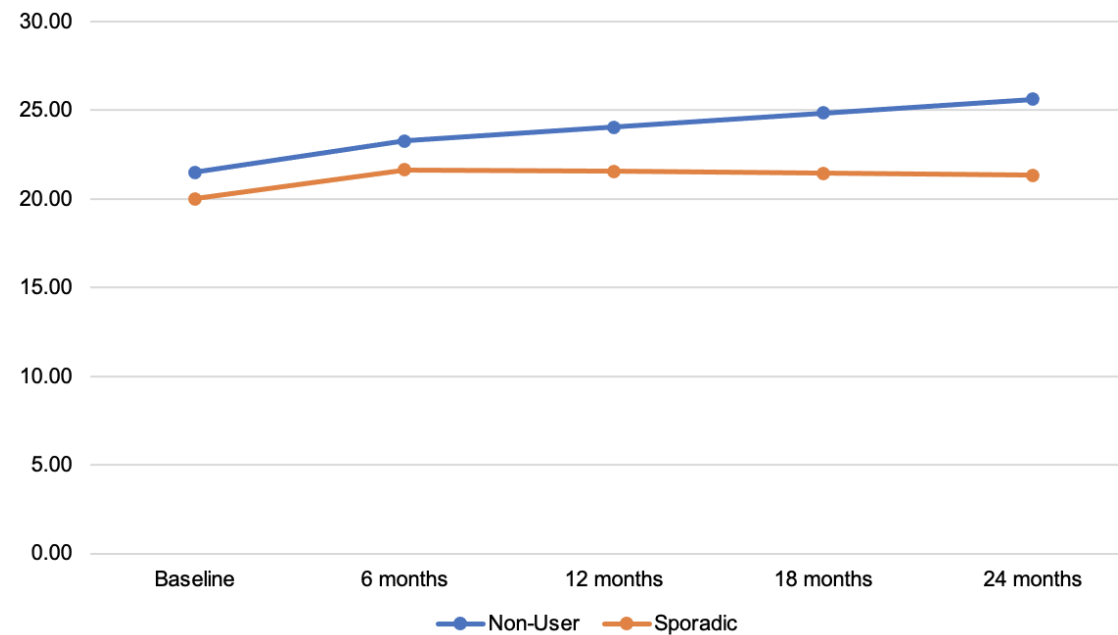
Symptom and Functional Outcome Trajectory Analysis of Cannabis Subgroups

- Mixed effects linear regression analyses conducted to evaluate differences in changes in outcomes (PANSS, QLS, CDSS) over 2 years between cannabis groups, treatment group, time, and their interactions over follow-up assessments, with baseline included as covariate
- Analyses first compared never used group with stopped use group
 - No significant cannabis group main effects or interactions found for any outcomes
- Subsequent analyses combined never used and stopped use groups, and compared with consistent and sporadic use groups with no use group as reference
- Focused on consistent effects for cannabis group or cannabis group interactions found on two or more outcome variables

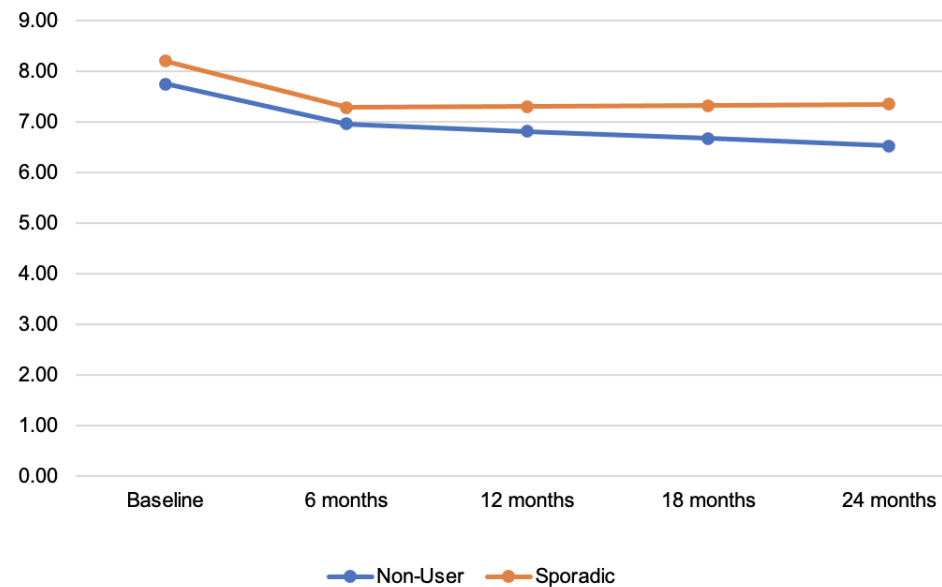
Consistent Findings of Trajectory Analyses

- There were significant cannabis group by time interactions for 2 variables, each for sporadic vs. non-users:
 - Controlling for baseline, sporadic cannabis users improved less than non-users from 6 months to 2 years in QLS intrapsychic foundations (e.g., motivation, curiosity, sense of purpose)
 - Similar effects were found for PANSS depression
- There were significant cannabis group by treatment group interactions for 2 variables, each comparing sporadic vs. non-users:
 - Controlling for baseline, sporadic cannabis users in NAVIGATE improved more than sporadic-users in CC from 6 months to 2 years in QLS Total
 - Similar effects were found for PANSS Total
- Consistent cannabis users in NAVIGATE improved significantly more than consistent users in CC, but similar effect not found for another variable

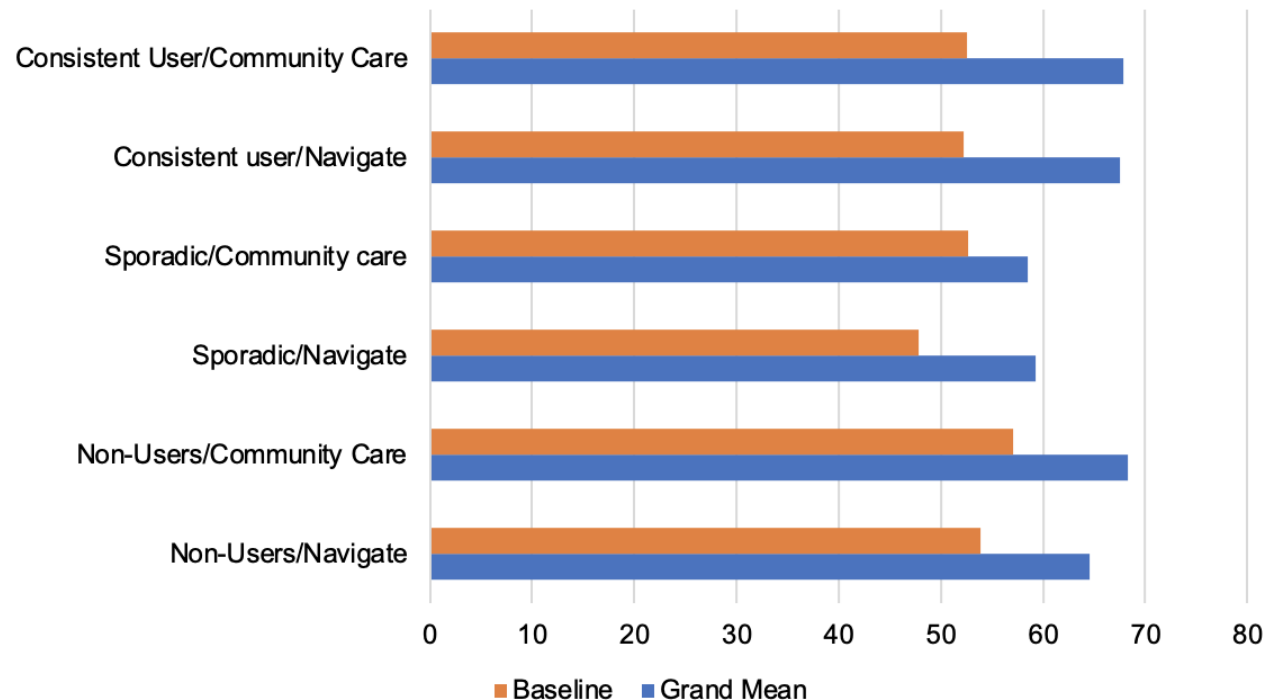
TWO-WAY INTERACTION FOR QLS INTRAPSYCHIC SUBSCALE BETWEEN CANNABIS USE GROUP (NON-USER VS. SPORADIC) IN BOTH TREATMENT GROUPS AND 4 TIME POINTS (BASELINE INCLUDED)



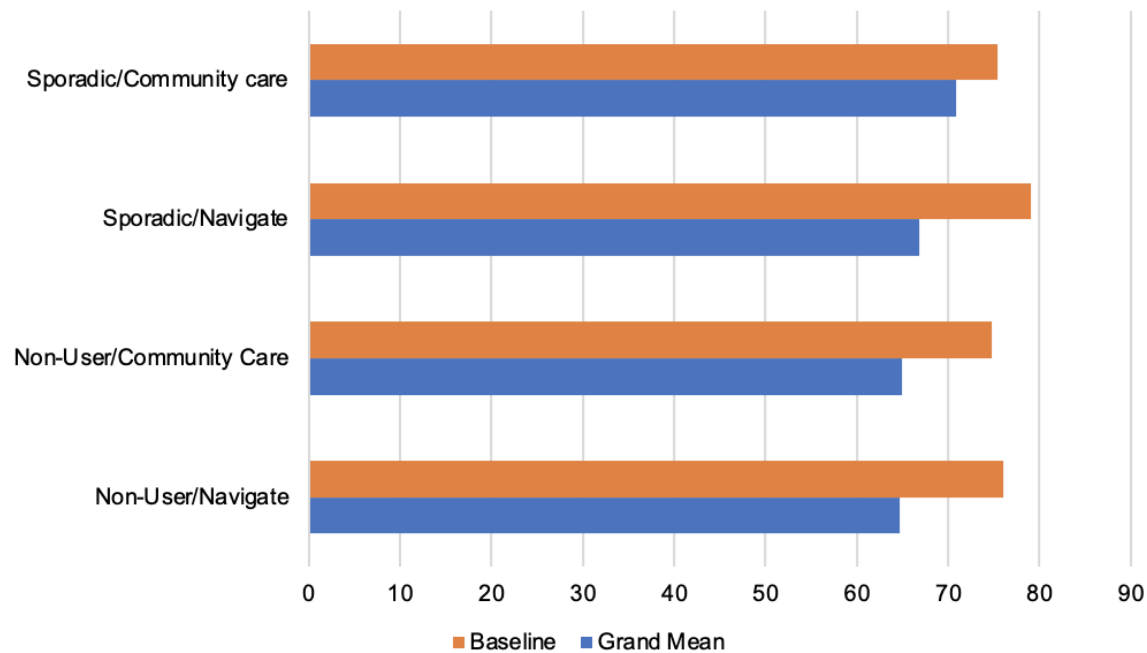
TWO-WAY INTERACTION FOR PANSS DEPRESSION SUBSCALE BETWEEN CANNABIS USE GROUP (NON-USER VS. SPORADIC) AND 4 TIME POINTS (BASELINE INCLUDED)



TWO-WAY INTERACTION FOR QLS TOTAL SCORE BETWEEN CANNABIS USE GROUP (NON-USER VS SPORADIC USE VS. CONSISTENT USE) AND TREATMENT GROUP (NAVIGATE VS. CC) WITH BASELINE AND GRAND MEAN (AVERAGE ACROSS ALL FOLLOW-UP TIME POINTS)



SIGNIFICANT TWO-WAY INTERACTION FOR PANSS TOTAL SCORE
BETWEEN CANNABIS USE GROUP (NON-USER VS. SPORADIC USE) AND
TREATMENT GROUP (NAVIGATE VS. CC) WITH BASELINE AND GRAND
MEAN (AVERAGE ACROSS ALL FOLLOW-UP TIME POINTS)



Discussion

- 80% of sample had used cannabis before entry into EIS program
- Approximately one-third of cannabis users stopped using before or around the onset of their FEP
 - No one began using cannabis after onset of FEP (consistent with low rate reported by van der Meer et al., 2015)
- The older age of the stopped users suggests some stopped before onset of psychosis
- The classification of 4 subgroups of cannabis users based on first year of study was stable during second year
 - Validity supported by differences between groups in history of cannabis use disorder at baseline and other substance use patterns over 2 years
 - Validity also supported by significantly earlier age of onset of FEP for consistent users than other 3 groups

Discussion, cont'd

- Unexpected pattern of findings indicated that sporadic cannabis users, not consistent users, tended to fare more poorly
- At baseline, sporadic users had the worst role functioning, most severe depression (on CDSS), and (while not significant) the worst overall symptoms (PANSS) and psychosocial functioning (QLS)
- Controlling for baseline, sporadic users in both treatment groups also improved less over 2 years than non-users in depression (PANSS) and intrapsychic foundations (QLS)
- Compared to usual care (CC), the NAVIGATE intervention protected sporadic users from a worse outcomes over 2 years in overall symptom severity (PANSS) and functioning (QLS)

Discussion, cont'd

- Sporadic cannabis use may be driven by efforts to control intense periods of negative affect or the absence of positive emotions
- The NAVIGATE intervention (compared to CC) may give people tools for effectively combatting some of these intense periods of negative affect and preventing worse symptomatic or functional outcomes
- Lack of treatment effects of NAVIGATE on cannabis use may be (partly) due to low exposure to substance misuse module in psychotherapy component (Individual Resiliency Training: IRT) of program
- First study to examine interactions between EIS (vs. CC) and cannabis use
- Strength of study: routine (monthly) cannabis use assessment
- Weakness of study: cannabis use prospectively measured, but not cannabis use problems

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RAISE-ETP: Executive Committee

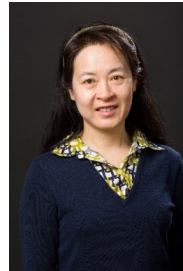


Principal NIMH Collaborators

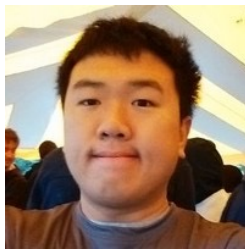
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