ADOLESCENT SUBSTANCE USE DISORDERS & CO-OCCURRING DEPRESSION: TREATMENT IMPLICATIONS

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A DISCLAIMER

I am presently receiving research support by NIAAA

I have been receiving royalties for authored and edited books on adolescent substance abuse by APPI, Hazelden and Routeledge

Struggling with sadness? Alcohol use getting in the way?

✓~ Are you 13-21 years of age?

✓~ Do you struggle with alcohol abuse (with or without other substance use) and depression?

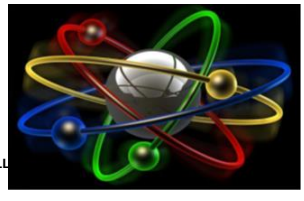
✓~ Do you want to get help?

If you are a teenager who is struggling with alcohol use and depression and would like to learn more about the ATOM Programs

T-TAAD Study at UCONN HEALTH, please call

➢**Rebecca @ (860) 679-8478 burke@uchc.edu**

*ALL



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PREVALENCE OF DISORDERS IN ADOLESCENTS WHO USE OR ABUSE SUBSTANCES

	Percentage	OR
Conduct disorder	25 to 50%	4
Anxiety	8 to 18%	1.5
Depression	20 to 30%	2-3*

*Meaning that comorbidity of AUD/SUD is X2-3 higher for those who suffer from depression than for those from the general population.

** Risky alcohol use is associated with a higher probability of developing affective D. than for not at-risk users

Armstrong, TD & Costello, EJ. (*J Consul Clin Psychology, 2002)*;

Swenden et al. (Compr Psychiatry, 1998); Bott et al. (J Stud Alcohol, 2005)

PREVALENCE OF DISORDERS IN ADOLESCENTS AND YOUNG ADULTS TREATED FOR SUD

	Percentage
Conduct disorder	24 to 82%
Depression	3 to 84%
Anxiety	1 to 38%

Couwenbergh, C. et al. (2006). Comorbid psychopathology in adolescents and young adults treated for substance use disorders. *European Child and Adolescent Psychiatry, 15*, 319-328.

NSDUH USA 2016

- **Major Depressive Episode (MDE):**

In 12.8% of youth aged 12-17 and 10.9% 0f those aged 18-25

- **Substance Use :**

Among MDE 31.7% Vs. Non MDE 13.4%

PREVALENCE AND RISK FACTORS

Prevalence of comorbid SUD and MDD in adulthood is 8.3%

Comorbidity in men is twice that for women (11.1% Vs. 5.7%)

Recognizing the heterogeneity among individuals with depression and/or SUD few risk factors may differ between mono and dual diagnosis.

For example:

Low SES and high family conflict related to developing MDD.

Dropping out from high school predicts developing SUD.

Green KM et al. (Addictive Behaviors, 2012)

IMPAIRED BUT UNDIAGNOSED

- individuals with psychosocial impairment not meeting DSM criteria for any of 29 well-defined disorders, but who have symptoms associated with psychosocial impairment should be regarded as suffering from a psychiatric disorder. Angold A, et al. (JAACAP, 1999)
- The prevalence of subthreshold MDD among youth in lit. review ranged between 5-29%. Elevated rates of psych comorbidity, suicidality, impaired function. Carrellas NW, et al. (2017)
- The clinical significance of depressive symptoms does not depend on crossing the major depressive diagnostic threshold. Lewinsohn et al. (2000)
- A third of youth with a subthershold diagnosis developed MDD during a follow-up period. Hill et al. (2014)

Why we can not ignore SA in patients with mental illness

- Overlapping developmental, environmental and genetic vulnerabilities.
- Drugs can trigger mental disorders in those that are vulnerable and can exacerbate their course.
- Patients with mental illness are at greater risk for substance abuse.
- Drugs contribute significantly to the morbidity and mortality of patients with mental illness. Compton W. (2010)

NEGATIVE CONSEQUENCES: DEPRESSION COMORBIDITY IN YOUTH

- **Compared to a single diagnosis:**

Elevated risk for suicide;

Greater treatment attrition and poorer outcomes;

Poorer overall quality of life including: social competence, mental and physical health (disability)

Babowitch JD, & Antshel KM (J. Affect Disorders, 2016)

MENTAL HEALTH GAPS FOR YOUTH

10-20% of youths in the U.S. meet diagnostic criteria for MH disorder.

Up to 50% of youth in the child welfare system and 70% in the JJ system have a diagnosable MH disorder.

Only 20-30% receive specialized MH care.

Youth comprise 25% of the population, only 1/9 of health care funding is directed to them. Kazak AE et al. (Am Psychol 65:85-97, 2010)

A TALE OF TWO SYSTEMS

Most adolescents receive substance abuse treatment separately from general medical and psychiatric services, typically in community-based programs. Differences across the three systems have perpetuated significant systemic barriers to access for youth with co-occurring problems, barriers reinforced by distinct funding mechanisms.

Hawkins EH: (Ann Rev Psychol 60:197-227, 2009)

BARRIERS FOR INTEGRATED SERVICES FOR THE DD YOUTH

The historical separation of substance abuse and mental health services.

The tendency to exclude youth with SUD from clinics for psychiatric disorders.

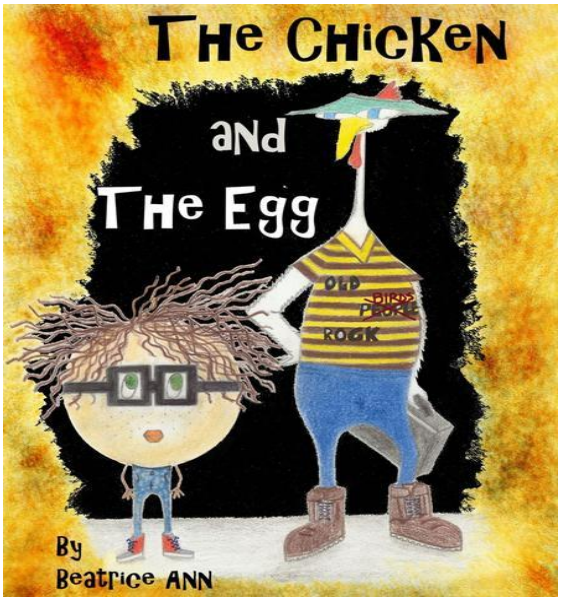
A limited # of clinicians and researchers who focus on dually diagnosed youth.

Few (<30%) providers respond using formal assessment practices or Tx protocols (10%).

Issues with billing and funding treatment of the Dually Diagnosed. Fishman M (2016)

EXPLAINING CO-OCCURRENCE: 5 MODELS

1) **Secondary substance use model: Self Medication?**
2) **Secondary psychopathology mode: Disease Model?**
3) **Bidirectional model: multiple factors are involved in triggering and maintaining MH and SU Disorders;**
4) **Common-factor model: proposed to independently increase the risk for both (e.g., neurobiological, etc);**
5) **Unrelatedness model: simply a co-probability of otherwise unrelated disorders** Kay-Lambkin et al. (2004)



CO-OCCURRING DISORDERS

May:

Precede as a risk factor of,

Develop as a consequence of,

Moderate the severity of,

OR

Originate from a common vulnerability as SUDs (TLI-transmissible liability index)

Tarter RE & Horner MS: Youth SUD and Co-occurring Disorders,

Edited by Kaminer, Y: (APPI, 2016)

In the ECA study (n=30,000; age range 18-30 Y.O.) a psychiatric disorder preceded the SUD in 3:4 participants.

Christie KA, et al. (Am J psychiatry, 1988)

SHARED LIABILITY

Substance use disorders and depression are bi-directionally associated Wilkinson et al. (AB, 2016)

That would suggest shared liability supported by studies of shared genetic origin among psychiatric disorders Pattersson E, et al. (Molecular Psychiatry, 2016); Cross-Disorder Group of Psych Genomic Consortium (Lancet 2013)

MOTIVATIONAL ASPECTS OF ONGOING DRUG USE

Allostatic Hypothesis: Emphasizes the secondary psycho-pathology that emerge after prolonged SU, including the compensatory use of other drugs. Koob et al. (2014)

The progression from occasional user to chronic user is a shift from SU as a positively reinforced reward-seeking behavior to a negatively reinforced compulsive behavior.

With respect to comorbid pathology, the model suggests that negative mood states related to SU cycles evolve into chronic conditions (i.e., Internalizing Disorders).

Progression to non cannabis SUD is anticipated/expanded effort for relief from reward deficiency & neg. mood states.

Olfson M. et al. (Cannabis use and risk for prescription opioid use disorder- Am J psychiatry, 2017); Kaminer Y. (editorial in Substance Abuse J. 2017)

PSYCH DISORDERS AS A RISK FACTOR FOR SUD

- Depression n=13, OR 2.03 Groenman AP et al. (JAACAP, 2017)
- MH disorders are a risk factor for SUD but this association works both ways. Wilkinson AL, et al. (Addict Behav, 2016)
- This would suggest shared liability (supported by shared genetic origin among common psychiatric disorders). Cross-Disorder Group of the Psychiatric Genomics Consortium (Lancet, 2013)
- COAs are at increased risk of developing other disorders, showing cross-disorder transfer. Hill SY et al. (1999)

ASSOCIATION OF PSYCHIATRIC COMORBIDITY WITH DURATION OF CUD

The following slides are based on a longitudinal study (n=816/173 CUD) from age 16 to 30 years Farmer RF et al. (2016)

Risk factors for the development of psychiatric disorders (PD) and CUD respectively have been well-researched.

Comparatively, little is known of factors associated with the persistence of CUD (P-CUD) with or without PD over time.

The initiation and persistence of co-occurring Internalizing and Externalizing disorders and their temporal sequencing (pre, during and post to) for ongoing CUD is explored.

Importance: recovery from a disorder becomes less probable over a longer period of time Patton, (2006)**.**

RESULTS-I

Any internalizing & mood disorder with onset Prior to that of the index CUD episode were each significantly and negatively associated with CUD duration.

Adjusted analyses controlling for putative confounds reduced the findings to a trend.

Subsequent occurrence of <u>any</u> Axis I disorder was significantly and positively associated with the duration of that episode in both unadjusted and adjusted episodes.

"PROTECTIVE FACTOR" OF INTERNALIZING D.

Associated with behavioral inhibition (BI);

BI may counteract reward seeking associated with negative consequences;

Persons with Int'l D. are less likely to affiliate with deviant peers;

Individuals with neg. moods and Int'l D. may experience cannabis to be less reinforcing;

Cannabis use may result with intensification of Int'l symptoms thus making cont'd use less likely

(Arendt M, et al. 2007)

CURRENT APPROACHES FOR DD INTERVENTION

- **Currently, clinicians have more info about the epidemiology than about approaches to DD Tx**
- **Traditional treatment of co-occurring MH and SUD have been designed around the Self Med and Disease models**
- **Utilizing existing uni-diagnosis Tx strategies**
- **Generally with the primary condition targeted for Tx**
- **The secondary condition is usually treated sequentially**
- **Failing to formulate co-morbidity Tx regimen leads to suboptimal Tx, poor outcomes, negative (and more costly) consequences** **Brady S, et al. (1996); Kay-Lambkin et al. (2004)**

TADS OUTCOMES

- Treatment for Adolescents with Depression study n=439 ; Age 12-17 years; assessments at 12 and 36 weeks
- Evaluate effectiveness of 4 Txs: FLX; CBT; FLX+CBT; PBO
- CBT+FLX superior in reducing depression in DSM-IV=MDD
- Suicidality improved across all TXs
  However, X2 with CBT or FLX+CBT
- Perhaps CBT protects against suicidality

March J, et al. (JAACAP, 2006)

ONSET OF SUD FOLLOWING TX FOR YOUTH DEPRESSION

- TADS study: N=192 adolescents treated for MDD (CBT; FLX; CBT/FLX; Placebo) without prior diagnosis of SUD were followed for 5 years
- Achieving a positive response to MDD was unrelated to AUD but predicted a lower rate of subsequent SUD
- More comorbid Disorders predicted SUD
- Type of MDD Tx was unrelated to either outcome. Curry JF, et al. (JCCP, 2012)
- TORIDA: 25% reported substance use $\geq$ 3 times during the study. Goldstein et al. (2009)

DEPRESSION RESPONSE TO AOSUD TX

- There is some evidence that CBT for AOSUD alone might improve depression after 1-year FU. Hawke JM, Kaminer Y, et al. Stability of comorbid psychiatric diagnoses in youths in treatment for alcohol use disorders. Substance Abuse, (2008)

% Responders at Week 4

- CBT+FLX 27.5%
- CBT+PBO 28% Riggs P, et al. (2007)
- In our ongoing study approx. 40% have been early depression responders to MET/CBT for AOSUD

CHANGES IN DEPRESSIVE SYMPTOMS OF YOUTH IN TX FOR CUD IN CYT STUDY

- METHOD
- Cannabis Use Treatment (CYT) study: N=600 (age 12-18 Y.)
- Five types of psychosocial therapies: MET/CBT-5 or 12; Incld. three family based interventions: MDFT; ACRA; FSN
- Cannabis use based on drug urinalysis and self reports
- Depression symptoms based on the GAIN-DSI; 6-item scale

Dennis M, et al. (JSAT; 2004)

CYT DEPRESSION OUTCOMES -II

RESULTS:

- **Baseline rates: DSM-IV-MDD and any depressive symptoms (18% and 70% respectively).**
- **A significant linear decrease in the depressive score, and cannabis use across 4 time points (up to 1 year FU)**
- **Improvement in both symptoms not correlated with type of Tx provided**
- **Improvement in cannabis use was not significantly influenced by depression severity at baseline**

Arias A., Burleson J, Kaminer Y, Curry J & Dennis M (Under review)

CYT DEPRESSION OUTCOMES -III

- **COMORBID ALCOHOL:**
- **Higher baseline alcohol use was inversely associated with improvement in depressive symptomatology**
- **However, the trend for depression improvement was still manifested across the entire cannabis using cohort**

TX OF COMORBID AUD & MDD WITH MI/CBT: A META-ANALYSIS

Based on 12 studies in adults; n=1721

Overall small effect size for depression response compared with controls P<0.001 confidence interval= 0.13-0.41

Digital interventions showed a higher effect size for depression than face-to-face interventions p=0.030.

Conclusion: combined MI/CBT has a small but clinically significant effect in Tx outcome compared with TAU.

Riper et al. (Addiction, 109, 394-406: 2013)

TX OF ADULT COMORBID AUD-DEPRESSION WITH CBT/MI

A meta-analysis of 12 studies with sufficient statistical power to detect small effect sizes (n=1721).

Combined CBT/MI for clinical and subclinical depressive and alcohol use disorders has a small but clinically significant effect in Tx outcome compared with Tx as usual.

For alcohol: g=0.17 confidence interval 0.07-0.28. After 12M (increase to g=0.32) (a "sleeper effect"):

Carroll KM, et al. (Arch Gen Psych,1994)

For depression; g=0.27 Confidence interval 0.13-0.41 (effect maintained after 12 M)

Riper H, et al. (Addiction, 2013)

INTERVENTIONS FOR CO-OCCURRING DEPRESSION IN YOUTH

Cognitive-behavioral Therapy (CBT)-singular or integrated such as the SHADEY protocol Hides et al. (J. Affect D., 2010)

Incorporating: Motivational interviewing and mindfulness skills delivered within a harm minimization framework.

SHADEY protocol includes: self-monitoring, activity scheduling, thought challenging, coping skills training and relapse prevention components.

Family-focused Therapy (FFT)

Medication (SSRI)

Integrative medical and psycho-therapies

COMORBID DEPRESSION AND THE OUTCOMES OF ADOLESCENT SUBSTANCE ABUSE TREATMENT

One might expect that the presence of any comorbid disorder would complicate SUD treatment and lead to poorer outcome

However, in a review of 12 studies comorbid depression at treatment baseline has been associated with all three possible influences on outcome: worse outcomes, better outcomes, and equivalent outcomes

Hersh, J, Curry, JF, & Kaminer, Y. (2014). What is the impact of comorbid depression on adolescent substance abuse treatment? *Substance Abuse, 35*, 364-375.

SUMMARY

Baseline depression has been associated with negative, neutral, or positive outcomes of substance abuse treatment in adolescents

Studies vary widely on certain key dimensions:

- Depression definition
- Method of depression assessment
- Duration and nature of treatment
- Time from baseline to outcome assessment
- Definition of outcome variable

POSITIVE IMPACT

Subjects were 106 adolescents and youths, ages 13-21 (Mean age = 17.2) with alcohol or cannabis use disorders

76% male, 24% female; 79% Caucasian

50% had Conduct Disorder; 38% had Major Depression; 27% had Traumatic Stress Disorder

Assessed at baseline and 3, 6, and 12 months post-baseline

Becker, SJ., Curry, JF, & Yang, C. (2011). Factors that influence trajectories of change in frequency of substance use and quality of life among adolescents receiving a brief intervention. *JSAT, 41*, 294-304.

TREATMENT AND OUTCOME VARIABLES

MET/CBT-5, consisting of two sessions of motivation enhancement therapy and three sessions of cognitive behavior therapy

Outcomes: Frequency of substance use; and Quality of Life

Outcome assessed based on trajectories of these outcomes over the 12 month period

RESULTS

Frequency of use declined significantly from baseline to month 3, then stabilized to month 12.

Quality of life increased modestly and significantly over the 12 months

Decreased frequency of use was associated with increased quality of life (with a time lag)

Severity of depression was associated with lower QoL at baseline but predicted greater improvement in QoL over the year

SEQUENCED VS. COORDINATED TX OF YOUTH WITH COMORBID DEPRESSION & SUD

N=170 (ages 13-18); 22%females; 61% Caucasian with comorbid depression (54% MDD; 18% dysthymia)

CWD-Coping with depression;

FFT-Functional family therapy (for SUD)

Three Tx sequences: FFT/CWD; CWD/FFT; FFT-CWD

FFT/CWD more efficacious for SU reductions

Depression reductions occurred early in all 3 Tx sequences

No Tx sequence resulted in more rapid depression recovery

Medication usage did not moderate change during or post Tx

Addressing depression early in Tx may improve substance use outcomes in the presence of MDD. Rhode P, et al. (JCCP, 2014)

LIMITATIONS

UNABLE TO RESTRICT FAMILIES FROM SEEKING ADDITIONAL TREATMENT.

UNCONTROLLED NONPROTOCOL INTERVENTIONS LIMIT THE INTERPRETETION OF THE FINDINGS

PROPOSED MECHANISMS FOR SYMPTOMS CHANGE

Dysfunctional reward processing might be a feature of comorbid depression and SUD that is responsive to Tx

Boger, et al. (J. Psychother. Integ., 2014)

Self-efficacy as a possible mediator between depression and substance use relapse Ramo, DE (Subst. Use Misuse 2010)

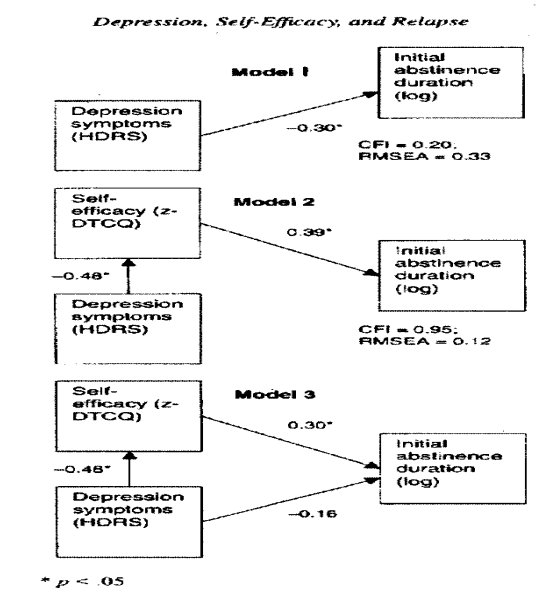


Figure 1. Three path models of the relationships between depression symptoms, drug-taking self-efficacy, and length of abstinence in adolescents.

RAMO DE (2010)

WHY ARE THESE DIFFERENCES IMPORTANT?

Depression can be a reactive adjustment problem or a diagnosed disorder

Depression is episodic

Depressive episodes vary greatly in severity and duration

When treated with psychotherapy, some proportion of patients with MDD (and not SUD) respond very quickly, suggesting a response to non-specific factors

To date no studies have investigated varying aspects of "depression" as they affect SUD treatment

Struggling with sadness? Alcohol use getting in the way?

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ADAPTIVE TREATMENT DESIGN

Begin treatment of SUD-MDD adolescents with CBT for SUD alone

Rapid depression responders will not need specific depression treatment

Begin depression treatment after ~ 4 weeks but only for those who need it

This will allow for better comparisons between an active depression treatment and a comparison condition

PRO'S OF THIS ADAPTIVE TREATMENT DESIGN

Allows for a more powerful comparison between any two interventions for depression, because it has removed from the comparison those likely to respond to non-specific factors

Provides a more robust test of any depression treatment because the "easy cases" are gone

Can lead to more personalized intervention

Analogous to a "placebo washout" lead-in to medication studies

CON'S OF THIS ADAPTIVE TREATMENT

Participants cannot be in obvious need of depression – specific treatment at baseline

Participants cannot be in need of treatment for serious suicidal risk at baseline

It may be challenging to add more sessions per week after week 4

It may be discouraging for those who do not achieve early depression response

CONCLUSIONS

The impact of comorbid depression on adolescent SUD treatment is currently not clear or consistent

There is a need to more carefully define and standardize the measurement of depression in studies of comorbid depression in youths

An adaptive treatment design may lead to a clearer picture of how depression affects adolescent SUD treatment

THE END

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SEVERAL MOTIVATIONAL MODELS OF SU INITIATION AND PERSISTENCE

Tension Reduction (Conger, 1956) and the Self-Medication (Khantzian, 1985) models-substance use is secondary to provide relief from negative mood and related stress;

Substance-induced enhancement model (Kushner et al, 1990) –multiple intoxication and withdrawal experiences increase susceptibility to anxious and depressed moods followed by additional cycles of abuse

REWARD DEFICIENCY & IMPULSIVITY MODELS

Despite differences in presumed underlying mechanisms of the following two models, Reward Processing dysfunction models suggest temporal continuity due to common causal factors between cannabis use and Externalizing pathology .

Reward Deficiency Hypothesis- (Bloom et al. 2012) attributes SU initiation, persistence, and habitual reward-seeking, risk-taking, and impulsive behaviors to hypo-responsive reward processing system. That is a compensatory response to reward-deficiency state.

RDIM-II

Impulsivity Hypothesis (Finn et al. 2002) conversely suggests that individuals with externalizing tendencies have a hyper-responsive reward system biased toward pursuit of immediate rewards, including SU initiation and the persistence of SUD over time.

RESULTS-II

These findings suggest:

Some modest protection against protracted episode when an Int'l disorder exist prior to the onset of the index CUD episode.

The emergence of psychopathology during or after the index episode including Int'l, Ext'l and non-cannabis SUD, is associated with greater disorder persistence.

TREATMENT AND OUTCOME MEASURE

Short-term (4-6 weeks) outpatient treatment in community clinics

Group and family therapy 3 times per week

Fully evaluated at baseline; alcohol use was evaluated monthly by telephone for 1 year

Outcome measure was Relapse = First use of alcohol after 7 days of abstinence **Cornelius (2004)**

RESULTS

MDD	Time to relapse
Yes	7 days
No	45 days

Survival analysis, *p* = .039

TREATMENT AND OUTCOME MEASURE

Weekly individual and group therapy sessions, family therapy, and urine drug screens

Average treatment duration was 3.7 months

Outcome: Days of non use in past month

Whitmore (2000)

RESULTS

Days of use in the past month increased from 4.1 to 7.6 (ns)

Percent with a diagnosis of Major Depression was not reduced

Severity of depressive symptoms did improve significantly on the Carroll Rating Scale

Baseline MDD did not predict substance use outcome

AATOM STUDY

In our study the focus is (TADS "light") on cognitive restructuring and behavioral activation.

There is less emphasis on coping skills and family intervention

FACULTY DISCLOSURE

	No, nothing to disclose
X	Yes, please specify:

Company Name	*Honoraria/ Expenses*	*Consulting/ Advisory Board*	*Funded Research*	*Royalties/ Patent*	*Stock Options*	*Ownership/ Equity Position*	*Employee*	*Other (please specify)*
NIAAA/NIDA			X					
Am Psychiatric Publishing Inc.				X				

IMPLICATIONS OF COMORBID SUD & MDD ON TREATMENT

- Exposure to "piecemeal" treatment targeting only one of the disorders increases risk of failure.

1) Increased risk of dropout from treatment.
2) Poorer treatment response (e.g., attention, affective response).
3) Risk for earlier relapse.

- improvement in drug use or depression may unexpectedly in some patients increase suicidality.
- Improved AOSUD outcomes during aftercare phase for treatment completers were associated with reduced suicidal ideation.

Kaminer et al. (2006)

THE FUTURE OF PSYCHOTHERAPY FOR YOUTH

- "Informed by the new field of translational developmental neuroscience, psychotherapy in the future will take aim at the developing brain similarly to psychosocial interventions in the rest of medicine"
- "The psychotherapy race is over: CBT wins" John March (2010)
- Interpersonal psychotherapy (Mufson et al. 2004) maybe considered a variant of CBT despite its Sullivanian origins . The emphasis is on family conflict, peer relationship, school experiences, etc.
- The field is moving from manual based (disorder focused) CBT toward a more individualized (broader) CBT that accounts for comorbidities and for patient's needs.

March JS: (J Child psychol Psychiat 50:170-9, 2009)

IMPLICATIONS OF COMORBID MDD & SUD: SUICIDAL BEHAVIOR

The likelihood of suicide attempts increased by X2.5 with each additional psychiatric disorder. Goldston et al. (2009)

Increased risk for suicidal behaviors is common for MDD or SUD (X10-14) and is higher for the dually diagnosed.

A WHO funded review of studies on youth completed suicide from Australia(2), Finland, G.B., Israel, Norway, Sweden(2), USA(5) (N=894 cases). It concluded that 42% had a mood disorder, 41% had SUD and 21% a disruptive disorder. Fleischmann et al. (2005)

39% of suicide cases were diagnosed with two or more disorders mostly mood, SUD, and disruptive disorders.

THE CRAFFT SCREENER

C: Have you ever ridden in a CAR driven by a person who was "high" or using alcohol or drugs (AOD)?

R: Do you ever use AOD to RELAX , feel better about yourself, or fit in?

A: Do you ever use AOD while you are by yourself, ALONE?

F: Do you ever FORGET things you did while you AOD?

F: Do your family or FRIENDS ever tell you that you should cut down on your drinking or drug use?

T: Have you ever gotten into TROUBLE while using AOD? Knight J. et al. (2001)

SELF MEDICATION?

Childhood Psychiatric D. as risk factor for subsequent SA: A Meta-analysis Groenman AP, et al. (JAACAP, 2017)

- **Focus on causal inference, directionality, the effect of comorbidity &gender**
- **A significant increased risk for ADHD, ODD, CD, and Depression Successful Tx of the primary D. would prevent the secondary D. (stimulants for ADHD have a protective effect against smoking:** -Schoenfelder et al. (Pediatrics, 2014. **Inconclusive** Humphreys et al. (JAMA Psych, 2013)

ANXIETY DISORDERS

Heterogeneity within Anxiety D.

Only increased risk for drug related disorders

Social anxiety does NOT increase the risk for CUD (OR 0.8) while Panic D. increases the risk (OR 5.9)

Groenman et al. (2017)

AGE OF ONSET

Younger age of onset have more severe outcomes, including more frequent adult pathology and worse functioning outcomes (lower SES) De Girolamo G, et al. (2012)

TABLE 3
Characteristics of Select Comprehensive Assessment Measures

Instrument	Settings in Which Studied	Format	Administration Time, min	Manual Available	Scoring Time, min	Computer Scoring	Fee for Use	Tobacco?	*DSM-IV*?	Source
GAIN	Clinic, drug treatment, juvenile detention	Semistructured interview	75–100	Yes	15	Yes	Yes	Yes	Yes	*http://lib.adai.washington.edu/instruments*
T-ASI	Clinic, drug treatment, juvenile detention	Semistructured interview	25–45	Yes	10	No	No	Yes	Yes	kaminer@psychiatry.uchc.edu
PEI	Clinic, drug treatment, juvenile detention	Self-report	45–60	Yes	10	Yes	Yes	Yes	No	*http://lib.adai.washington.edu/instruments*

Note: GAIN = Global Appraisal of Individual Needs; T-ASI = Teen Addiction Severity Index; PEI = Personal Experience Inventory.

Winters & Kaminer, JAACAP, 2008

WHAT ABOUT CONCURRENT TREATMENT OF DEPRESSION WITH MEDS AND SUD IN TEENS?

Fluoxetine and CBT study

Subjects: 126 adolescents ages 13-19 with at least one SUD, lifetime CD, and current MDD

Treatment:

- **16 weeks of CBT**
- **plus either fluoxetine or placebo**

Riggs, PD. et al. (2007). A randomized controlled trial of fluoxetine and cognitive behavioral therapy in adolescents with major depression, behavior problems and substance use disorders. *Archives of Pediatric and Adolescent Medicine, 161*, 1026-1034.

OUTCOME MEASURES

Depression :

- **(1) Children's Depression Rating Scale-Revised (CDRS-R)**
- **(2) Clinical Global Impression-Improvement (CGI-I)**

Substance use:

- **(1) days of use**
- **(2) proportion of "clean" weekly urine drug screens**

RESULTS

FLX surpassed PBO on the CDRS-R, but not on the CGI-I (depression response 76% versus 67%)

No significant difference on days of use, although both groups improved

PBO surpassed FLX on proportion of "clean" weekly urine drug screens

"The CBT may have contributed to higher-than-expected treatment response and mixed efficacy findings, despite its focus on SUD."

DEPRESSION TX IN CHILDREN & ADOLESCNETS

- **"Psychological therapies Vs. antidepressants alone and in combination for depression in children & adolescents"**

  Cox GR, et al. Cochrane Database Syst Rev (Nov 30; 2014)
- **Eleven studies, n=1307 subjects**
- **For majority of outcomes no statistically significant difference between interventions compared**
- **Limitations for comparability of results: different severities of the disorder, variety of comorbid disorders, blind assessors in 6/11 studies, incomplete data analysis methods.**
- **In 2 studies, n=220; Meds>Psych for a quicker post Tx remission**
- **In 3 studies, n=378; Comb>Meds for a quicker post Tx remission**
- **In 1 study , n=188; suicidal ideation significantly higher and persistent 6-9 months in Meds>Psych**
- **Conclusion: There is a limited evidence for comparison of effectiveness**

NEGATIVE IMPACT

Subjects: 116 adolescents ages 14-18

65% male (n = 75); 35% female (n = 41) mostly Caucasian;

50 of 116 had current Major Depression at baseline

Those with MDD did not differ from others on any baseline measure of alcohol or drug use

Cornelius, JR, et al. (2004). Major depression associated with earlier alcohol relapse in treated teens with AUD. *Addictive Behaviors*

NEUTRAL IMPACT

Subjects were 46 (of 60 eligible) adolescent females, ages 13-19, (Mean age = 15.5)

Followed up post-discharge (Mean = 13 months)

At baseline, 22.2% (n = 10) had Major Depression

All had lifetime Conduct Disorder, and 40 of the 46 had current Conduct Disorder

Whitmore, EA, et al. (2000). One-year outcome of adolescent females referred for conduct disorder and substance abuse/dependence. *Drug and Alcohol Dependence, 59*, 131-141.