Opioid agonist treatment and the opioid crisis

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Presenter disclosure

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THE OPIOID CRISIS

The opioid crisis in Ontario

- ODPRN: 2050 opioid-related deaths March-December 2020, vs 1,162 deaths in same period in 2019
- Northern public health units have the greatest per capita death rate and the greatest increase in rate:
- Sudbury – increase from 28 per 100,000 to 53 per 100,000
- Ontario average – increase from 11/100,000 to 17/100,000

Opioid crisis (2)

- COVID is a major factor:
  - Social isolation (risk of death is far greater when opioids used alone)
  - Depression, anxiety, quarantine, loss of income, housing
  - Attendance at addiction and general health care services has declined
  - Weekly ED visits for mental health aged 0-29:
  - Seven days in Feb 2020: 2000 visits
  - Seven days in Feb 2021: 1500 visits
- Drug supply is increasingly toxic
- Content of drug supply is a business decision made by fentanyl manfacturers
- They are responding to, and creating, a demand for potent opioids

EFFECTIVENESS OF OAT BEFORE AND DURING THE OPIOID CRISIS

OAT protects against fentanyl overdose

- OAT is by far the most important public health strategy to prevent opioid overdose deaths
- Systematic review (Sordo 2017): mortality rate while on methadone = 2.6/ 1000 patient years, rising to 12.7/1000 patient years while off methadone
- Methadone's protective effect is relatively greater in the fentanyl era than before
- Retrospective cohort study in BC (Pearce 2020): relative risk of death while off methadone was 2.1, rising to 3.4 after fentanyl use became common in 2016
- Mortality rate while on OAT remained stable during this period, suggesting that OAT remained protective against fentanyl overdose
- Buprenorphine offers comparable protection against overdose

OAT protects against fentanyl overdose (2)

- OAT protects against overdose even in people who continue to use fentanyl
- In a retrospective cohort study of 127 people who used fentanyl (Stone 2020), there were no deaths while on methadone, and four deaths among people who left methadone treatment
- OAT protects against overdose by reducing the frequency and amount of fentanyl use, and by building tolerance to fentanyl-induced respiratory depression
- Protection for both methadone and buprenorphine is probably dose related
- In one study, among 20 people who died of an overdose while on methadone, all were on < 60 mg and half were on 30 mg
- Other positive outcomes of OAT: Reduced crime and incarceration rates, reduced HIV risk behaviours, decreased ED visits and hospital admissions, reduced hospital AMA rates (Farrell 1994, Sun 2015, Malta 2019, Karki 2016, Ti 2015)

Treatment engagement and retention rates

- Number of individuals on OAT increased from 51,000 in Jan 2020 to 53,000 in March 2021
- Treatment retention rates are low and may be declining
- Six-month treatment retention rates among patients on OAT in Ontario dropped from 55.9% in 2013 to 49.6% in 2018 (Leece 2020)
- Treatment drop out is associated with a high risk of death
- Factors associated with treatment drop-out:
  - Fentanyl use
  - Concurrent mental illness

REASONS FOR DECLINING TREATMENT RETENTION

Suboptimal dosing

- Fentanyl use increases likelihood of treatment dropout (Arfken 2017)
- Because fentanyl is so potent, high doses of methadone are needed to relieve fentanyl cravings and withdrawal symptoms
- Methadone must be titrated gradually to prevent methadone toxicity
- Highly tolerant patients report that they don't even feel the starting dose of 30 mg
- Why bother going to the pharmacy if methadone doesn't help and fentanyl is available
- Missed doses force prescribers to delay or reverse dose increases
- Post on listserv: Most methadone patients who use the Supervised Consumption Site are on doses of 30 mg

Effect of clinic practices on retention and dosing

- Some clinics require patients to attend once or twice per week to leave a urine drug screen and receive a prescription (Guan 2017)
- Patients who miss an appointment, or several appointments, may have trouble getting a script and will be more likely to drop out of treatment
- CPSO standards and Guidelines (2010) contain numerous rules which make it difficult to restart or maintain treatment or to quickly titrate to an effective dose
  - E.g., patients who have missed three consecutive doses must attend the clinic in person to get a new script

Mental illness and treatment retention

- In a study involving methadone patients experiencing homelessness and mental illness in BC, the “Medication Possession Ratio” was only 0.47 (i.e., they only took methadone on every 2nd day on average) (Parpouchi 2017)
- High prevalence of mental illness among people who inject opioids (Arfken 2017, Parpouchi 2017)
- Difficult to achieve a dose of 80 mg or more if methadone is taken only every 2nd day
- Most patients receive OAT in community clinics funded entirely by OHIP
- Ontario Health does not give stipends to physicians for nonpaid clinical work, and does not support FFS clinics with case management etc.
- This makes it very difficult to provide care for patients with OUD and concurrent mental and substance use disorders

OAT IN THE ED AND OTHER HEALTH CARE SETTINGS

OAT in the ED (1)

- In the early 2000s, most patients with opioid use disorder were addicted to OxyContin
- OxyContin is far less potent than fentanyl
- Most patients tolerated gradual methadone titration
- Most patients were stable and could make and keep appointments at OAT clinics
- In contrast, people who use fentanyl are more likely to attend the ED
- The ED presents an opportunity to intervene:
- Study of 1,257 people who had one or more opioid overdoses in Simcoe county:
  - 69% had visited the ED at least once in the year prior to the overdose
  - 36% had visited three or more times.
- In a retrospective cohort study of 6140 people who were seen in an Ontario ED for a non-fatal overdose, the risk of death in the year following the overdose was 5.3% (Leece 2020)

OAT in the ED (2)

- Controlled trials: giving buprenorphine in the ED is far more effective at engaging patients in treatment than referral only (D'Onofrio 2017, Srivastava 2019)
- A significant proportion of patients will accept buprenorphine and attend an outpatient addiction clinic
- Retrospective cohort study at Lakeridge ED: 88% of 49 patients in opioid withdrawal agreed to receive buprenorphine in the ED, and 54% attended the initial appointment at the RAAM clinic (Hu 2019)
- Canadian Association of Emergency Physicians endorses the use of buprenorphine in the ED (CJEM 2020)
- Yet only a few EDs in Ontario offer buprenorphine on site to our knowledge
- A national survey of Canadian ED physicians found that that only 7% prescribed buprenorphine regularly, even though the large majority reported seeing opioid withdrawal frequently in their EDs (Hoyeck 2020)

OAT in other addiction and health care settings

- Withdrawal Management Services are beginning to initiate OAT but most WMS only have one NP on staff so coverage is spotty
- Hospitals with addiction consult services routinely provide OAT but only a minority of hospitals have ACS
- Family physicians are reluctant to initiate OAT or to accept patients in transfer
- RAAM clinics are increasing in number, but many RAAM clinics have limited hours
- Residential psychosocial programs: An increasing number will maintain patients on OAT but not all are able to initiate OAT

STRENGTHENING THE OAT SYSTEM

The goal

- Patients should be able to receive medication assisted treatment, on-site and immediately, in all health care and addiction treatment settings: EDs, hospitals, primary care, withdrawal management services
- Once treatment is initiated in an acute care setting, patients should have convenient, low barrier access to ongoing OAT
- Once stable, patients should be able to receive ongoing treatment in primary care

Clinical standards and integrated care pathways

- Steps needed to create a strong OAT system:
  - Define clinical standards for opioid use disorder in all addiction and health care settings, ie
  - Hospitals, WMS, RAAM clinics should offer buprenorphine, methadone, SROM on site
  - Ensure that addiction and health care settings have appropriate training and staffing to meet these standards
  - Build integrated care pathways involving RAAM clinics, WMS, EDs, residential programs, primary care
- The overall cost of such an initiative would be far less than the cost of the public health response to COVID

Methadone dosing protocols and practices

- **META:PHI's recommendations for prescribing methadone**
- Several recommendations designed to make it easy to remain in treatment
- Eg faxed scripts for missed appointments
- Leave a script for 30 mg at the pharmacy if patient missed 3+ doses
- Flexibility regarding frequency of office visits and UDS

Methadone dosing protocols (2)

- Add slow release oral morphine to methadone during initial titration
- Helps relieve withdrawal symptoms and cravings as methadone effects wear off
- Does not need to be tapered when maintenance methadone dose reached
- Little published evidence base to support this recommendation
- But Listserv posts and personal communications: clinicians report good results with combining methadone and SROM
- Risks of treatment drop-out vastly outweigh the risks of methadone/morphine toxicity

Buprenorphine or methadone first?

- Buprenorphine is safer, and more convenient for patient
  - more flexible take-home policies, more easily available than methadone
- But buprenorphine is harder to start and less effective for some patients
- Controlled trials and systematic reviews have consistently shown that methadone has higher treatment retention rates than buprenorphine
- Therefore, start buprenorphine first if:
  - Patient doesn't want methadone, has done well on buprenorphine in the past, or is high risk for methadone toxicity
- Titrate to optimal dose (16-32 mg) as quickly as possible, and consider depot buprenorphine

Buprenorphine or methadone (2)

- **Start methadone if**:
- Induction onto buprenorphine is unsuccessful
- Repeatedly drops out and restarts buprenorphine
- Continued high risk fentanyl use despite optimal buprenorphine dose

Induction methods for buprenorphine

- Choose induction method that patient finds most convenient and acceptable
- Office/ED induction for patients in active withdrawal, or willing to stop their opioid for 12+ hours and attend the office
- Home induction for patients who would rather go through withdrawal and start buprenorphine at home
- Micro-induction for patients who don’t want to endure withdrawal and are willing to wait 4-10 days

Macrodosing

- Can administer bup when COWS score is 4+
- First buprenorphine dose is 8-16 mg, followed by 8-16 mg q 2H prn, to maximum of 32 mg on day one
- This dose gives a full mu agonist effect, relieving symptoms of precipitated withdrawal
- May be a good fit for the ED:
  - Patient doesn't have to be in full withdrawal to start treatment
  - A full therapeutic dose is reached quickly
  - Patient's time in withdrawal (precipitated or otherwise) is limited
- Many California EDs use this protocol (Snyder 2021), but not much outcome research

Depot buprenorphine

- SC injection lasting 28-42 days
- Has several potential advantages over SL buprenorphine:
- Higher and more constant serum level than sl buprenorphine, so may be better at relieving withdrawal symptoms and cravings (though no head to head comparison of SL vs depot)
- No need for daily pharmacy visits; injection only needed every 28 days and is ok if several days or even a week or two missed
- So treatment retention rates may be better (but further research needed)

SROM (as stand-alone OAT treatment)

- SROM is recommended as 3rd line opioid agonist treatment by CRISM (Canadian Research Initiative in Substance Misuse)
- Indicated for patients who have failed at or can't tolerate methadone and buprenorphine
- RCTs have found that SROM is of comparable effectiveness to methadone
- Illicit opioid users should have daily observed dosing (Klimas 2019)
- Usual therapeutic range 800-1500 mg

IMPROVING ACCESS TO OAT

Educational, training initiatives

- There are many local, regional and provincial initiatives for education, training, mentorship and communities of practice
- META:PHI's initiatives:
- ED toolkit for managing opioid use disorder in the ED
- Guidelines on OAT for residential programs and for withdrawal management services
- Recommendations on prescribing methadone for people who use fentanyl
- Nurse practitioner manual
- Primary care handbook, Best Practices handbook

Implementation initiatives

- ED Change project: META:PHI has given grants to five EDs across Ontario to implement buprenorphine protocols
- Nurse practitioners working in WMS are developing protocols and building communities of practice and mentorship networks
- RAAM clinics are working to expand hours, expand access, and build strong connections with EDs
- Hospitals are funding addiction clinical consult services and patient navigators
- Individual clinicians and hospitals doing ground breaking work
- Virtual care systems being developed
  - Alberta's virtual opioid dependency program is a good model
  - OAT can be started on the same day regardless of where patient resides – home, ED, shelter, WMS
  - 2000 new OAT starts in one year

THANK YOU!