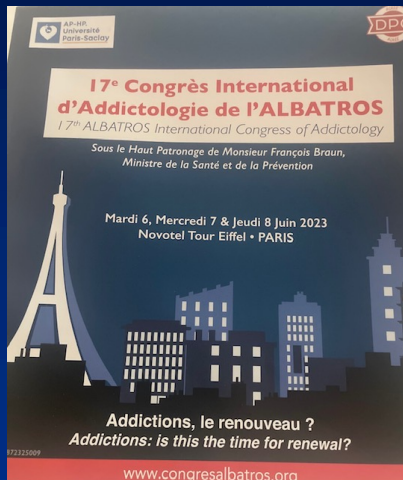




MEDICAL UNIVERSITY  
OF VIENNA

# Sex/Gender (♀) and Substance Use disorder



*Paris, June 8th, 2023*

Univ. Prof. Dr. Gabriele Fischer

Center of Public Health

Department of Psychiatry & Psychotherapy

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# COI relevant for topic

I have received travel support & financial fees for lectures & expert meetings related to that topic in the last 5 years

- Camurus
- Boehringer Ingelheim
- Takeda
  
- Consultancy activities with UNODC, WHO, European Parliament
- Member of Scientific Committee of EMCDDA



MEDIZINISCHER UNIVERSITÄTSCAMPUS



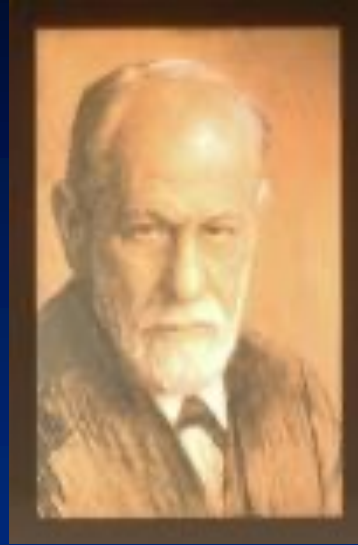
MEDIZINISCHE  
UNIVERSITÄT WIEN



Allgemeines Krankenhaus  
der Stadt Wien

# Sigmund Freud

6.5.1856 - 3.9.1939







# Structure

- General aspects
- Addiction related aspects
  
- 3 examples
  - Co-morbidity
  - Preventive medicine – NAS
  - Prison





# Key note der Literatin Chimamanda Ngozi Adichie bei der Chatham House Konferenz in London, UK – Juni 2018

“In our world,

a man is confident, but a women is arrogant.

A man is uncompromising, but a women is a ball-breaker.

A man is assertive, a women is aggressive.

A man is strategic, a women is manipulative.

A man is a leader, a women is controlling.

A man is authoritative, a women is annoying.

The characteristic of behavior is the same, what is different is the sex. And based on the sex, the world makes assumptions and treats us differently (...)”

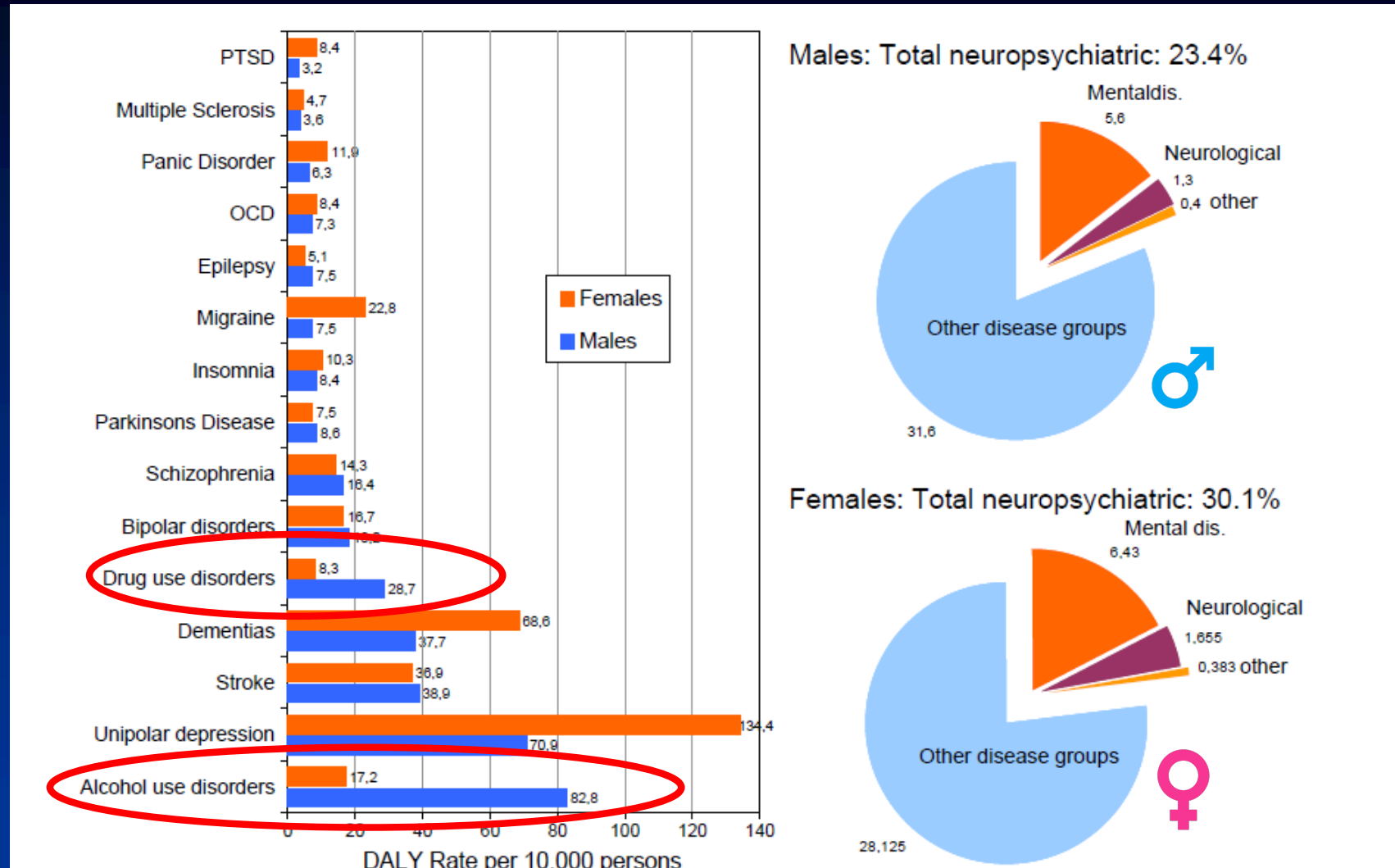
<https://ChathamHouse/>



# „Priorities“ in Health care system

- ♂ have a lower life expectation
- ♂ have a higher neonatal mortality rate
- ♀ have a higher life expectation rate – but more years living with higher burden of disease & lower quality of life
- ♀ health focus is not pregnancy or breast cancer –
- ♂ health focus is not prostate cancer

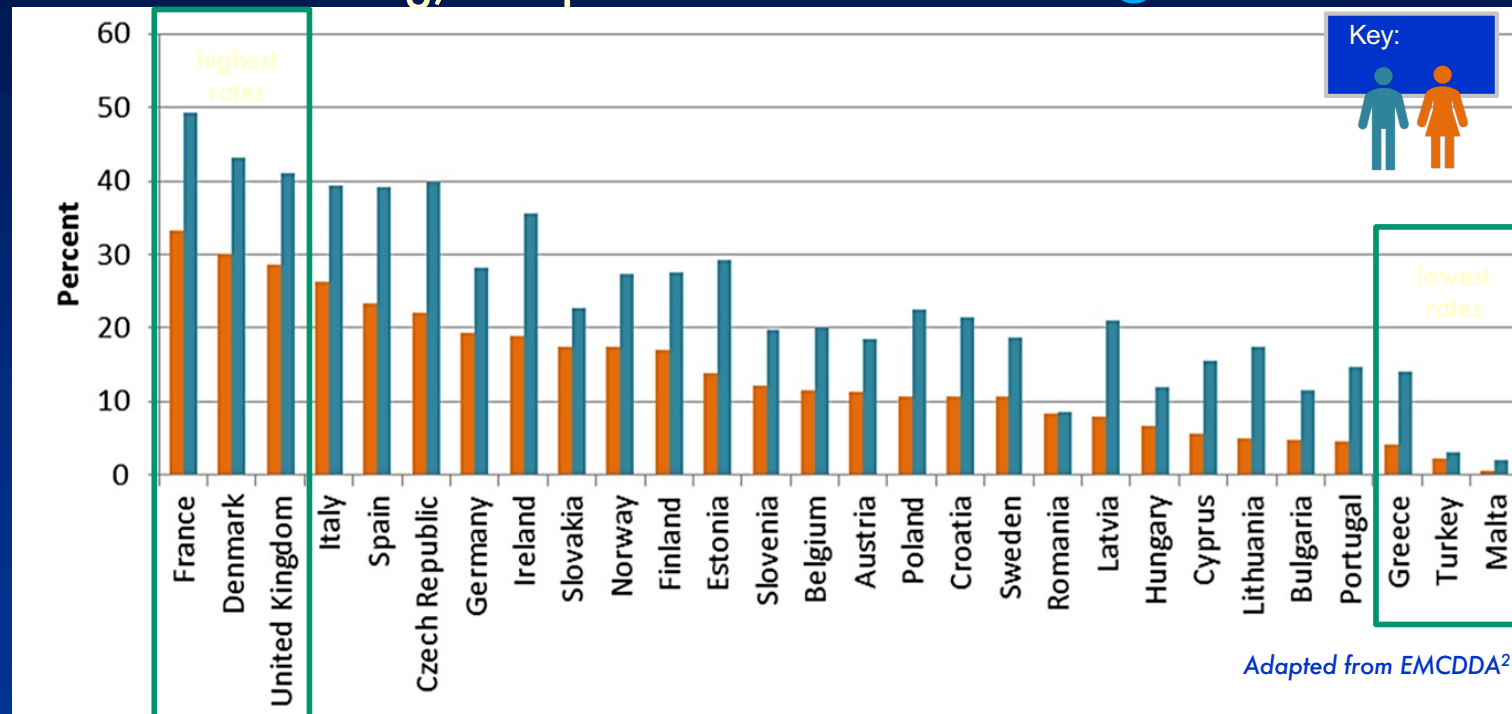
# Gender/sex - related differences in psychiatric and neurological disease burden



DALY: disability-adjusted life-years; OCD: obsessive-compulsive disorder  
 Wittchen HU, et al. *Eur Neuropsychopharmacol.* 2011;21:655-79

## Prevalence of illicit drug use: Differences between ♂ and ♀

- In the EU, 34.8 million ♀ aged 15 to 64 were reported to have previously tried an illicit drug, compared with 54.3 million ♂<sup>1</sup>



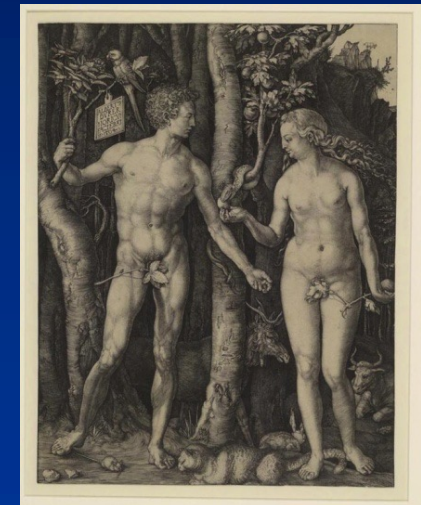
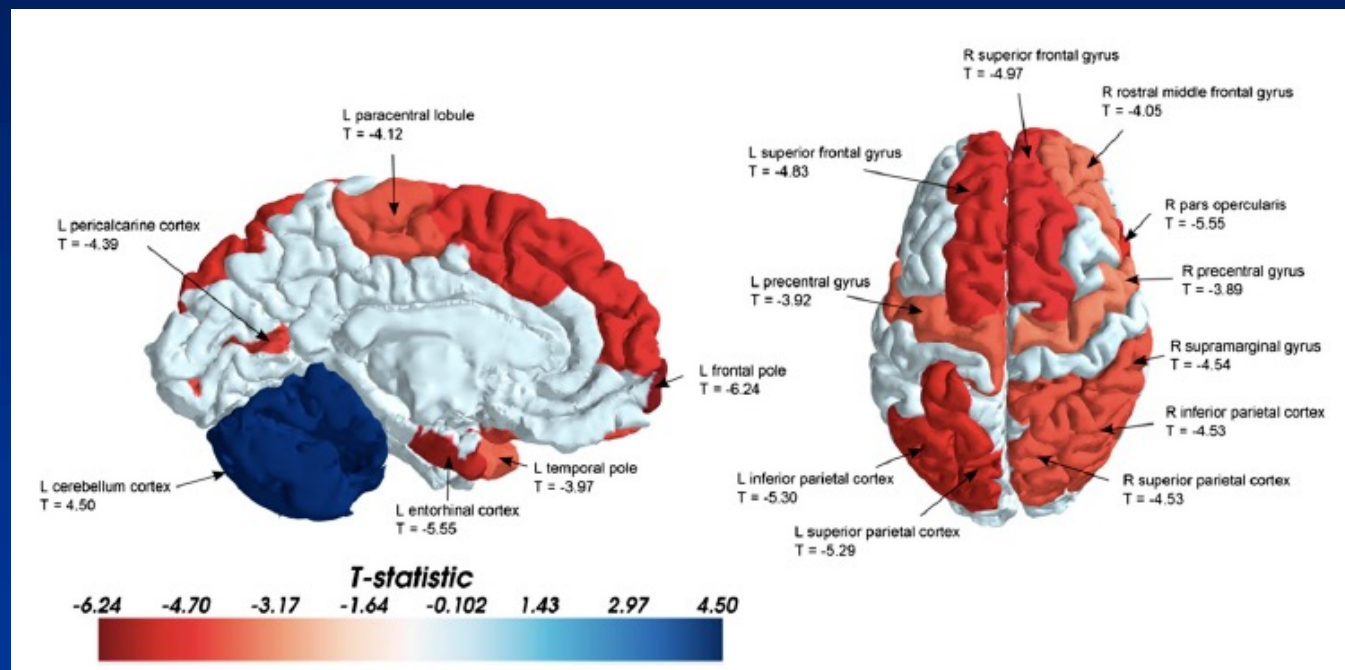
- 1. EMCDDA (European Monitoring Centre for Drugs and Drug Addiction) (2016a). European drug report 2016: trends and developments. Publications Office of the European Union, Luxembourg. 2. EMCDDA (European Monitoring Centre for Drugs and Drug Addiction) (2016b). Statistical bulletin 2016 (data tables). Available at: <http://www.emcdda.europa.eu/data/stats2016> [accessed Feb 2020]

# Sex differences in the structural connectome of the human brain

Madhura Ingalhalikar<sup>a,1</sup>, Alex Smith<sup>a,1</sup>, Drew Parker<sup>a</sup>, Theodore D. Satterthwaite<sup>b</sup>, Mark A. Elliott<sup>c</sup>, Kosha Ruparel<sup>b</sup>, Hakon Hakonarson<sup>d</sup>, Raquel E. Gur<sup>b</sup>, Ruben C. Gur<sup>b</sup>, and Ragini Verma<sup>a,2</sup>

<sup>a</sup>Section of Biomedical Image Analysis and <sup>c</sup>Center for Magnetic Resonance and Optical Imaging, Department of Radiology, and <sup>b</sup>Department of Neuropsychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA 19104; and <sup>d</sup>Center for Applied Genomics, Children's Hospital of Philadelphia, Philadelphia, PA 19104

Edited by Charles Gross, Princeton University, Princeton, NJ, and approved November 1, 2013 (received for review September 9, 2013)



# Gender - specific differences (aside biology)

- *Awareness of health* (nutrition, risk behaviour, physical activity, prevention medical check up, ...)
- *Perception* and willingness to accept the occurrence 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 con`t)

- **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

# Men & Women are different

In addition also

➤ cultural background, *ethnicity* and ***economics*** play a major role in addition

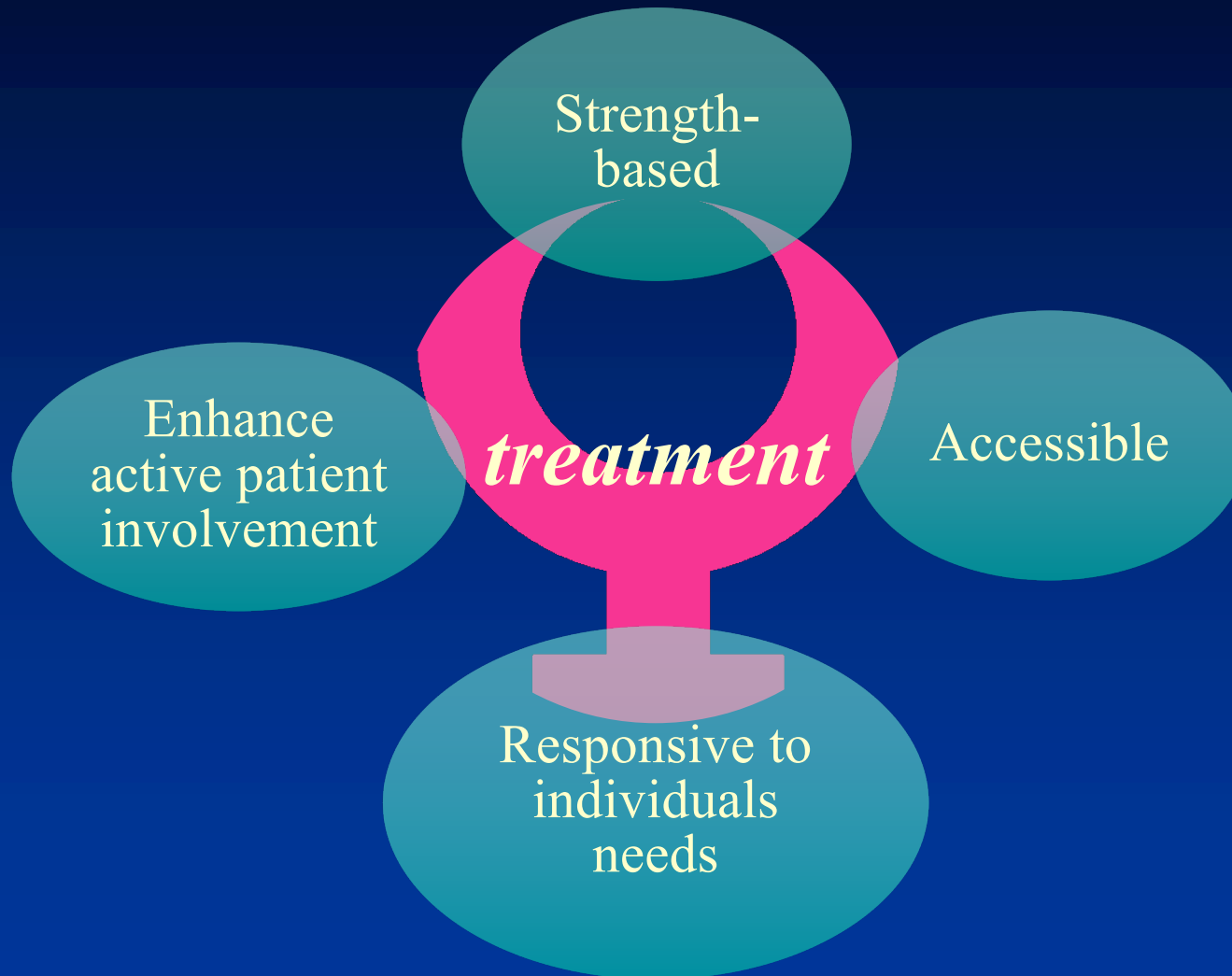
➤ to higher stigma in ♀



In the spectrum of medical diseases *women* do have a higher retention rate in all disorders, ***but not in substance use disorder*** - related to limited access to treatment.



# ♀ centered treatment should be...



# Overview - Guiding principles for gender responsive treatment

## **BOX 14**

### GUIDING PRINCIPLES FOR GENDER-RESPONSIVE TREATMENT

**Gender:** Acknowledge that gender makes a difference.

**Environment:** Create an environment based on safety, respect and dignity.

**Relationships:** Develop policies, practices and programmes that are relational and promote healthy connections to children, family, significant others and the community.

**Services:** Address the issues of substance abuse, trauma and mental health through comprehensive, integrated, culturally relevant services.

**Economic and social status:** Provide women with opportunities to improve their socio-economic conditions.

**Community:** Establish a system of community care with comprehensive, collaborative services [5].

*United Nations Office on Drugs and Crime* - Substance abuse treatment and care for women: Case studies and lessons learned. 2004.

# Gender/sex differences in addiction – substance use disorder

- prevalence/incidence
- age of onset
- **treatment access**
- **comorbidity**
- consumption patterns
- metabolism
- secondary damage
- mortality
- abstinence behaviour



# Gender-differences in drug-abuse

- Men 2-3 times more likely drug abuse/dependence disorder; 4 times more often alcohol use disorder
- Different biological response to drugs
- Disease progression
- Vulnerability: more rapid organ damage, e.g. brain atrophy, or heart, muscle, liver damage in women - e.g. telescoping
- Socio-economical disadvantages for women
- Pattern of consumption with alcohol/nicotine different: women lower levels, less binge, shorter periods of abstinence
- Negative stigma associated with drug abuse and child custody issues in women
- Different access to treatment for substance abuse (women more often in mental health facilities)

(Lynch et al., 2002)

[www.nature.com/nature](http://www.nature.com/nature)

Vol 465 | Issue no. 7299 | 10 June 2010

## **Putting gender on the agenda**

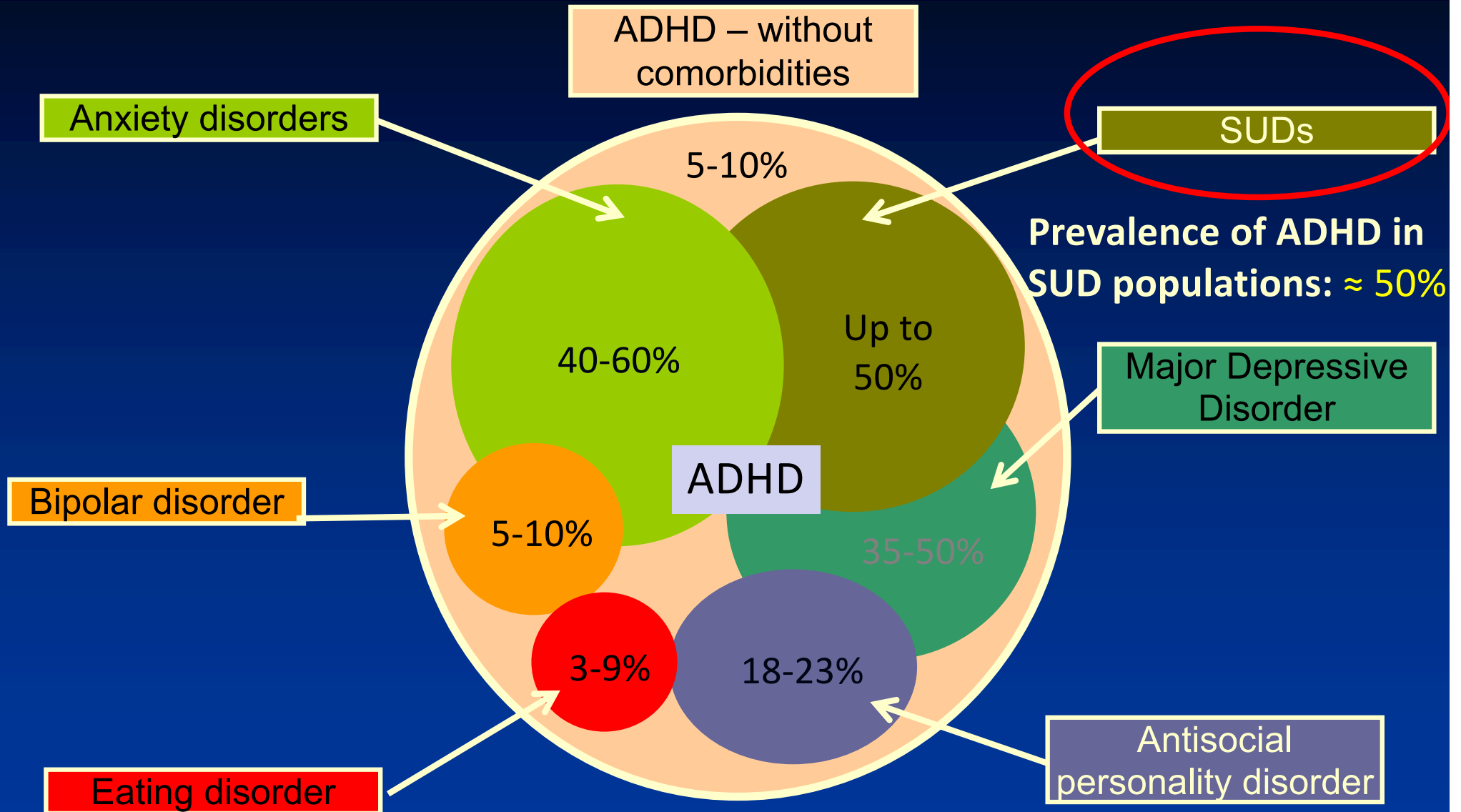
(Editorial)

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

# Example

- Co – morbidity: ADHD



# Psychiatric co-morbidities of ADHD



Sobanski, E. (2006). *European Archives of Psychiatry and Clinical Neuroscience*, 256 (1), 26-31.; van Emmerik-van Oortmerssen, et al. (2012). *Drug and alcohol dependence*, 122 (1), 11-19;

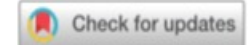
# ADHD & criminality: Role of pharmacologic treatment

Pharmacological treatment of ADHD has the potential to reduce criminality <sup>1</sup>:

- Reduction of crime rates for  : 32%  
 : 41%
- During periods with pharmacological treatment of ADHD in former prisoners (drugs used for ADHD treatment according to the prescribed drug register; stimulants and non-stimulants).
  - Reduction of all types of delicts.
  - No prove of long-term effects after the end of treatment.

<sup>1</sup>Lichtenstein et al. (2012).*NEJM*, 367:2006-14.





## Comorbidity Patterns Among Patients With Opioid Use Disorder and Problem Gambling: ADHD Status Predicts Class Membership

Marisa Silbernagl<sup>a</sup>, Takuya Yanagida<sup>b</sup>, Rudolf Slamanig<sup>c</sup>, Gabriele Fischer<sup>a</sup>, and Laura Brandt<sup>b</sup>

<sup>a</sup>Center for Public Health, Medical University of Vienna, Vienna, Austria; <sup>b</sup>Department for Applied Psychology: Work Education and Economy, University of Vienna, Vienna, Austria; <sup>c</sup>Department of Psychiatry and Psychotherapy, Medical University of Vienna, Vienna, Austria

Silbernagl, M., Yanagida, T., Slamanig, R., Fischer, G., & Brandt, L. (2019). Comorbidity patterns among patients with opioid use disorder and problem gambling: ADHD status predicts class membership. *Journal of Dual Diagnosis*, 15(39): 147-158.

### 3 - class solution (predictors of class: sample, ADHD status)

- PrG patients were more likely members of the “most burdened class” (compared to OMT from the community or prisons)
- Inmates enrolled in OMT (prison and those recruited from the community) did not significantly differ concerning their probabilities of class membership
- **Adult ADHD** was the strongest predictor for class membership

**Individuals with adult ADHD had 10 times higher odds of being a member of the “most burdened class”**

# Example

- Preventive medicine: NAS - costs

# Abused Prescription Opioids

**Fentanyl**

**Tramadol**

**Codeine**



**Hydromorphone  
(Dilaudid<sup>®</sup>,  
Palladone<sup>®</sup>)**

**Oxycodone (OxyContin<sup>®</sup>)**

**Aspirin & Oxycodone  
(Percodan<sup>®</sup>)**

# Publications - Opioid crisis

LETTERS TO THE EDITOR

World Psychiatry 18:2 - June 2019

## Addressing the opioid crisis globally

Nora D. Volkow<sup>1</sup>, María Elena Medina-Mora Icaza<sup>2</sup>, Vladimir Poznyak<sup>3</sup>,  
Shekhar Saxena<sup>3</sup>, Gilberto Gerra<sup>4</sup>, and the UNODC-WHO Informal  
Scientific Network

<sup>1</sup>National Institute on Drug Abuse, National Institutes of Health, Bethesda, MD, USA; <sup>2</sup>National Institute of Psychiatry Ramón de la Fuente, Mexico City, Mexico; <sup>3</sup>Department of Mental Health and Substance Abuse, World Health Organization, Geneva, Switzerland; <sup>4</sup>Drug Prevention and Health Branch, United Nations Office on Drugs and Crime, Vienna, Austria

# TIME

They're the most  
**powerful  
painkillers**  
ever invented.

And they're creating  
the worst addiction  
crisis America  
has ever seen.

By Massimo Calabresi



## FIGHTING A HIDDEN HEALTH CRISIS

*Tennessee leads the way  
in treating Neonatal  
Abstinence Syndrome*





# What & How are we measuring NAS related to opioid exposure ?



- Many publications are retrospectively - no information about the medication & substance abuse during pregnancy
  - NAS reports „related“ to methadone ? - This doesn't seem to be justified
  - The only good references are prospectively controlled evidence plus consideration of nicotine consumption & other concomitant use
  - Are preterm deliveries separately investigated from term deliveries ?
  - Many „Finnegan“ versions + different medications applied
  - Do publications differentiate between breastfeeding & bottle nursing ?
- Do we have any information about pharmacodynamics & pharmacokinetics of medication in neonates ? Increased pharmacogenomic evidence

# Association of *OPRM1* and *COMT* Single-Nucleotide Polymorphisms With Hospital Length of Stay and Treatment of Neonatal Abstinence Syndrome

Elisha M. Wachman, MD

Marie J. Hayes, PhD

Mark S. Brown, MD, MSPH

Jonathan Paul, PhD

Karen Harvey-Wilkes, MD

Norma Terrin, PhD

Gordon S. Huggins, MD

Jacob V. Aranda, MD, PhD

Jonathan M. Davis, MD

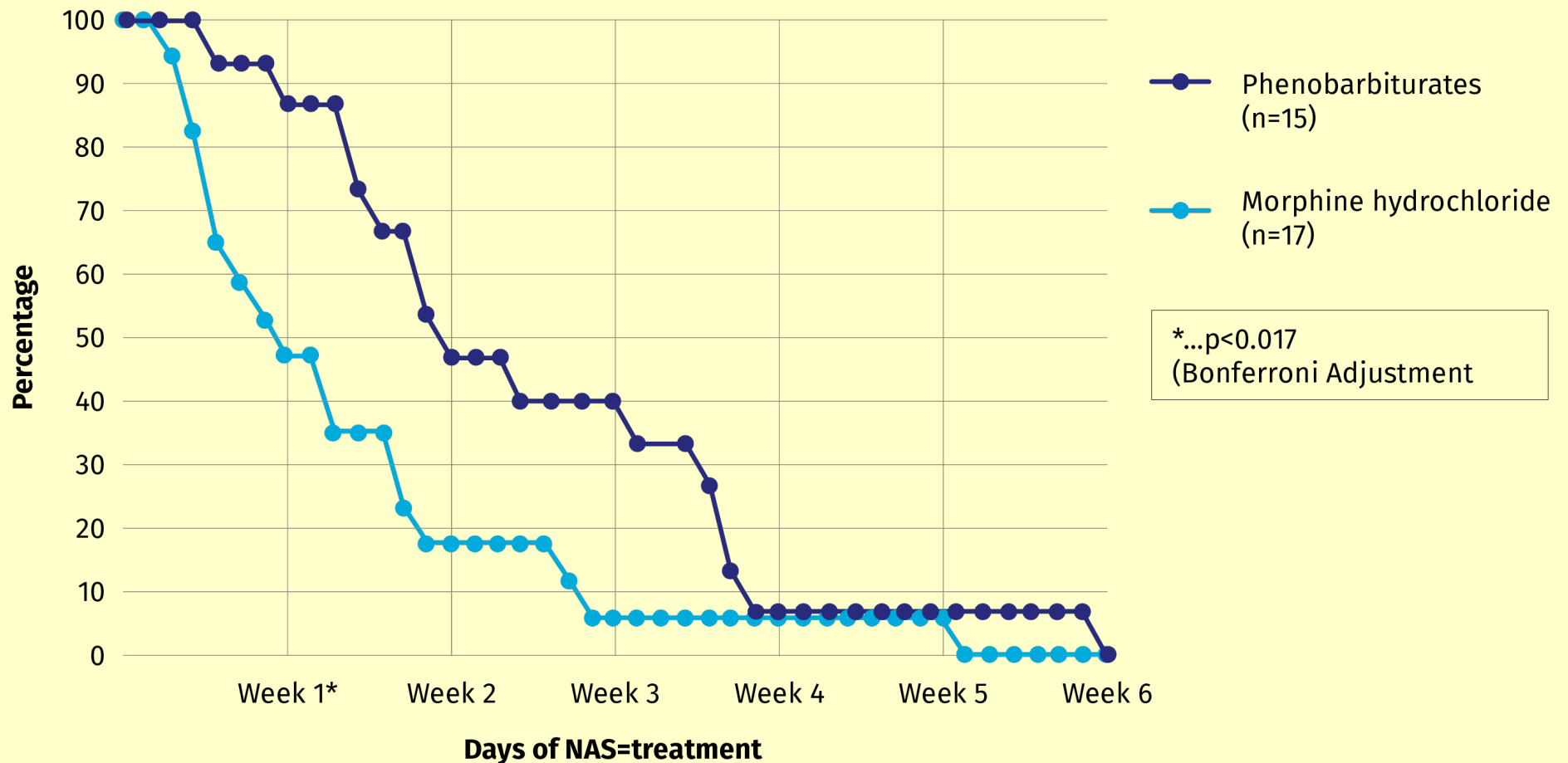
**Importance** Neonatal abstinence syndrome (NAS) caused by in utero opioid exposure is a growing problem; genetic factors influencing the incidence and severity have not been previously examined. Single-nucleotide polymorphisms (SNPs) in the  $\mu$ -opioid receptor (*OPRM1*), multidrug resistance (*ABCB1*), and catechol-o-methyltransferase (*COMT*) genes are associated with risk for opioid addiction in adults.

**Objective** To determine whether SNPs in the *OPRM1*, *ABCB1*, and *COMT* genes are associated with length of hospital stay and the need for treatment of NAS.

**Design, Setting, and Participants** Prospective multicenter cohort study conducted at 5 tertiary care centers and community hospitals in Massachusetts and Maine between July 2011 and July 2012. DNA samples were genotyped for SNPs, and then NAS outcomes were correlated with genotype. Eighty-six of 140 eligible



# NAS treatment: morphine compared to phenobarbiturates





Original Investigation | Pediatrics

# Prenatal Risk Factors and Perinatal and Postnatal Outcomes Associated With Maternal Opioid Exposure in an Urban, Low-Income, Multiethnic US Population

Romuladus E. Azuine, DrPH, MPH, RN; Yuelong Ji, PhD; Hsing-Yuan Chang, MD, MPH; Yoona Kim, MPH; Hongkai Ji, PhD; Jessica DiBari, PhD; Xiumei Hong, MD, PhD; Guoying Wang, MD, PhD; Gopal K. Singh, PhD; Colleen Pearson, BA; Barry Zuckerman, MD; Pamela J. Surkan, ScD; Xiaobin Wang, MD, MPH, ScD

## Sample:

**8509 Boston Birth Cohort mother-newborn pairs for prenatal and perinatal analyses**

- Overall, 454 of the 8509 children (5.3%) had in utero opioid exposure.

## **At birth, opioid exposure was associated**

- with higher risks of fetal growth restriction (odds ratio [OR], 1.87; 95%CI, 1.41-2.47)
- Preterm birth (OR, 1.49; 95%CI, 1.19-1.86)



Original Investigation | Pediatrics

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## Sample: cont`d

### Opioid exposure was associated with

- increased risks of lack of expected physiological development (OR, 1.80; 95%CI, 1.17-2.79)
- conduct disorder/emotional disturbance (OR, 2.13; 95%CI, 1.20-3.77) among preschool-aged children.

### In school-aged children, opioid exposure was associated with

- a higher risk of attention-deficit/hyperactivity disorder (OR, 2.55; 95%CI, 1.42-4.57)

## Costs of preterm deliveries in UK in €/ infant

	Preterm delivery ( < 37 weeks)	Early preterm delivery ( < 33 weeks)	Very early preterm delivery ( < 28 weeks)
Prevalence of live births	7.17	1.71	0.48
Costs for delivery	443,-	974,-	2.425,-
Costs for neonatal care	28.993,-	79.447,-	116.230,-
Costs for inpatient treatment until age of 18 yrs	29.762,-	81.152,-	120.495,-
Costs for outpatient treatment until age of 18 yrs	761,-	1.104,-	2.187,-
Costs for medical and social care until age of 18 yrs	30.775,-	83.015,-	124.913,-
<b>TOTAL</b>	<b>90.734,-</b>	<b>245.692,-</b>	<b>466.250,-</b>



# Health system costs of Fetal Alcohol Syndrome (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

\*\*Oppositional Defiant Disorder

# Example

- Prison





# Health issues in prison

Most relevant health problems in jail (according WHO):

- Infections diseases , **Addiction** and teeth related problems

	Men	Women
Psychotic illness <sup>1</sup>	4% (3-4)	4% (3-5)
Major depression <sup>1</sup>	10% (9-12)	14% (10-18)
Alcohol misuse <sup>2</sup>	18-30%	10-24%
Drug misuse <sup>2</sup>	10-48%	30-60%

Data are % (95% CI) or %.

**Table 1: Prevalence of different psychiatric diagnoses in adult prisoners based on systematic reviews**

**TABLE 2—Percentage of Inmates Reporting Chronic Medical Conditions, Psychiatric Disorders, Substance Abuse, or Substance Dependence, by Gender: Survey of Inmates in Local Jails, 2002**

	Men, Weighted %	Women, Weighted %	P
<b>Medical condition</b>			
Cancer	1.1	8.3	<.001
Diabetes	3.2	6.5	<.001
Hypertension	17.3	21.9	<.001
Heart problem	8.6	11.4	.002
Asthma	13.9	24.4	<.001
Arthritis	12.7	20.2	<.001
Hepatitis	4.9	9.6	<.001
Cirrhosis	1.2	2.1	.006
Any medical condition	40.0	56.8	<.001
<b>Psychiatric disorder</b>			
Depressive	17.4	35.5	<.001
Bipolar	8.7	20.7	<.001
Psychotic	4.4	6.0	.013
Posttraumatic stress	4.4	11.3	<.001
Other anxiety	6.1	18.5	<.001
Personality	4.7	8.7	<.001
Any psychiatric	21.6	43.6	<.001
<b>Drug-use disorder</b>			
Drug abuse	18.2	13.6	<.001
Drug dependence	34.5	45.7	<.001
Drug abuse or dependence	52.7	59.3	<.001
<b>Alcohol-use disorder</b>			
Alcohol abuse	24.6	18.0	<.001
Alcohol dependence	23.3	18.9	<.001
Alcohol abuse or dependence	47.9	36.9	<.001
History of injection drug use	17.1	24.4	<.001

## Gender Differences in Chronic Medical, Psychiatric, and Substance-Dependence Disorders Among Jail Inmates

Ingrid A. Binswanger et al. 2010  
American Journal  
of Public Health

### Investigation on 6982 inmates in the USA

Inmates are of higher risk for somatic & psychiatric diseases  
→ this is especially relevant for female inmates



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Contents lists available at ScienceDirect

## Drug and Alcohol Dependence

journal homepage: [www.elsevier.com/locate/drugalcdep](http://www.elsevier.com/locate/drugalcdep)

### Incarceration exposure and prescription opioid use during pregnancy

Alexander Testa<sup>a,\*</sup>, Chantal Fahmy<sup>b</sup>, Dylan B. Jackson<sup>c</sup>

<sup>a</sup> Department of Management, Policy & Community Health, University of Texas at Health Science Center at Houston, USA

<sup>b</sup> Department of Criminology & Criminal Justice, University of Texas at San Antonio, USA

<sup>c</sup> Johns Hopkins Bloomberg School of Public Health, Johns Hopkins University, USA

#### ARTICLE INFO

**Keywords:**

Incarceration

Opioids

Pregnancy

Women's health

Substance use

#### ABSTRACT

**Background:** Prior research demonstrates a high prevalence of substance use, including cocaine and alcohol, among individuals who have had personal or vicarious contact with the correctional system. Relatedly, although there is evidence of increased opioid use in general, opioid use during pregnancy is becoming a growing public health concern. However, little is known for prescription opioid use during pregnancy remain understudied. This study is the first to examine the relationship between a women's personal or vicarious exposure to incarceration in the 12 months prior to pregnancy and prenatal opioid use.

# Risk of substance-related death after imprisonment in England u. Wales

(Farrell & Marsden, *Addiction* 103:251-255, 2007)

■ Opioids: included in 95% of substance-related deaths

Substance	Percentage of deaths
Opioids	95% (primarily <2 weeks after release)
Heroin	66% (primarily in males)
Cocaine	21%
Benzodiazepines	20%
Antidepressants (trizycl.)	10% (primarily females)

# Acute risk of drug-related death among newly released prisoners in England and Wales

(Farrell & Marsden, *Addiction* 103:251-255, 2007)

## Methods:

Database linkage study. National sample of N = 48,771 released female and male prisoners in England and Wales in 1998-2000.

All causes*	substance-related causes	substance-related among Women	substance-related among Men
442	59%	73%	55%

\*within 1 year after release

# Acute risk of drug-related death among newly released prisoners in England and Wales

(Farrell & Marsden, *Addiction* 103:251-255, 2007)

## ■ Mortality ratio among released prisoners vs. general population

Mortality ratio	♀	♂
1 week after release	69 times higher	29 times higher

### Risk reduction through:

- Psychoeducation
- Opioid maintenance therapy
- Initiated referral to local treatment centers after release

# LIFE IS A RACE BETWEEN EDUCATION AND DISASTER

H.G. Wells - 1904



Drugs of Abuse Engage Systems in the *Motivation and Pleasure Pathways of the Brain*



**Thank you for your  
attention!**