ADDICTIVE DISORDERS IN WOMEN

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Addiction Medicine

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DISCLOSURE

Minnesota Psychiatric Society CME
Sheila Specker, MD

- I have no financial relationships to disclose:

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- Cresta Jones, MD, Maternal-Fetal Medicine
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OBJECTIVES

The participant will be able to:

- Discuss the gender differences in development and course of substance use disorders
- Highlight neurobiologic aspects in addiction
- Describe substance use in pregnancy
- List medical and psychiatric problems in women with substance use disorders
- Identify specific needs of women in treatment and recovery

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ADDICTIVE AND CO-OCCURRING PSYCHIATRIC DISORDERS IN WOMEN

- Epidemiology
- Neurobiology
- Pregnancy
- Co-occurring conditions
- Course and Treatment

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BOTTOM LINE

- Women use drugs differently
- Women respond to drugs differently
- There are unique obstacles to effective treatment

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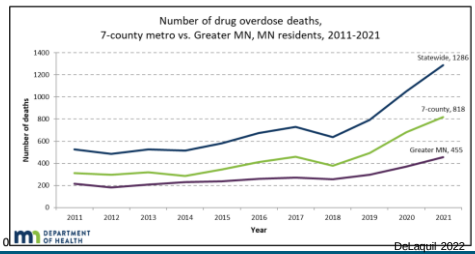
Figure 1: The number of drug overdose deaths in 2021 was the highest annual number ever recorded



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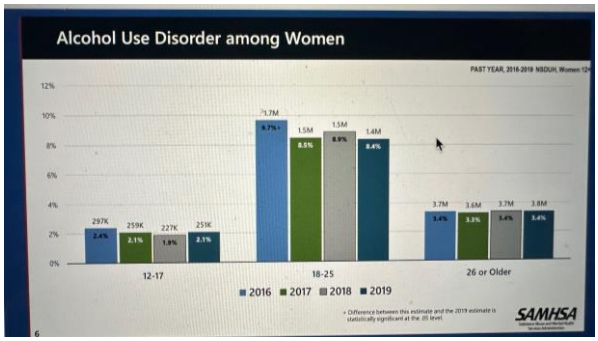

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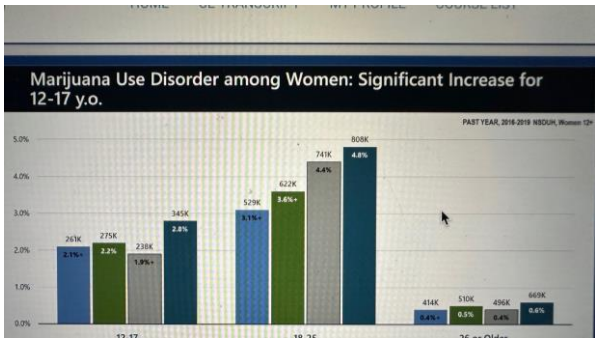

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ADDICTIVE DISORDERS IN WOMEN
Epidemiology

RATES OF ADDICTION (LIFETIME):*

	Women(%)	Men(%)
Alcohol abuse/depd.	4.4%	24%
Drug abuse/depd.	4.4%	7%
Alcohol depd.	8.4%	18%

*Epidemiologic catchment area data 1984

**Nat. Longitudinal Alcoholic Epidemiological Survey (N=43,000, DSM-IV)

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Epidemiology: Alcoholism Rates 2022 *(WHO)*

COUNTRY	MALE	FEMALE	TOTAL
Hungary	36.90%	7.20%	21.20%
Russia	36.90%	7.40%	20.90%
Belarus	33.90%	6.20%	18.80%
Latvia	28.80%	4.60%	15.50%
Slovenia	23.50%	4.50%	13.90%
South Korea	21.20%	6.80%	13.90%
United States	17.60%	10.40%	13.90%
Tanzania.	11.5%.	2.2%.	6.8%

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ADDICTIVE DISORDERS IN WOMEN
Epidemiology

- Adolescent girls begin alcohol/drug use slightly later than boys.
- Increase in heavy drinking in adolescent girls and college women, converge with male patterns
- Women more likely to obtain drugs via "licit" medical channels
- Smoking rates have fallen less in females
- Girls = boys on rates of smoking

*National Household survey; Harrison and Hoffman 1989; Opland, Winters, Stinchfield 1995

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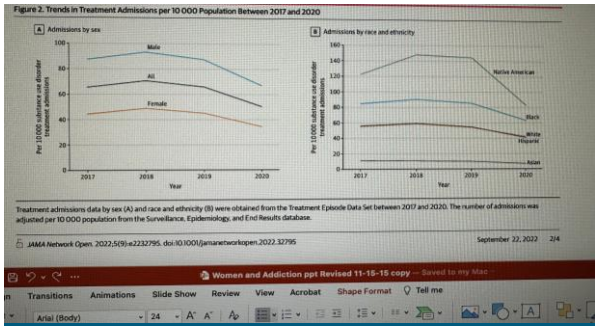

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ADDICTIVE DISORDERS IN WOMEN
Trends

- Gender differences in drinking and alcohol related problems narrowing
- Both genders have earlier onset of drinking and problems
- Gender gap in binge drinking in high school students decreased from 23% (1975) to 12% (2001)

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ADDICTIVE DISORDERS IN WOMEN
Predisposing Factors

Genetic

- Clear evidence in men, less clear in women
- Twin study in 2000 female pairs* demonstrated importance of environment in modifying heredity:

	% variance of drinking
Unmarried twins	60%
Married twins	31%

* Heath, et al 1989

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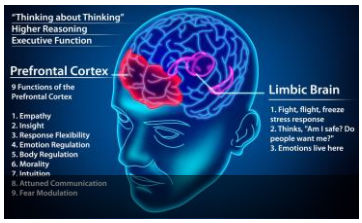
NEUROBIOLOGY



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Preclinical Studies

- Progesterone attenuates the drive for cocaine in rats
- Estrogen enhances drive and acquisition of cocaine self-administration

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SEX DIFFERENCES IN VULNERABILITY TO DRUG ABUSE: PRECLINICAL

- Female rats compared to males:
  - More vulnerable to stimulant self-medication: acquisition, escalation, reinstatement
  - More vulnerable to reinstatement of cocaine-seeking behavior
  - Self administered higher levels of cocaine
  - Maintained greater levels of ethanol intake

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Human Laboratory Study
Effect of Progesterone on Cocaine Craving, Physiology, Use

- **Inpatient trial with progesterone/placebo in men and women (N=38), cross-over, PC, Cocaine/placebo cocaine**

- Women used more than men but had fewer treatments
- Women had more craving
- Higher progesterone levels associated with:
  - Decreased stimulation, decreased craving, decreased effects of last dose
  - Decreased BP elevation
- Men had more heart racing, more "high" in response to cocaine

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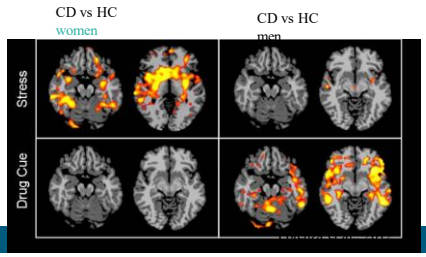
Neuroimaging Evidence for Sex Differences in Stress and Reward Circuits in Cocaine-Dependence (Potenza et al., 2012)



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Role of Neuroimaging/Neuromodulation

- **Neuroimaging** has identified neural networks that support abstinence
- **Neuromodulation** can be used to target these networks and boost them to support abstinence
  - --Non-invasive Transcranial direct current stimulation (tDCS)

Camchong, 2022

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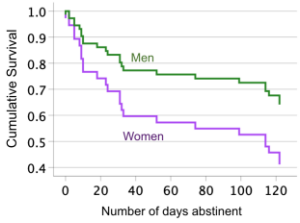
Relapse Rate by Sex



Pearson Chi Square = 5.02; **p=0.025**; Phi effect size = 0.29

Camchong, in preparation

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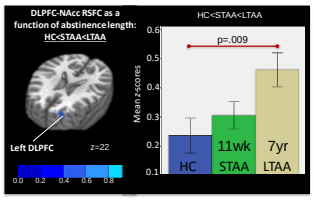
Higher DLPFC-NAcc RSFC in long-term abstinence from alcohol



Camchong et al, Alcohol Clin Exp Res, May 2013

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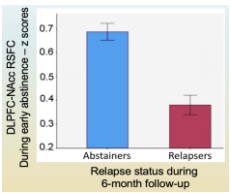
Lower DLPFC-NAcc RSFC associated with relapse

- N=69 short-term abstinent
  - –28 AUD + 41 AUD/SUD
- Rest fMRI data collected at **11 weeks** of abstinence
  - –Measured DLPFC-NAcc
- 6-month follow-up:
  - –Abstainers → n=40
  - –Relapsers → n=29



Camchong et al., Cerebral Cortex 2013

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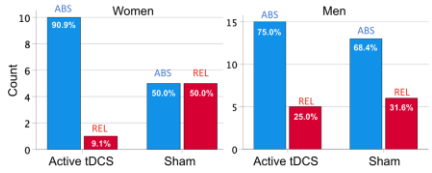
Sex-stratified Intervention Effect on **Binary Relapse Outcome**



Pearson Chi Square = 4.30; **p=0.038**; Phi effect size = 0.452

Pearson Chi Square = 0.21; **p=0.648**; Phi effect size = 0.073

Camchong, in preparation

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Pregnancy and Substance Use

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Pregnancy and Substance Use Challenges

- Conflicting interests: mother/ baby
  - Recovery support for mother
  - Infant effects of substance use maximize long term recover + minimize infant effects
- Social stigma, avoiding care
- Legal issues in pregnancy

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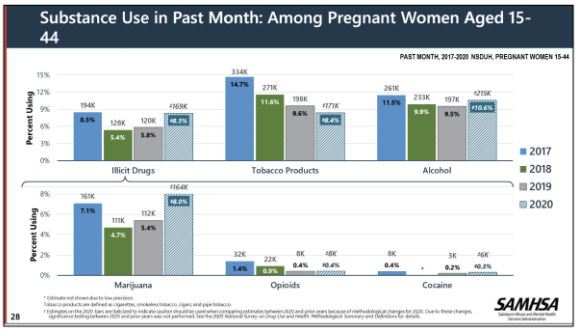

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State of Minnesota Legal System

- Prior to July 2021:

  Any perinatal substance use must be reported *except alcohol and cannabis*

  Barrier to universal screening

  Decreased prenatal care

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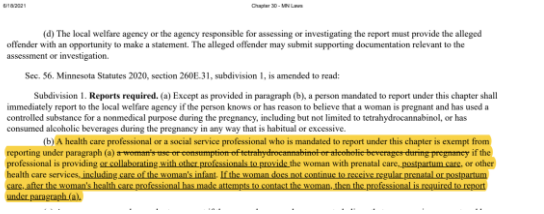

6/18/2021 Chapter 30 - MN Laws

(d) The local welfare agency or the agency responsible for assessing or investigating the report must provide the alleged offender with an opportunity to make a statement. The alleged offender may submit supporting documentation relevant to the assessment or investigation.

Sec. 56. Minnesota Statutes 2020, section 260E.31, subdivision 1, is amended to read:

Subdivision 1. **Reports required.** (a) Except as provided in paragraph (b), a person mandated to report under this chapter shall immediately report to the local welfare agency if the person knows or has reason to believe that a woman is pregnant and has used a controlled substance for a nonmedical purpose during the pregnancy, including but not limited to tetrahydrocannabinol, or has consumed alcoholic beverages during the pregnancy in any way that is habitual or excessive.

(b) A health care professional or a social service professional who is mandated to report under this chapter is exempt from reporting under paragraph (a) ~~a woman's use or consumption of tetrahydrocannabinol or alcoholic beverages during pregnancy~~ if the professional is providing or collaborating with other professionals to provide the woman with prenatal care, postpartum care, or other health care services, including care of the woman's infant. If the woman does not continue to receive regular prenatal or postpartum care, after the woman's health care professional has made attempts to contact the woman, then the professional is required to report under paragraph (a).

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RESULT OF CHANGES IN LAW 2021

-- Enhanced therapeutic relationship with patients using substances
-- Allows preparation time to arrange treatment
-- Prenatal care even without substance use treatment
-- More consistent care
-- Option to report
-- Requirement to report – if lost to follow up

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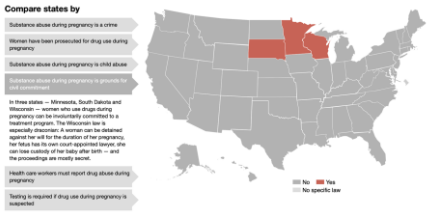

www.projects.propublica.org

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The Data: Involuntary Commitment: not the solution?

-- Individuals subjected to involuntary treatment 2.2 x more likely to die from overdose compared to voluntary treatment
-- 34% patients reported relapsing to drug use the day they were released from civil commitment
-- Less than 20% patients received medication treatment during commitment
-- 7% followed up with addiction treatment after release

Messinger and Beletsky, Chau et al, Jain

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GOALS IN PREGNANCY

- Establish rapport and trust
- Identify social, psychological, family issues
- Treat co-occurring psychiatric disorders
- Motivational approach for treatment/cessation
- Use opioid pharmacotherapies
- Easy access to care
- Team approach

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WOMEN AND ADDICTION
Other Risk Factors for Alcohol Use/problems

Factor	Evidence
▪ Alcohol reactivity	▪ Association of FH and low reactivity ▪ Women more cognitive, motor impairment at low doses
▪ Social sanctions	▪ Greater for women
▪ Gender roles	▪ Feminine traits (nurturance, warmth) association with less use, fewer problems. ▪ Undesirable masculine traits (aggressiveness, over-control) association with problematic use

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WOMEN AND ADDICTION
Other Risk Factors for Alcohol Use/problems

Factor	Evidence
▪ Motives	▪ Stronger relationship in women alcoholics between distress and alcohol
▪ Behavioral	▪ Men show greater impulsivity, under-control which are consistently associated with alcohol problems in men, less in women
▪ Antisocial	▪ Associated with alcohol disorders in both genders
▪ Interpersonal	▪ Strong similarities in drinking patterns in partners

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ADDICTIVE DISORDERS IN WOMEN Differences

Women with alcohol problems differ from men:

- Attribute onset of problem drinking to life stress
- Drink alone
- More likely to be separated/divorced
- Sexual abuse common (23 - 67%)
- More psychiatric symptoms and prior psychiatric treatments
- 20-40% of married women alcoholics report abuse in spouse

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The Stress-Addiction Connection: Gender Differences

- Women greater craving to negative emotional cues compared to men
- Women endorse stress/interpersonal conflict as relapse precipitant
- Men more responsive to drug-related cues

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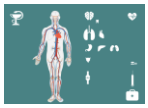
Co-occurring Medical, Psychiatric Conditions



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WOMEN AND ADDICTION

Women who drink excessively may be more prone to:

- Alcohol-induced depressive disorders
- Associate with others who drink excessively and thereby increase risk for domestic violence
- Increased risk for HIV exposure while intoxicated

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WOMEN AND ADDICTION
Psychiatric Factors (cont.)

Traumatic events:

- 67% of alcohol women versus 28% of control women had been victim of sexual abuse during childhood.
- Higher rate in alcohol women than general psychiatric outpatients.

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WOMEN AND ADDICTION
Domestic Violence

- Increased likelihood of violence by partner as consequence of substance use
- Domestic abuse may lead to higher rates of substance abuse in women who are victimized
- Link between physical/sexual abuse and greater use of cocaine, marijuana, alcohol among girls
- Increased prior suicidality in teenage girls with history of physical/sexual abuse

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Stress-Addiction Connection

- Childhood adverse events strongly associated with SUD's – particularly for women
  - –ACES
- PTSD, mood/anxiety disorders strongly associated with SUD's - 2-3 times more common in women

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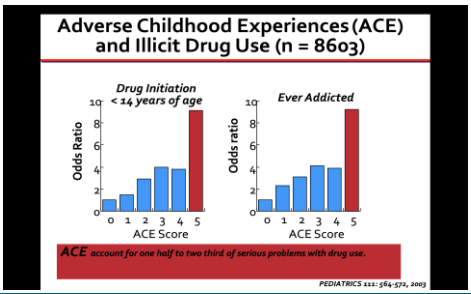

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ADDICTIVE DISORDERS IN WOMEN
Physical

How are women using alcohol different from men?

- Single doses of alcohol produce higher BAC even corrected for weight (lower body water content in women, lower levels of alcohol dehydrogenase)
- Increased BAC variability in women (e.g.pre-menstrually)
- Less acute tolerance
- OCP's may slow rate of alcohol clearance
- Women have a longer half-life for lipid soluble drugs (e.g. benzo's)

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ADDICTIVE DISORDERS IN WOMEN
Medical Effects of Alcohol

- Women develop adverse health effects more rapidly than men: fatty liver, cirrhosis, ulcer,hypertension, anemia, malnutrition, GI bleed
- Many effects on reproduction/sexual functioning: inhibits ovulation, obstetrical complications, FAS, irregular menses, early menopause, ↓ arousal
- Linkage to early cardiovascular mortality
- **"Telescoping"**

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WOMEN AND ADDICTION
Psychiatric Comorbidity

- ECA data:
  - 65% of women alcoholics vs. 48% of men alcoholics had additional psychiatric diagnosis
  - Women alcoholics had four times the ratio of MDD than women in the general population

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WOMEN AND ADDICTION
Psychological/Social

- Depression and anxiety are found more in women; antisocial personality trait disorder more in men.
- Prospective study: low self-esteem, impaired coping ability in high school predicted later problem drinking in girls.
- Longitudinal study: college women who drank to change feeling state predicted later drinking problems.
- Use influenced by male partners

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WOMEN AND ADDICTION
Psychiatric Comorbidity (cont.)

- Depression preceded the alcoholic problem in two-thirds of alcoholic women.
- Depressive symptoms predicted higher alcohol consumption years later.
- Both depression and sexual dysfunction predicted chronicity of alcohol problems.

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Course, Treatment, Outcomes

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WOMEN AND ADDICTION
Course

- Women drink less than men but gender gap in binge drinking decreased from 23% in 1975 to 12% in 2001.
- Women start drinking later than men but have shorter times from use to dependence and treatment (“telescoping”)
- Women drink to reach intoxication earlier than men
- Women have higher severity of alcohol problems on treatment entry
- Telescoping probably occurs with other drugs
- Telescoping does not occur in younger women

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ADDICTIVE DISORDERS IN WOMEN
Course

Study: More rapid progression to treatment among opioid, cannabis or alcohol dependent women (N = 271)*

- No gender differences in age of onset of regular use
- Women: fewer years regular use opioid, cannabis, alcohol before entering treatment
- Women reported more severe psychiatric, medical and employment complications
- Same severity of drug and alcohol dependence

*Hernandez-Avila, Rounsaville, Kranzler: Drug and Alcohol Dependence, 74(3), 2004

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ADDICTIVE DISORDERS IN WOMEN Course of Alcoholism

- Consequences differ
- Continuous versus episodic
- Higher socioeconomic women had later age of onset, older at treatment, less alcohol problems, drink less, lower rates of spouse alcoholism

Gomberg 1991, 1986; Smart 1979; Corrigan 1980; Ross 1989

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Stress and Substance Use Disorders: Clinical Considerations

- Careful assessment/aggressive treatment of co-occurring stress sensitive disorders
- Importance of social support in mediating effects of stress
- Careful attention to environmental factors – ongoing stress/abuse
- Coping Skills/Stress Management Techniques

K. Brady

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ADDICTIVE DISORDERS IN WOMEN Treatment Issues

- Good psychiatric history essential
- Attention to medical complications (e.g. STD's)
- Special skills acquisition (e.g. assertiveness)
- Integration of 12 step and other treatment modalities (e.g. CBT)
- Individual therapy or all women's groups
- Family therapy desirable

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WOMEN AND ADDICTION Treatment

1. Attention to Hx abuse
2. Careful physical/psychiatric dxs
3. Evaluate, treat family members
4. Parenting education
5. Child care services
6. Skill building: assertiveness, etc.
7. Social role issues
8. Women role models

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Medication Trials for Addiction: Gender Differences

Inconsistent results:

- Naltrexone associated with reduced craving for alcohol, more efficacious in women (Kiefer 2005)
- Naltrexone augments NRT in women smokers (Byars 2005)
- Pooled data: female gender associated with poorer outcome in med trials in cocaine use disorder
- Acamprosate US trial: not efficacious for women

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ADDICTIVE DISORDERS IN WOMEN
Barriers to Treatment

- Parenting responsibilities (lack of child care)
- Economic dependency
- Stigma
- Few social supports
- Housing
- Legal system which equates drug misuse with child abuse/neglect
- Lack of insurance coverage

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ADDICTIVE DISORDERS IN WOMEN
Outcome

- Gender as factor is understudied
- Most studies show similar outcome in women as compared to men when controlling for demographic and clinical variables *(Vannicelli, 1986, McLellan et al 1986)*
- Factors influencing outcome: supportive social network, number of life problems *(Macdonald 1987)*
- Higher mortality rates than men compared to expected *(Lindberg & Agren 1988)*

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ADDICTIVE DISORDERS IN WOMEN
Relapse Dynamics

STUDY:

60 cocaine dependent women, recently abstinent, participated in a 90 day longitudinal study on relapse dynamics. The group was largely African-American (58%), single (58%), unemployed (83%) with mean age 32 years.

- Baseline structured psychiatric interview (SCID-P, SCID-II), Addiction Severity Index (ASI)
- At 30 and 90 days, Minnesota Relapse and Coping Skills Questionnaire, ASI

- Specker 1996

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ADDICTIVE DISORDERS IN WOMEN
Relapse Dynamics

Antecedents to relapse:

Relapse Factor	% Reporting "Most Important" Factor
Negative emotional state	21%
Interpersonal conflict	16%
Environmental	16%
Craving	16%
Situational	11%
Impulse	10%
Pressure to use	5%
Withdrawal	5%
Physical pain	0%
Positive emotional state	0%

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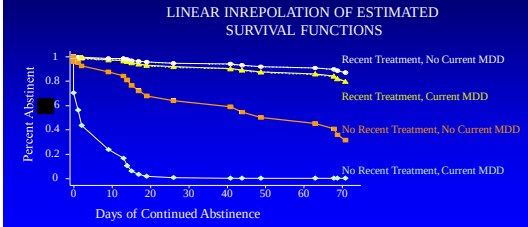
RELAPSE DYNAMICS IN COCAINE USING WOMEN



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ADDICTIVE DISORDERS IN WOMEN
Conclusions

- Women have a more severe course of addiction
- High rates of psychiatric co-morbidity are found
- Coping skills are essential in preventing relapse
- Broader treatment services are needed

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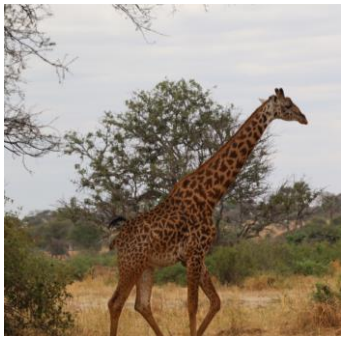

Thank you

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