Sex, Gender and Opioids



Given the current health crisis, and evidence on the impact of sex, gender and trauma on risk factors and patterns of use, there is an urgent need for the development and testing of sex and gender-tailored, trauma-informed approaches to screening, monitoring, prevention, harm reduction, treatment and policy.

DEFINITIONS

Sex-related factors affect how your body reacts to substances, including how substances are metabolized, what effects they may have on your brain, and the development of tolerance and dependence. Female and male bodies have different genetic and physiological characteristics that affect these processes.

Gender-related factors affect your risks for use, exposure to marketing or exploitation, access to care and services, and the societal response to problematic use. Men, women, and gender diverse individuals experience these elements differently. In part, this is based on social roles and expectations that are dependent upon cultural context.

Canada is in the midst of an opioid crisis. Opioid overdoses are particularly high in British Columbia, yet opioid misuse and related fatalities are evident across the country. There is growing evidence on the need for sex- and gender-informed approaches to prevention, treatment and harm reduction to address opioid misuse.

Key Sex-Related Factors

- The impact of female hormones on pain processing may increase
 women's vulnerability to opioid use and misuse; fluctuations in estrogen
 during the menstrual cycle and menopausal transition can increase pain
 sensitivity, and susceptibility to the side effects of opioids.^[1,2]
- Various opioids are metabolized by males and females differently.^[1]
 Evidence suggests the effects of fentanyl may be lower in females, and the effects of codeine may be lower in males.^[1]
- Since opioids dissolve in fats, body weight and body fat have an effect on the blood concertation level of opioids.^[1] As females tend to have a higher body fat percentage compared to males, fixed doses, as opposed to doses adjusted according to body weight, can result in higher blood concentration levels for women.^[1]
- Compared to men, women more frequently report higher dose and longer term prescription opioid use as a result of having more chronic pain. [3,4]
- Women with opioid use disorder have higher rates of simultaneous mental health issues such as depression or anxiety. [6-8]
- Recent research may suggest that high levels of estradiol and progesterone levels during the reproductive cycle may help to hinder the development or maintenance of problematic opioid use.^[3]

Sex, Gender and Opioids

Key Gender-Related Factors

- Deaths from opioid pain medication increased 400% between 1999 and 2010 for women, and 265% times for men.^[3,9,10] The increase in heroin use by women has resulted in 3x the number of women dying from heroin overdose within a three-year period (2010-2013).^[3]
- In British Columbia in 2019, preliminary data suggest that men account for 79% of fentanyl-detected deaths (21% for women).[11]
- From 2016–2017, the rate of hospitalization due to opioid overdoses in Canada was higher among males than females.^[12] Women with prescription opioid use disorder (POUD) are more likely than males with POUD to be administered through the emergency department.^[7]
- The greater risk of opioid overdose and deaths may be, in part, due to riskier forms of substance use by men. Men are more likely to: escalate their opioid medication doses;^[13] ingest opioid medications non-orally;^[5,14] and obtain prescription opioids via an illegitimate source (71% of men vs. 46% of women).^[5,15-17]
- For women the greatest risk for opioid addiction is receiving a prescription for an opioid medication. [4,7,18,19] Women are also more likely than men to "doctor shop", hoard unused prescriptions, use additional medications to enhance the effectiveness of pain medication, and report dependence on and craving of opioids. [3,14]
- Women often begin opioid use at an older age compared to men, but progress more rapidly to hazardous use, even with smaller amounts. [3,6,7,20]
- Older adults are increasingly being hospitalized for opioid overdose. [21] Elderly women may be particularly vulnerable due to prescribing practices, social isolation, and relatively longer life expectancies. [22]

- Compared to other types of substance use, both women and men who are addicted to prescription opioids are more likely to report a traumatic event, and also report higher rates of childhood trauma.^[23]
- Emerging evidence suggests women are more likely to use prescription opioids to manage negative emotions.^[5]
- Men are more likely to use other substances in conjunction with opioids.^[4]
- Women report higher rates of sharing needles compared to men.^[25]
- Transgender populations experience very high rates of gender-based discrimination, harassment and violence. While research on opioid misuse among transgender individuals is lacking, the prevalence of non-medical prescription opioid use among transgender adults is high. Higher rates of non-medical prescription pain medication use have also been reported among transgender youth, compared to cisgender youth.
- Non-heterosexual young adults are more likely to report misuse of prescription opioids.^[29] Bisexualidentified women in particular are more likely to use opiates than heterosexual and lesbian-identified women.^[30]
- Among Indigenous women and men, colonization and intergenerational trauma are closely linked with substance use, including opioid misuse, and is a key barrier to accessing support services.^[24]

For information about opioids and its effects while pregnant, breastfeeding, and parenting, visit: bccewh.bc.ca

Sex, Gender and Opioids

REFERENCES

- Pisanu, C., et al., Sex differences in the response to opioids for pain relief: A systematic review and meta-analysis. Pharmacological Research, 2019: p. 104447.
- Lee, C.W.-S. and I.-K. Ho, Sex differences in opioid analgesia and addiction: Interactions among opioid receptors and estrogen receptors. 2013, SAGE Publications: Los Angeles, CA. p. 45.
- 3. Ait-Daoud, N., et al., *Women and addiction: An update.* Medical Clinics of North America, 2019. **103**(4): p. 699-711.
- Bawor, M., et al., Sex differences in substance use, health, and social functioning among opioid users receiving methadone treatment: A multicenter cohort study. Biology of Sex Differences, 2015. 6(1): p. 21.
- McHugh, R.K.P.D., et al., Gender differences in a clinical trial for prescription opioid dependence. Journal of Substance Abuse Treatment, 2013. 45(1): p. 38-43.
- Jacobs, A.A.M.D. and M.M.D. Cangiano, Medication-assisted treatment considerations for women with opiate addiction disorders. Primary Care: Clinics in Office Practice, 2018.
 45(4): p. 731-742.
- 7. John, W.S. and L.-T. Wu, Sex differences in the prevalence and correlates of emergency department utilization among adults with prescription opioid use disorder. Substance Use & Misuse, 2019. 54(7): p. 1178-1190.
- Huhn, A.S., M.S. Berry, and K.E. Dunn, Review: Sex-based differences in treatment outcomes for persons with Opioid Use Disorder. The American Journal on Addictions, 2019. 28(4): p. 246-261.
- Mack, K.A., et al., Vital signs: Overdoses of prescription opioid pain relievers and other drugs among women – United States, 1999–2010. Morbidity and Mortality Weekly Report, 2013. 62(26): p. 537-542.
- 10. McHugh, R.K., et al., Sex and gender differences in substance use disorders. Clinical Psychology Review, 2018. **66**: p. 12–23.
- British Columbia Ministry of Public Safety and Solicitor General, BC Coroners Service fentanyl-detected suspected illicit drug toxicity deaths, 2012-2019. 2019.
- 12. Canadian Institute for Health Information, *Opioid-related harms in Canada*. 2017, Ottawa, ON: CIHI.
- Kaplovitch, E., et al., Sex differences in dose escalation and overdose death during Chronic Opioid Therapy: A populationbased cohort study. PloS One, 2015. 10(8): p. e0134550.
- Back, S.E., et al., Prescription opioid aberrant behaviors:
 A pilot study of sex differences. Clinical Journal of Pain, 2009.
 25(6): p. 477-484.
- Back, S.E., et al., Gender and prescription opioids: Findings from the National Survey on Drug Use and Health. Addictive Behaviors, 2010. 35(11): p. 1001-1007.
- Green, T.C., et al., Women who abuse prescription opioids: Findings from the Addiction Severity Index-Multimedia Version Connect prescription opioid database. Drug & Alcohol Dependence, 2009. 103(1-2): p. 65-73.

- Gladstone, E.J., K. Smolina, and S.G. Morgan, Trends and sex differences in prescription opioid deaths in British Columbia, Canada. Injury Prevention: Journal of the International Society for Child and Adolescent Injury Prevention, 2016. 22(4): p. 288-290.
- Schepis, T.S. and S. Krishnan-Sarin, Sources of prescriptions for misuse by adolescents: Differences in sex, ethnicity, and severity of misuse in a population-based study. Journal of the American Academy of Child & Adolescent Psychiatry, 2009. 48(8): p. 828-836.
- Hachey, L.M., et al., Health implications and management of women with opioid use disorder. Journal of Nursing Education and Practice, 2017. 7(8): p. 57.
- Back, S.E., et al., Characteristics and correlates of men and women with prescription opioid dependence. Addictive Behaviors, 2011. 36(8): p. 829-834.
- 21. Canadian Institute for Health Information and Canadian Centre on Substance Abuse, Hospitalizations and emergency department visits due to opioid poisoning in Canada, CIHI, Editor. 2016: Ottawa, ON.
- 22. Hemsing, N., et al., Misuse of prescription opioid medication among Women: A scoping review. Pain Research and Management, 2016. **2016**: p. 1-8.
- Lawson, K.M., et al., A comparison of trauma profiles among individuals with prescription opioid, nicotine, or cocaine dependence. The American Journal on Addictions, 2013. 22(2): p. 127-131.
- First Nations Health, A., Overdose data and first nations in B.C: preliminary findings. 2017, Vancouver, B.C: First Nations Health Authority.
- Vigna-Taglianti, F.D., et al., Gender differences in heroin addiction and treatment: Results from the VEdeTTE Cohort. Substance Use & Misuse, 2016. 51(3): p. 295-309.
- Gonzalez, C.A., J.D. Gallego, and W.O. Bockting, Demographic characteristics, components of sexuality and gender, and minority stress and their associations to excessive alcohol, cannabis, and illicit (noncannabis) drug use among a large sample of transgender people in the United States. The Journal of Primary Prevention, 2017. 38(4): p. 419-445.
- Benotsch, E.G., et al., Non-medical use of prescription drugs, polysubstance use, and mental health in transgender adults. Drug and Alcohol Dependence, 2013. 132(1): p. 391-394.
- De Pedro, K.T., et al., Substance use among transgender students in California public middle and high schools. Journal of School Health, 2017. 87(5): p. 303-309.
- Kecojevic, A., et al., Initiation into prescription drug misuse: Differences between lesbian, gay, bisexual, transgender (LGBT) and heterosexual high-risk young adults in Los Angeles and New York. Addictive Behaviors, 2012. 37(11): p. 1289-1293.
- Kerr, D., et al., An alcohol, tobacco, and other drug use comparison of lesbian, bisexual, and heterosexual undergraduate women. Substance Use & Misuse, 2015. 50(3): p. 340-349.