Responding to the Challenge of Treatment of Individuals with Co-occurring Substance Abuse and Psychotic Disorders: A Focus on Youth and Young Adults

Lisa Dixon, M.D., M.P.H.
New York State Psychiatric Institute
Columbia University

Tina

Outline

- Understanding the Problem
- Lessons from previous research
- RAISE Connection Experience

Understanding the Problem: Co-occurring Substance Use

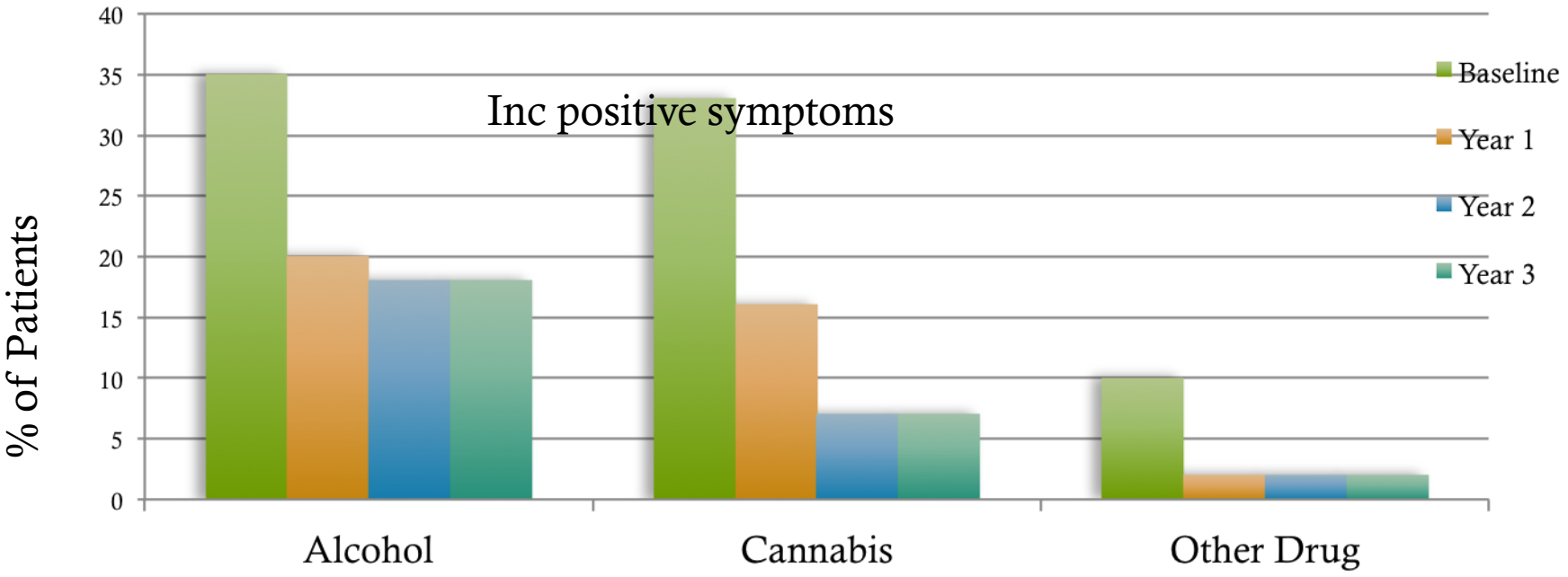
- A barrier to recovery for individuals experiencing long-standing mental disorders
- Associated with increased hospitalization, relapse, treatment drop out, increased positive symptoms and medical problems, homelessness, though possibly better premorbid functioning

Understanding the Problem: Co-occurring Substance Use

- Effective treatment requires
  - Integrated approach
  - Stage based care
  - Attention to both disorders

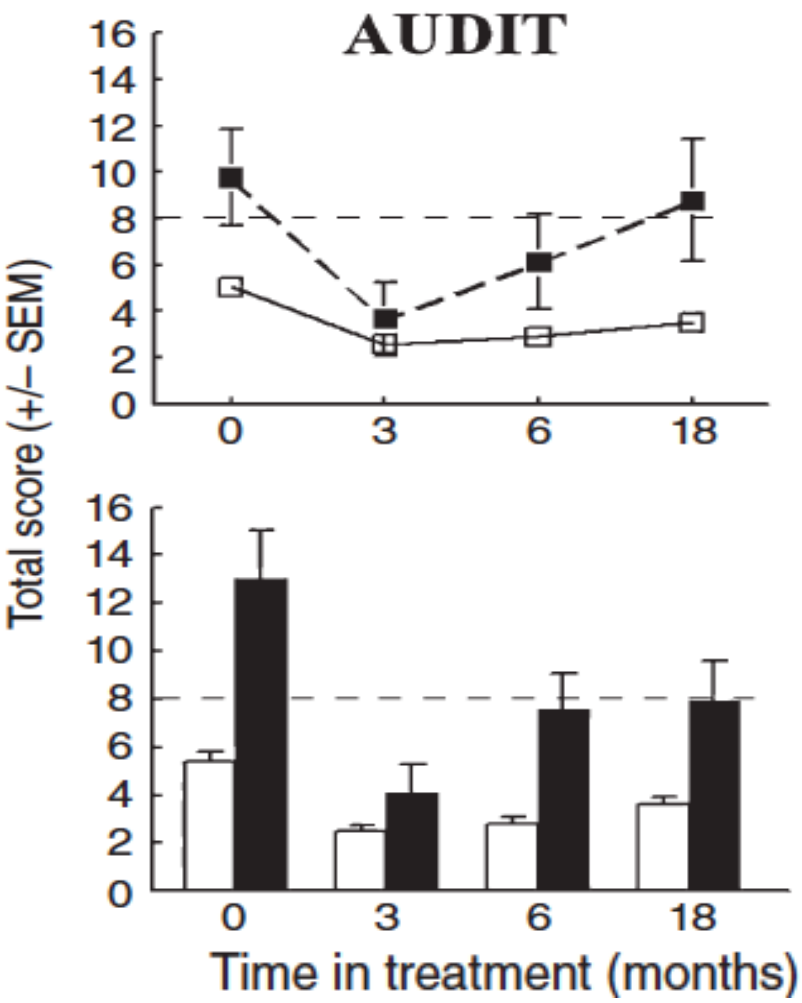
Prevalence and Outcome in FEP

Calgary Early Psychosis Program:
Alcohol and Substance Misuse (N=203)



Addington and Addington, Patterns, predictors and impact of substance use I n early psychosis: a longitudinal study. Acta Psychiatr Scand. **2007** Apr;115(4):304-9

Substance misuse over the first 18 months of specialized intervention for first episode psychosis



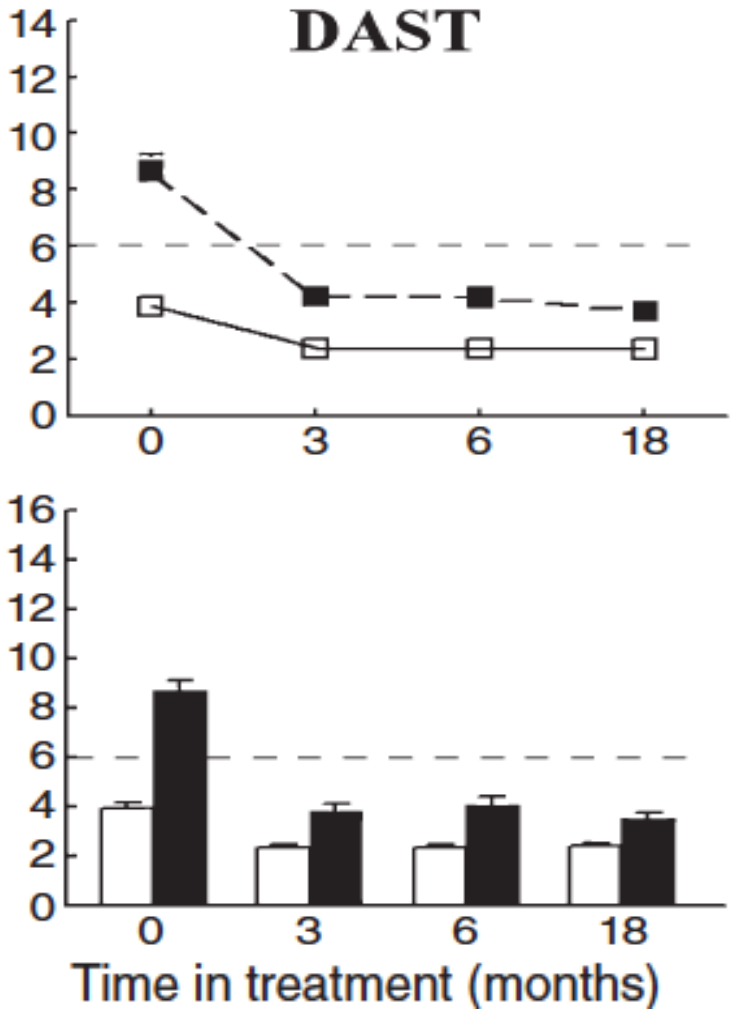
PEPP-London, Ontario
N=243 at baseline

Met criteria for alcohol (AUDIT) or drug (DAST) abuse or dependence on entry

Did not meet criteria for alcohol (AUDIT) or drug (DAST) abuse or dependence on entry

Carr et al. Early Intervention in Psychiatry, 2009

Substance misuse over the first 18 months of specialized intervention for first episode psychosis



PEPP-London, Ontario
N=243 at baseline

Met criteria for alcohol (AUDIT) or drug (DAST) abuse or dependence on entry

Did not meet criteria for alcohol (AUDIT) or drug (DAST) abuse or dependence on entry

Carr et al. Early Intervention in Psychiatry, 2009

Naturalistic follow-up of co-morbid substance use in schizophrenia: the West London first-episode study

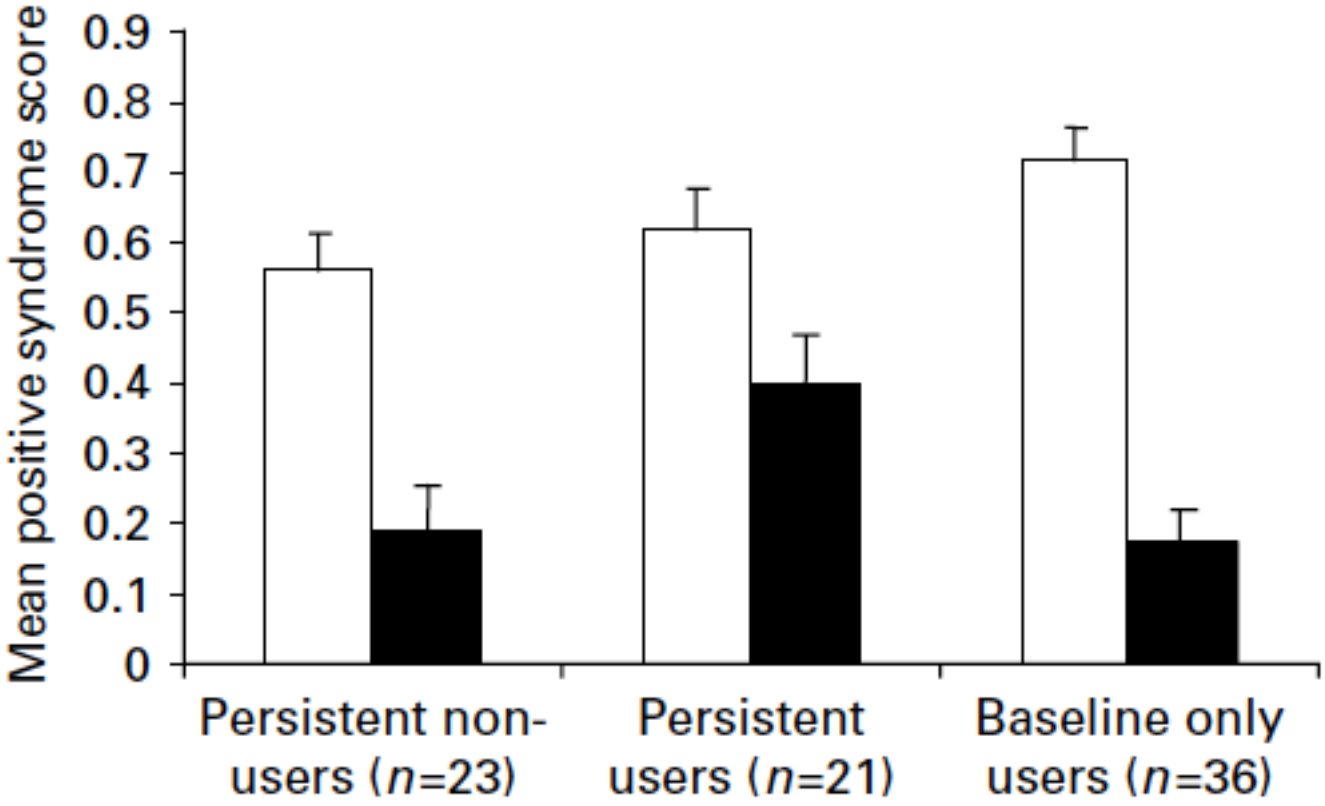
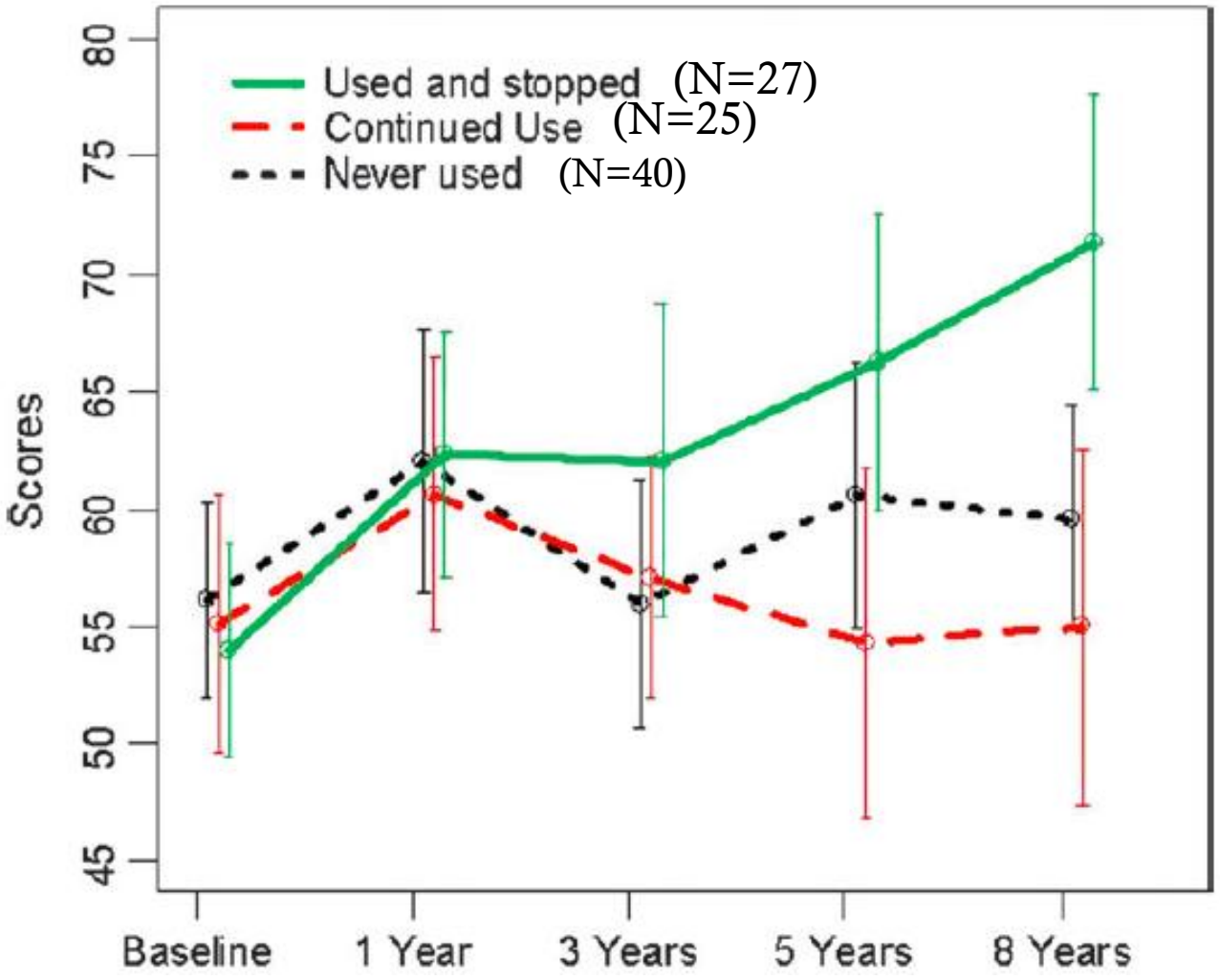


Fig. 1. Comparison of three main substance use follow-up subgroups at baseline (□) and follow-up (■): positive symptom syndrome.

Harrison, Joyce et al. *Psychological Medicine* (2008), 38, 79–88.

Cannabis and First-Episode Psychosis:

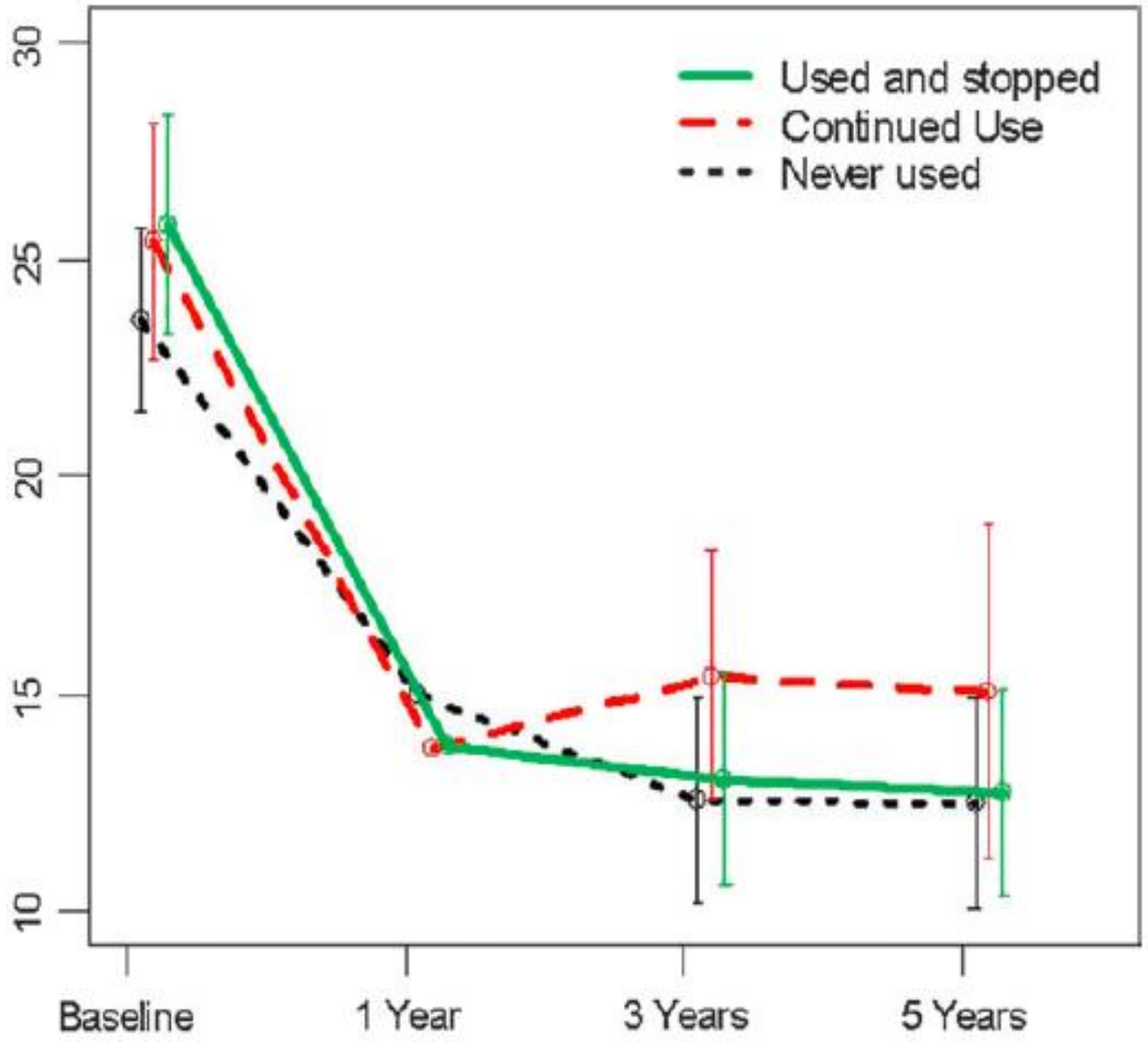


Global Assessment Of Functioning

Spanish Basque Country

Gonazalez-Pinto et al. **Schizophrenia Bulletin** vol. 37 no. 3 pp. 631–639, 2011

Cannabis and First-Episode Psychosis:

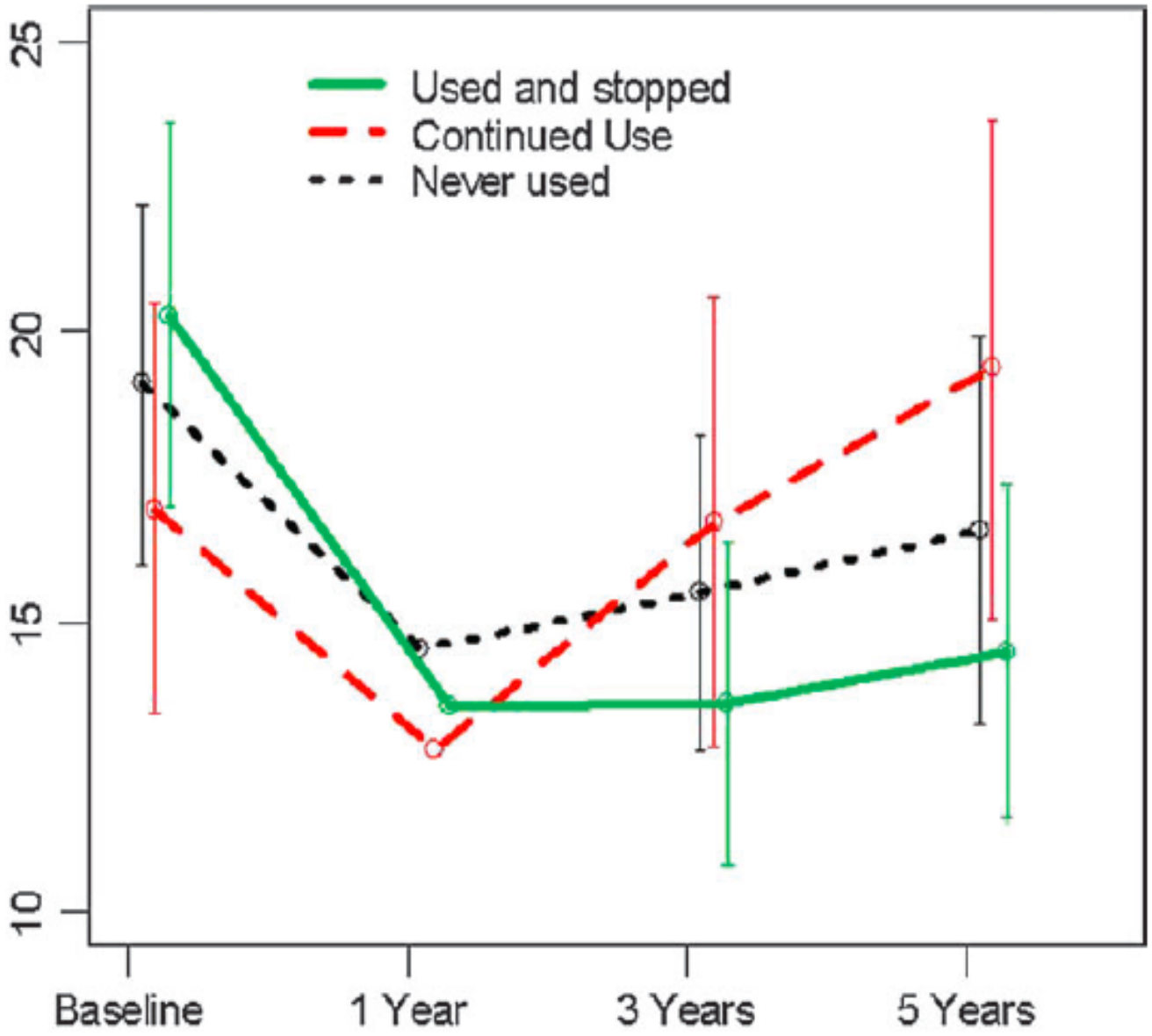


PANSS Positive Symptoms

Spanish Basque Country

Gonazalez-Pinto et al. **Schizophrenia Bulletin** vol. 37 no. 3 pp. 631–639, 2011

Cannabis and First-Episode Psychosis:



PANSS Negative Symptoms

Spanish Basque Country

Gonazalez-Pinto et al. **Schizophrenia Bulletin** vol. 37 no. 3 pp. 631–639, 2011

Psychotic symptom and cannabis relapse in recent-onset psychosis

Table 3 Cox regression survival analysis on BPRS psychotic relapse with cannabis use and other predictor variables in one model

Variable	B	s.e.	Wald	d.f.	*P*	Hazard ratio
Baseline psychotic symptoms	0.09	0.05	2.83	1	0.09	1.09
Baseline depression-anxiety symptoms	0.23	0.07	10.65	1	0.00	1.26
Duration of untreated psychosis	0.00	0.00	0.49	1	0.49	1.00
Medication adherence	−0.01	0.01	0.58	1	0.45	0.99
Subjective life stress	0.01	0.02	0.53	1	0.47	1.01
Days of other substance use	−0.01	0.04	0.06	1	0.82	0.99
Days of cannabis use	0.06	0.02	8.61	1	0.00	1.06

N=84 at baseline: N=81 at 6 months: Brisbane, Australia

Hides, Dawe et al.

BRITISH JOURNAL OF PSYCHIATRY (2006), 189, 137–143.

Psychotic symptom and cannabis relapse in recent-onset psychosis

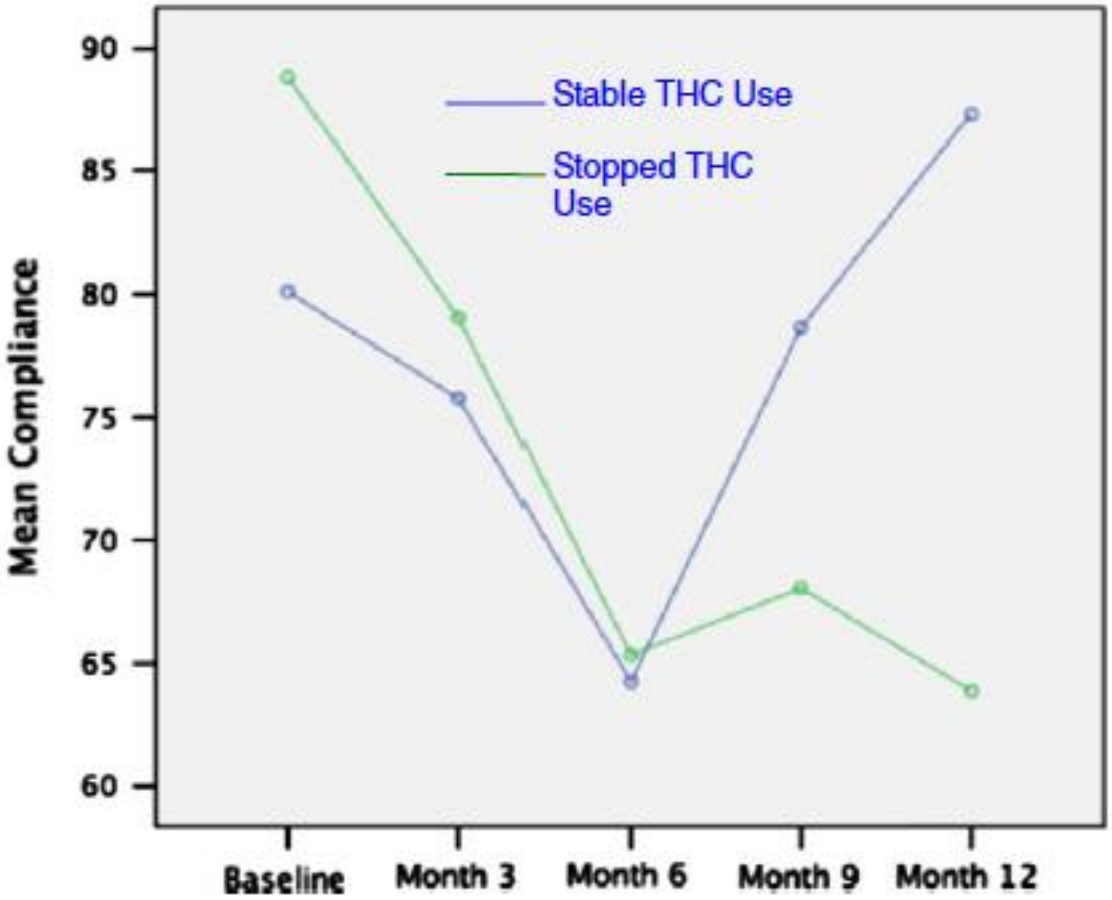
Table 4 Cox regression survival analysis on cannabis relapse with psychotic symptom severity and other predictor variables in one model

Variables	B	s.e.	Wald	d.f.	*P*	Hazard ratio
Baseline cannabis use	0.02	0.01	2.40	1	0.12	1.02
Age at onset of regular cannabis use	0.03	0.04	0.42	1	0.52	1.03
Medication adherence	−0.02	0.01	4.21	1	0.04	0.99
Subjective life stress	0.00	0.01	0.05	1	0.82	1.00
Days of other substance use	0.02	0.01	1.64	1	0.20	1.02
Psychotic symptom severity	0.03	0.01	8.02	1	0.00	1.03

N=84 at baseline: N=81 at 6 months: Brisbane, Australia

Hides, Dawe et al. BRITISH JOURNAL OF PSYCHIATRY (2006), 189, 137–143.

Medication adherence mediates the impact of sustained cannabis use on symptom levels in first-episode psychosis



PEPP-Montreal

PANSS total greater among individuals who did not stop when controlling for adherence

Faridi e tal. Schizophrenia Research 141 (2012) 78–82

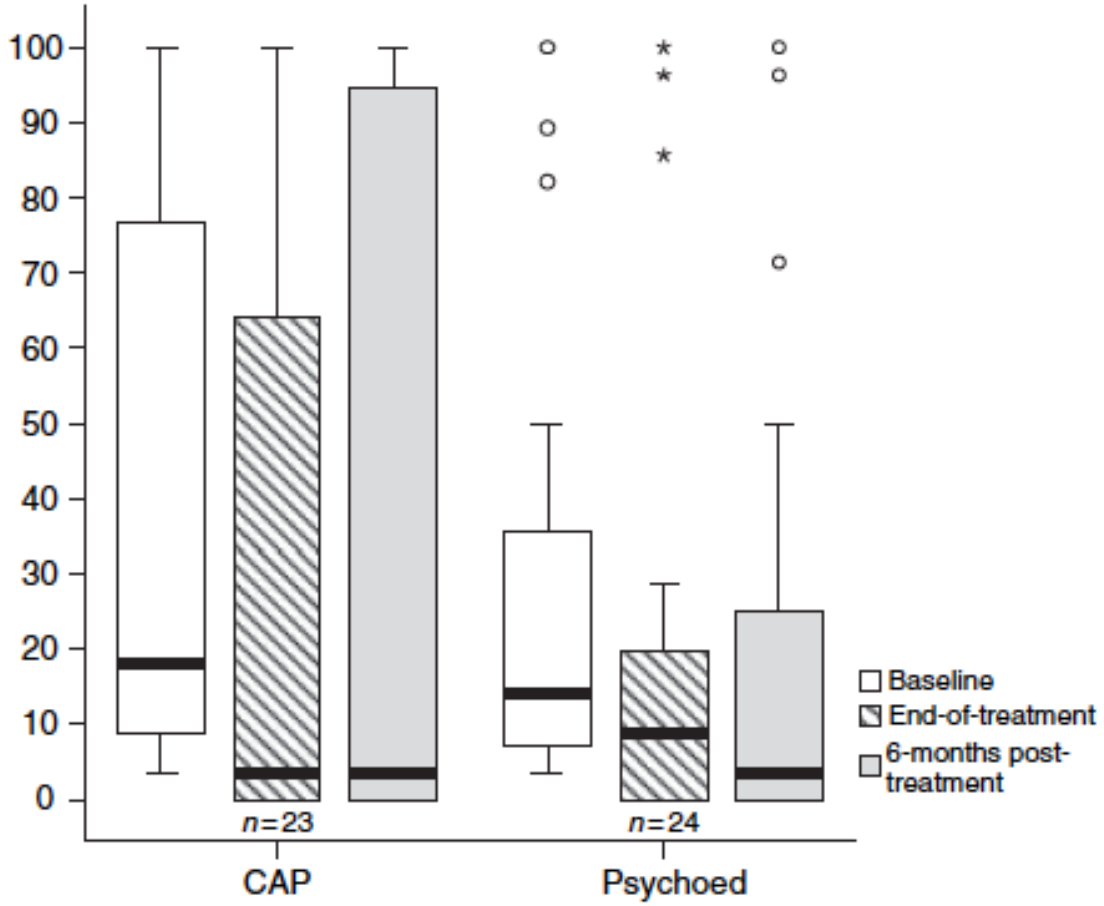
Randomized controlled trial of a cannabis-focused intervention for young people with first-episode psychosis

- RCT comparing Cannabis and Psychosis Therapy (CAP) (N=23) to Psychoeducation (N=24)
- Individuals enrolled at 10 weeks, 3 months or 9 months after program enrollment if using cannabis in the 4 weeks prior to the assessment
- Conducted at EPPIC

Edwards J, Elkins K, .et al *Acta Psychiatr Scand 2006: 114: 109–117*

Treatment Conditions

- CAP
  - Individually administered
  - Cognitive Behavioral
  - Harm minimization
  - 10 weekly sessions over 3 months
  - Content phase specific
- Psychoeducation
  - 10 Sessions guided by powerpoint
  - Covered psychosis, medication, relapse prevention
  - Avoided mention of cannabis



Both Groups Improved
No Group Differences

Fig. 1. Box plots for percentage of days used cannabis in the previous 4 weeks (last observation carried forward) at baseline (□), end-of-treatment (▨), and 6-month post-intervention (■) for cannabis and psychosis therapy (CAP, $N = 23$) and psychoeducation (PE, $N = 24$). ○ = outlier, ★ = extreme value.

A multi-center, randomized controlled trial of a group psychological intervention for psychosis with comorbid cannabis dependence over the early course of illness

- RCT comparing Group Psychological Intervention (GPI)(N=59) to TAU (N=29)
- Individuals with psychosis and cannabis dependence
- Evaluated at baseline, three months and one year
- Presented to DETECT first episode service in South County Dublin/ North Wicklow

Kevin Madigan [a,b,*], Daria Brennan [a,b], Elizabeth Lawlor [a,b], Niall Turner [a,b], Anthony Kinsella [b,c], John J. O'Connor [d], Vincent Russell [e,f], John L. Waddington [c,e], Eadbhard O'Callaghan [a,b,†]

Schizophrenia Research 143 (2013) 138–142

Group Psychological Intervention

- Weekly sessions of anxiety management, motivational interviewing, and CBT Techniques
- Six phases:
  - Entry, commitment, goal setting, challenges, relapse prevention and lifestyle, maintenance, exit
- Once per week for twelve weeks with booster 6 weeks later

Results

- Improved subjective quality of life (WHOQOL, BREF) score at three months and one year in GPI
- No difference in
  - Cannabis use
  - Insight
  - Attitude to treatment
  - Positive symptoms
  - Negative symptoms
  - Depressive symptoms
  - GAF

Understanding factors influencing substance use in people with recent onset psychosis: A qualitative study

- Aim to understand factors influencing use of substances among group of individuals with recent onset psychosis
- Purposive sampling of 19 individuals age 16 to 35 within three years of admission to Early Intervention Service
- All misused substances currently or in the six months prior to intervention to the service
- All had been regular cannabis users, and for 13 it was priamry durg of choice

Fiona Lobbana [a,*], Christine Barrowclough [b], Sophie Jeffery [b], Sandra Bucci [b], Katherine Taylor [a], Sara Mallinson [c], Mike Fitzsimmons [d], Max Marshall [d]

Social Science & Medicine 70 (2010) 1141–1147

Understanding factors influencing substance use in people with recent onset psychosis: A qualitative study

THEME 1: influence of perceived drug norms on behaviour

When people were asked to talk about how they began using drugs they often talked about how 'normal' drug taking was in their neighbourhood or community. Drug taking was often described as an integral part of local landscapes:

Fiona Lobbana [a,*], Christine Barrowclough [b], Sophie Jeffery [b], Sandra Bucci [b], Katherine Taylor [a], Sara Mallinson [c], Mike Fitzsimmons [d], Max Marshall [d]

Social Science & Medicine 70 (2010) 1141–1147

Understanding factors influencing substance use in people with recent onset psychosis: A qualitative study

THEME 2: Attributions for initial and ongoing drug-taking behaviour

Some, but not all, participants were able to identify specific reasons for their drug use and amongst this group there were two types of attribution: internal attributions (i.e., that it was an active personal choice) and external attributions (i.e., that it was due to the influence of others). Those people who made internal attributions described seeking out information, and weighing up pros and cons in order to make their decisions:

Fiona Lobbana [a,*], Christine Barrowclough [b], Sophie Jeffery [b], Sandra Bucci [b], Katherine Taylor [a], Sara Mallinson [c], Mike Fitzsimmons [d], Max Marshall [d]

Social Science & Medicine 70 (2010) 1141–1147

Understanding factors influencing substance use in people with recent onset psychosis: A qualitative study

THEME 3: changes in life goals affecting drug use

In many accounts a key reason for reducing or stopping substance misuse was a change in personal life goals, especially an increase in the perceived value of health, disposable income and close family relationships. These were largely identified by older participants who had reduced their use of substances and were reflecting on the reasons for this:

Fiona Lobbana [a,*], Christine Barrowclough [b], Sophie Jeffery [b], Sandra Bucci [b], Katherine Taylor [a], Sara Mallinson [c], Mike Fitzsimmons [d], Max Marshall [d]

Social Science & Medicine 70 (2010) 1141–1147

Understanding factors influencing substance use in people with recent onset psychosis: A qualitative study

THEME 4: beliefs about the links between mental health and drug use

Many participants expressed theories about the connection between drugs and the onset of psychosis which were clearly influencing behaviour. Some drew on fairly sophisticated formulations in which drug use mediated between biological and/or life events and the onset of mental health problems:

Fiona Lobbana [a,*], Christine Barrowclough [b], Sophie Jeffery [b], Sandra Bucci [b], Katherine Taylor [a], Sara Mallinson [c], Mike Fitzsimmons [d], Max Marshall [d]

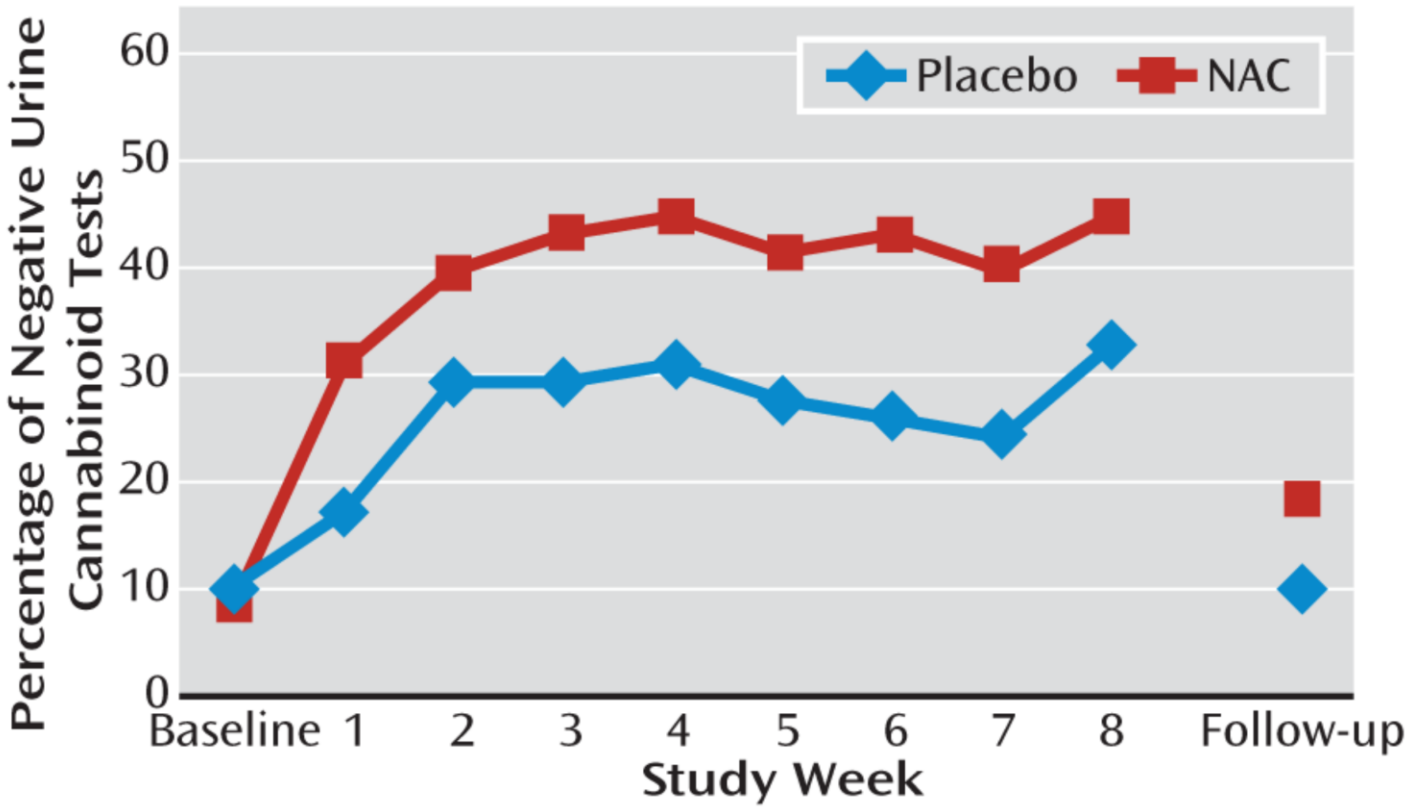
Social Science & Medicine 70 (2010) 1141–1147

N-Acetyl Cysteine for Cannabis Dependence

- NAC is a precursor of cysteine which is a precursor of glutathione, a potent antioxidant—oxidative stress may contribute to the development of schizophrenia
- Cysteine also competes with glutamate for reuptake and may increase glutamate levels.
- Preclinical findings suggest that NAC, via glutamate modulation in the nucleus accumbens, holds promise as a pharmacotherapy for substance dependence.

From: A Double-Blind Randomized Controlled Trial of N-Acetylcysteine in Cannabis-Dependent Adolescents

Am J Psychiatry. 2012;169(8):805-812. doi:10.1176/appi.ajp.2012.12010055



Figure

Proportion of Negative Urine Cannabinoid Tests Over Time Among Cannabis-Dependent Adolescents in a Randomized Controlled Trial of N-Acetylcysteine (NAC)[a]

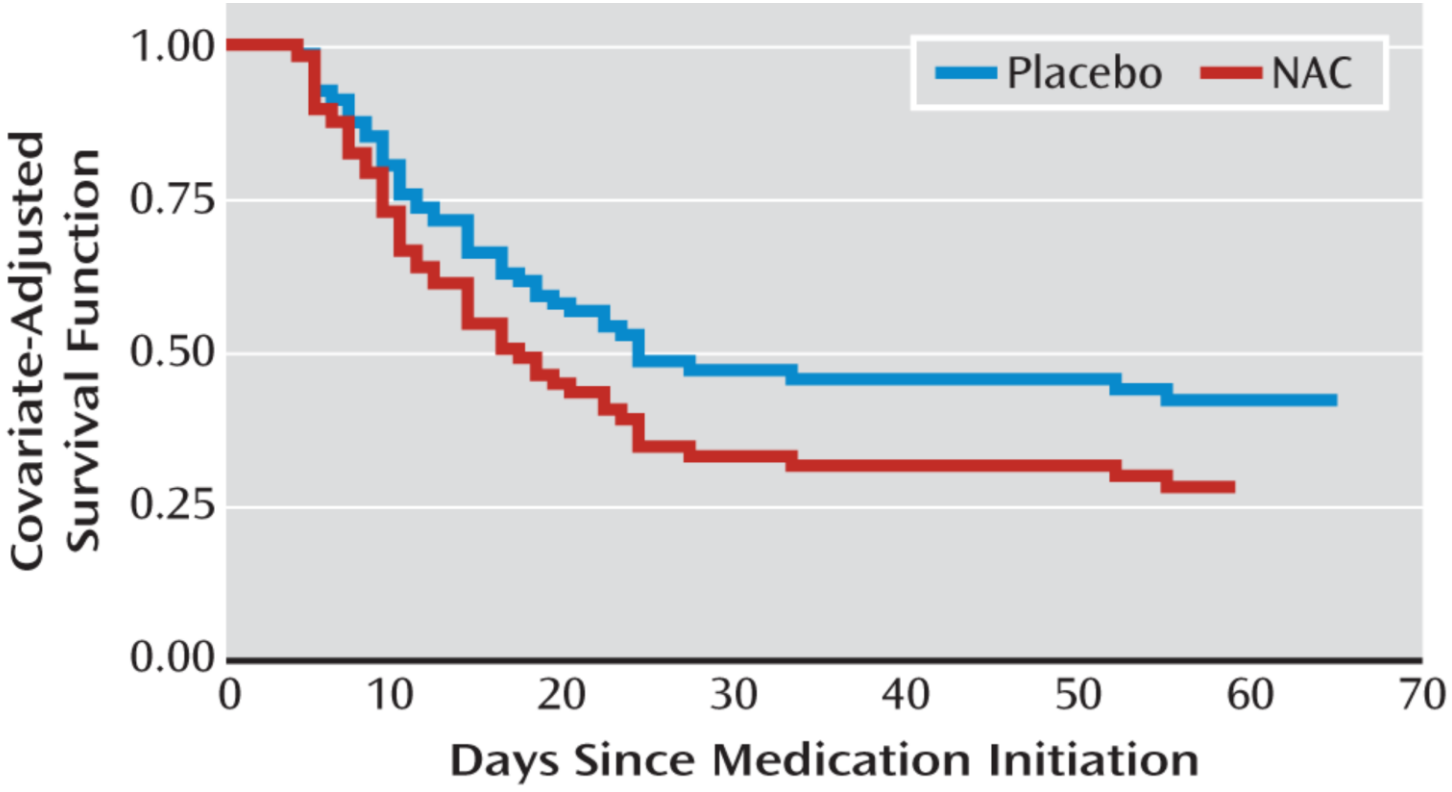
[a] In this intent-to-treat analysis, all randomized participants (N=116) were included, and urine cannabinoid tests were assumed to be positive for all missed visits. With adjustment for years of cannabis use, baseline urine cannabinoid test results, and major depressive disorder, odds ratio=2.4, 95% CI=1.1–5.2; χ^2=4.72, p=0.029.

THE AMERICAN JOURNAL OF PSYCHIATRY

psychiatryonline

From: A Double-Blind Randomized Controlled Trial of N-Acetylcysteine in Cannabis-Dependent Adolescents

Am J Psychiatry. 2012;169(8):805-812. doi:10.1176/appi.ajp.2012.12010055



Survivorship Function for Time to First Negative Urine Cannabinoid Test Among Cannabis-Dependent Adolescents in a Randomized Controlled Trial of N-Acetylcysteine (NAC)[a]

[a] The graph shows the estimated survival function for NAC compared with placebo participants, adjusted for years of cannabis use and baseline urine cannabinoid test results.

Summary of Lessons from Current Research

- Misuse of substances, especially cannabis, common among individuals with recent psychosis.
- Half or more of individuals misusing substances will stop using with the onset of standard Early intervention treatment
- The remaining group who misuse persistently are likely to have worse outcomes with respect to positive symptoms and perhaps other outcomes
- Effective treatments for the persistent users remain elusive
- Greater understanding of contextual and biological factors is needed.