



Impact of COVID-19 Pandemic on Seriously Mentally Ill (SMI) Subjects in Clinical Trials

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Conflict of Interest Disclosure -- Robert E. Litman, M.D.

Speakers Bureau: Johnson & Johnson, AbbVie Inc.

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Psychiatry Clinical Trial Concerns During the COVID-19 Pandemic

Disruption of Clinical Trial Programs due to COVID-19 Restrictions

- Design modification
- Missed data
- Remote assessments
- Operational snags & shut-downs
- Lost recruitment



Paused/postponed drug trial programs

Subject Safety: Are SMI a COVID high-risk group?

- **Increased risk of COVID-19 mortality** in SMI population (Fond G et al, 2021)
- Need for increased preventative & disease management strategies in SMI

Data Integrity: Implications for Drug Efficacy & Safety

- Neuropsychiatric symptoms of acute/chronic COVID-19
- Pandemic stress: relationship to psychiatric symptoms, behavior, morbidity
- How to interpret efficacy & safety data during a pandemic?

Survey of SMI Patients at Clinical Trial Sites (Jun - Sep 2020)

1st Survey regarding Covid-19

- Convenience sample (N=94)
- SMI clinical trial subjects at 3 sites (FL, GA, MD)
- Jun – Sep 2020



Objectives

- **Subject Safety:** Investigate SMI ability to function during the pandemic
 - Knowledge
 - Risk perception
 - Use PPE
 - Social distance
- **Stress:** Investigate levels of pandemic-induced stress in SMI patients

Key Findings

- 9 patients (10%) tested positive for SARS-CoV-2 infection
- 51% of patients reported worsening of psychiatric symptoms at time of survey
- Majority of patients (~75%) reported use of PPE (similar to general population)
- Higher stress levels observed in MDD patients compared to other diagnoses ($p < 0.05$)

2nd Survey: Expanded Sample and Data (Apr – Jul 2021)

Impact of COVID-19 Pandemic on SMI Patient Safety

- Comparison with non-psychiatric clinical trial control subjects (NPC)
- Increase sample size to N=300 (SMI N=150, NPC N=150)

Impact of COVID-19 Pandemic on Psychiatric Morbidity

- Symptoms
- Outcome
- Mental health care

Impact of Pandemic-induced Stress on Psychiatric Symptoms, Behavior, Outcomes

Methods: Expanded Survey

Convenience Cross-sectional Survey Conducted

- Clinical trial participants from previous 2 years or currently in trials (n=287)
- **SMI psychiatric diagnoses (n=138)**
 - Bipolar 1 F31 (n=23, 16.7%)
 - Major Depression, Recurrent F33 (n=46, 33.3%)
 - Schizophrenia F20.9 (n=69, 50%)
- **Non-psychiatric controls (NPC) (n=149)**

Questionnaire

- 60+ items
- Written, informed consent
- Interviewer administered
- Responses gathered via Qualtrics



Methods (cont): Expanded Survey

Subjects surveyed at 7 clinical trial sites in distinct geographic areas in the U.S.

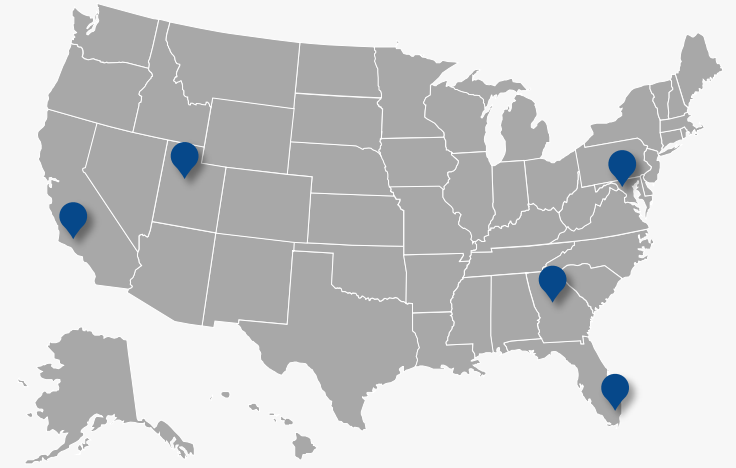
(CA, FL, GA, MD, UT)

Kessler Psychological Distress (K10)

- All subjects categorized as Low-Stress (Median K10 Total 10-19) or High-Stress (Median K10 Total 20-50)

Data analysis

- T-test used to compare numerical variables between two SMI/NPC
- ANOVA performed to identify differences when comparing 3 or more groups



Questionnaire Design: Expanded Survey

Driven by Literature on COVID-19 & Previous Pandemics (H1N1, Influenza)

60+ Questions -- 15 – 30 min

Components

- Demographics
- Clinical information & mental health care during COVID-19 (SMI patients only)
- Substance use
- COVID-19 health and medical care
- COVID-19 contact history
- Knowledge about COVID-19
- Concerns about COVID-19
- Risk perceptions
- Use of precautionary measures (PPE, social distancing)
- COVID-19 vaccine

Kessler's Psychological Distress Scale (K10)

The following questions ask about how you have been feeling during the **past 30 days**. For each question, please circle the number that best describes how often you had this feeling.

Q1. During that month, how often did you feel ...	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. ... tired out for no good reason?	1	2	3	4	5
b. ...nervous?	1	2	3	4	5
c. ...so nervous that nothing could calm you down?	1	2	3	4	5
d. ...hopeless?	1	2	3	4	5
e. ...restless or fidgety?	1	2	3	4	5
f. ...so restless that you could not sit still?	1	2	3	4	5
g. ...depressed?	1	2	3	4	5
h. ...so depressed that nothing could cheer you up?	1	2	3	4	5
i. ...that everything was an effort?	1	2	3	4	5
j. ...worthless?	1	2	3	4	5

Demographics

Total Sample (n=277)	Non-Psychiatric Controls (NPC) (n=139)	Seriously Mentally Ill (SMI) (n=138)	Significance
Average Age	38.0 (\pm 14.0)	41.5 (\pm 12.9)	p = .03
Female / Male	99/40	70/66	p<.001
African-American / White / Other	42/76/21	83/45/10	p<.001
Employed / Unemployed	95/23	41/73	p<.001
Income < \$30K / > \$30K	55/84	96/40	p<.001
Did Not Complete High School	4	18	p = .04
Married / Single	44/95	22/116	p = .01
Living Arrangement Family / Alone / Supervised / Homeless	89/47/0/2	53/73/5/6	p<.001

COVID-19 Disease Management

	All Subjects (n=277)	NPC (n=139)	SMI (n=138)	Significance
COVID-19 Exposure	93 (32.4)	61 (43.9)	29 (21.0)	p <.001
Quarantine	51 (18.4)	32 (23.0)	19 (13.8)	
COVID-19 Testing	203 (73.2)	103 (74.1)	93 (67.4)	
Clinical Trial Site	36 (17.7)	14 (13.6)	22 (23.7)	
Public / Community	84 (41.4)	51 (49.5)	29 (31.2)	
Doctor / Hospital	70 (34.5)	31 (30.1)	36 (38.7)	
Other (home, work)	13 (6.4)	7 (6.8)	6 (6.5)	
Positive COVID-19 Diagnosis	27 (9.4)	19 (13.7)	7 (5.1)	p <.05
Vaccinated for COVID-19	146 (51.0)	76 (55.1)	70 (51.0)	
Vaccine Concern	86 (29.9)	43 (30.9)	43 (31.4)	

Use of Precautionary Measures

Total Sample (n=277)	NPC (n=139)	SMI (n=138)	Significance
Wearing Face Masks *	4.32 (\pm 1.19)	4.55 (\pm 0.83)	
Social Distancing*	3.93 (\pm 1.32)	4.49 (\pm 0.89)	p < 0.001
Handwashing *	4.60 (\pm 0.91)	4.72 (\pm 0.58)	
Avoiding Large Gatherings *	3.93 (\pm 1.32)	4.49 (\pm 0.89)	p < 0.001
Use of PM after Vaccine	102 (73.9)	128 (93.4)	p < 0.001

* Responses to items scored on a Likert scale ranging from 1 (Never) to 5 (Always)

Psychiatric Morbidity Among SMI

Category	Sample Prevalence (n=138)
Worsening of Psychiatric Symptoms During Pandemic	97 (70.3)
Symptoms	
Depression	MDD: 16 out of 38 pts
Voices	SCZ: 14 out of 43 pts
Paranoia	SCZ: 14 out of 43 pts
Suicidal Ideation During Pandemic	48 (35.0)
Attempt(s)	8 (17.0)
Increase in Mental Health Care Due to COVID-19 Distress	66 (47.8)
More frequent appointments with MH providers	40 (60.6)
Increase or changes in medication	39 (59.1)
Visits to ER for psychiatric symptoms	13 (19.7)
Admission to hospital for psychiatric symptoms	10 (15.2)

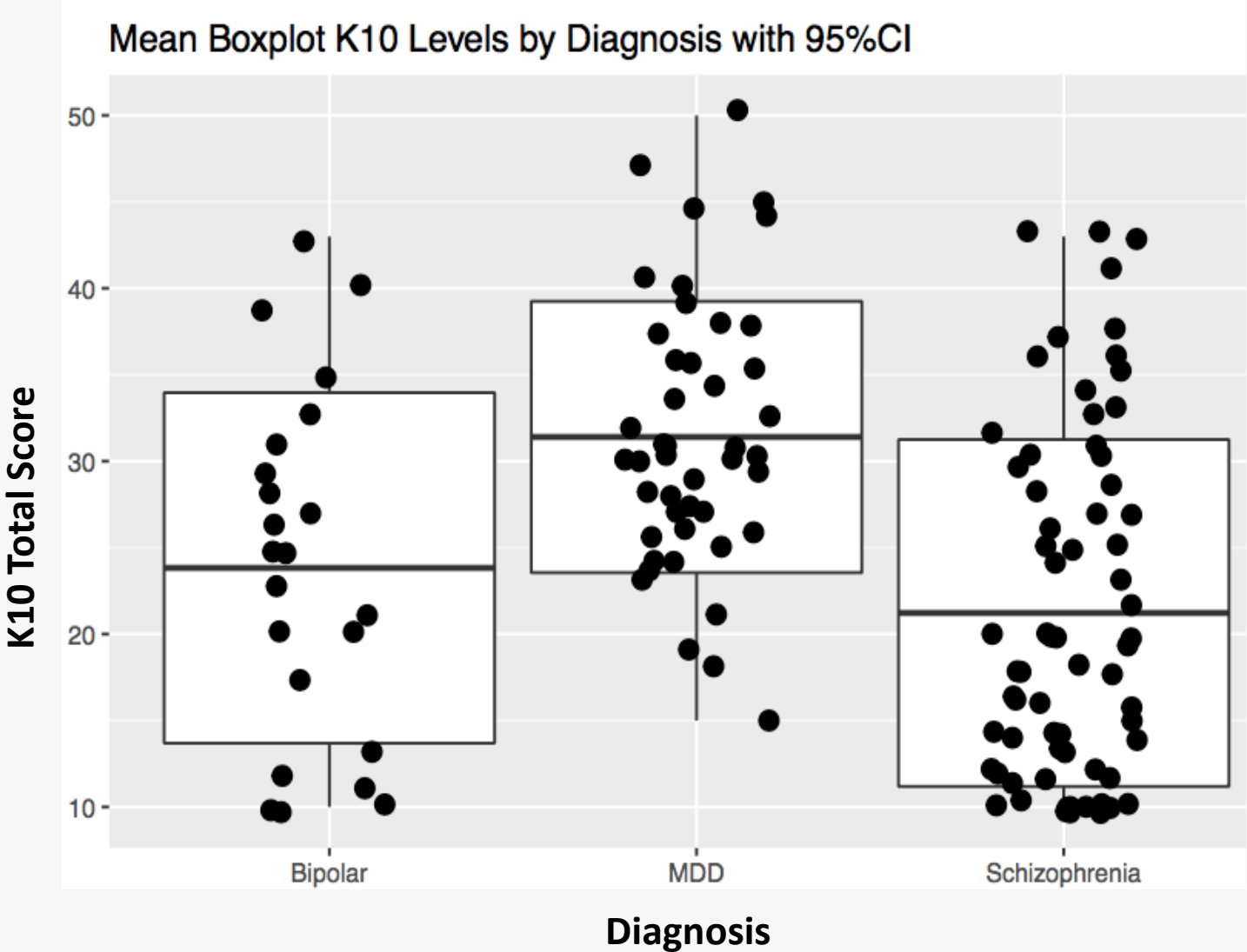
Kessler Psychological Distress (K10)

	NPC (N=139)	SMI (N=138)	SCZ (N=69)	BP (N=23)	MDD (N=46)
K10 Total Score	15.50* (± 6.59)	25.03* (± 10.39)	21.22* (± 10.03)	23.83* (± 10.14)	31.40* (± 7.85)
K10 High Stress (%)	37 (27.0)	93* (68.4)	34 (49.0)	16 (69.6)	43* (93.5)

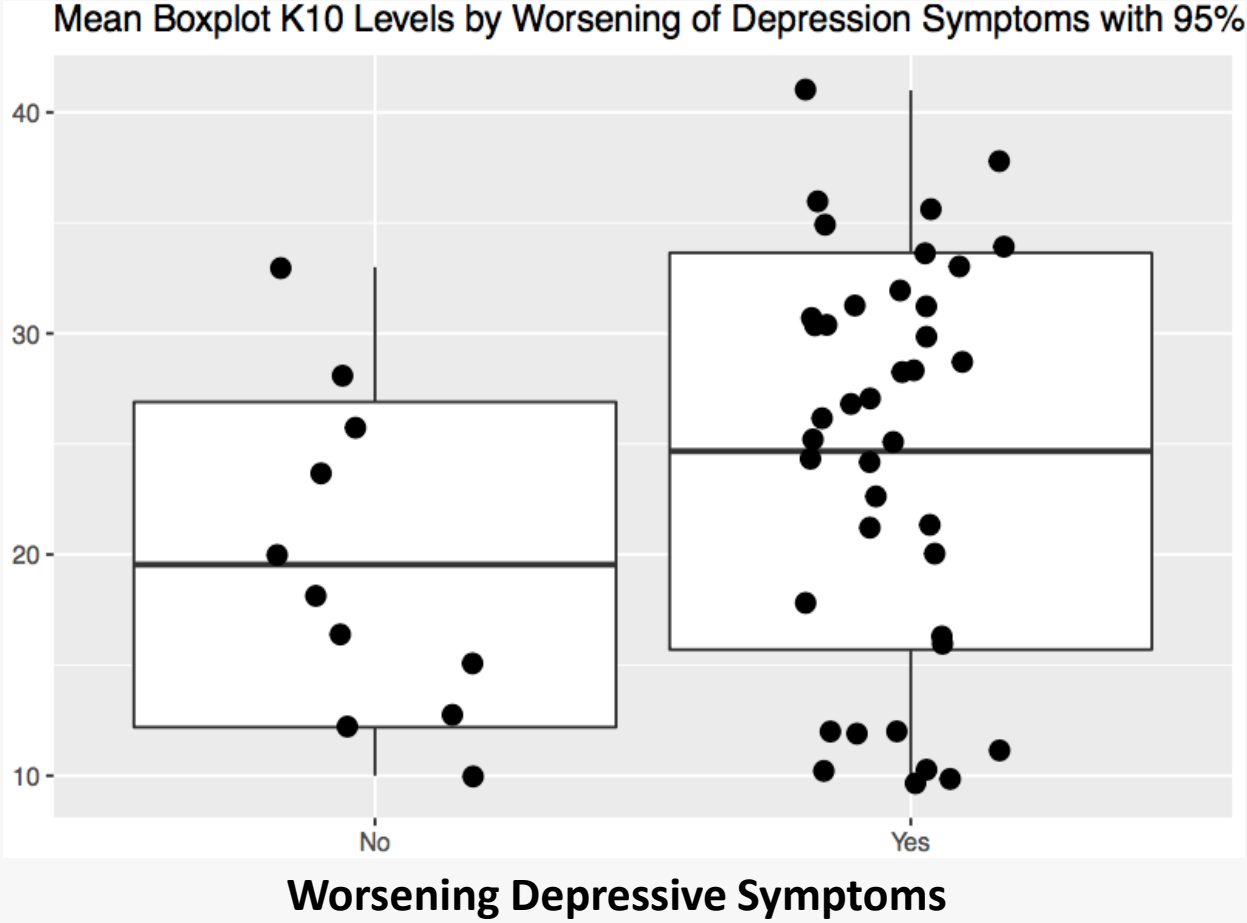
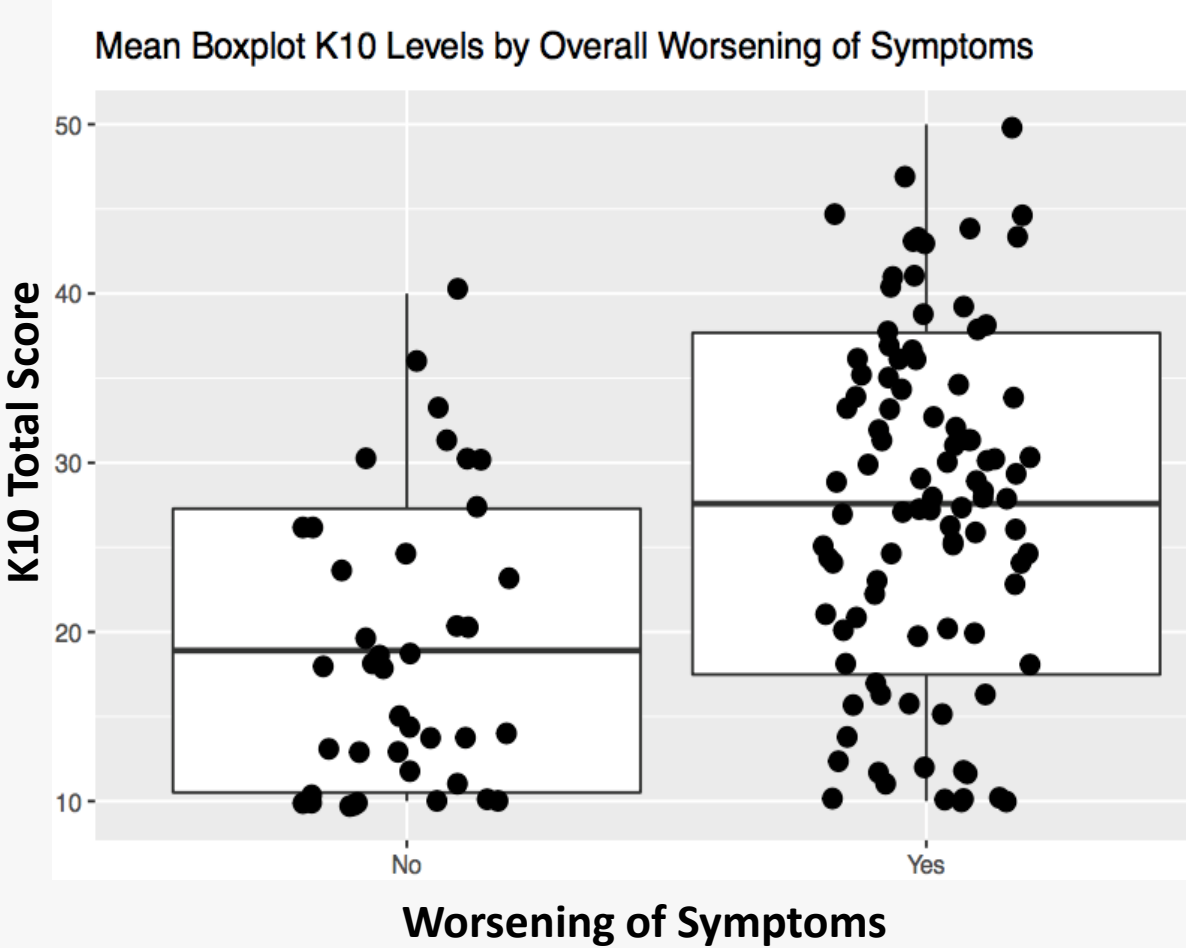
K10 Total Score: * $p < 0.001$ NPC vs SMI, Bipolar vs. MDD vs Schiz

K10 High Stress: * $p < .001$, NPC vs SMI, MDD vs Schiz

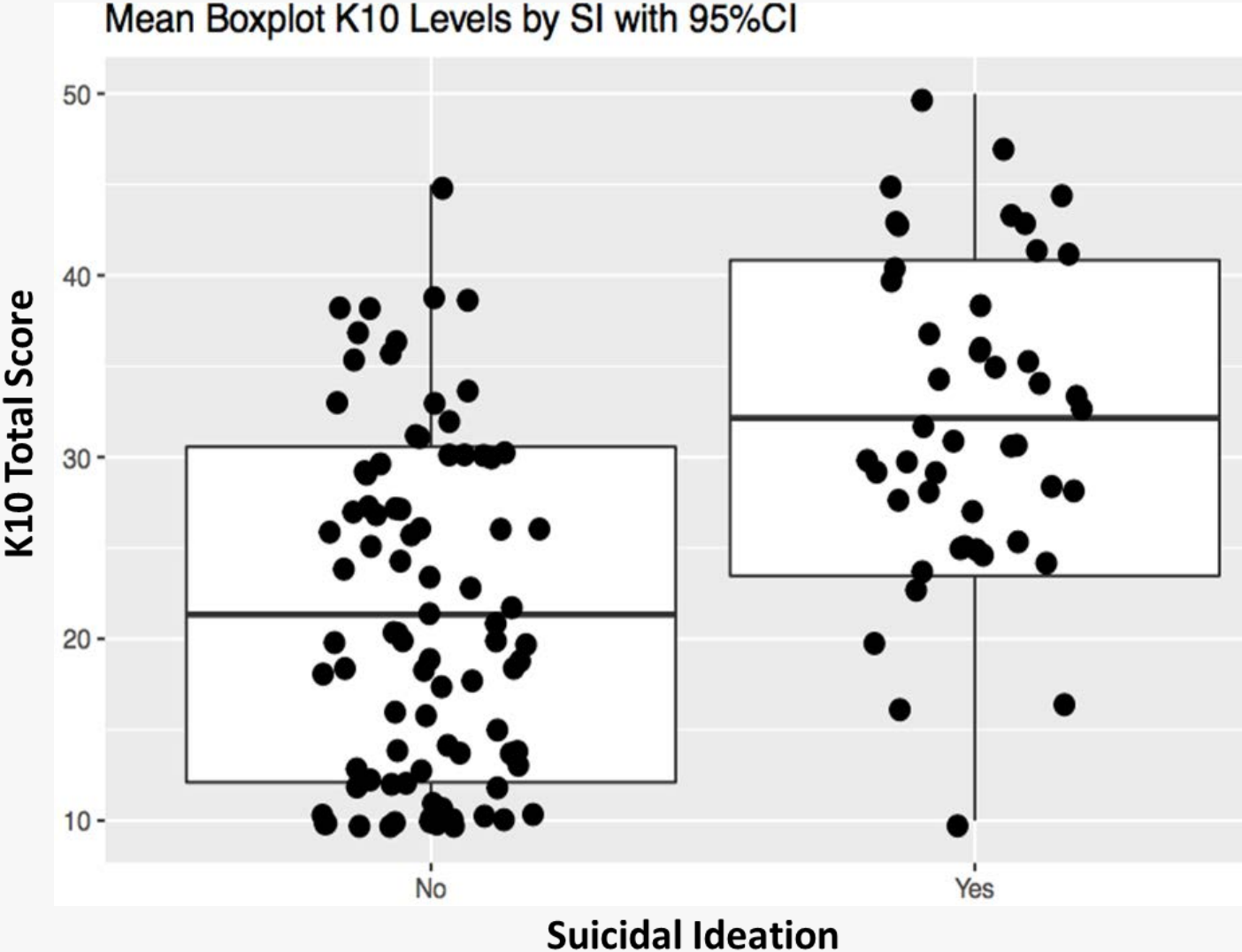
Psychological Stress (K10) in MDD > SCZ



Psychological Distress and Symptoms



Psychological Distress and Suicide



Lessons Learned

SMI Research Subjects Can Participate Safely in Clinical Trials

- SMI comparable to NPC in maintaining safety and protecting against infection
- SMI endorse use PPE = NPC, and social distancing > NPC
- SMI sought medical care & received vaccinations at rates similar to NPC
- Sites/Sponsors can be reassured regarding SMI safely participating in clinical trials during the Covid 19 pandemic

Clinical Trial Participation May be Protective for SMI Subjects

- Clinical trial SMI select for subjects without characteristics conferring high mortality risk (chronic unstable medical illnesses, obesity, substance use disorder)
- Clinical trial sites provide preventative and targeted disease management strategies (testing) advocated for protection of SMI from infection risk

Pandemic-induced Stress Confound for Efficacy/Outcomes, especially in MDD study population

- Worsening of psychiatric symptoms
- Suicidal ideation

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