



## ADDICTIVE DISORDERS IN WOMEN

Sheila Specker, M.D.  
Department of Psychiatry and Behavioral Sciences  
University of Minnesota



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### DISCLOSURE

Minnesota Psychiatric Society CME  
Sheila Specker, MD

▪ I have no financial relationships to disclose:



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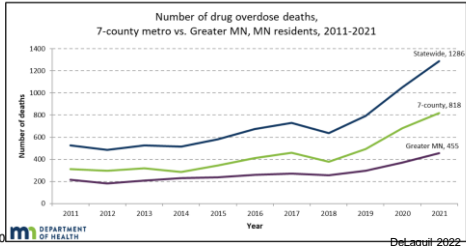
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Figure 1: The number of drug overdose deaths in 2021 was the highest annual number ever recorded



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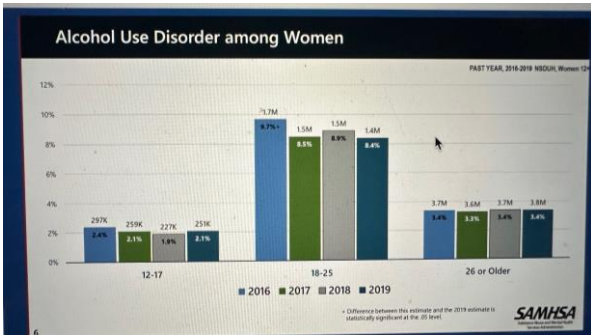
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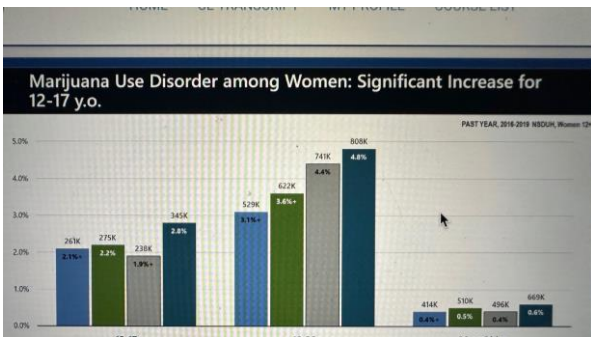
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**ADDICTIVE DISORDERS IN WOMEN**  
Epidemiology

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; Hamison and Hoffman 1989; Opland, Winters, Stinchfield 1995



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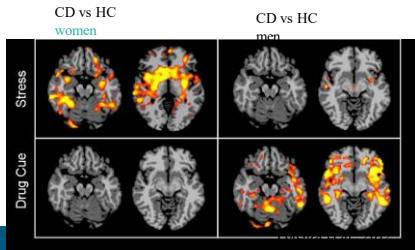
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### Neuroimaging Evidence for Sex Differences in Stress and Reward Circuits in Cocaine-Dependence (Potenza et al., 2012)



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### Role of Neuroimaging/Neuromodulation

- ⑩ **Neuroimaging** has identified neural networks that support abstinence
- ⑩ **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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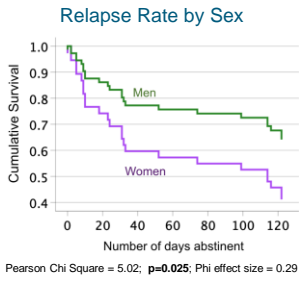
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Camchong, in preparation

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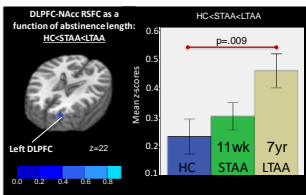
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### Higher DLPFC-NAcc RSFC in long-term abstinence from alcohol



Camchong et al., Alcohol Clin Exp Res, May 2013

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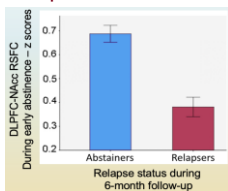
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### Lower DLPFC-NAcc RSFC associated with relapse

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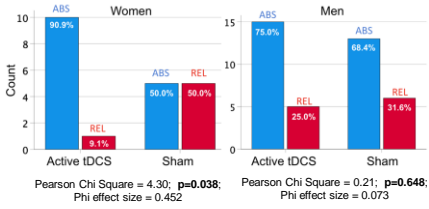
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### Sex-stratified Intervention Effect on Binary Relapse Outcome



Camchong, in preparation



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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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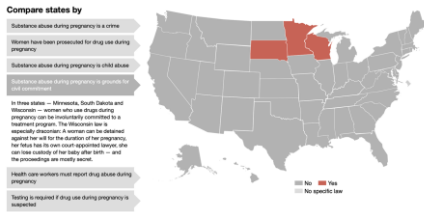


### RESULT OF CHANGES IN LAW 2021

- 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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### 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

C. Jones



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**WOMEN AND ADDICTION**  
**Other Risk Factors for Alcohol Use/problems**

Factor	Evidence
▪ Alcohol reactivity	<ul style="list-style-type: none"> <li>▪ Association of FH and low reactivity</li> <li>▪ Women more cognitive, motor impairment at low doses</li> </ul>
▪ Social sanctions	<ul style="list-style-type: none"> <li>▪ Greater for women</li> </ul>
▪ Gender roles	<ul style="list-style-type: none"> <li>▪ Feminine traits (nurturance, warmth) association with less use, fewer problems.</li> <li>▪ Undesirable masculine traits (aggressiveness, over-control) association with problematic use</li> </ul>



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**WOMEN AND ADDICTION**  
**Other Risk Factors for Alcohol Use/problems**

Factor	Evidence
▪ Motives	<ul style="list-style-type: none"> <li>▪ Stronger relationship in women alcoholics between distress and alcohol</li> </ul>
▪ Behavioral	<ul style="list-style-type: none"> <li>▪ Men show greater impulsivity, under-control which are consistently associated with alcohol problems in men, less in women</li> </ul>
▪ Antisocial	<ul style="list-style-type: none"> <li>▪ Associated with alcohol disorders in both genders</li> </ul>
▪ Interpersonal	<ul style="list-style-type: none"> <li>▪ Strong similarities in drinking patterns in partners</li> </ul>



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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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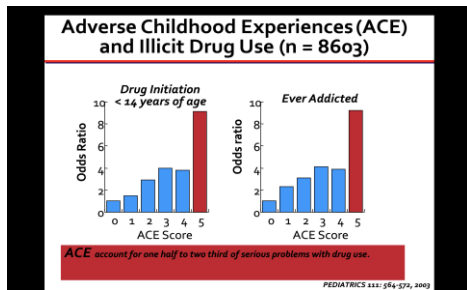
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K. Brady



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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
- Acamprostate 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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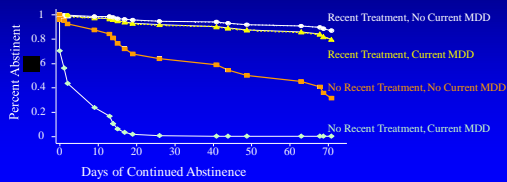
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### RELAPSE DYNAMICS IN COCAINE USING WOMEN

LINEAR INTERPOLATION OF ESTIMATED SURVIVAL FUNCTIONS



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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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