VOLKSANWALTSCHAFT

MEDICAL UNIVERSITY OF VIENNA

Chair: OPCAT Commission 3 Austrian Ombudsmen Board - NPM: National Prevention Mechanism

Substance dependent women and pregnancy - Research & policy under the human right´s mandate

APSAD – Melbourne 2017

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COI relevant for topic

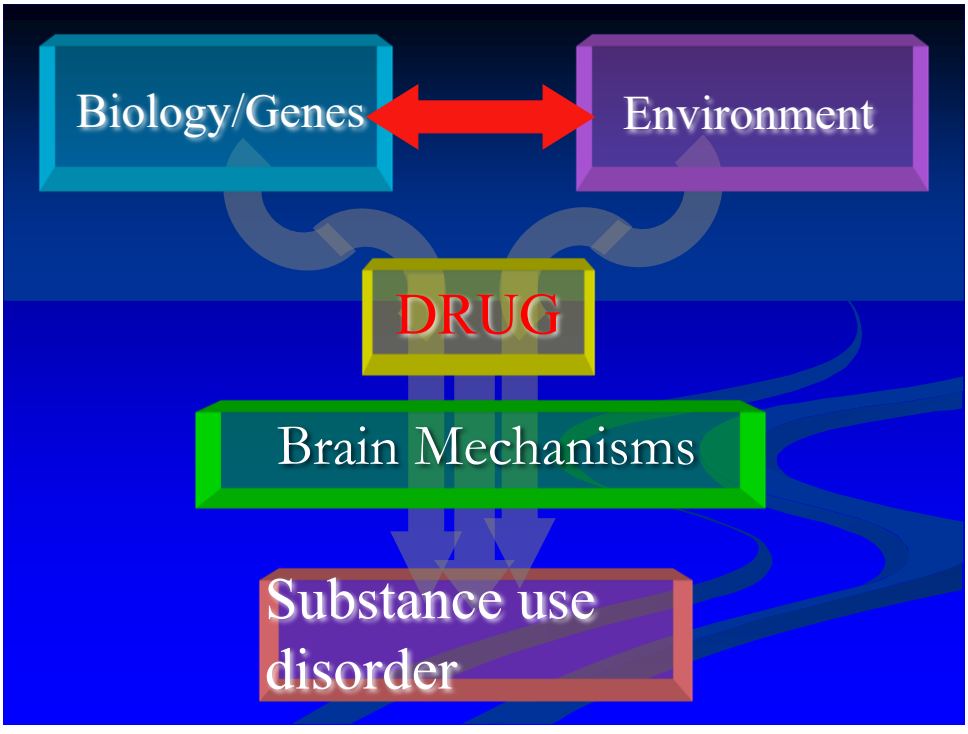
I have received travel support & financial fees for lectures & expert meetings related to that topic in the past years

- Astra Zenica
- MSD, Abbvie, Gilead
- Indivior
- GL Pharma
- Mundipharma/Nepp;
- Reckitt Benckiser/Schering Plough

- Consultancy activities with UNODC, WHO, European Parlament
- Member of Scientific Committee of EMCDDA


How does addiction influence the outcome of pregnancy?


Addiction
Medical
NEUROTOXICITY
OBESITY
AIDS
CANCER
MENTAL ILLNESS
DRUGS
Economic
HEALTH CARE COSTS
PRODUCTIVITY LOSS
ACCIDENTS
Social
HOMELESSNESS
CRIME
VIOLENCE

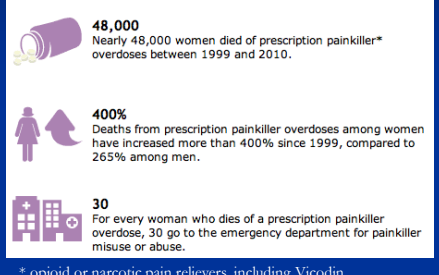


Heritability of psychiatric disorders

Autismus	80 - 93 %
Bipolare affektive disorder	60 - 93 %
ADHS	***60 - 90 %***
Nicotine dependence	***67 %***
Schizophrenia	60 - 85 %
Tourette Syndrome	57 %
Dementia (M. Alzheimer)	50 - 70 %
Eating disorder (Anorexia/ bulimia nerv.)	45 - 60 %
Substance dependence	**40 - 60 %**
Recurrent depressive disorder	M 29 & F 42%
Obsessive compulsive disorder	30 – 70 %
Panic disorder	30 – 50 %

Davis L et al. PLOS Genetics 9, October 2013, e1003864; Nurnberger J WCPG 2013, Boston; Craddock N et al. (2013) Lancet 381:1654; Cross-Disorder Group of PGC (2013) Nature Genetics 45:984; Schwab S et al. (2013) Eur Arch Psychiatry Clin Neurosci 263 (Suppl 2):S147; Sullivan PF et al. (2012) Nature Rev Genetics 13:537; Costain G et al. (2012) The Application of Clin Genetics 5:1; Burmeister M et al. (2008) Nature Reviews Genetics 9:527

Prescription painkiller overdoses
- A growing epidemic, especially among women (US)



* opioid or narcotic pain relievers, including Vicodin (hydrocodone), OxyContin (oxycodone), Opana (oxymorphone), and methadone

- 18 ♀ die every day of a prescription painkiller overdose in the US (>6,600 deaths in 2010)

→ under-recognized and growing problem for ♀

→ ♂ are still more likely to die of prescription painkiller overdoses (>10,000 deaths in 2010)

→ But gap is closing

- **Deaths from prescription painkiller overdose have risen more sharply among ♀ than among ♂**
- **Since 1999:** > 400% increase in deaths among ♀ compared to 265% in ♂

Centers for Disease Control and Prevention (2013): http://www.cdc.gov/vitalsigns/PrescriptionPainkillerOverdoses/

Abused Prescription Opioids

Fentanyl

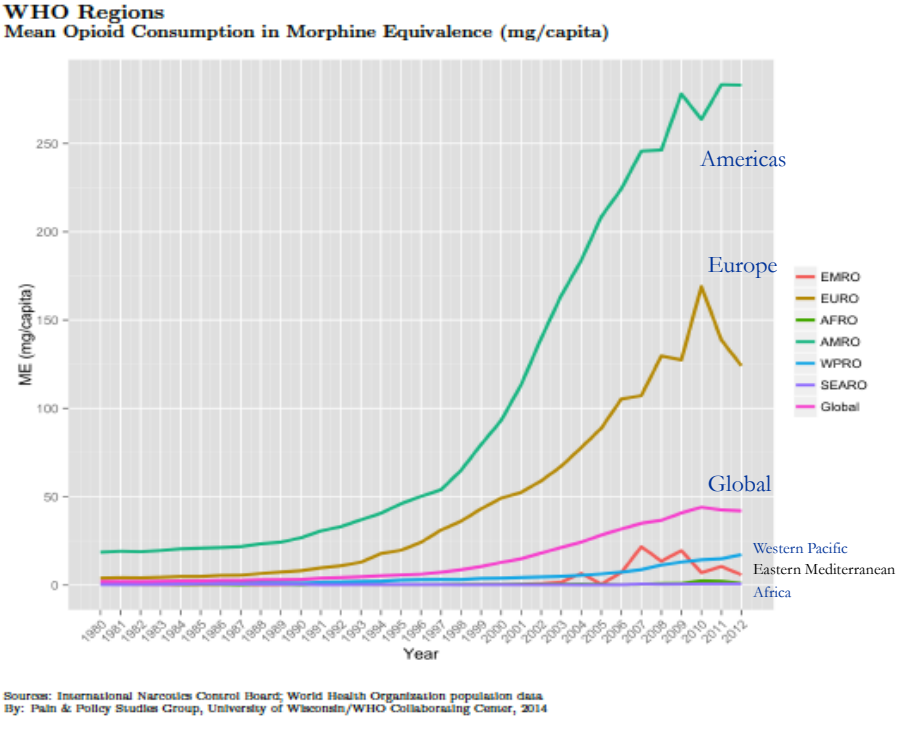
Tramadol

Hydromorphone (Dilaudid^{R}, Palladone^{R})

Codeine

Oxycodone (OxyContin^{R})

Aspirin & Oxycodone (Percodan^{R})

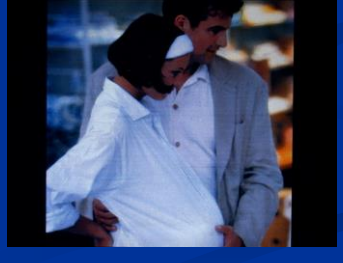


Black Market in Vienna 1949

POLICE INVESTIGATOR: "…Stage three was when the organizers decided that the profits were not large enough.

Penicillin would not always be impossible to obtain legitimately; they wanted more money and quicker money while the going was good. They began to dilute…… ***A number of children*** simply died, and a number went off their heads. You can see them now in the mental ward…"

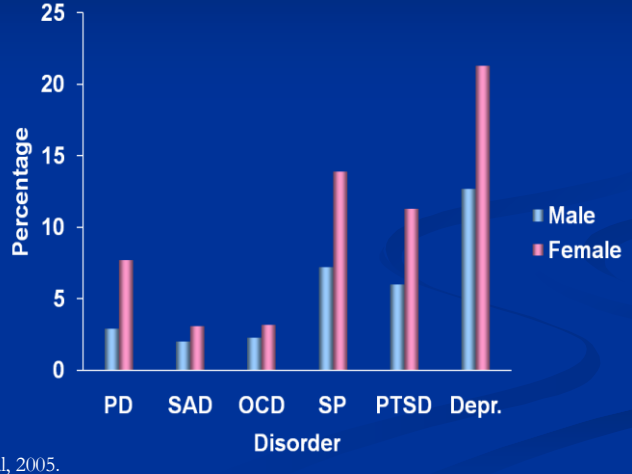
Pregnancy in a vulnerable population



The great gender equalizer

The Tourist ....

Sex and mood disorders: prevalence



Wittchen et al, 2005.

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.

- Pregnant women get ill, and sick women get pregnant...
  - Optimal: no need for medication
- 50% unplanned pregnancies in the general poplulation…

Results: Prevalence of psychiatric symptoms (n=174)

Psychiatric Symptoms	In %
One or more psychiatric diagnosis	65
Major Depression (MDD)	32
Dysthymia	31
Hypomanic episode	39
Anxiety disorders	
- Generalized anxiety disorder (GAD)	40
- Panic disorder	26
- Agoraphobia	22
Social Phobia	16
Post-traumatic Stress Disorder (PTSP)	16
Obsessive–compulsive disorder (OCD)	3
Bulimia	<1

Symtoms at some point in the past 30 days	in %
Mood symptoms	49
Anxiety symptoms	40
Suicial thinking	13

Benningfield, M.M., Arria, A.M., Kaltenbach, K., Heil, S.H., Stine, S.M., Coyle, M.G., Fischer, G., Jones, H.E., Martin, P.R. Co-occurring Psychiatric Symptoms are Associated with Increased Psychological, Social & Medical Impairment in Opioid Dependent Pregnant Women. AM J Addict, 2010, 19(5): 416-421.

Convention on the Rights of Persons with Disabilities (Art 1 CRPD)

Persons with disabilities **include** those who have long-term physical, mental*, intellectual or sensory impairments which in interaction with **various barriers** may hinder their full and effective participation in society on an equal basis with others.

**This includes of course: substance use disorder*
= chronic relapsing psychiatric disorder

The Human Right for a reproductive Health

Substance Abuse

ISSN: 0889-7077 (Print) 1547-0164 (Online) Journal homepage: http://www.tandfonline.com/loi/wsub20

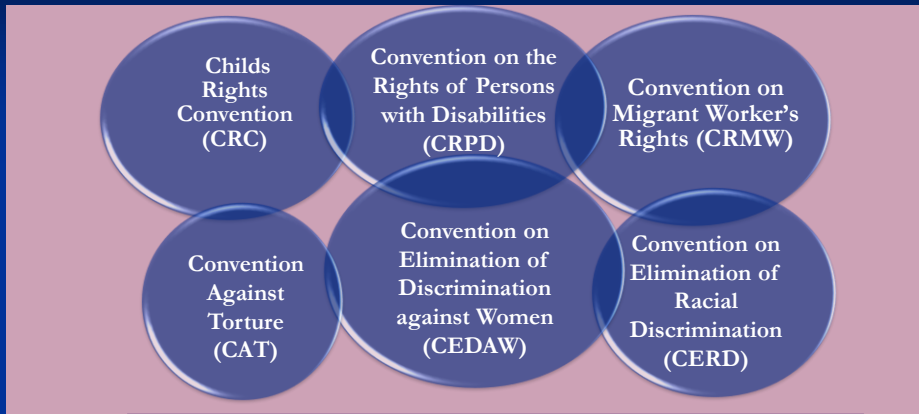
Monitoring Neonatal Abstinence Syndrome in buprenorphine-exposed IVF twins: A case study

Laura Brandt PhD, Patrick Swoboda MD, Gabriele Fischer MD & Annemarie Unger MD

To cite this article: Laura Brandt PhD, Patrick Swoboda MD, Gabriele Fischer MD & Annemarie Unger MD (2016): Monitoring Neonatal Abstinence Syndrome in buprenorphine-exposed IVF twins: A case study, Substance Abuse, DOI: 10.1080/08897077.2016.1184738

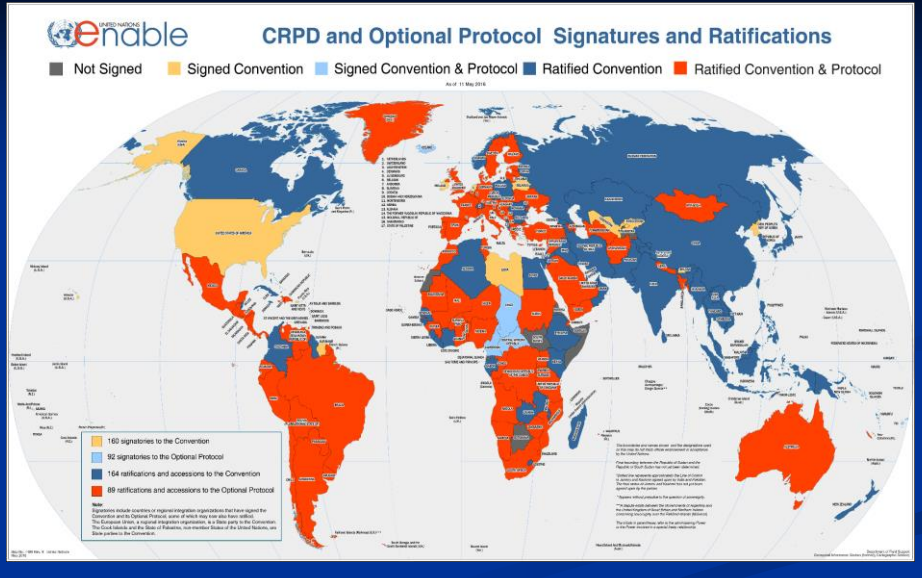
The rights of women "include their right to have control over and decide freely and responsibly on matters related to their sexuality, including sexual and reproductive health, free of coercion, discrimination and violence.
http://www.ohchr.org/Documents/Issues/Women/WRGS/SexualHealth/INFO_Contra_Fam Plan_WEB.pdf

Human Rights Treaties - UN Principles



"Bill of Rights"

- Covenant on Economic & Social & Cultural Rights (CESCR)
- Covenant on Civil & Political Rights (CCPR)
- Universal Declaration of Human Rights (UDHR)



Convention on the Rights of Persons with Disabilities (CRPD)

Quelle: United Nations. Abgerufen von https://www.un.org/development/desa/disabilities/convention-on-the-rights-of-persons-with-disabilities.html am 13.3.2017 um 18:00.

Pregnant women with substance use disorder
Ethical & legal guidelines

The ethical principle of respect for persons makes the woman the autonomous decision maker for herself and her fetus.

A pregnant woman and her fetus ought to be thought of as a unit or dyad.

Intervention strategies during pregnancy ought to benefit both the woman and the fetus.

Treatment Improvement Protocol (TIP) Series, No. 5. Center for Substance Abuse Treatment. Rockville (MD): Substance Abuse and Mental Health Services Administration (US): 1993.

Convention on the Elimination of All Forms of Discrimination Against Women
(Right to Health – Article 12 CEDAW)

- States Parties shall take all appropriate measures to eliminate discrimination against women in the field of health care in order to ensure, on a basis of equality of men and women, access to health care services, including those related to family planning.
- (..) States Parties shall ensure to women appropriate services in connection with pregnancy, confinement and the post-natal period, granting free services where necessary, as well as adequate nutrition during pregnancy and lactation.

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Covenant on Economic, Social and Cultural Rights *(CESCR)*

Right to Health – Article 12 CESCR

1. The States Parties to the present Covenant recognize the right of everyone to the enjoyment of the ***highest attainable standard of physical and mental health.***

Benefits of Scientific Progress – Article 15 CESCR

The States Parties to the present Covenant recognize the right of everyone:

(b) *To enjoy the benefits of scientific progress and its applications* (eg: positive discrimination – women as more marginalized group should benefit early & comprehensively on new medical options)

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Obligation to ensure participation: Art 4/3 CRPD

In the development and implementation of legislation and policies to implement the present Convention and in other decision-making processes concerning issues relating to persons with disabilities, States Parties shall closely consult with and actively involve persons with disabilities, including children with disabilities, through their representative organizations.

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Liberty & Security of the Person Art (Art 14/1 CRPD)

States Parties shall ensure that persons with disabilities - on an equal basis with others:

(a) *Enjoy the right to liberty and security of person;*

(b) Are *not deprived of their liberty unlawfully or arbitrarily*,
and that any deprivation of liberty is in conformity with the law, and that the existence of a disability shall in no case justify a deprivation of liberty.

(This is only the first paragraph, the entire provision is too long for one slide).

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Best interest of the child (Art 3 Child Rights Convention)

1. Right
2. Legal principle
3. Procedural rule

Ad 1: *Must be determined on a case-by-case basis*

Ad 2: Resolve any conflicts **with other human rights treaties** (eg under consideration ESCR; CRPD..)

Ad 3: Attention must be paid to all solutions, which are in the child's best interests (eg full information & disclosure to parents, including information on diagnosis & course of treatment)

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Determination of the child's best interests:

Protection of the family has to be ensured (Right to Privacy, European Convention Human Rights-ECHR)

- *Support for parents to fulfill their parental responsibilities*
- *Economic reasons no justification for separation (Art 10 ESCR)*
- *Child's life and development have to be considered holistically*
- Future consequences of decision have to be taken into account
- *Decision making has to be fair & give due respect to parents' views*
- *Non-discrimination: eg regarding health-status, social origin, cultural background etc.*

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Human rights consideration in regard: opioid dependent/maintained pregnant women & neonates

In some countries/institutions women are **forced to withdraw** from **methadone/burprenorphine** during pregnancy:

- no scientific evidence in favour of forced withdrawal during pregnancy- contrary - "quasi-voluntary": increased risk of mortality & morbidity
- sometimes institutions follow even an extortive approach: women have to "show treatment motivation" to be entitled to care for their child

➢ *Practices against scientific evidence are not in line with the right of highest standard of care and the right of scientific progress ..*

  ➢ *"methadone/ buprenorphine maintenance" etc.*

➢ *See:* The States Parties to the present Covenant recognize the right of everyone (…) to enjoy the benefits of scientific progress and its applications (…)[1].

➢ Forced withdrawal during pregnancy could even lead to harm of the unborn child due to physical and psychological stress of the mother

[1] Article 15, International Covenant on Economic, Social and Cultural Rights

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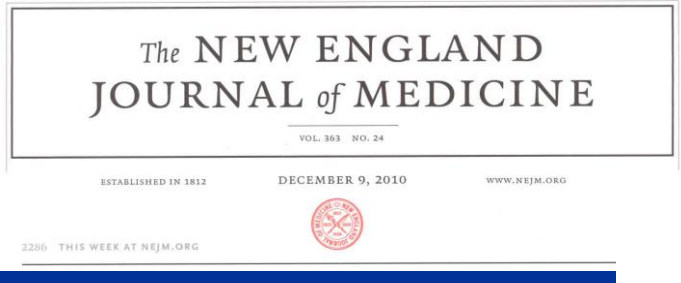
Gold Standard in research:
Double blind, double dummy prospective controlled

Copyright:
Rael Strauss



- 6 US Sites
  - leading site = Johns Hopkins
- 1 Canadian (Toronto)
- 1 European (Vienna)

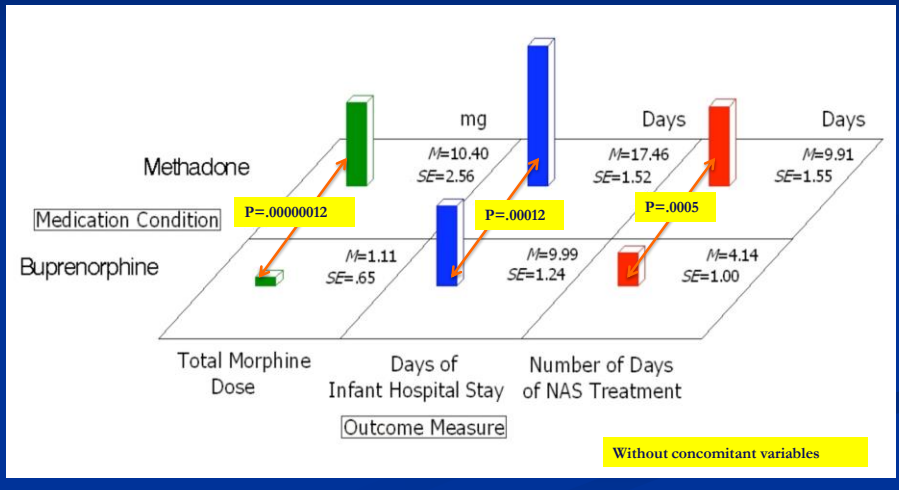
ORIGINAL ARTICLE

Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure

Hendrée E. Jones, Ph.D., Karol Kaltenbach, Ph.D., Sarah H. Heil, Ph.D., Susan M. Stine, M.D., Ph.D., Mara G. Coyle, M.D., Amelia M. Arria, Ph.D., Kevin E. O'Grady, Ph.D., Peter Selby, M.B., B.S., Peter R. Martin, M.D., and Gabriele Fischer, M.D.

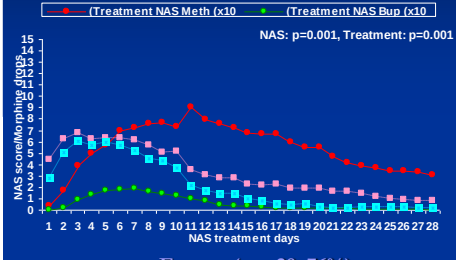
„ Mother Study“:
Maternal Opioid Treatment:
Human Experimental Research
R01 NHI DA018417-01

Total Morphine Dose, Days of Infant Hospital Stay, and Number of Days of NAS Treatment

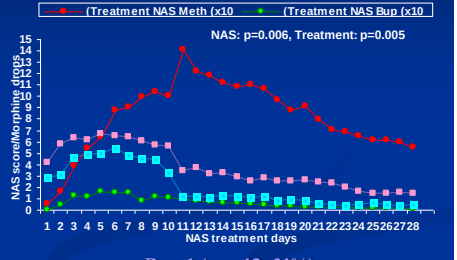


NAS

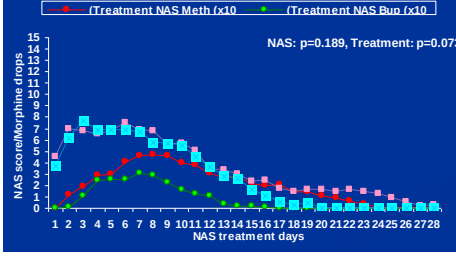
All Sites (n = 68; 52%)



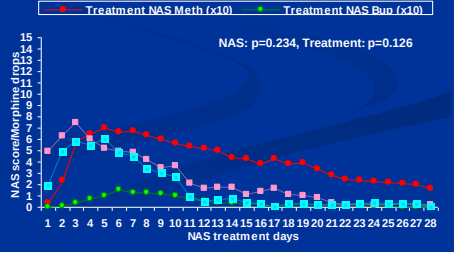
Urban (n = 28; 51%)

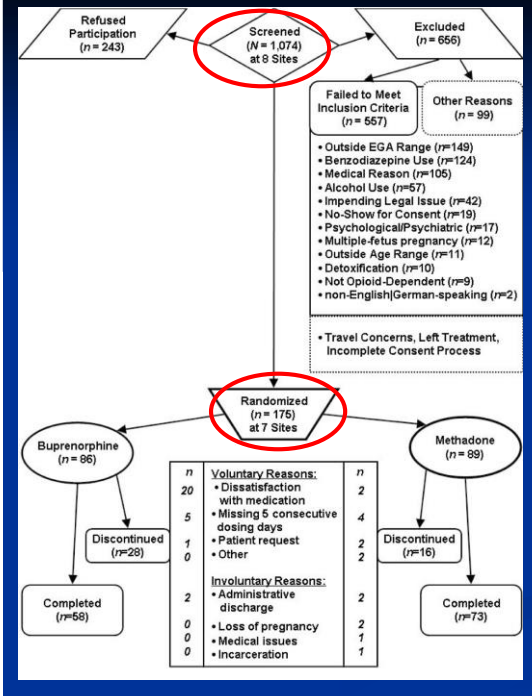


Europe (n = 28; 76%)



Rural (n = 12; 31%)





Population

Peripartum pain management i opioid dependent women

Following cesarean delivery opioid maintained women 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 A, Langer M, Jagsch R, Baewert A, Winklbaur B, Fischer G., Unger A.,: Peripartum pain management in opioid dependent women. European Journal of Pain 16 (4) (2012)

Human rights concerns - examples

During the *postpartal period*, some institutions do not inform mothers about medication and diagnostic procedures concerning their new born. This is seen critically, as the ***legal guardian has the right to full information*** about therapy and examinations concerning the child in order to give informed consent.

- Implementation of the right to health[1] must take into account all human rights principles, especially the guiding principles of the Convention, and must be shaped by evidence-based public health standards and best practices.[2]
- It is essential that supportive policies are in place and that children, parents and health workers have adequate rights-based guidance on consent, assent and confidentiality.[2]

[1] Article 24, Child Rights Convention
[2] General Comment 15, Child Rights Committee, Right to Health

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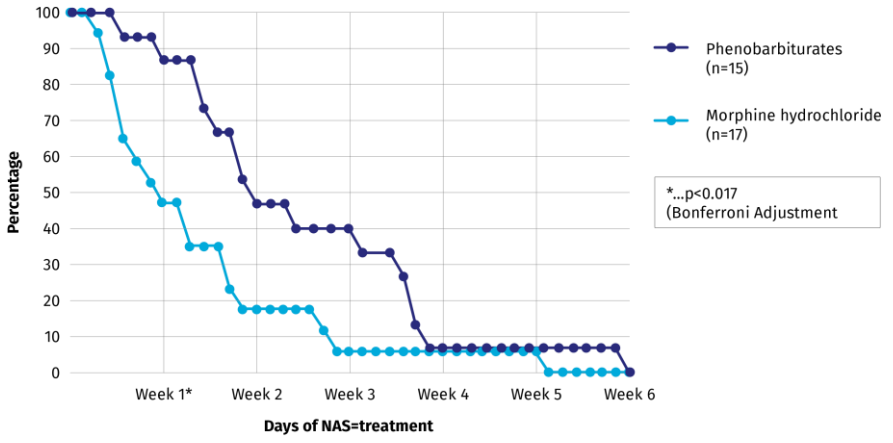
What & How are we measuring NAS related to opioid exposure ?

- Many publications are retrospectivley - 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 prospectivley controlled evidence plus consideration of nicotine consumption & other concomitant use
  - Are preterm deliveries seperatly 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

NAS treatment: morphine compared to phenobarbiturates



only opioid positive urinetoxicology last trimester of pregnancy

Elmer N., Rohrmeister K., Winklhaur B., Baewert A., Jagsch R., Peternell A., Thau K., Fischer G. Management of neonatal abstinence syndrome in neonates born to opioid maintained women. Drug & Alcohol Dependence 87 (2007) 131-138

Violation of Human rights: example

- In some, ***treatment of neonatal abstinence syndrome*** (NAS) is prolonged, which indicates a separation of long duration between the child and the mother (> 1 month), except visiting hours.

Scientific evidence reports mean treatment durations for NAS after intrauterine opioid exposure of around 10 days & only about 60% show treatable NAS[3]

- related to oral morphine application to neonates & administered rating; treatment duration differs between methadone/buprenorphine intrauterine exposure, also sign. influence of prepartal cigarette consumption[3]
- *Breastfeeding as a human right* [1,2]
- Sometimes breathing monitoring devices are used over a time period up to 6 months (in case of non-compliance mothers are threaten with abduction of the child)

- Act of discrimination, stigmatization & paternalism
- Maternal and new born care following delivery should ensure no unnecessary separation of the mother from her child[1]:The State Parties to the present Covenant recognize the right of everyone (…) to enjoy the benefits of scientific progress and its applications (…).[2]

[1] General Comment 15, Child Rights Committee, Right to Health
[2] Article 15, International Covenant on Economic, Social and Cultural Rightts; 3. Jones et al; Winklbauer et al; Tuten et al

JOGNN

REVIEW

Breastfeeding Promotion for Management of Neonatal Abstinence Syndrome

Ursula A. Pritham

JOGNN, 42, 517-526; 2013. DOI: 10.1111/1552-6909.12242

Pritham , U.A. (2013). Breastfeeding promotion for management of neonatal abstinence syndrome. JOGNN, 42: 517-526.

2. Safety of Methadone and Buprenorphine while breastfeeding

- Amount of *buprenorphine* or methadone level found in breast milk and passed to the neonate is considered to be small – regardless of maternal dose (f.e. see Lindemalm et al., 2009)
- Neonates exposed to in-utero methadone and who were breast feed were less likely to require treatment for NAS
  - They also had a shorter mean hospital stay of 9 days compared to those who were formula fed (Pritham et al., 2012)
- Breastfeeding is associated with a decreased rate of treatment for methadone or buprenorphine withdrawal
  - Breast feeding may be a protective factor for neonates withdrawing from opioids (Brown et al., 2011)

Safety of breastfeeding for women is emphasized by the American college of Obstetricians and Gynecologists (ACOG) as long as no contraindication exists (see next slide)

Pritham , U.A. (2013). Breastfeeding promotion for management of neonatal abstinence syndrome. JOGNN, 42: 517-526.

2. Safety of Methadone and Buprenorphine while breastfeeding

- Many mothers suffer from feelings of guilt due to their neonates in utero exposures and resulting NAS (Bogen et al., 2011)
  - breastfeeding allows the mother to take an active role in the management of NAS
  - Promotes maternal/infant bonding
  - Provides newborns with passive immunity (Riordan & Wambach, 2010)
- Although these benefits, breastfeeding rates are generally low among opioid-dependent women (Wachman et al., 2010)
- Also more than 50% of women who initiate breastfeeding stop within one week (Wachman et al., 2010)

To increase breastfeeding rates, **early and established education** on the established benefits of breastfeeding is required

Pritham , U.A. (2013). Breastfeeding promotion for management of neonatal abstinence syndrome. JOGNN, 42: 517-526.

3. Rooming in

- Rooming-in allows more maternal/newborn contact and leads ***to a significant decrease*** in the need for treatment for NAS (and a reduced length of hospital stays)
- Neonates with severe NAS may be separated from the mothers and transferred to a NICU, which presents barriers to successful breastfeeding (Rivera et al., 2008)
- If transference to a NICU is not necessary → creating an environment for safe bed sharing – also known as **bed-in rooming** is recommended to promote breastfeeding (Smith, 2013)
- If feeding does not work as expected it might have been due to the neonates ability to latch
  - When this occurs, skin-to skin holding of the infant is recommended (Riordan & Wambach, 2010)

Pritham , U.A. (2013). Breastfeeding promotion for management of neonatal abstinence syndrome. JOGNN, 42: 517-526.

Conclusion

- Opioid depended mothers should be **reassured and educated** about the **benefits of breastfeeding** for maternal and infant health
  - Breastfeeding has been associated with an increased need for NAS treatment and promotes infants attachment and bonding
  - Length of hospital stays is shortened if a mother selected breastfeeding over formula feeding

Further research is needed concerning :

- Potential differences between neonates with NAS who were breastfed and those who where fed pumped breast milk
- Safety of breastfeeding while on psychotropic medication with opioid replacement therapy

Pritham , U.A. (2013). Breastfeeding promotion for management of neonatal abstinence syndrome. JOGNN, 42: 517-526.

REVIEW ARTICLE

The Opioid Dependent Mother and Newborn Dyad: Nonpharmacologic Care

Martha Velez, MD, and Lauren M. Jansson, MD

J Addict Med • Volume 2, Number 3, September 2008

REVIEW

Neonatal abstinence syndrome: where are we, and where do we go from here?

Laura Brandt[a] and Loretta P. Finnegan[b]

Curr Opin Psychiatry 2017, 30:268–274
DOI:10.1097/YCO.0000000000000334

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The emergence of neonatal abstinence syndrome – from the beginning until today

- **1875:** first case report on NAS (named "congenital morphinism")[1]
- **1903:** first case was successfully treated with morphine[2]
- **1975:** first scoring tool for NAS published: Finnegan Scale (Finnegan, 1975) → Still most frequent used assessment tool for NAS today.

[1] Menninger-Lerchenthal (1943). *Mütetter. Monatschr f Kinderh.*; [2] OD (1903). *JAMA*; [3] Jones et al. (2010). *NEJM*; Osborn et al. (2010). *Cochrane Database Syst Rev.*; [4] Osborn et al. (2010). *Cochrane Database Syst Rev.*

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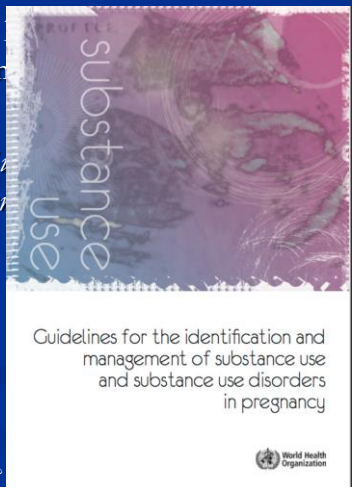
Also .....

- Focus on NAS increased in past decade → increase in prescription opioid misuse and use, especially in the U.S.
- With drug abuse going *stigmatization* often barriers, especially for dependent (pregnan
- WHO released guideline on this issue: *"Ga identification and management of substance use a*



Brandt & Finnegan (2017). Neonatal abstinence syndrome: where are we, and where do we go from here?

...and the conclusion?

One can not predict at birth whether a newborn will develop NAS and how severe the degree will be → there exists too many different variables which could have an influence on these factors.

„ Not everything that counts can be counted, and not everything that can be counted counts!"

Albert Einstein

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Brandt & Finnegan (2017). Neonatal abstinence syndrome: where are we, and where do we go from here? *Curr Opin Psychiatry*, 30: 268-274.

ORIGINAL CONTRIBUTION

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 μ-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

JAMA. 2013;309(17):1821-1827 www.jama.com

Neonatal Abstinence Syndrome and High School Performance

Estimated Dose Exposure of the Neonate to Buprenorphine and Its Metabolite Norbuprenorphine via Breastmilk During Maternal Buprenorphine Substitution Treatment

natal drug withdrawal syndrome: cross-country arison using hospital administrative data in d, the USA, Western Australia and Ontario,

Hilary Davies,[1] Ruth Gilbert,[2] Kathryn Johnson,[3] Irene Petersen,[1] Irwin Nazareth,[1] Melissa O'Donnell,[4] Astrid Guttmann,[5] Arturo Gonzalez-Izquierdo[6]

To cite: Oei JL, Melhuish E, Uebel H, et ... Abstinence Syndrome and High ... *Pediatrics*. 2017;139(2):e201...

ACTA PÆDIATRICA

Prematurity reduces the severity and need for treatment of neonatal abstinence syndrome

Original article

Journal of Paediatrics and Child Health

ORIGINAL ARTICLE

How long should infants at risk of drug withdrawal be monitored after birth?

Dop... gene polymorphisms in newl... of drug-using women

Ju Lee Oei, ... Hong Xiu Xu,[1] Mohamed E Abdel-Latif,[3,4] Krishna Vunnam,[1] Adil Al-Amry, Sara Clews,[5] Janet Falconer,[5] John M Feller,[6] Kei Lui[1,2]

ACTA PÆDIATRICA

REGULAR ARTICLE

Home-based detoxification for neonatal abstinence syn length of hospital admission without prolonging treatn

Paediatric and Perinatal Epidemiology

Epidemiological Evidence for a Decreasing Incidence of Neonatal Abstinence Syndrome, 2000–11

Oei et al. (2017). Neonatal Abstinence Syndrome and

Violation of Human rights: example

- **In many cases, institutions demand postpartally quasi-voluntary "rehabilitation" admission of women & neonates with substance dependence.**
  - Right to respect for private and family life, his home & correspondance[1]
    - Mostly, these women can only have limited contact to their partners (restriction of intimacy, sexuality) during these periods.

- Article 10 CESCR[2]
- The widest possible protection and assistance should be accorded to the family(…).
- Special protection should be accorded to mothers during a reasonable period before and after childbirth (...).

[1] European Convention of Human Rights, Article 8, Right to respect for private and family life
[2] Committee on Economic, Social and Cultural Rights, Article 10

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Reasons for Rehospitalization in Children Who Had Neonatal Abstinence Syndrome

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- All infants born in the state of New South Wales (NSW), Australia,between 2000 and 2011 woth NAS
- Results were compared with details from children without a diagnosis of NAS

Uebel et al. (2014). Reasons for rehospitalization in children who had neonatal abstinence syndrome. *Pediatrics*, 136: 811-820.

Methods

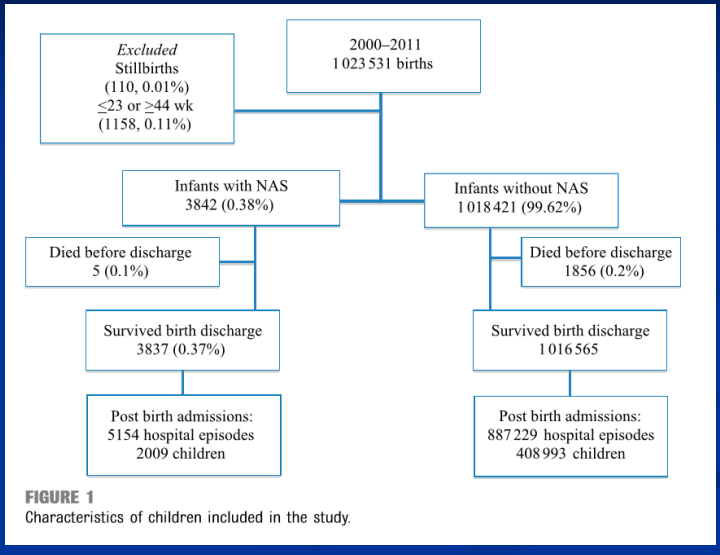


FIGURE 1
Characteristics of children included in the study.

Uebel et al. (2014). Reasons for rehospitalization in children who had neonatal abstinence syndrome. *Pediatrics*, 136: 811-820.

Results

Total of **1 023 531** live born infants between July 1, 2000, and December 21, 2011 were observed:

- 3842 **(0.38%)** were diagnosed with NAS (P96.1) during the birth admission
- Five **(0.1%)** NAS and 1856 **(0.2%)** non-NAS infants died before discharge from hospital after birth
- The number of episodes of care per child were significantly higher in children with NAS (2.6 episodes per child) than without NAS (2.2 episodes per child, $p < .001$)
- Forty-five (1.2%) children with NAS died by the end of the study period, compared with 3665 (0.4%) non-NAS children ($p < .001$).

Uebel et al. (2014). Reasons for rehospitalization in children who had neonatal abstinence syndrome. *Pediatrics*, 136: 811-820.

Results

Children with NAS

- were more likely to be rehospitalized (OR 1.6, CI:1.5– 1.7),
- die during hospitalization (OR 3.3, CI: 2.1– 5.1),
- be hospitalized for
  - assaults (OR 15.2, CI: 11.3– 20.6),
  - maltreatment (OR 21.0, CI: 14.3– 30.9),
  - poisoning (OR 3.6, CI: 2.6– 4.8),
  - mental/behavioral (OR 2.6, CI: 2.1– 3.2)
  - and visual disorders (OR 2.9, CI: 2.5-3.5)

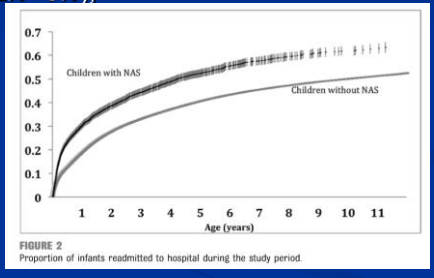


FIGURE 2
Proportion of infants readmitted to hospital during the study period.

Regression analyses demonstrated

- that NAS was the most important predictor of admissions for maltreatment (odds ratio 4.5, 95% confidence interval: 3.4– 6.1)
- mental and behavioral disorders (odds ratio 2.3, CI: 1.9– 2.9),
- even after accounting for prematurity, maternal age and Indigenous status

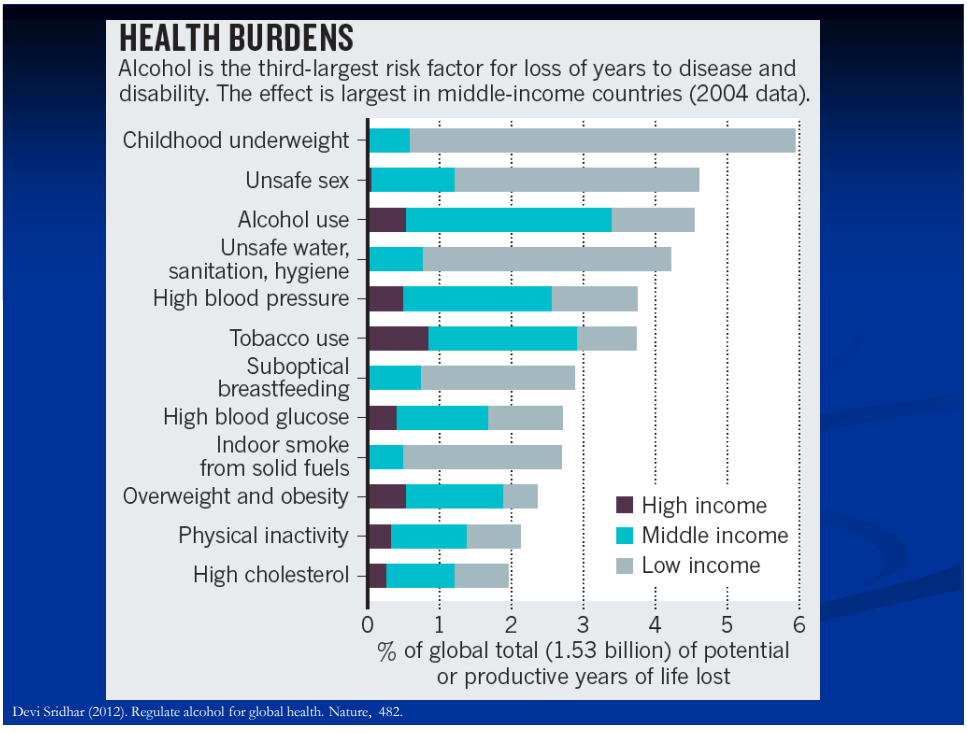
Uebel et al. (2014). Reasons for rehospitalization in children who had neonatal abstinence syndrome. *Pediatrics*, 136: 811-820.

"Regulate alcohol for global health"

- 4% of all mortality cases worldwide are related to alcohol consumption
- > number as caused through HIV/AIDS, tuberculosis or malaria

- Alcohol consumption is the 3. largest health risk factor
- In middle income countries (1/2 of the world population) is alcohol the largest risk factor
- Consumption during pregnancy leads to neonatal sbstinence syndrome & fetal alcohol (spectrum) disorder

Devi Sridhar (2012). Regulate alcohol for global health. Nature, 482.



Devi Sridhar (2012). Regulate alcohol for global health. Nature, 482.

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

**Opositional Defiant Disorder

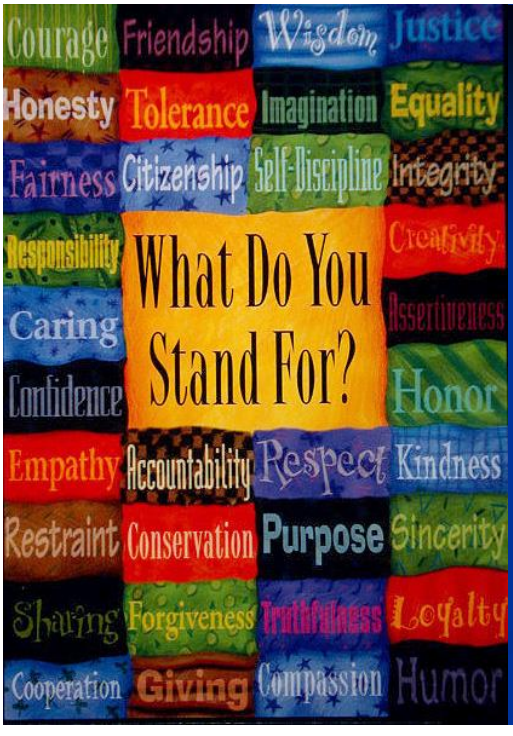
Klug, M. G., & Burd, L. (2003). *Neurotoxicology and teratology*, *25*(6), 763-765.

Ergebnisse

Table 3
Child characteristics for Lazio region sample by FASD diagnosis and randomly-selected controls.

Measure	FASD mean (SD) (n = 46)	Randomly selected controls mean (SD) (n = 116)	Test score	p
Child physical characteristics				
Age (months)	79.8	79.5	t = −.442	.659
Sex (% male)	50.0	52.6	χ^2 = .09	.766
Height	38.2 (29.5)	60.7 (26.1)	t = 4.76	<.001
Weight	41.4 (30.5)	67.2 (25.6)	t = 5.05	<.001
Head circumference (OFC) centile	24.8 (28.1)	55.2 (26.8)	t = 6.42	<.001
Palprebral fissure length (PFL) centile	20.1 (18.8)	31.1 (16.6)	t = 3.67	<.001
Narrow vermilion border of the upper lip (% Yes; a score of 4 and 5)	93.5	21.6	χ^2 = 69.96	<.001
Smooth Philtrum (% Yes; a score of 4 and 5)	89.1	13.8	χ^2 = 81.98	<.001
Total dysmorphology score	11.9 (4.1)	3.6 (2.9)	t = 210.19	<.001
Child neurocognitive performance				
Raven centile	53.9 (23.2)	71.0 (21.2)	t = 4.48	<.001
Rustioni (number of errors made)	8.0 (2.3)	5.3 (2.5)	t = −4.41	<.001
PBCL-36	9.1 (6.1)	3.9 (3.7)	t = −3.31	.004
Inattention (Pelham)	6.7 (7.9)	2.2 (3.7)	t = −3.65	.001
Hyperactivity (Pelham)	4.2 (6.2)	2.2 (4.3)	t = −2.03	.047
WISC verbal	91.8 (15.3)	103.1 (16.0)	t = 2.85	.006
WISC nonverbal	94.6 (16.9)	113.7 (17.5)	t = 4.41	<.001
WISC overall	92.3 (15.9)	109.3 (17.7)	t = 3.97	<.001

Ceccanti, M. et al. (2014). *Drug and alcohol dependence*, *145*, 201-208.



...and evidence-based medicine

Thank you for your time

This situation calls for a strong and diffuse campain fighting that ongoing discrimination

The Nelson Mandela Rules - an updated Guide for Prison Management in line with Human Rights - Dec 2015 UN- General assembly

https://www.unodc.org/unodc/index.html