TWIST Training With Stakeholders
Applying EU Addiction Research

Sex & Gender Differences

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Structure – bullet points

- Sex
- Gender
- Epidemiology
- Co-morbidity
- Pharmakodynamic,- Pharmakokinetic
- Substances
- “Aging” population
- Prescription drug use
- Gambling
- Special population: pregnancy
- Human rights

Declarations of interest GF

- Funding received over the past 5 years from Reckitt Benckiser, Indivior, GL Pharma, Gilead, Mundipharma, Shire, Pfizer, AOP-Orphan, Abbvie, MSD and Lundbeck (honorarium for travel expenses & delivery of speeches)

Declarations of interest MT

- Funding received over the past 5 years from, Indivior, Gilead, Mundipharma, Elsevier, MSD and Lundbeck (honorarium for consulting & delivery of speeches)

Definition of sex and gender

Sex — **The biological sex**

Gender — **Includes psychosocial aspects**

Gender mainstreaming – consideration in all areas

Gender-specific differences aside biology I

- ***Awareness*** *of health* (nutrition, risk behaviour, physical activity, prevention medical check up, ...)
- ***Perception*** and **willingness to accept** the occurance of medical conditions as well as setting adequate *actions* (to take symptoms serious, consultations in due time, symptom-presentation at the doctor, compliance, ...)
- ***Exposure*** *to* and *coping* of diseases

Gender-specific differences aside biology II

- **The way how** to talk about disease, health and condition and to present themselves respectively (health-reporting-behavior).
- ***Men´s and women´s report*** differ regarding treatment duration and presentation of their needs.
- ***Previous experience*** with the health care system and the health care supply

Sex differences in the structural connectome of the human brain

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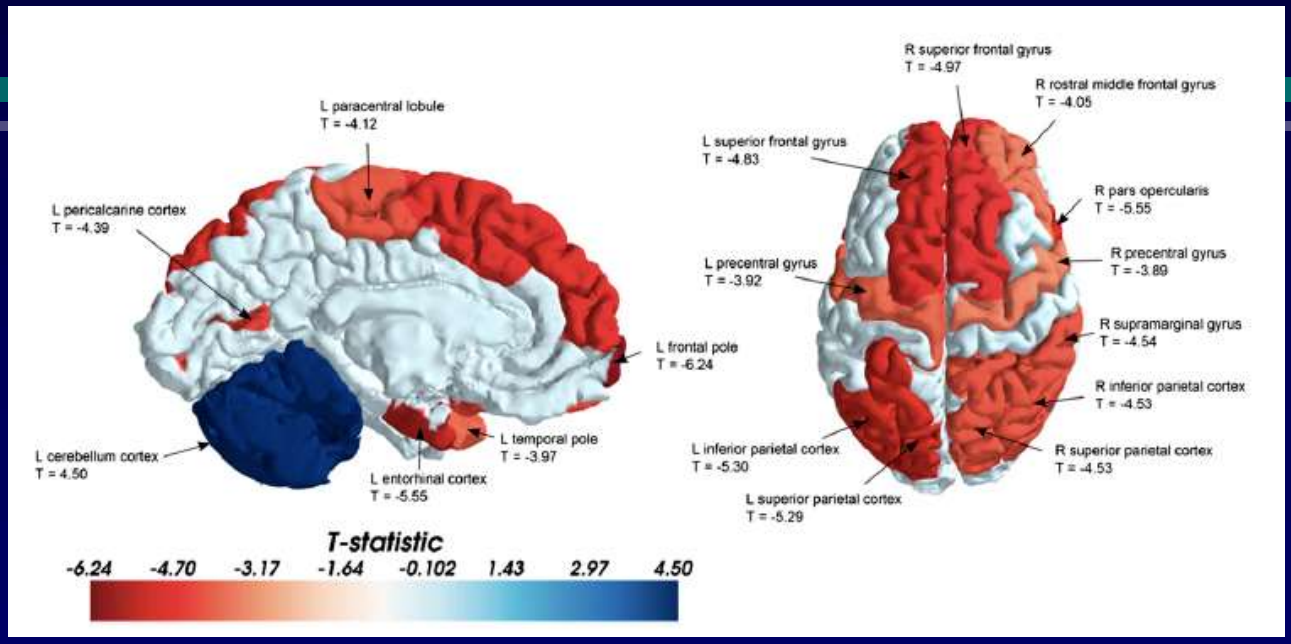


Reporting differences - substance use disorder higher stigma in women

Lifetime prevalence of substance exposure

National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-US)

- 85.7% of the sample (n= 43,093,> 18years) reported any lifetime exposure (49.2% ♀)
- Lifetime prevalence of exposure was significantly higher for ♂ compared to ♀ in all categories (after adjusting for sociodemographic variables, all ORs > 1)

TABLE 1. Comparison of lifetime exposure to substances among females and males in the NESARC 2001–2002

Substance	Female (% [CI])	Male (% [CI])	Unadjusted OR† (CI)	Adjusted OR†,‡ (CI)
Heroin	0.2 (0.1–0.2)	0.5 (0.4–0.6)	3.23 (2.09–4.97)	3.37 (2.12–5.37)
Cocaine	4.2 (3.8–4.7)	8.3 (7.6–8.9)	2.04 (1.83–2.28)	2.06 (1.84–2.31)
Cannabis	16.6 (15.6–17.7)	24.9 (23.7–26.0)	1.66 (1.56–1.77)	1.67 (1.57–1.78)
Nicotine*	38.1 (36.7–39.6)	49.7 (48.2–51.2)	1.60 (1.53–1.68)	1.77 (1.68–1.87)
Alcohol	77.5 (75.7–79.1)	88.4 (87.4–89.4)	2.22 (2.04–2.42)	2.31 (2.12–2.52)
Hallucinogens	3.9 (3.5–4.3)	7.9 (7.3–8.6)	2.14 (1.94–2.36)	2.12 (1.91–2.35)
Inhalants	.9 (.7–1.0)	2.7 (2.4–3.0)	3.18 (2.57–3.93)	3.10 (2.50–3.84)
Sedatives	3.1 (2.8–3.4)	5.2 (4.7–5.6)	1.69 (1.51–1.89)	1.72 (1.53–1.92)
Tranquilizers	2.4 (2.2–2.7)	4.5 (4.1–5.0)	1.91 (1.66–2.18)	1.90 (1.65–2.18)
Opioids*	3.5 (3.2–3.9)	6.1 (5.5–6.7)	1.77 (1.57–2.00)	1.79 (1.57–2.03)
Amphetamines	3.4 (2.9–3.8)	6.1 (5.5–6.7)	1.87 (1.65–2.11)	1.88 (1.66–2.13)

All percentages are weighted. CI, Confidence interval; OR, Odds ratio.
*Lifetime exposure to nicotine was defined as at least 100 cigarettes smoked; †Female is the reference group (OR = 1.0); ‡Adjusted for age, race, educational level, household income, marital status, urbanicity, and region.

*prescription opioids

Lev-Ran et al, 2013.

Lifetime prevalence of substance dependence

- ♂ had a significantly higher prevalence for alcohol and cannabis dependence
- ♀ had a significantly higher prevalence of amphetamine dependence

TABLE 2. Comparison of lifetime prevalence of substance dependence among females and males with lifetime exposure to substances in the NESARC 2001–2002

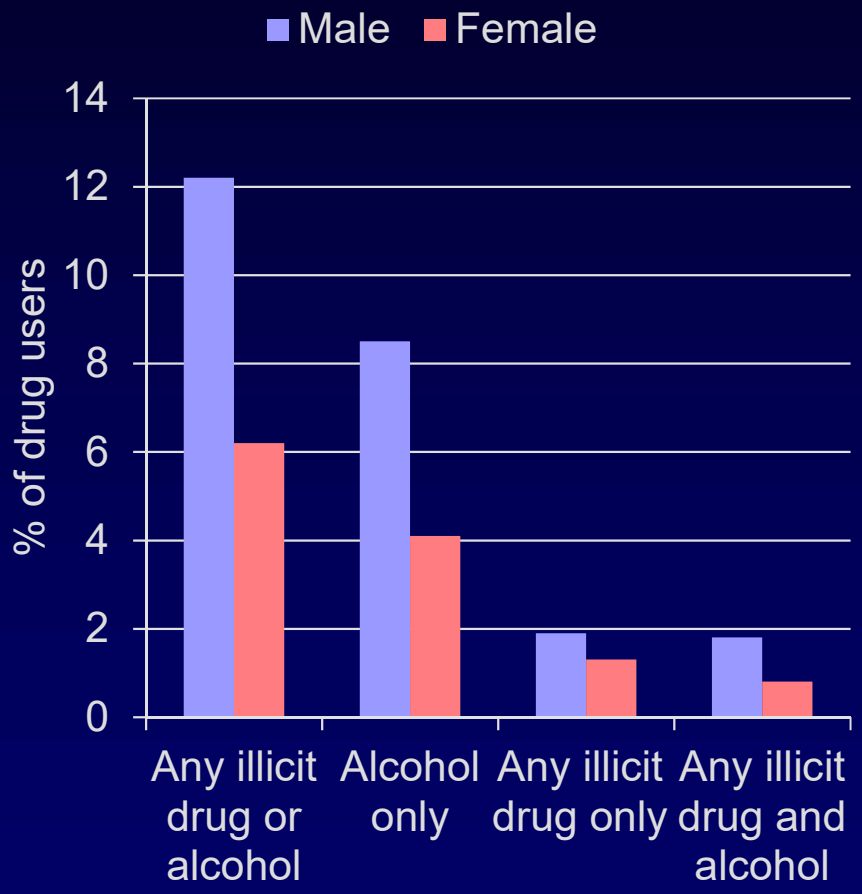
Substance	Female (% [CI])	Male (% [CI])	Unadjusted OR† (CI)	Adjusted OR†,‡ (CI)
Heroin	25.6 (14.7–40.6)	29.1 (20.7–39.2)	1.20 (0.54–2.66)	1.24 (0.51–3.00)
Cocaine	17.8 (14.8–21.1)	15.0 (13.0–17.3)	0.82 (0.62–1.07)	0.85 (0.65–1.11)
Cannabis	5.3 (4.5–6.3)	7.0 (6.1–8.1)	1.35 (1.08–1.68)	1.37 (1.09–1.72)
Nicotine*	40.6 (39.1–42.1)	32.3 (36.4–39.7)	0.90 (0.83–0.97)	0.97 (0.89–1.05)
Alcohol	10.3 (9.6–11.1)	19.6 (18.6–20.8)	2.13 (1.96–2.30)	2.27 (2.09–2.47)
Hallucinogens	3.1 (2.1–4.6)	4.8 (3.4–6.6)	1.56 (0.89–2.72)	1.52 (0.87–2.66)
Inhalants	2.5 (1.0–6.0)	2.2 (1.0–4.7)	0.85 (0.25–2.88)	0.76 (3.16–3.58)
Sedatives	6.6 (4.8–8.9)	5.8 (4.2–7.9)	0.88 (0.54–1.43)	0.96 (0.60–1.55)
Tranquilizers	7.7 (5.5–10.7)	5.9 (4.0–8.4)	0.74 (0.44–1.26)	0.79 (0.47–1.33)
Opioids*	7.9 (6.0–10.4)	6.8 (4.9–9.2)	0.84 (0.55–1.29)	0.86 (0.55–1.32)
Amphetamines	17.6 (14.1–21.7)	10.2 (8.0–12.9)	0.53 (0.36–0.78)	0.55 (0.37–0.81)

All percentages are weighted.
CI, Confidence interval; OR, Odds ratio.
*Lifetime exposure to nicotine was defined as at least 100 cigarettes smoked; †Female is the reference group (OR = 1.0); ‡Adjusted for age, race, educational level, household income, marital status, urbanicity, and region.

*prescription opioids

Lev-Ran et al, 2013.

Sex differences in prevalence are narrowing



- Percentage of persons aged 12 years or under abusing alcohol or illicit drugs in 2003

SAMHSA, 2005.

Drug use in ♂ compared to ♀

	♂	♀
Comorbid psychiatric disorders[1,2]	Depression (27.2%)	Depressive (29.4%)
	Anxiety (25.0%)	Anxiety (46.8%)
	PTSD (24.0%)	PTSD (45%)
	ADHD (28.0%)	ADHD (19%)
	Antisocial personality disorders[5]	Borderline personality disorders
Behaviors[5]	Externalizing	Internalizing behaviors: alleviate physical or emotional pain
	Hedonistic reason and sensation seeking	Initiated into drug use by ♂ partners
	Mortality 13 times higher than age- and sex-matched controls[6]	Higher HIV/AIDS-risk behaviors: sex workers[4]

1) Lynch et al, 2002. 2) Callaly et al, 2001. 3) Schubiner et al, 2000. 4) McCance-Katz et al, 1999. 5) Deykin et al, 1997. 6) Rowan-Szal et al, 2000.

pharmacokinetic/pharmacodynamic differences: ♀

Physiologic factors

- lower body weight and organ size
- Higher percentage of body fat
- Lower glomerular filtration rate
- Different gastric motility in women (slower in luteal phase)
- Ovarian hormones

Drug transporters and drug-metabolizing enzymes (CYP450-is modulated by sex hormones; women clear some CYP3A4 - enzymes drugs faster than men - might needs higher dosing ?)

Different pharmacological responses,
but clinically relevance mostly unproven !

(Meibohm, 2002)

Physiology in ♀	Drug transporters & drug-metabolizing enzymes	Sex-specific factors in ♀
Lower body weight and organ size	***Pharmacokinetics:*** One drug can interfere with the absorption, distribution, metabolization or excretion of another	Menstrual cycle (pre-, post-ovulation)
Higher percentage of body fat	***Pharmacodynamics:*** Clinical response to a given drug is either enhanced or inhibited – "drug–drug interaction"	Oral contraception
Lower glomerular filtration rate	Drug transporters & drug metabolizing enzymes (eg CYP450) are modulated by sex hormones	Pregnancy
Different gastric motility in ♀ (slower in luteal phase)	♀ clear some CYP3A4 - enzymes drugs faster than men (might needs higher dosing ?)	Menopause
Ovarian hormones		

Different pharmacological responses, but clinical relevance mostly unproven! ...Clinical trials are getting much *more expensive* - Meibohm et al, 2002

The importance of sex/ gender

Nature 465 | Issue no. 7299 | 2010

Putting gender on the agenda (editorial)

"Medicine as it is currently applied to women is less evidence-based than that being applied to men"

Science 308 | 2005

Gender in the pharmacy: Does it matter?

Best investigated	Opioids	Antidepressants

• "Drugs" who interact with heart rhythm:
  • Antiarrhythmic
  • Antihistamine
  • Antibiotics
  • Antipsychotics
	• 1990 Jon Levine's group - kappa-receptor opioids work much better in ♀ & caused fewer side-effects[1]
	• Controversial/confirmative results
		• Susan Kornstein's study (2000) - SSRI/tricyclics[2]

1) Gear et al, 1996. 2) Kornstein et al, 2000.

Medication examples & sex differences

Drug	Drug class	Incidence	I_{kr} blocker
Amiodarone	Anti-arrhythmic	F>M	Yes [43]
Bepridil	Anti-anginal	F>M	Yes [44]
Cisapride	Gastrointestinal stimulant	F>M	Yes [45,46]
Disopryamide	Anti-arrhythmic	F>M	Yes [47]
Erythromycin	Antibiotic	F>M	Yes [48]
Halofantrine	Anti-malarial	F>M	Yes [49]
Ibutilide	Anti-arrhythmic	F>M	Yes [50]
Methadone	**Opioid agonist**	**F>M**	**Yes [51]**
Pentamidine	Anti-infective	F>M	?
Pimozide	Anti-psychotic	F>M	Yes [52]
Quinidine	Anti-arrhythmic	F>M	Yes [53]
Sotalol	Anti-arrhythmic	F>M	Yes [54]

F, female; M, male; F>M, substantial evidence indicated a greater risk (usually ≥ twofold) of TdP in women Ikr, rapid delayed rectifier potassium current.

Abi-Gerges et al, 2004.

- Cardial interaction: ♀ experience a longer QTc interval & increased propensity toward drug-induced Torsade de Pointes
  - Methadone: Kaufmann et al., J Pharmacol. Exp.Ther., 2002

Differences in opioid effects

- Higher μ-opioid receptor binding in ♀[1]
  - Gender-by-age interactions in thalamus & amygdala
- Subjective feelings more frequent and intense in ♀:
  - The feeling of being "high" (spaced out)
  - A "heavy" feeling and dry mouth[2]
- ♀ *experienced more severe postoperative pain and required higher morphine doses (+11%)*[3]
- No differences in:
  - Degree of psychomotor impairment
  - Physiological effects (miosis, respiration rate)

1) Zubieta et al, 1999. 2) Zacny et al, 2001. 3) Aubrun et al, 2005.

Peripartum pain management in opioid maintained ♀

Following Cesarean delivery opioid maintained ♀ (methadone & buprenorphine) received **significantly less opioid analgesics** (day of delivery p = 0.038; day 1: p = 0.02), NSAIDs were administered more frequently than to the comparison group during cesarean section and postpartum.

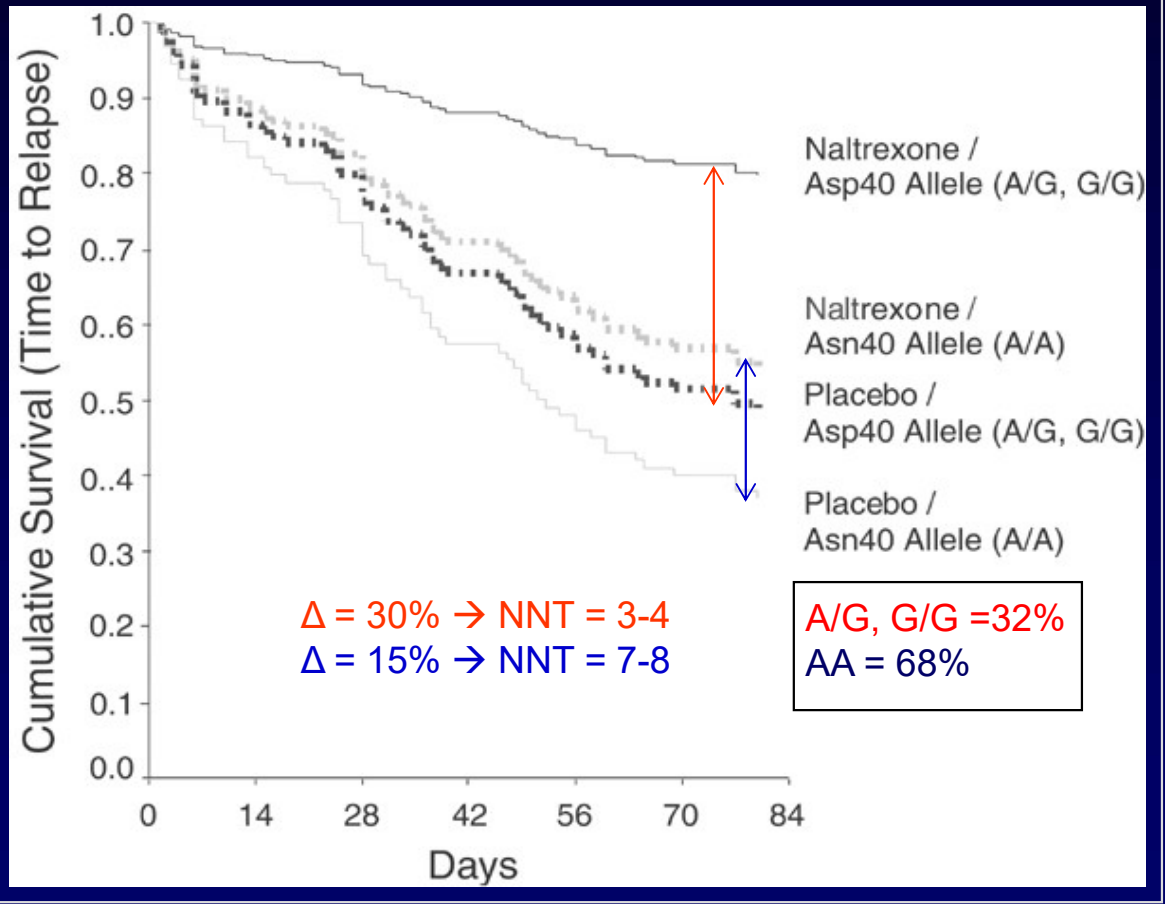
Hoeflich et al, European Journal of Pain 16 (4) (2012)

Alcohol dependence

- Alcohol dependence prevalence rates: 3:1
- Consequences more severe and rapid in ♀
  - Develop higher alcohol concentration after equivalent amounts of alcohol/kg
  - Show a faster progression of alcohol dependence ("Telescoping")
  - Have heightened susceptibility to organ damage
  - Have increased sensitivity to alcohol-induced brain damage
- ♀ are less likely to have received treatment for alcohol dependence: 15% vs. 23%
- Gender differences in comorbidity:
  - Higher rates of comorbid **major depression**: 52% vs. 32%
  - No gender difference in **anxiety** prevalence but **higher severity** for ♀
  - Lower rates of comorbid antisocial personality disorder: 20% vs. 49%

Boykoff et al, 2010.

Pharmacogenomics



Oslin et al. 2003	+
McGeary et al. 2006	+
Anton et al. 2008	+
Kim et al. 2008	+
Ooteman et al. 2009	+
Gerlernter et al. 2007	-
Tidey et al. 2008	-

The importance of gender in substance abuse research

- Historically, participants in substance abuse research were largely ♂
- ♀ view SUD more negatively and are more concerned about social stigma than ♂
  - Pregnancy:
    - Large stigma associated with SUD in pregnant ♀
    - Lack on special services for pregnant ♀
- Treatment entry for ♀ is less facilitated by social institutions (employers or criminal justice system) as for ♂
- ♀ with SUD are more likely to
  - Come from families where members are addicted
  - Be in relationships with drug-abusing partners
  - Experience more affective disorders (♂ higher criminal behaviour)
  - Support their addiction through prostitution (♂ robbery, burglary…)

Tuchman, 2010.

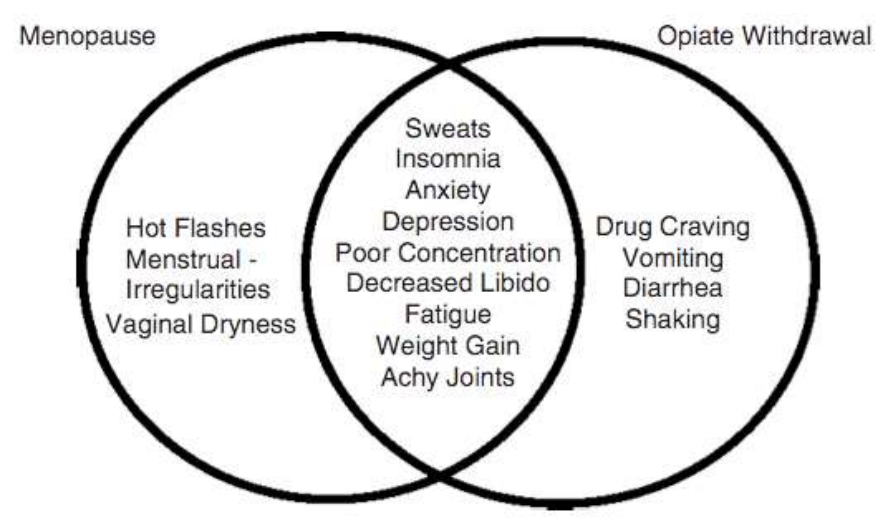
Gender differences in treatment outcomes

- Higher treatment drop-out rates in ♀
- Factors other than dose adequacy contribute to improved outcomes (eg, therapeutic relationship)
- History of physical, sexual and emotional abuse may have negative impact on treatment outcome
- Remaining abstinent after treatment – no difference?
  - Continued abstinence 7 months after completion of treatment: ♀ who complete multiprofessional treatment do better than ♂ [6]

1) Hser et al, 1990. 2) Kosten et al, 1993. 3) Pettinati et al, 1997. 4) Weiss et al, 1997. 5) Lynch et al, 2002. 6) Green et al, 2004.

Menopause symptoms of ♀ in MMT

- 15.6% of adults receiving treatment for opioid dependence in 2004 were >50 years old (up from 5.5% in 1994)[1]
- High rates of vasomotor symptoms
- Mood overshadows classical menopause symptoms
- Multiplicity of symptom-producing entities[2]
- Need menopause research agenda for ♀ in MMT



1) Rosen et al, 2008. 2) Tuchman, 2007.

♂ Erectile dysfunction in maintenance therapy

- Methadone versus buprenorphine patients or healthy controls[1]
  - M: Lower plasma testosterone (p<0.00001)
  - M: Higher rates of impaired libido (p<0.0001)
  - Higher frequency of sexual dysfunction (p<0.00001) (M)
- Risk factors for erectile dysfunction in maintenance treatment[2]:
  - Methadone maintenance (p=0.0135 vs buprenorphine)
  - Not living with a partner (p=0.0018)
  - Depression (p<0.001)
  - Homo- or bi-sexuality (p=0.0427)
  - Partner with history of drug abuse (p=0.0078)
- No significant association found with methadone or buprenorphine dose or treatment duration[1]

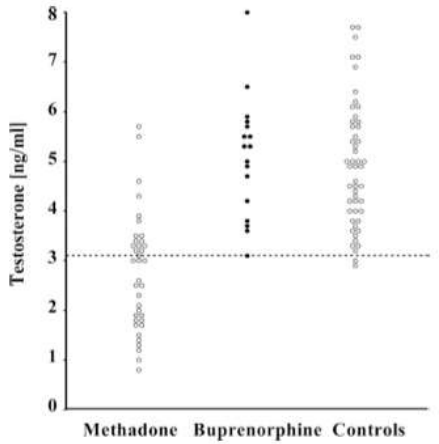


FIG. 1. Comparison of serum testosterone levels in 17 patients treated with buprenorphine, 37 patients treated with methadone, and 51 healthy controls. *Dashed line*, Lower limit.

1) Bliesener et al, 2005. 2) Quaglio et al. 2008.

Bone density in patients receiving methadone maintenance treatment (MMT)

- Cross-sectional study of 59 ♀ and 33 ♂ in MMT (mean age 42 years):
  - Low bone mineral density (BMD) significantly associated with
    - Male gender ($p<0.001$)
    - Lower weight ($p=0.009$)
    - More years of heavy alcohol use ($p=0.02$)
  - Reasons for the high proportion of the ♂ sample with abnormal BMD are unknown, but may reflect the high prevalence of secondary causes of osteoporosis
  - Current heroin use, methadone dosage and duration of MMT were not associated with lower BMD

Kim et al, 2006.

Mental and physical health in "older" methadone patients

- Documentation of prevalence and range of medical and mental health disorders in a population of "older" methadone patients
  - Mean age: 53.9 years (SD=4.01, range 50–67)
  - SF-12: measure of severity of physical and mental health symptoms

Results

Diagnosis	N=140 Overall sample	n=92 ♂	n=48 ♀	p
Hypertension	44.9%	*52.2%*	*29.2%*	*0.002*
Diabetes	11.4%	*16.3%*	*2.1%*	*0.03*
Major depression episode	32.9%	27.2%	43.8%	0.06
Generalized anxiety disorder	29.7%	25.0%	37.5%	0.09
Agoraphobia	13.6%	9.8%	20.8%	0.07
Panic disorder	13.6%	12.0%	22.9%	0.09

- Scores for cohort aged 50–54 years worse than population norms for individuals aged 55–67 years

Rosen et al, 2008.

Abused Prescription Opioids

Oxycodone (OxyContin^{R})
Aspirin & Oxycodone (Percodan^{R})
Hydromorphone (Dilaudid^{R}, Palladone^{R})

♀ who abuse prescription opioids:
Findings from the ASI-MV® Connect database

29,906 US adults entering substance abuse treatment

Gender Differences	Limitations
• ♀ more likely to use and abuse prescription opioids	• Some important risk factors not assessed; smoking, medical/psychiatric diagnoses
• ♀ prefer fast-release, ♂ prefer extended-release	• Cross-sectional design
• Strongest predictor: prescription of pain medication	• No causation can be concluded from correlations
• Need gender-specific strategies for monitoring/prevention/Rx	• Potential selection bias (treatment program attendees)
	• Large number of associations examined (type I error?)
	• Time frame used for obtaining covariates (past month)

Green et al, 2009.

Pathological Gambling

Gambling Behaviour

Strategic vs. non-strategic Gambling

- ♀ prefer non-strategic gambling (e.g. Slot machines, Bingo, Lotto)
- ♂ prefer strategic gambling (e.g. sports bets) or „face to face“ gambling (e.g. Black Jack, Poker)

Gambling motivation

- ♀ gamble as avoidance strategy
- ♀often gamble primarily in/for company
- ♀ start to gamble as leisure activity
- ♂„Sensation-seeking” or to avoid emptiness and negative feelings
- ♂ Gambling as stimulant and for winning money

Nower & Blaszczynski, 2005; Ladd & Petry, 2002; Potenza et al., 2001; Potenza, Maciejewski & Mazure, 2006

Pathological Gambling – Telescoping Effect

Telescoping effect – (Grant & Kim, 2002; Ibanez et al., 2003; Ladd & Petry, 2002; Potenza et al., 2001; Tavares et al., 2001)

Characteristics	♀ (n=39)	♂ (n=38)	p
Age			
•At gambling onset	34,2	20,4	<0,001
•At seeking treatment	44,7	42,3	n.s.
Years of intensiv gambling (until first gambling problems)	1,0	4,6	0,017
Years of probleme gambling (from first gam. problemes until treatment)	1,8	8,6	<0,001
Max. abstinence length (in months)	2,6	10,1	0,015

Tavares et al., 2001

Smoking

Nicotine – Smoking rates

- Male and female smoking rates over a period of 32 years

	1980			2012		
	Total	♀	♂	Total	♀	♂
Global	26%	11%	41%	19%	6%	32%
EU	32%	24%	42%	27%	22%	33%
US	30%	28%	33%	15%	14%	17%
Australia	30%	28%	34%	17%	15%	18%
Asia	19%	6%	33%	19%	3%	35%

Ng, M., et al. (2014). Smoking Prevalence and Cigarette Consumption in 187 Countries, 1980-2012. *JAMA, 311*(2):183-192

Gender differences in nicotine metabolism

- Main cytochrome (CYP) responsible for nicotine metabolism (CYP2A6) is upregulated in ♀ compared to ♂
- Higher CYP expression is associated with faster nicotine metabolism
- ♀ may consume more cigarettes than ♂ in accordance with greater CYP expression

→ ♀ experience more difficulty quitting smoking than ♂

→ ♀ may be at greater risk of developing smoking-related diseases

Rahmanian, Diaz, & Wewers, 2011; Allen, Oncken, & Hatsukami, 2014; Mucha, Stephenson, Morandi, & Dirani, 2006

Smoking cessation during pregnancy

- Increased intrinsic motivation to deliver a healthy baby = important window of opportunity for quitting smoking[1]
- Up to 45% of smoking ♀ quit without assistance between learning of pregnancy and first prenatal visit[2]
- BUT: up to 70-80% of these ♀ relapse after the postpartum period[3]

- Promising: Contingency management (CM), based on principles of operant conditioning that offer incentives to encourage smoking abstinence
- CM can improve smoking cessation in the postpartum period: 12 weeks postpartum, 24% of women in CM were still abstinent compared to 3% of women without CM[4]
- CM interventions have also shown a positive impact on fetal growth, birth weight and breastfeeding duration[5]

1) Su & Buttenheim, 2013; 2) Lumley, et al., 2009; 3) Shaw, et al., 2006; 4) Heil, et al., 2006; 5) Higgins, et al., 2012

Nicotine

- Double-blind, placebo-controlled study with nicotine (2 mg by inhaler) to investigate changes in cognitive performance
- Nicotine did not improve attention and memory; exposure to stress increased anxiety and aggression in ♀, which were blocked through nicotine, but not in ♂
- *Smoking in women correlated to stress situation*

- File, S., Fluck, E., & Leahy, A. (2001). Nicotine has calming effects on stress-induced mood changes in females, but enhances aggressive mood in males. *International Journal of Neuropsychopharmacology, 4:* 371–376.

Alcohol consumption during pregnancy

- Canada: 13,8% of pregnant women show mild to moderate alcohol consumption*[1]
- US: 12,5% mild to moderate use*, 1,6% regular use or binge-drinking[2]
- Europe: prevalence of alcohol use in pregnant women comparable to estimates for Canada and US[3]
  - For comparison: In Europe, 62,9% of all women show mild to moderate use*, 13.9% regular (≥ 20g Alcohol/day) and 5,2% problematic consumption (≥ 40g alcohol: 1l beer or 3/8 wine/day)[4]
- Potential consequence: Fetal alcohol syndrome (FAS) → prevalence up to 1%

*max. 1 alcoholic bevarage/day

[1]Walker, et al., 2011; [2]Floyd, & Sidhu, 2004; [3] 2005 Comparative Risk Assessment study; [4] Rehm et al., 2012

Health system costs of FAS (US)

Health system costs of FAS and comorbid disorders (US) until 21 years of age

	Mean costs per year (US$)	Additional costs per year * (US$)	Potential cumulative savings per case and year (US$)	
			After 10 years	After 20 years
FAS	2.842	2.342	128.810	491.820
ADHD	649	154	8.470	32.340
Learning disability	1.302	806	44.330	169.260
Developmental disorder	2.286	1.797	98.835	377.370
ODD**	1.377	883	48.565	185.430
Epileptic seizures	2.181	1.689	92.895	345.690

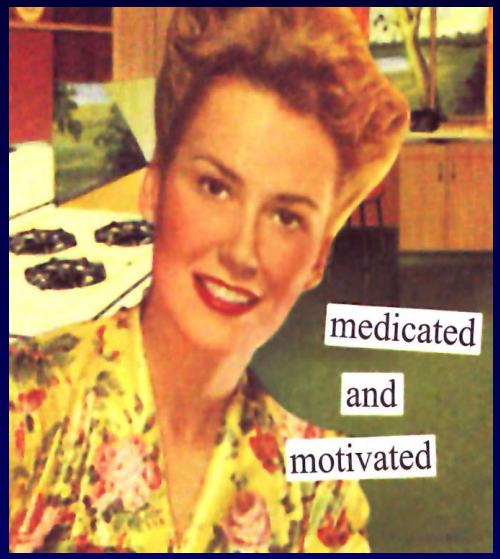
*Additional costs: Costs of a child with the disorder minus costs of a child without the disorder

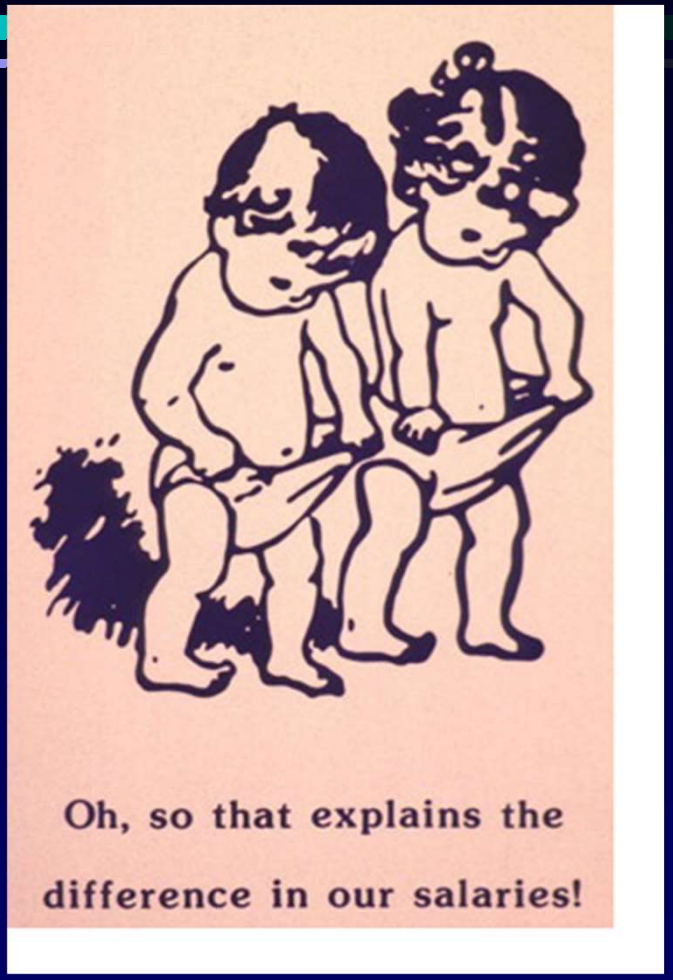
**Opositional Defiant Disorder

Klug, M. G., & Burd, L. (2003). *Neurotoxicology and teratology*, *25*(6), 763-765.

Conclusion

Treating him, treating her:
both sex and gender matter





Thank you for your attention!

Psychiatric comorbidity & Substance Use Disorder

Dual diagnosis

Relevance ?

- More emergency admissions
- Higher prevalence of suicide (OR=14)
- Increased rates of medical co-morbidity (risk behaviours and related infections: HIV & HCV)
- Worse prognosis: More risk of relapse in drug use and psychiatric disorder
- Higher unemployment and homelessness rates
- Greater incident of violent or criminal behaviour

Increased clinical & social severity
High cost for society

Martín-Santos et al 2006 ; Langas et al 2011; Schmoll 2015; Lambert et al, 2003; Stahler et al, 2009; Aharonovich 2002; Conner , 2111, Marmorstein 2011, Szerman 2012; King et al, 2000; Carey et al, 2001; Durvasula and Miller, 2014; Vazquez et al, 1997; Krauz 2013; Soyka 2000; Greenberg & Rosenheck, 2014

Epidemiology?

- **40%-70%** of substance abusers have other psychiatric disorders
- The most prevalent psychiatric diagnoses are:
  - Depression
  - Anxiety disorders (Panic disorder, Post-traumatic stress disorder)
  - Eating Disorder
  - Borderline Personality disorder
  - Antisocial Personality disorder
  - ADHD
- Gender differences: **female present more mental disorders than male**

Gender ?

Estudio PsyCoBarcelona

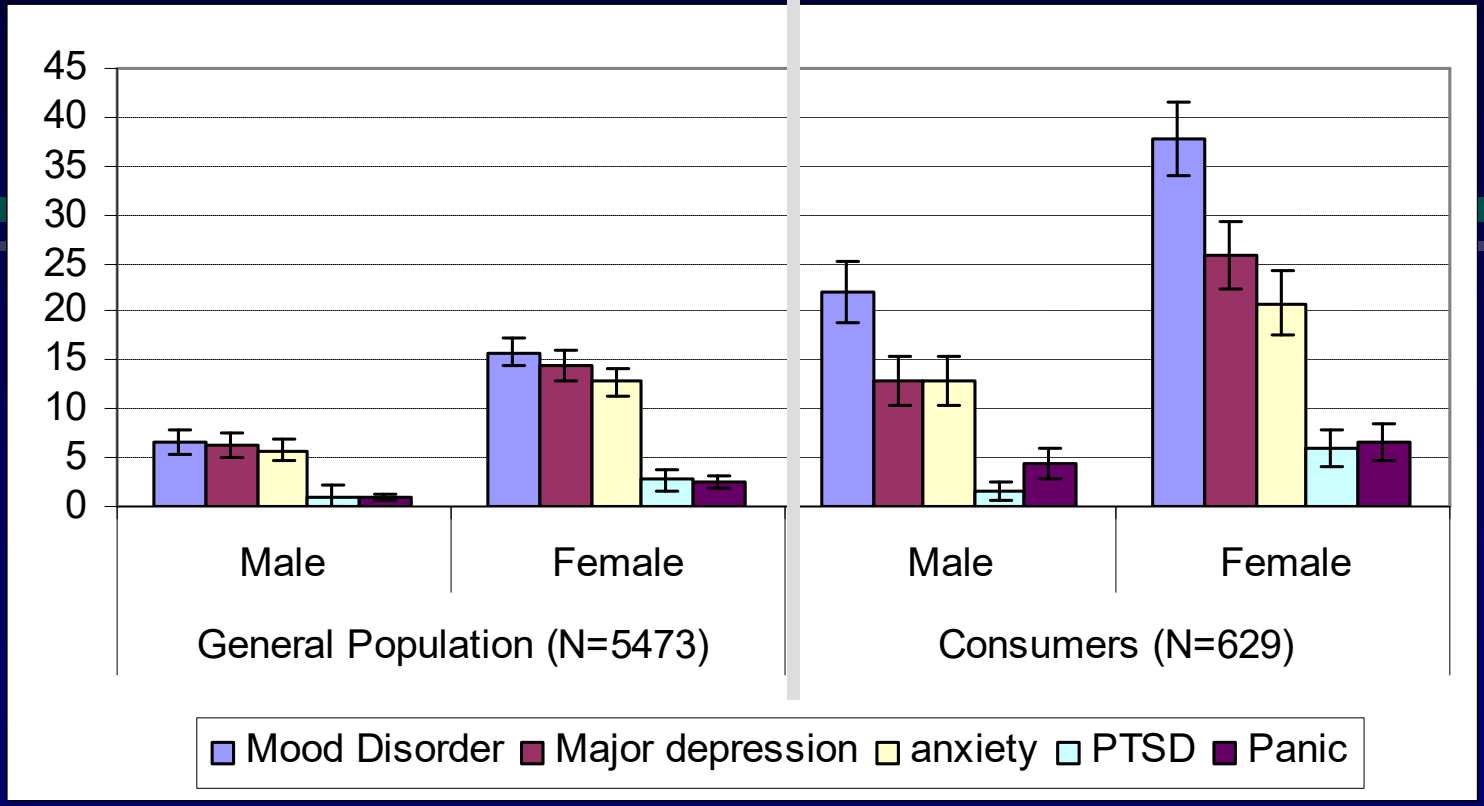
N=629

Gilchrist, Torrens & Domingo (2011)

** p<0.001; * p<0.05

SUD & Gender: Psychiatric comorbidity

Lifetime prevalence of mental disorders in general population and substance abusers by gender (%)



Haro et al., 2006; Gilchrist et al, in press

Gender differences in lifetime psychiatric and substance use disorders among people who use substances in Barcelona, Spain

Yasmina Frem, Marta Torrens, Antonia Domingo-Salvany and Gail Gilchrist

VOL. 10 NO. 2 2017, pp. 45-56, © Emerald Publishing Limited, ISSN 1757-0972 | ADVANCES IN DUAL DIAGNOSIS

Table II Factors associated with lifetime Axis I non-substance use disorder (non-SUD) among females who use substances

	No lifetime Axis I non-SUD (%)	*Lifetime Axis I non-SUD (%)*	*Unadjusted OR and 95%CI*	*OR and 95%CI Adjusted for age and study*
Demographics				
Marital status				
Single/never married/divorced/separated/widowed	72.8	65.1	1.00	1.00
Married/cohabiting	27.2	24.9	0.70 (0.28, 1.28)	0.71 (0.38, 1.31)
Highest level of education attained				
Secondary school or university studies (vs no or primary schooling)	46.7	47.7	1.04 (0.60, 1.81)	1.06 (0.59, 1.88)
Employment				
Working or studying	42.4	38.9	0.86 (0.49, 1.52)	0.86 (0.48, 1.55)
Criminal history				
Ever in prison	33.0	52.3	2.23 (1.25, 3.97)	2.57 (1.35, 4.86)
Living arrangements				
Lives alone	5.4	11.9	1.00	1.00
Flatmate/family	72.8	65.1	0.41 (0.14, 1.21)	0.41 (0.14, 1.21)
Squatting/homeless	21.8	22.9	0.48 (0.15, 1.58)	0.50 (0.15, 1.68)
Blood borne virus status				
HIV	17.3	21.8	1.33 (0.63, 2.81)	1.36 (0.62, 2.96)
Hepatitis C	28.4	48.0	2.33 (1.24, 4.34)	3.05 (1.48, 6.29)
Recruited from out of treatment settings	58.7	59.6	1.04 (0.59, 1.83)	1.99 (0.58, 6.80)

Table IV Associations between specific lifetime substance use disorders and non-substance use disorder among females who use substances

Lifetime substance use disorders OR (95%CI)	*Lifetime (non-substance use) psychiatric disorders OR (95%CI)*					
	Mood	*Anxiety*	*Eating*	*Psychotic*	*Antisocial and/or borderline personality*	*Any substance induced*
Alcohol	1.84 (1.03, 3.29)	1.82 (0.92, 3.60)	1.21 (0.48, 3.07)	1.10 (0.37, 3.28)	1.71 (0.87, 3.37)	2.92 (1.40, 6.11)
Opiates	1.58 (0.85, 2.93)	1.58 (0.74, 3.37)	0.59 (0.23, 1.50)	7.26 (0.93, 56.71)	2.68 (1.17, 6.16)	1.75 (0.77, 3.95)
Cocaine	1.36 (0.71, 2.60)	2.67 (1.06, 6.76)	2.28 (0.64, 8.13)	5.28 (0.67, 41.35)	10.34 (2.41, 44.43)	2.81 (1.03, 7.63)
Sedatives	1.44 (0.79, 2.61)	1.40 (0.70, 2.82)	0.45 (0.14, 1.39)	3.81 (1.22, 11.86)	1.93 (0.97, 3.85)	1.93 (0.89, 3.78)
Stimulants	1.31 (0.71, 2.40)	1.62 (0.80, 3.28)	2.35 (0.93, 5.98)	3.12 (1.03, 9.41)	1.54 (0.77, 3.11)	2.12 (1.02, 4.39)
Cannabis	1.32 (0.74, 2.36)	1.06 (0.53, 2.13)	1.62 (0.64, 4.10)	3.01 (0.97, 9.34)	4.47 (2.18, 9.20)	3.66 (1.73, 7.74)
Hallucinogens	2.13 (1.06, 4.29)	2.19 (1.01, 4,75)	3.10 (1.17, 8.21)	0.65 (0.14, 3.05)	1.80 (0.82, 3.93)	2.75 (1.25, 6.06)
Polysubstance	1.52 (0.75, 3.09)	2.57 (0.95, 6.98)	0.88 (0.30, 2.56)	–	7.91 (1.83, 34.11)	6.42 (1.48, 7.80)

Note: Extremely low cell count for some variables precluded statistical analysis

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Psychiatric comorbidity among women who inject drugs

- Among 226 women who injected drugs, 87% had a psychiatric comorbidity

Country	Panic	Generalised Anxiety Disorder	Social Phobia	Agora phobia	Depression	PTSD
Austria	46.0%	32.0%	12.0%	18.0%	80.0%	62.0%
Italy	57.1%	36.7%	30.6%	24.5%	77.6%	53.1%
Poland	46.0%	40.0%	38.0%	32.0%	82.0%	56.0%
Scotland	80.0%	63.3%	73.3%	66.7%	93.3%	76.7%
Spain	52.0%	18.0%	8.0%	14.0%	54.0%	24.0%
Total	54.1%	35.8%	28.8%	27.9%	76.0%	52.4%

Factors associated to psychiatric comorbidity in females with SUD

- Women with SUD are more likely than men to:
  - come from families with other addicted/psychiatric members (genetic vulnerability, family history, or environmental stress)
  - have experienced more disruption in their families
  - be in relationships with drug use partner
  - support their habits through prostitution
  - suffer high prevalence of intimate partner violence

Psychiatric Comorbidity and intimate partner violence

ADVANCES IN DUAL DIAGNOSIS | VOL. 5 NO. 2 2012,

Exploring the relationship between intimate partner violence, childhood abuse and psychiatric disorders among female drug users in Barcelona

Gail Gilchrist, Alicia Blázquez and Marta Torrens

The probability of experiencing intimate partner violence were:

- Over twice greater among those with any depressive disorder
- Over three times greater for those who reported ever attempting suicide, had borderline personality disorder, had been abused in childhood or currently lived with a substance user

Psychiatric Comorbidity and intimate partner violence

JOURNAL OF WOMEN'S HEALTH
Volume 24, Number 1, 2015

DOI: 10.1089/jwh.2014.4866

Original Articles

Identifying and Intervening with Substance-Using Women Exposed to Intimate Partner Violence: Phenomenology, Comorbidities, and Integrated Approaches Within Primary Care and Other Agency Settings

Terri L. Weaver, PhD,[1] Louisa Gilbert, PhD,[2] Nabila El-Bassel, PhD,[2]
Heidi S. Resnick, PhD,[3] and Samia Noursi, PhD[4]

Women with SUD and Depression or PTSD have more probabilities of:

- Be suffering Intimate Partner Violence
- Be less able to detect the signs that lead to episodes of violence
- Reduced search capacity and access to resources that can improve security

Intimate partner violence and HIV and HCV

- Prevalence rates of intimate partner violence:
  - among non-drug using women range between 1.5% to 16%
  - among women in drug treatment range between 25% and 57%
- Women who experience intimate partner violence
  - Less use of condoms
  - More share needles
  - Multiple sexual partners
  - Trade sex

➔ **HIV and HCV infections**

➔ **Continued drug use and relapse**

Psychiatric Comorbidity and HIV

	All participants $n = 118$ (%)[a]	HIV		
		Negative $n = 86$ (%)[a]	Positive $n = 32$ (%)[a]	OR (95 CI)
Psychiatric risk factors				
Mental disorders				
Any major depression	68 (58.6)	44 (52.4)	24 (75.0)	2.73[b] (1.10, 6.76)
Primary major depression	41 (35.3)	31 (36.9)	10 (31.3)	0.78 (0.33, 1.85)
Substance-induced major depression	35 (30.4)	19 (22.9)	16 (50.0)	3.37[b] (1.42, 7.97)
Post traumatic stress	32 (27.1)	20 (23.3)	12 (37.5)	1.98 (0.83, 4.74)
Borderline personality	39 (33.1)	24 (27.9)	15 (46.9)	2.28 (0.99, 5.28)
Antisocial personality	27 (22.9)	12 (14.0)	15 (46.9)	5.44[b] (2.16, 13.71)
Behavioural risk factors				
Unprotected sex	42 (36.5)	25 (29.8)	17 (54.8)	2.87[b] (1.23, 6.69)
Ever traded sex	39 (34.8)	18 (22.2)	21 (67.7)	7.35[b] (2.94, 18.39)
Ever injected regularly	56 (47.9)	29 (33.7)	27 (87.1)	13.27[b] (4.24, 41.54)
Ever injected with used syringe	44 (38.6)	19 (22.6)	25 (83.3)	17.11[b] (5.76, 50.76)
Any Partner IDU	67 (65.0)	41 (54.7)	26 (92.9)	10.78[b] (2.39, 48.72)
Any Partner HIV + ve	38 (41.3)	16 (23.9)	22 (88.0)	23.38[b] (6.18, 88.44)
Hepatitis C positive	55 (46.6)	24 (27.9)	31 (96.9)	80.08[b] (10.35, 619.79)
Social risk factors				
Mean age (SD)	39.07 (7.75)	37.98 (8.13)	42.00 (5.79)	1.07[b] (1.01, 1.14)
Primary studies or no schooling (vs. secondary studies)	57 (48.3)	37 (43.0)	20 (62.5)	2.21 (0.96, 5.08)
IPV (past 12 months)	67 (57.3)	47 (55.3)	20 (62.5)	1.35 (0.59, 3.10)
Childhood Abuse	82 (71.3)	57 (68.7)	25 (78.1)	1.63 (0.63, 4.25)
Ever been homeless	35 (30.4)	21 (25.3)	14 (43.8)	2.30 (0.98, 5.41)
Ever been in prison	66 (55.9)	44 (51.2)	22 (68.8)	2.10 (0.89, 4.96)

Psychiatric comorbidity and pregnancy

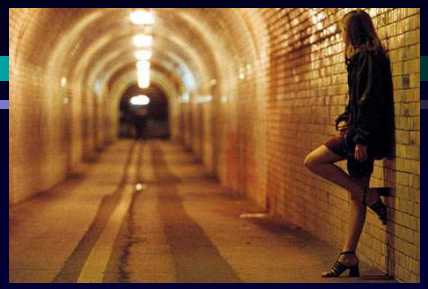
- Prevalence of psychiatric comorbidity among substance misusing pregnant women: 91% to 57% (*Coleman-Cowger, 2012 Strengell, 2015)*

- Postpartum mood disorders affect approximately 10-20% of women and this prevalence increase in women with lifetime substance use *(Prevatt, 2016).*

Addiction & Gender & Mental disorders

Pregnancy

Mental disorders



Prostitution

HIV-AIDS

Hepatitis C Virus

Gender Violence

Conclusions

1. Women with SUD present more psychiatric comorbidity than men with SUD and women without SUD
2. Depression, anxiety and PTSD are the most frequent mental disorders
3. Women with SUD and psychiatric comorbidity present more risk of be suffering Intimate partner violence
4. Women with SUD and psychiatric comorbidity present more risk of HIV and HCV infection

Conclusions

- Policy makers must guarantee the access to appropriate treatment of females with mental disorders and substance use disorder

Thank you!

TWIST **Training With Stakeholders**
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