



GENDER AND ALCOHOL

DR ABHIJNA CHATTOPADHYAY

MBBS, MD PSYCHIATRY NIMHANS, MRCPSYCH (UK)

Trust the science...!!

A randomized trial of low-dose aspirin in the primary prevention of cardiovascular disease in women

Paul M Ridker¹, Nancy R Cook, I-Min Lee, David Gordon, J Michael Gaziano, Joann E Manson, Charles H Hennekens, Julie E Buring

Affiliations + expand

PMID: 15753114 DOI: 10.1056/NEJMoa050613

Free article

COMMENTARIES

Zolpidem and Gender: Are Women Really At Risk?

Greenblatt, David J.^{*}; Harmatz, Jerold S.^{*}; Roth, Thomas[†]

Author Information

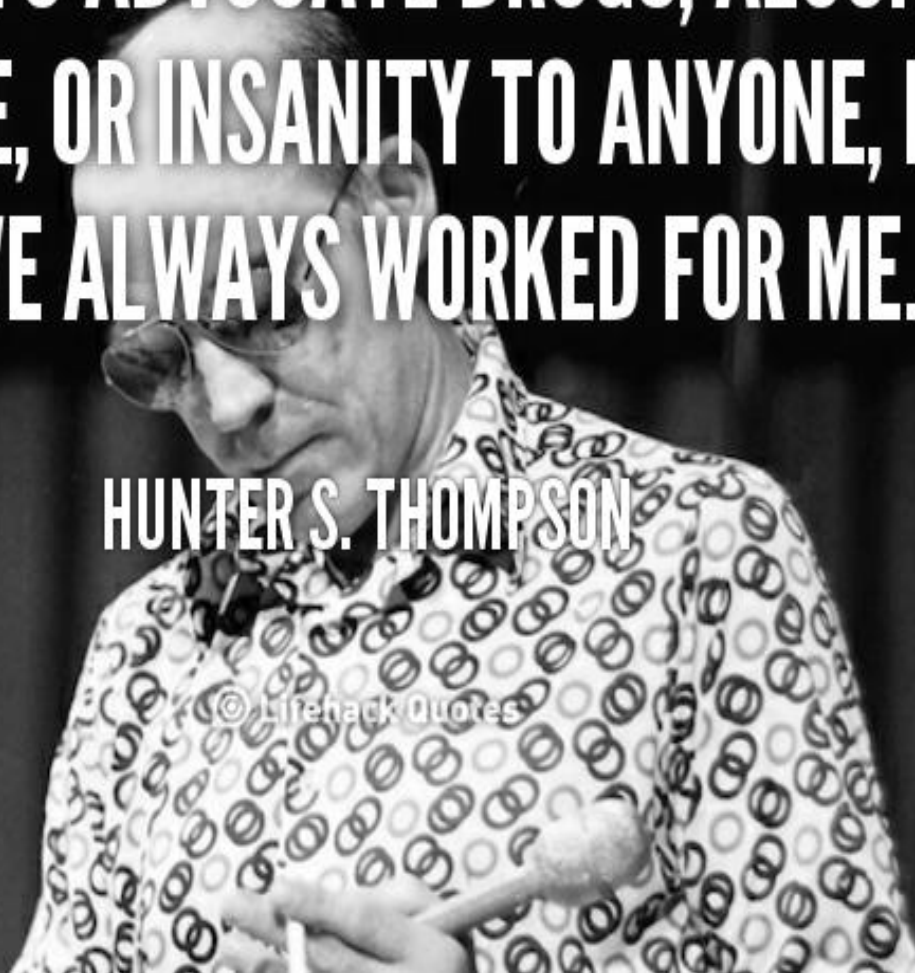
Journal of Clinical Psychopharmacology 39(3):p 189-199, 5/6 2019. | DOI:

10.1097/JCP.0000000000001026

**“I HATE TO ADVOCATE DRUGS, ALCOHOL,
VIOLENCE, OR INSANITY TO ANYONE, BUT
THEY’VE ALWAYS WORKED FOR ME.”**

HUNTER S. THOMPSON

© Lifehack Quotes



- ▶ India- 10 gms.
- ▶ small glass of red wine
- ▶ beer (375 ml)
- ▶ spirits (30 ml)

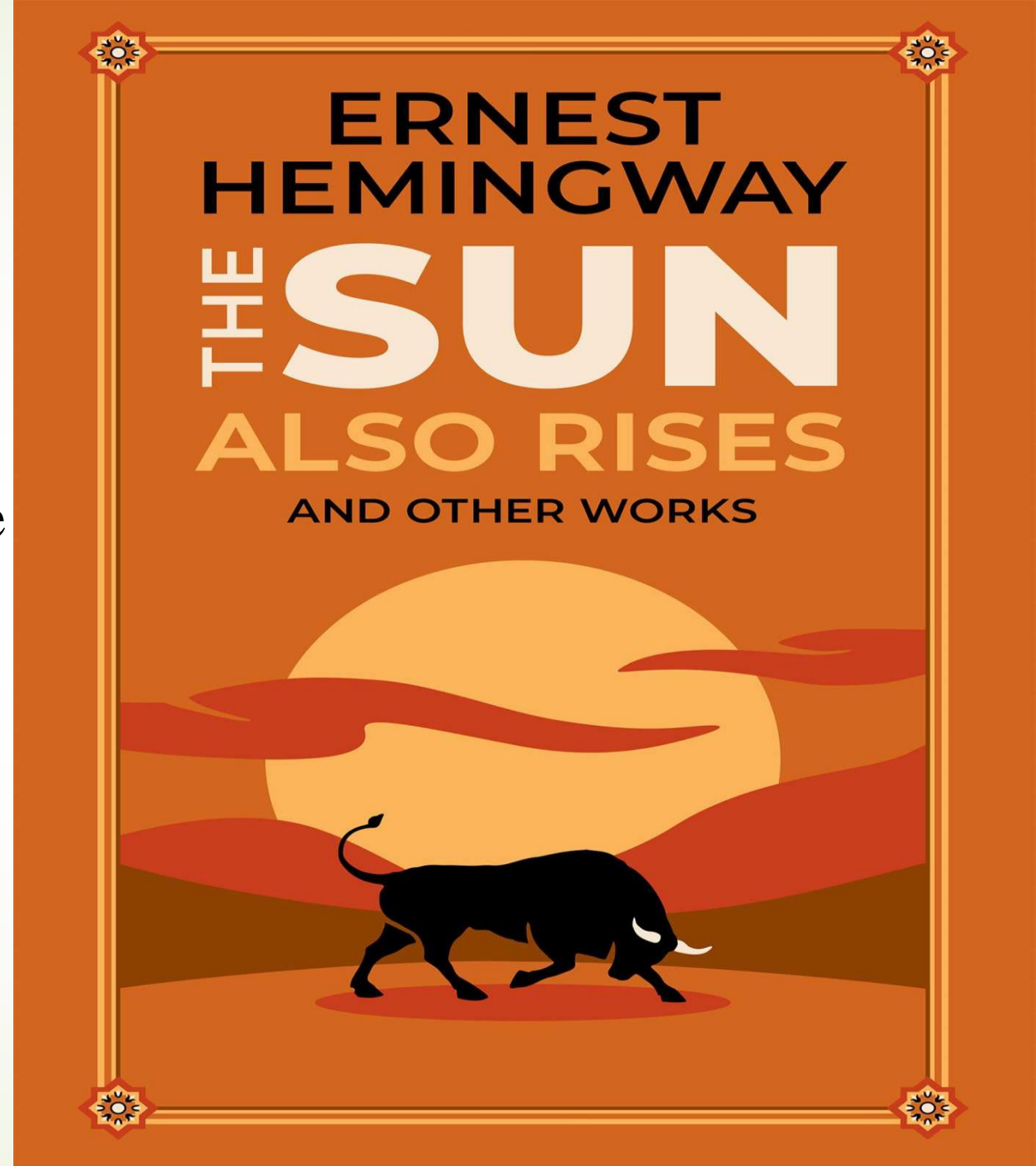


TABLE 1. Adult alcohol consumption and male-female consumption in 14 WHO sub-regions, 2000

WHO sub-region	Total consumption (litres of absolute alcohol)	Consumption per drinker	% Male current drinkers	% Female current drinkers
Africa D (e.g., Nigeria, Algeria)	4.9	13.3	47	27
Africa E (e.g., Ethiopia, South Africa)	7.1	16.6	55	30
Americas A (Canada, Cuba, USA)	9.3	14.3	73	58
Americas B (e.g., Brazil, Mexico)	9.0	14.1	75	53
Americas D (e.g., Bolivia, Peru)	5.1	7.6	74	60
Eastern Mediterranean B (e.g., Iran, Saudi Arabia)	1.3	11.0	18	4
Eastern Mediterranean D (e.g., Afghanistan, Pakistan)	0.6	6.0	17	1
Europe A (e.g., Germany, France, UK)	12.9	15.1	90	81
Europe B (e.g., Bulgaria, Poland, Turkey)	8.3	13.4	72	52
Europe C (e.g., Russian Federation, Ukraine)	13.9	16.5	89	81
Southeast Asia B (e.g., Indonesia, Thailand)	3.1	13.7	35	9
Southeast Asia D (e.g., Bangladesh, India)	2.0	12.9	26	4
Western Pacific A (e.g., Australia, Japan)	8.5	10.4	87	77
Western Pacific B (e.g., China, Philippines, Vietnam)	5.0	8.8	84	30

Source: World Health Organization, 2004a

5.1% (DALYs),
men's (**7.1%**)
women's (**2.2%**)

alcohol-attributable
deaths **7.7%** of all
deaths worldwide
among men versus
2.6% among women



Tell me why

1. Metabolism

➤ 2. Cultural

➤ 3. False assumptions/consequences-

➤ taking custody of children

(Dolgin, 1991; Nishimoto & Roberts, 2001)

➤ forcing alcohol abusing women to be hospitalized or incarcerated if pregnant

(Abel & Kruger, 2002; DeVille & Kopelman)



VENUS AND MARS

- EPIDEMIOLOGICAL=POPULATION LEVEL
- NEUROBIOLOGY- selected
- GENETICS AND HERITABILITY
- CLINICAL COURSE- TELESCOPING/ CHARACTERISTICS & RISK
- **PSYCHIATRIC COMORBIDITIES/ MEDICAL COMORBIDITIES**
- **OUTCOME**
- TREATMENT- PROGRAMS/PHARMACOTHERAPY
- POLICY LEVEL
- ADIEU

TRENDS IN ALCOHOL CONSUMPTION


- APC-
- 5.7 litres in 2010
- 5.5 litres in 2019 (relative reduction of 4.5%)
- 27 grams of pure alcohol per day

- Alcohol consumption increasing in India from
- 1.6 litres in 2003–2005
- 2.2 litres in 2010
- 5.5 litres in 2016–2018

TALE OF 2 INDIA'S-Parmar et al (IJP)- 2023

Prevalence of various substance use among women

	STUDY	SURVEILLANCE	PREVALENCE	DEPENDENT
Alcohol	NFHS-3	Current use	32%	2.2%
	NMHS	Alcohol use disorder	9.1%	0.5%
	NFHS-4	Current use	29.5%	1.2%
	NNCDMS	Current use	28.3%	2.4%
	NFHS-5	Current use	18.7%	1.3%
	Ambekar <i>et al.</i> , 2019	Current use	27.3% (one in 5 dependent)	1.6% (one in 16 dependent)
Cannabis	Ambekar <i>et al.</i> ,	Current use	5.0%	0.6%

- 
- high per-capita consumption among the drinkers
 - high prevalence of heavy episodic drinking
 - Higher disease burden
 - there was an increase in the proportion of men who reported use ‘almost every day’ among men.
 - AUD:

WORLD- 7%

INDIA- 4.7%

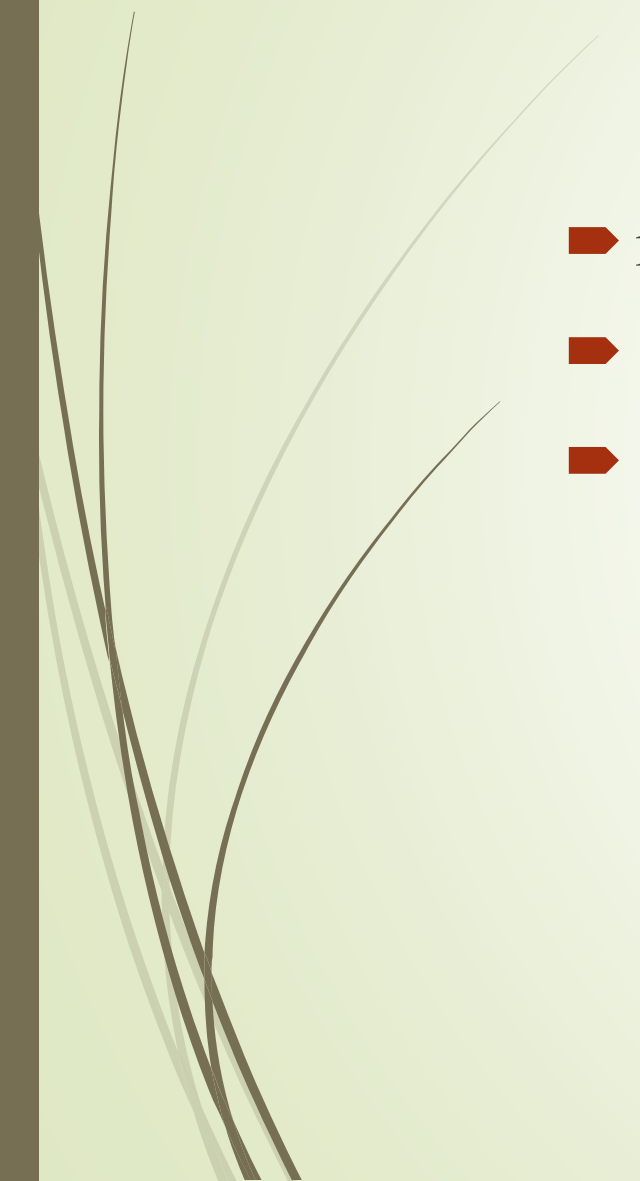
Alcohol, Gender and Drinking Problems

Perspectives from Low and Middle Income Countries





GENDER CONVERGENCE

- ▶ in low- and lower-middle-income countries-1.8 to 1
 - ▶ In upper-middle-income countries-1.5 to 1
 - ▶ high-income countries- 1.2 to 1
- 

BMJ Open Birth cohort trends in the global epidemiology of alcohol use and alcohol-related harms in men and women: systematic review and metaregression

Tim Slade,¹ Cath Chapman,¹ Wendy Swift,¹ Katherine Keyes,² Zoe Tonks,¹ Maree Teesson¹

To cite: Slade T, Chapman C, Swift W, *et al.* Birth cohort trends in the global epidemiology of alcohol use and alcohol-related harms in men and women: systematic review and metaregression. *BMJ Open* 2016;**6**:e011827. doi:10.1136/bmjopen-2016-011827

► Prepublication history and additional material is available. To view please visit the journal (<http://dx.doi.org/10.1136/bmjopen-2016-011827>).

Received 8 March 2016
Revised 10 June 2016
Accepted 1 August 2016

ABSTRACT

Objective: Historically, alcohol use and related harms are more prevalent in men than in women. However, emerging evidence suggests the epidemiology of alcohol use is changing in younger cohorts. The current study aimed to systematically summarise published literature on birth cohort changes in male-to-female ratios in indicators of alcohol use and related harms.

Methods: We identified 68 studies that met inclusion criteria. We calculated male-to-female ratios for 3 broad categories of alcohol use and harms (any alcohol use, problematic alcohol use and alcohol-related harms) stratified by 5-year birth cohorts ranging from 1891 to 2001, generating 1568 sex ratios. Random-effects meta-analyses produced pooled sex ratios within these 3 categories separately for each birth cohort.

Findings: There was a linear decrease over time in the sex ratio for all 3 categories of alcohol use and related harms. Among those born in the early 1900s, males were 2.2 (95% CI 1.9 to 2.5) times more likely than females to consume alcohol. 3.0 (95% CI 1.5 to 6.0)

Strengths and limitations of this study

- Prior to this study, the evidence around gender convergence in alcohol use and alcohol-related harms was fragmented. This study systematically summarised all available literature and provided a quantification of the rate of gender convergence through the derivation of a single metric—the male-to-female ratio in alcohol use and alcohol-related harms.
- This study was strengthened by its examination of 11 separate indicators of alcohol use and alcohol-related harms, summarised in three broad categories and showed that gender convergence was evident across all indicator categories.
- While the derivation of a single metric facilitated numerical synthesis of data, the analyses are not independent of measurement variance.
- The current study did not test specific hypotheses for why the male–female gap in alcohol use and alcohol-related harms is closing.



REASONS

Labour force by age 35

Education levels in the upper quartile of the income distribution

Median age of first marriage.

strongest in those countries where female and male roles were converging over time. (Seedat et al)

Original Investigation

FREE

August 2014

Generational Increase in Young Women's Drinking

A Prospective Analysis of Mother-Daughter Dyads

Rosa Alati, PhD, MAppSc¹; Kim S. Betts, MPH²; Gail M. Williams, PhD, MSc²; et al

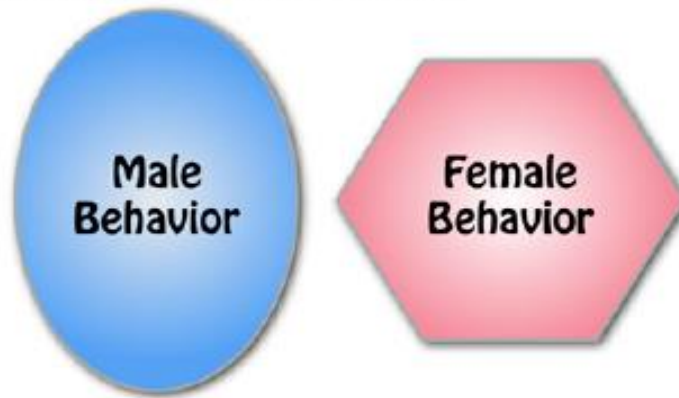
» [Author Affiliations](#) | [Article Information](#)

JAMA Psychiatry. 2014;71(8):952-957. doi:10.1001/jamapsychiatry.2014.513

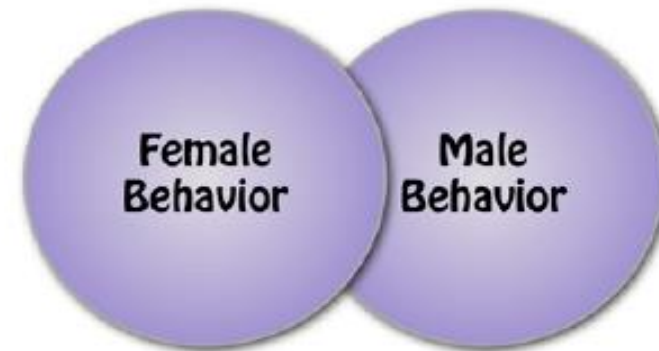
SEX DIFFERENCES IN NEUROBIOLOGY

Becker and Koob

A Qualitative Differences



B Quantitative Differences



C Population Differences



D Underlying Mechanisms Differ



Sex differences in addiction to different classes of drugs^a

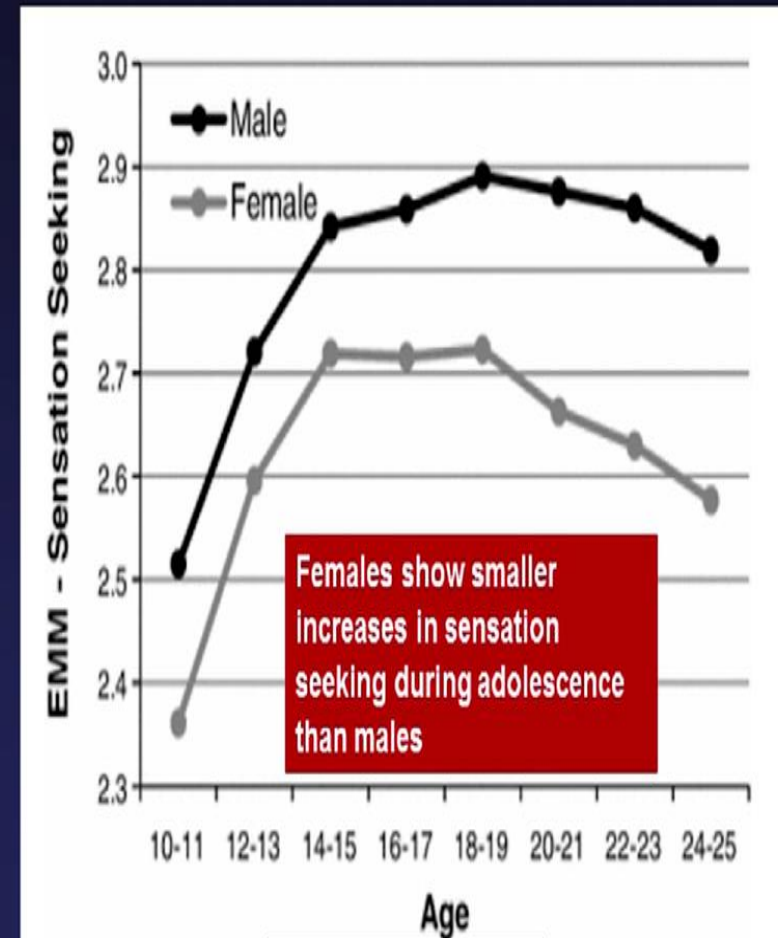
Drug	Species	Stage of Addiction Cycle		
		Binge/Intoxication	Withdrawal/Negative Affect	Preoccupation/Anticipation
Alcohol	Humans	<ul style="list-style-type: none"> • Escalation of use $F > M$ (qualitative) • Amount of intake $M > F$ (quantitative) • Incidence $M > F$ (population) 	<ul style="list-style-type: none"> • Negative affect $F > M$ (qualitative) 	<ul style="list-style-type: none"> • Stress or anxiety-induced relapse $F > M$ (qualitative)
	Rodents	<ul style="list-style-type: none"> • Amount of intake $F > M$ (quantitative) • In some studies intake does not differ $F = M$ 	<ul style="list-style-type: none"> • Withdrawal symptoms $M > F$ (quantitative) 	<ul style="list-style-type: none"> • Stress-induced reinstatement $F > M$ (qualitative)

Females might be More Motivated to Drink Alcohol for Negative Reinforcement than Males

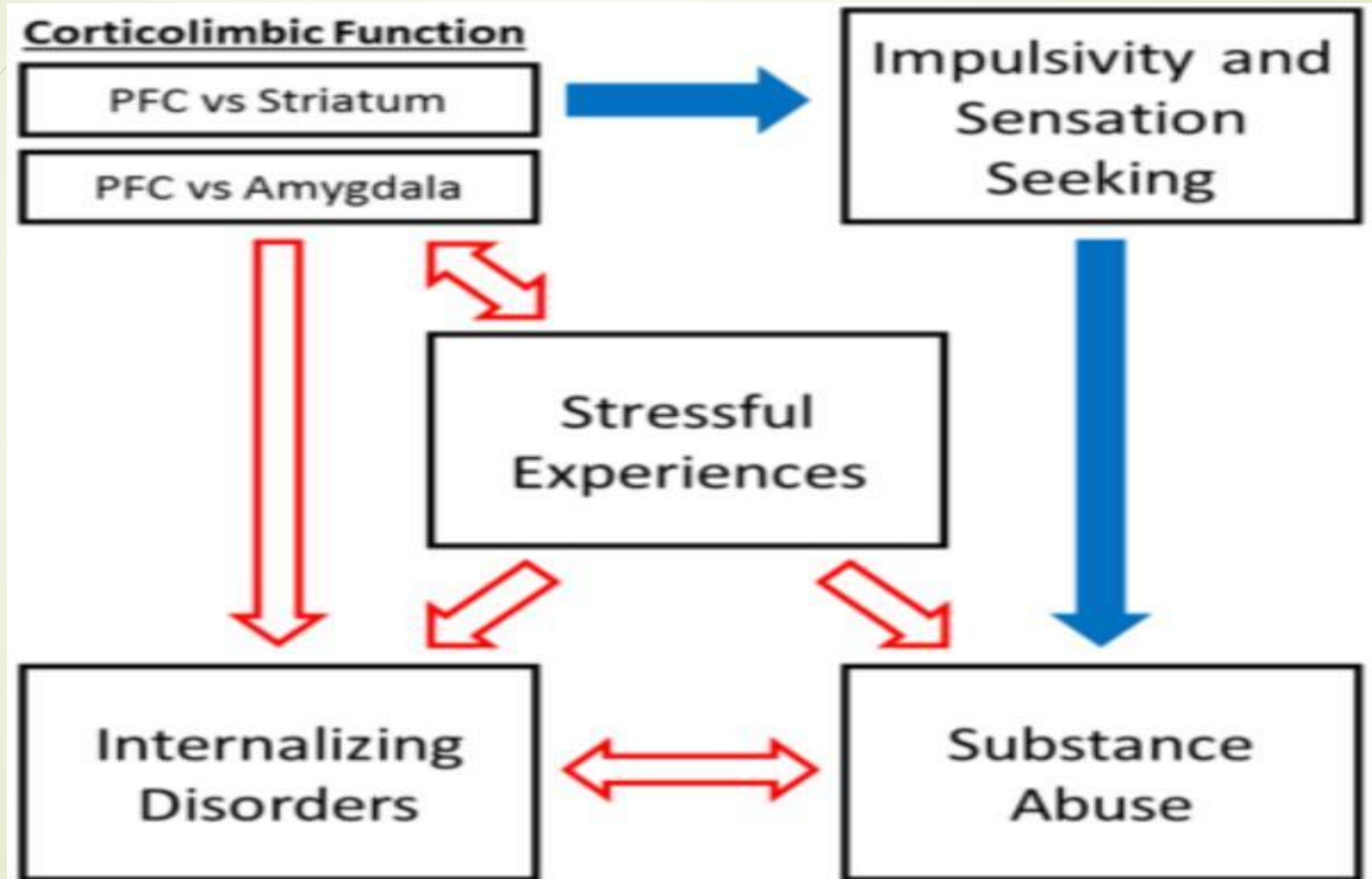
“The results from the largest drinking motive study conducted to date suggest that gender-specific prevention should take differences in the motivational pathways toward (heavy) drinking into account, that is, **positive reinforcement seems to be more important for boys and negative reinforcement for girls.**”

-- Kuntsche et al., 2015

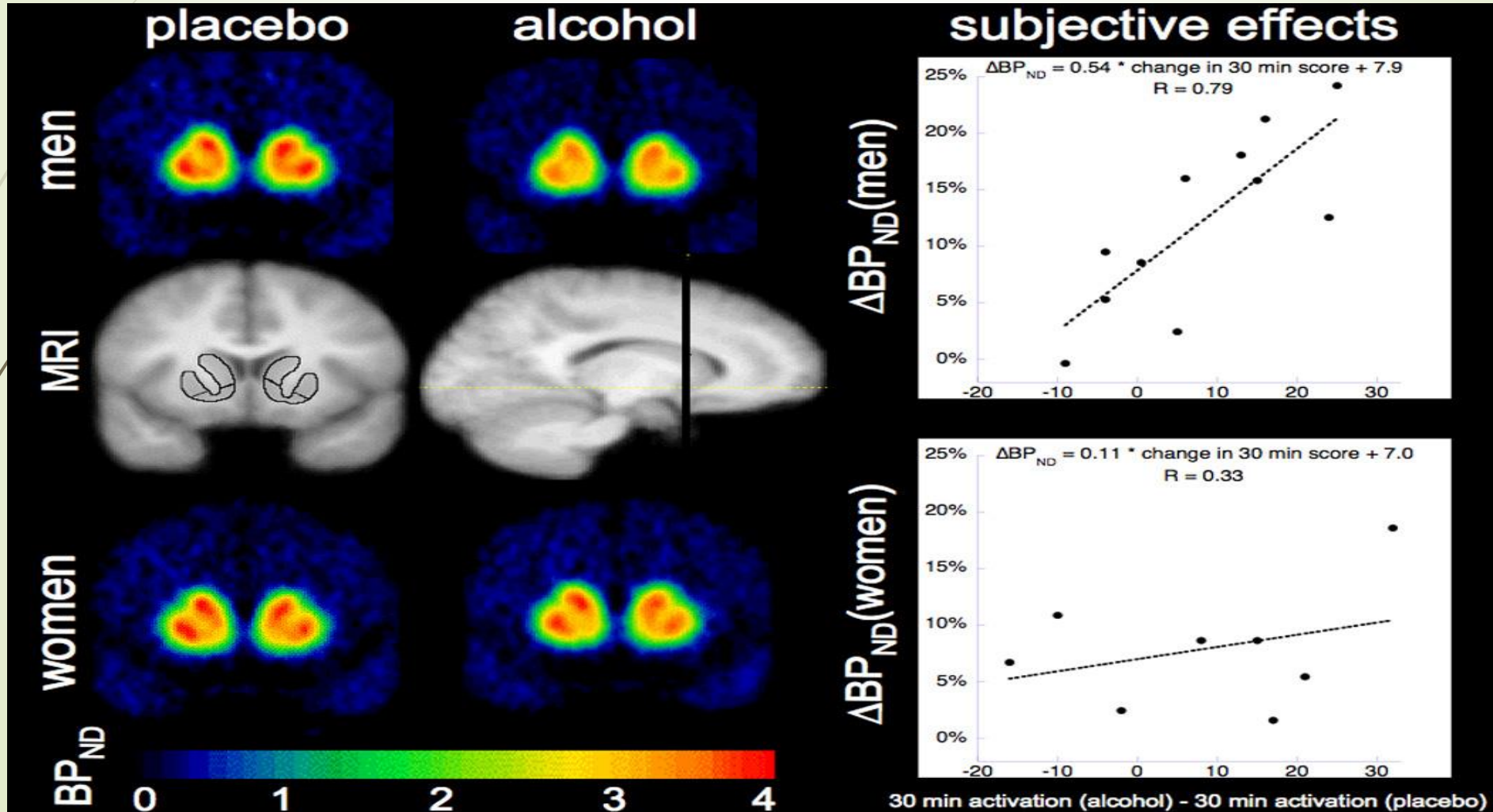
Sensation Seeking Motivates Substance Use During Adolescence -- but maybe More for Males



Hammerslag et al 2016



Alcohol causes less dopamine release in F>M
Nucleus Accumbens(Urban NGL et al 2010)





HORMONES- GENDER - ALCOHOL

- ▶ acute and chronic alcohol administration disrupts functioning of the endocrine system (Rachdaoui and Sarkar et al)
- ▶ HPA VS HPG axis
- ▶ gonadal sex steroid hormones exert organizational (permanent) and activational (transient) effects on the brain
- ▶ Gonadal steroids also influence the stress response (HPA) axis,
- ▶ elevated stress hormones (HPG) axis
- ▶ reciprocal interaction between the stress and reproductive axes



STEROID HORMONES-(SEX STEROID/STRESS STEROID

- ▶ Progestins, such as progesterone and dihydroprogesterone, bind to two progesterone receptor isoforms: A and B
- ▶ Estrogens, such as 17beta-estradiol, bind to two distinct receptor subtypes: estrogen receptor-alpha and estrogen receptor-beta
- ▶ Androgens, such as testosterone and dihydrotestosterone, bind to androgen receptors
- ▶ Glucocorticoids, such as corticosterone in rodents and cortisol in humans and monkeys, bind to mineralocorticoid receptors (type I) and glucocorticoid receptors (type II)
- ▶ “neuroactive steroids” and “neurosteroids”



WHAT IT MEANS FOR US

- ▶ Two studies with small cohorts of male and female patients with co-occurring AUD and cocaine use disorder found that progesterone administration **decreased** cue-induced craving and cortisol responses
- ▶ **(SPECIES SPECIFIC)**-, a significant reduction in allopregnanolone, progesterone, and estradiol levels was detected upon detoxification, and levels recovered to baseline values after 4 months of abstinence **HUMANS VS RODENTS/PRIMATES**
- ▶ 2. studies have shown that exposure to predator odor stress (PS), which is considered a traumatic stress and used as a model of PTSD, significantly increases alcohol drinking and self administration in rodents.
- ▶ Evidence supports greater PS-enhanced drinking among female versus male mice .(Finn et al)
- ▶ 5 Plasma corticosterone levels following PS exposure have been shown to be significantly higher in female versus male mice(Nentwig et al 2019)



ORPHAN NEUROPEPTIDES

G- PROTEIN COUPLED RECEPTOR SYSTEMS



- ▶ orphaned neuropeptide systems and receptors (oGPCR), which have no known cognate receptor or ligand, remain understudied in drug discovery and development
- ▶ GPCRs, also termed seven-transmembrane (7TM) domain receptors, are the largest class of receptors in the mammalian genome (Alexander et al., 2019)
- ▶ GPCRs are currently classed into five main categories based on phylogenetic studies, forming the GRAFS classification—Glutamate (Class C), Rhodopsin (Class A), Adhesion, Secretin, and Frizzled/Taste2
- ▶ EX Cocaine and amphetamine regulated transcript
- ▶ GPR26



ARTICLE



OPEN

Cocaine and amphetamine regulated transcript (CART) mediates sex differences in binge drinking through central taste circuits

Xavier J. Maddern^{1,2}, Bethany Letherby^{1,2}, Sarah S. Ch'ng^{1,2}, Amy Pearl^{1,2}, Andrea Gogos^{1,2}, Andrew J. Lawrence^{1,2} ^{1,2} and Leigh C. Walker^{1,2} 

© The Author(s) 2023

- ▶ The neuropeptide cocaine- and amphetamine-regulated transcript (CART) is encoded by the *Cartpt* gene
- ▶ There are two biologically active forms of CART in humans, CART42-89 and CART49-89
- ▶ CART has been implicated in a diverse range of physiological and pathophysiological functions, including energy balance, depression, anxiety, and reward related behaviours, including AUD
- ▶ CART mediates a number of factors that promote alcohol consumption, including stress/anxiety, reward seeking/motivation, taste and social interaction

- 
- 
- ▶ sexually dimorphic effect of CART in binge drinking and
 - ▶ highlight a novel, sex-specific behavioural mechanism in females, whereby CART mediates binge drinking through changes in bitter taste sensitivity, in part through CART signalling in the CeA
 - ▶ Specifically, male CART KO mice showed heightened alcohol consumption, while female CART KO mice showed reduced alcohol consumption
 - ▶ differences in taste preference, specifically a heightened bitter taste sensitivity in female CART KO mice.



GENETICS- GENDER- ALCOHOL

- AUDs strongly run in families (Cotton, 1979).
 - While twin and adoption studies have unequivocally demonstrated a substantial genetic contribution to the etiology of AUDs
 - (e.g., Cadoret et al., 1987; Cloninger et al., 1981)
 - 3 QUESTIONS REMAIN
- A. Familial-environmental influences on risk for AUDs
 - B. quantitative sex effects in the genetic factors for AUD — that genetic effects were stronger in males than in females
 - C. qualitative sex effects for AUDs — that the genetic risk factors were not entirely the same in males and females.

GENETICS AND GENDER

Inheritance of the Susceptibility to Alcohol Abuse in Adoptees Participating in the Stockholm Adoption Study

Alcohol Abuse in the Biological Parents		Percentage of Adoptees With These Parents Who Abuse Alcohol	
Father	Mother	Sons	Daughters
No	No	14.7 %	2.8 %
Yes	No	22.4 %	3.5 %
No	Yes	26.0 %	10.3 %
Yes	Yes	33.3 %	9.1 %

SOURCE: Adapted from Sigvardsson et al. in press.


CIONINGER'S TYPOLOGY


Distinguishing Differences Between Type I and Type II Alcoholism¹

Characteristic	Type I Alcoholism	Type II Alcoholism
Contributing factors	Genetic and environmental	Primarily genetic
Gender distribution	Affects both men and women	Affects men more often than women
Usual age of onset	After age 25	Before age 25
Common alcohol-related problems	Loss of control over drinking; binge drinking; guilt about drinking; progressive severity of alcohol abuse	Inability to abstain from alcohol; drinking frequently associated with fighting and arrests; severity of alcohol abuse usually not progressive
Characteristic personality traits	High harm avoidance and low novelty seeking; person drinks to relieve anxiety	High novelty seeking; person drinks to induce euphoria



VERHUSLT ET AL 2015

- ▶ meta-analysis of twin and adoption studies of AUD
 - ▶ genetic factors account for roughly 50% of the variance in AUD, and this estimate applies to both males and females.
 - ▶ contrast to mixed findings from earlier studies
- 



A National Swedish Twin-Sibling Study of Alcohol Use Disorders

Kenneth S. Kendler^{1,2,3}, MirNabi PirouziFard⁴, Sara Lönn⁴, Alexis C. Edwards^{1,2}, Hermine H. Maes^{1,3}, Paul Lichtenstein⁵, Jan Sundquist⁴, and Kristina Sundquist⁴

- ▶ three registers in Sweden: medical, crime, and pharmacy.
- ▶ substantial differences in heritability of AUD emerged between the sexes, with estimates in **males more than twice as high** as those observed in females.
- ▶ consistent evidence for **strong shared environmental influences** (and hence reduced heritability) on AUD in the **female–female twin and sibling pairs**
- ▶ No qualitative sex differences

TELESCOPING

Telescoping of Alcoholism in Women Alcoholics

Nick J. Piazza,* PhD

*The University of Toledo
Toledo, Ohio*

Jean L. Vrbka, MA

*Kitsap Mental Health Services
Bremerton, Washington*

Rebecca D. Yeager, PhD

*Lincoln-Lancaster Drug Projects
Lincoln, Nebraska*

Abstract

The accelerated progression of alcoholism, or *telescoping*, was examined among women alcoholics. Three aspects of telescoping in women were examined: the age of onset of four landmark symptoms, the number of years between landmark symptoms, and the number of symptoms occurring within each interval between landmarks. Women alcoholics were found to report a significantly shorter interval between the age at which they first began experiencing alcohol-related problems and the time they sought treatment than did male alcoholics.



CLINICAL PRESENTATION AND CYCLE OF TREATMENT

- Women are more likely to start drinking at a later age.
- If they do start, likely to consume less than men.
- Men are twice as likely to binge drink & four times more likely to be heavy drinkers
- women at baseline generally presenting with more severe clinical issues
- women initially presented with more financial, family/social, and psychiatric problems.
- **More likely to be seen by primary care services**



LETS NOT FORGET

- Women experience disproportionate second-hand harm from alcohol-consuming spouses, partners, ex-partners or family members
- Men, on the contrary, are more likely to demonstrate hazardous patterns of alcohol use and to engage in drink-driving or aggressive or antisocial behaviour
- Women are also more likely than men to support alcohol-control policies



Predictors of treatment


- Good- stable marriage, employment, education, children
- Poor – divorce, unemployment, no children contribute to higher consumption
- **Preexisting mood disorder/anxiety disorder**
- **Marriage- risk factor for women /protective in men**



Service delivery

Specific program components that women identify as helpful include:

- ▶ women's only groups
- ▶ childcare services
- ▶ individual counseling
- ▶ Specialized women's services have shown to be particularly effective for women who are pregnant, trauma-affected or experiencing comorbid psychiatric disorder (dual diagnosis)

- 
- ▶ women may do better in women-only residential and outpatient settings that offer enriched wrap-around services
 - ▶ (e.g., childcare parenting training, assertiveness training, family planning).
 - ▶ Across studies, patients in women-only treatment averaged significantly more days in care, were more than twice as likely to complete treatment and were more than two times less likely to report substance abuse at follow-up compared with women in mixed-gender treatment



OUTCOMES





SHORT TERM :

- ▶ women tend to have longer inpatient stays and that longer inpatient stays are associated with an increase in sustained abstinence for women but not for men (Green et al)
- ▶ demographic variables, such as lower psychiatric impairment, higher socioeconomic status, and greater social support and stability

LONG TERM:

Results have been more mixed regarding women's long-term outcomes compared to men.⁶ In the same study from Spain described above, women had superior drinking outcomes compared to men

Litt and colleagues found that women had worse drinking outcomes than men in the 2 years following outpatient AUD treatment

- 
- 
- ▶ during the first 5 years of recovery, women report lower quality of life and self-esteem and greater psychological distress compared with men
 - ▶ **Project MATCH / COMBINE study/ United Kingdom Alcohol Treatment Trial-**
 - ▶ Women were more likely than men to be in the abstinent recovery or asymptomatic, low-risk drinking categories than in the persistent AUD category



LIVER

- Different first-pass metabolism, because of oestrogen-caused diminished gastric alcohol-dehydrogenase (ADH) activity.
- Women develop more liver damage
- More liver fatty acids under alcohol consumption.
- Women are more likely than men to develop alcoholic hepatitis and to die of cirrhosis
- Women are also more likely than men to develop rapidly progressing liver disease, which frequently persists even after abstaining from alcohol



CARDIAC

- increased risk of cardiac diseases, including cardiomyopathy, arrhythmia, hypertension
- Females more sensitive to cardiac contractile depression due to acetaldehyde possibly accounting for sex differences in AICM (Duan et al 2003)
- The level of drinking at which more cardiac harm than benefit is seen is **considerably lower** for women than for men.
- (Linnet al., 1993) (Klatsky,2001)



BREAST CANCER

- In one study, there was a 12% increase in breast cancer risk per 1 drink/day increase in average alcohol consumption.
- There is dose-response relationship between alcohol consumption and risk of breast cancer
-



BRAIN/CNS




- Women who drink have also been shown to have faster progression of brain damage compared to men.
- Both genders develop a comparable amount of brain atrophy but the brain atrophy occurs faster in women than in men.
- Moderate drinking is associated with higher risk for subarachnoid hemorrhage in women than men.

(Mann et al., 2005)



Fetal alcohol spectrum disorder



- abortion, fetal death, premature birth, low birth weight, abnormalities in mental and physical development, somatic alterations.
- The teratogenic effects of alcohol are globally defined as fetal alcohol spectrum disorders (FASD) and the fetal alcohol syndrome (FAS) is the worst manifestation.
- Fetal damage is not dose-related and may occur even at low levels of maternal alcohol intake, especially if ingested in early pregnancy.
- 48% COMORBIDITY WITH ADHD



COMORBIDITIES- PSYCHIATRIC

- ▶ Most common mood disorder among women with alcohol or drug use disorders was major depressive disorder (15.4%) and the most common anxiety disorder was specific phobia (15.6%)
- Secondary depression is also more common in women than men
(NIAAA)
- ▶ PTSD
 - Prevalence of PTSD is 1.4 to 5 times higher compared to those without substance use disorders

(Lowinson and Ruiz, 2010)

- 
- 
- ▶ NCS-R estimated that rates of lifetime AUDs occurred in up to 34% of individuals with EDs, which is significantly higher than rates of alcohol use disorders in the general population

TREATMENT (PREVENTION TO PHARMA)



World Health
Organization

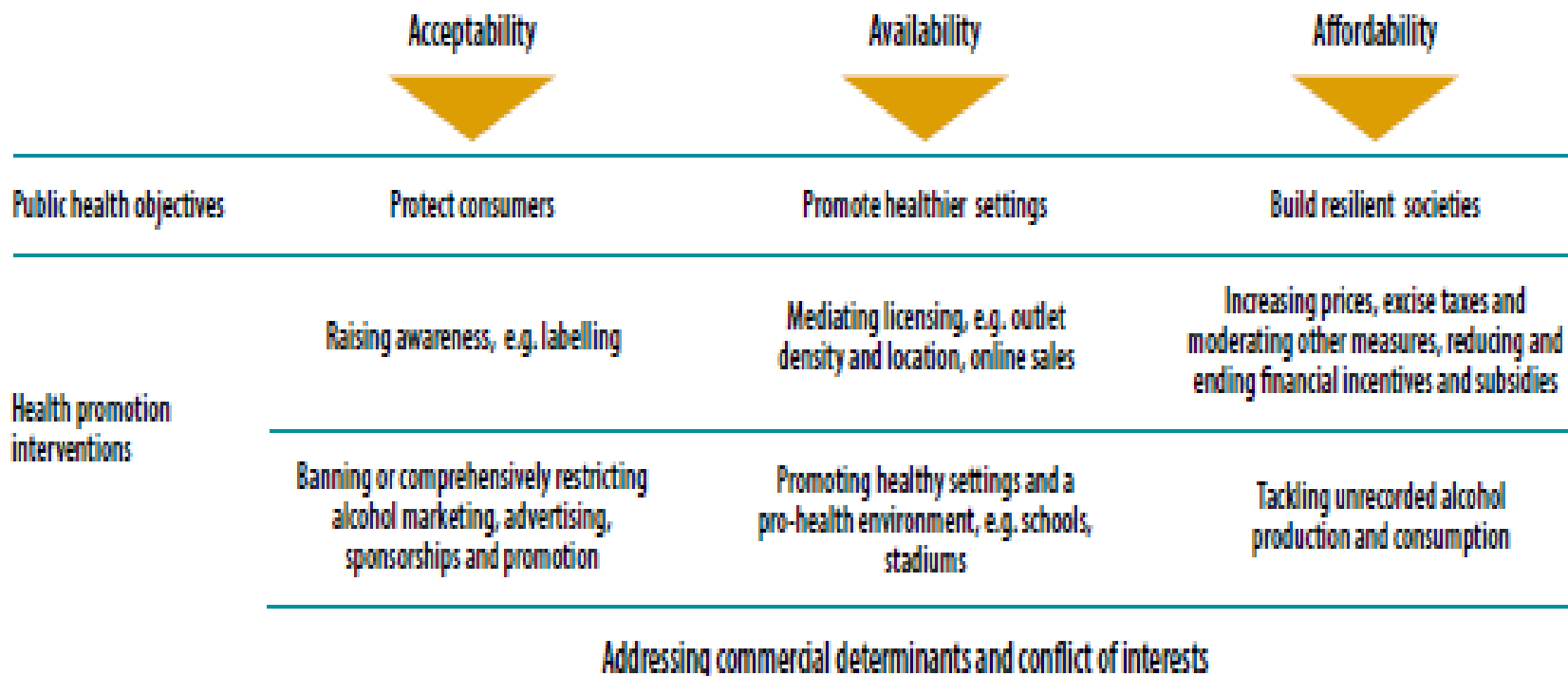
Gender-responsive
approaches to the
acceptability, availability
and affordability of alcohol

Brief 11

Snapshot series on alcohol
control policies and practice

GENDER BLINDNESS

Determinants driving the consumption of alcohol





POLICY



- ▶ **ACCEPTABILITY**-men were more likely to be exposed to or influenced by broadcast advertising than women, especially for beer. young women may be more exposed to and affected by billboard and print media advertising.
- ▶ alcohol labelling can be used to enable informed decisions about the products individuals purchase and consume.
- ▶ these messages are effective in prompting conversations about risks for women of childbearing age. Labeling helps reduce drinking among low-risk,first-time pregnant women
- ▶ **AVAILABILITY**-earlier bar closing times in Brazil were associated with a significant reduction in homicides and a non-significant reduction in assaults against women.
- ▶ **AFFORDABILITY**-women drinkers may be slightly more likely than men to respond to changes in the price of alcohol . 1% modelled increase in the price of alcohol was associated with a reduction of 3.1 – 3.5% in self-reported wife abuse,



Social initiatives



- 1. Supporting women to turn away from home-brewed alcohol in the United Republic of Tanzania
- 2. AUD in Pakistan-**Peace Inn**
- 2. Māori wardens -provided with specific alcohol related statutory functions and powers.



TARGETTING WOMEN-GENDERED APPROACHES

- ▶ The industry has aligned alcohol consumption with culturally desirable notions of masculinity, such as strength, humour and success, and desirable aspects of femininity, such as being attractive, sociable, caring and empowered, across the globe
- ▶ 1. **Pinking** - developing drinks that are colourful, stylized, pretty and appealing to look. Flavored.. Alcopops/wine
- ▶ 2. aligning products to health and weight concerns- **surrogate marketing**
- ▶ 3. draws on notions of feminism, including equality and independence,
- ▶ 4. celebrity endorsements and linking to gendered -highly feminine accessories such as make-up, clothes, fashion
- ▶ 5. Sponsorships- inclu gender based violence!!!



ACAMPROSATE

- ▶ The effect size of acamprosate in women was comparable to that of men, and comparable to or better than effect sizes reported in non sex-specific literature-based meta-analysis (**Barbara J Mason et al, 2012**)
- ▶ despite a history of significantly more anxiety, depression, suicide attempts, drug abuse, interpersonal loss and greater liver impairment at baseline than men, women responded comparably well to alcoholism treatment.
- ▶ Women were more likely to have side effect complaints of greater severity than men, with either acamprosate or placebo treatment. (**did not affect dropout rates**)
- ▶ Recent findings of a beneficial effect of acamprosate on sleep (Staner et al., 2006) may be particularly germane to comorbid disorders in which sleep disruption is a factor



NALTREXONE

Treatment effects among men taking long acting injectable naltrexone versus placebo was highly significant, whereas naltrexone was **not** significantly better than placebo in women

nausea was significantly greater in women at the lowest dose examined - a noted clinical phenomenon (**Garbutt et al, 2005**)

only men showed a greater reduction in drinks per day following daily oral naltrexone (**Hernandez-Avila et al., 2006**)

-The largest study of behavioral and pharmacologic treatment outcomes of alcohol dependence is the COMBINE study . alcohol-dependent women responded to naltrexone with medical management, similar to the alcohol-dependent men, on a wide range of outcome measures

More data is needed to elucidate the differences in men and women in naltrexone responsiveness for alcohol dependence.



DISULFIRAM

- ▶ Research was primarily conducted in males and there is insufficient data to determine if there are sex differences in treatment response [94].
- ▶ A meta-analytic study found that women only accounted for 1% of all study participants evaluating the efficacy of disulfiram negating any possible sex-based analysis.
- ▶ Cocaine use- worsened outcomes



BACLOFEN

- ▶ studies are often designed with lower doses of baclofen for women but then, do not analyze for sex differences

- ▶ To date, two studies have addressed sex:

Garbutt et al- non-significant findings

Reynauld et al-women administered baclofen were almost 11× more likely to achieve abstinence than men



ONDANSETRON

Kenna et al:

Genetic polymorphisms interacted with sex on medication response.

Women, but not men, who had LL genotype and equal or greater than 7 exon III repeats on dopamine receptor D4 gene, had significantly reduced alcohol intake when taking ondansetron



**I know I was an alcoholic
because I was
preoccupied whether
alcohol was going to be
served or not.**

BETTY FORD