MODELLING THE IMPACT ON OVERDOSE AND OVERDOSE DEATHS OF UNSUPERVISED INJECTABLE OPIOID AGONIST THERAPY WITH OTHER OPIOID THERAPIES

Wai Chung Tse MD Candidate

Dr Nick Scott BSc (Hons), PhD

Prof. Paul Dietze BSc (Hons), PhD

Assoc. Prof. Suzanne Nielsen BPharm (Hons), PhD

MONASH University

DISCLOSURE OF INTERESTS

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ACKNOWLEDGEMENT OF COMMUNITY AND COUNTRY

WHAT IS OPIOID AGONIST THERAPY?

- Opioid agonist therapy (OAT) is a **cost-effective treatment** for people who inject drugs
- Historically, OAT is an oral therapy
- OAT involving methadone and buprenorphine have a large evidence base demonstrating their effectiveness in reducing opioid use and related mortality
- An estimated **5-10% of people** who use opioids are not attracted to, or do not benefit from current OAT therapies

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WHAT TO DO FOR THOSE REFRACTORY TO OAT?

ORIGINAL ARTICLE

Diacetylmorphine versus Methadone for the Treatment of Opioid Addiction

Eugenia Oviedo-Joekes, Ph.D., Suzanne Brissette, M.D., David C. Marsh, M.D., Pierre Lauzon, M.D., Daphne Guh, M.Sc., Aslam Anis, Ph.D., and Martin T. Schechter, M.D., Ph.D.

Article Figures/Media

25 References 197 Citing Articles Letters

August 20, 2009
N Engl J Med 2009; 361:777-786
DOI: 10.1056/NEJMoa0810635

Abstract

BACKGROUND
Studies in Europe have suggested that injectable diacetylmorphine, the active ingredient in heroin, can be an effective adjunctive treatment for chronic, relapsing opioid dependence.

METHODS
In an open-label, phase 3, randomized, controlled trial in Canada, we compared injectable diacetylmorphine with oral methadone maintenance therapy in patients with opioid dependence that was refractory to treatment. Long-term users of injectable heroin who had not benefited from at least two previous attempts at treatment for addiction (including at least one methadone treatment) were randomly assigned to receive methadone (111 patients) or diacetylmorphine (115 patients). The primary outcomes, assessed at 12 months, were retention in addiction treatment or drug-free status and a reduction in illicit-drug use or other illegal activity according to the European Addiction Severity Index.

RESULTS
The primary outcomes were determined in 95.2% of the participants. On the basis of an intention-to-treat analysis, the rate of retention in addiction treatment in the diacetylmorphine group was 87.8%, as compared with 54.1% in the methadone group (rate ratio for retention, 1.62; 95% confidence interval [CI], 1.35 to 1.95; P<0.001). The reduction in rates of illicit-drug use or other illegal activity was 67.0% in the diacetylmorphine group and 47.7% in the methadone group (rate ratio, 1.40; 95% CI, 1.11 to 1.77; P=0.004). The most common serious adverse events associated with diacetylmorphine injections were overdoses (in 10 patients) and seizures (in 6 patients).

CONCLUSIONS
Injectable diacetylmorphine was more effective than oral methadone. Because of a risk of overdoses and seizures, diacetylmorphine maintenance therapy should be delivered in settings where prompt medical intervention is available. (ClinicalTrials.gov number, NCT00175357.)

Related Articles

EDITORIAL AUG 20, 2009
Heroin Prescription and History
V. Berridge

CORRESPONDENCE NOV 26, 2009
Diacetylmorphine versus Methadone for Opioid Addiction

- Injectable OAT (iOAT), typically involving self-administration of short-acting opioids such as diacetylmorphine and hydromorphone
- Has proven to be effective in treating those opioid-dependent people who inject drugs who do not respond to treatment with conventional OAT
- iOAT may provide increased treatment coverage for people who inject drugs

CONCLUSIONS

Injectable diacetylmorphine was more effective than oral methadone. Because of a risk of overdoses and seizures, diacetylmorphine maintenance therapy should be delivered in settings where prompt medical intervention is available. (ClinicalTrials.gov number, NCT00175357.)

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SUPERVISED IOAT DOESN'T SOLVE EVERYTHING

- iOAT carries a greater risk relative to oral/sublingual OAT
- Provided in a **highly structured way** with supervised administration requiring dedicated infrastructure and oversight by medical and nursing staff
- Those receiving iOAT must come to a dedicated service to self-administer **supervised injections 2-3 times a day**
- Not all at-risk clients who might benefit from iOAT are willing to enter this form of treatment

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WHAT ABOUT UNSUPERVISED IOAT THEN?

ADDICTION
SSA
RESEARCH REPORT
doi:10.1111/add.15297

Perceptions of injectable opioid agonist treatment (iOAT) among people who regularly use opioids in Australia: findings from a cross-sectional study in three Australian cities

Suzanne Nielsen[1,2], Paul Sanfilippo[1], Vendula Belackova[3,4], Carolyn Day[3,5], Ed Silins[2,3], Nicholas Lintzeris[5,6], Raimondo Bruno[7], Jason Grebely[8], Kari Lancaster[4], Robert Ali[9], James Bell[3,4], Paul Dietze[10], Louisa Degenhardt[2], Michael Farrell[2] & Briony Larance[2,11]

Background and aims Not all people experiencing opioid dependence benefit from oral opioid agonist treatment. The aim of this study was to examine perceptions of (supervised) injectable opioid agonist treatment (iOAT) (described as 'an opioid similar to heroin self-injected at a clinic several times a day') among people who regularly use opioids and determine how common iOAT eligibility criteria accord with interest in iOAT. **Design** Cross-sectional survey **Setting** Sydney, Melbourne and Hobart, Australia **Participants** A total of 344 people (63% male) who use opioids regularly and had ever injected opioids, interviewed December 2017–March 2018. The mean age of participants was 41.5 years [standard deviation (SD) = 8.5]. **Measurements** Primary outcome measures were interest in iOAT, factors associated with interest and the proportion of participants who would be eligible using common criteria from trials and guidelines. We examined willingness to travel for iOAT, medication preferences and perspectives on whom should receive iOAT. **Findings** Overall, 53% of participants (n = 182) believed that iOAT would be a good treatment option for them. Participants who believed that iOAT was a good treatment option for them were more likely to be male [adjusted odds ratio (aOR) = 1.76, 95% confidence interval (CI) = 1.10–2.82], have used heroin in the past month (aOR = 6.03, 95% CI = 2.86–12.71), currently regularly inject opioids (aOR = 1.84, 95% CI = 1.16–2.91) and have met ICD-10 criteria for opioid dependence (aOR = 3.46, 95% CI = 1.65–7.24). Those interested in iOAT had commenced more treatment episodes (aOR = 1.06, 95% CI = 1.00–1.12). Among those interested in iOAT (n = 182), 26% (n = 48) met common eligibility criteria for iOAT.
Conclusions Interest in injectable opioid agonist treatment does not appear
use opioids. Among study participants who expressed interest in injectable o
common eligibility criteria.

- An alternative to supervised iOAT has been proposed where clients are given iOAT <u>without</u> the need the administer on site
- Increases treatment access for clients who do not respond to conventional OAT and are unable or unwilling to enroll in current supervised iOAT settings
- We currently **don't know** the risks vs benefits or cost effectiveness of unsupervised iOAT vs existing treatments

Conclusions Interest in injectable opioid agonist treatment does not appear to be universal among people who regularly use opioids. Among study participants who expressed interest in injectable opioid agonist treatment, most did not meet common eligibility criteria.

What are the **risks and benefits** for **unsupervised iOAT** in the context on overdoses and overdose deaths?

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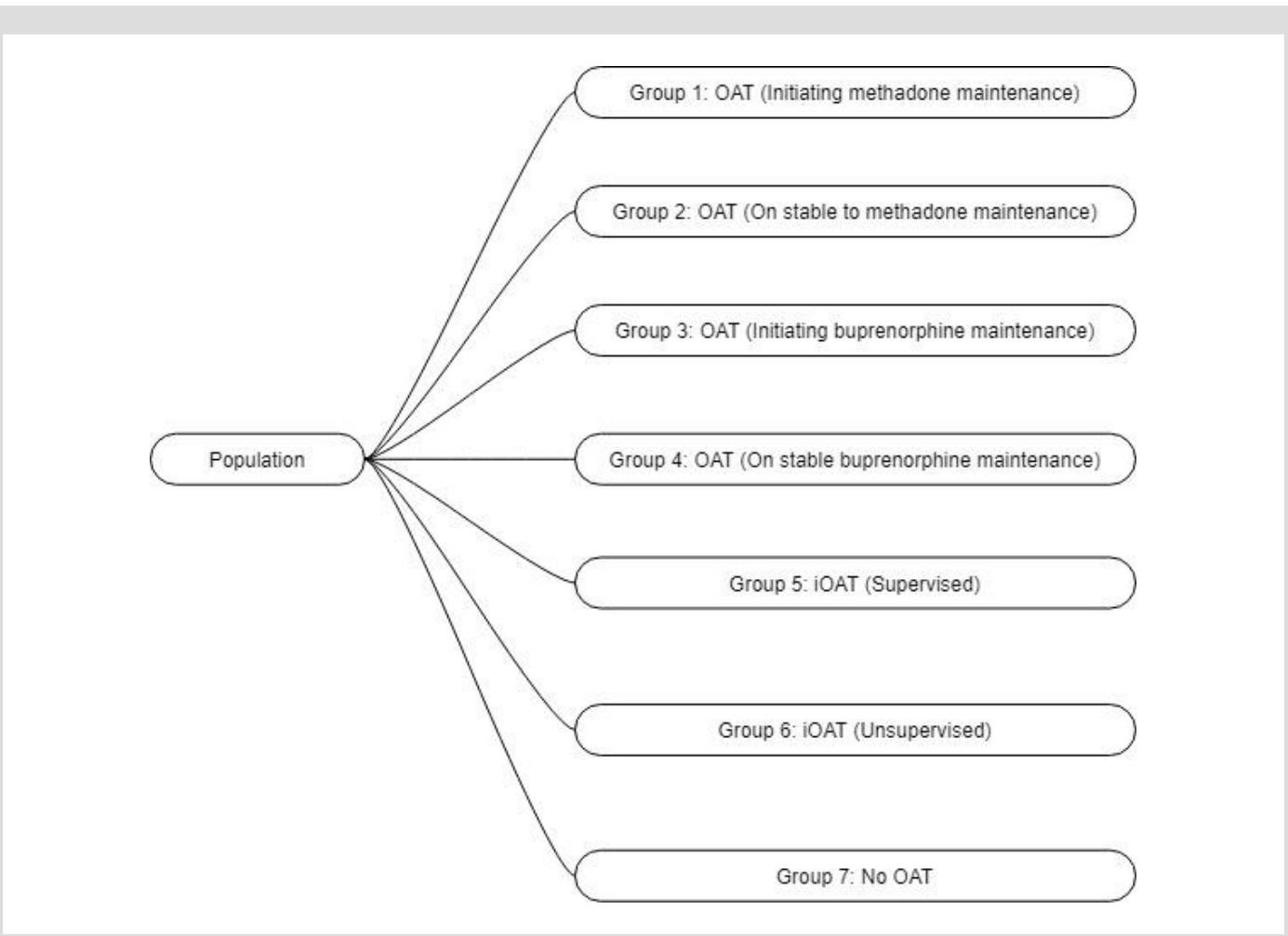
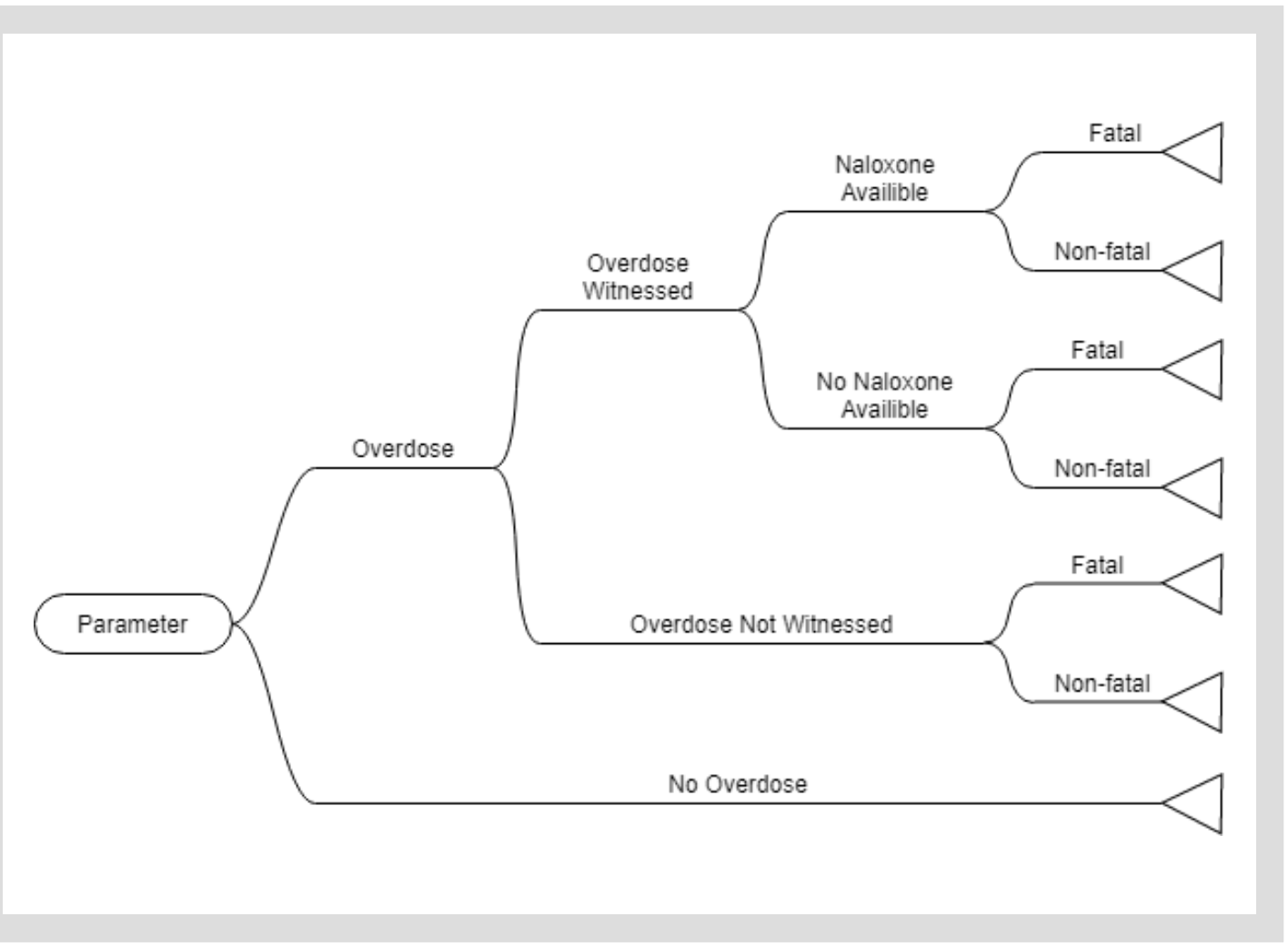
METHODS

- We used a **decision tree model** to model the impacts of different unsupervised iOAT coverage scenarios to **estimate** overdoses (fatal and non-fatal) and treatment costs per 10,000 people per annum
- In our simulated population of 10,000 people in Australia we had 7 groups



METHODS

- Each group had an associated parameter of risks of OD which led to **3 end outcomes**
- Overdose (OD) & OD mortality **depends on a sequence of probabilities**:
  - The probability of overdose
  - Being witnessed when overdose
  - Naloxone available when being witnessed
  - Fatal overdose when naloxone administered



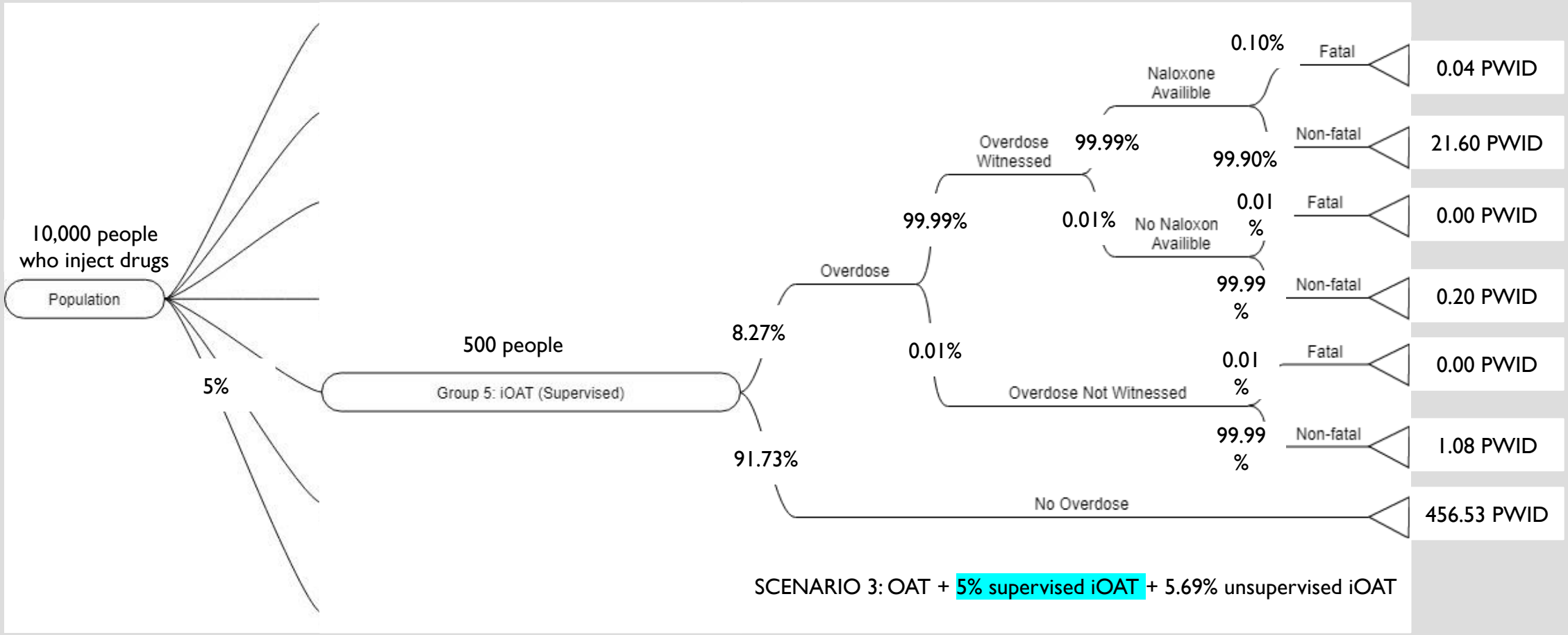
METHODS

- Parameters identified through PubMed with keywords (injectable opioid agonist therapy, methadone, buprenorphine, naloxone, maintenance therapy, hydromorphone, diacetylmorphine) and search from the reference list of key systematic reviews
- Our measurements
  - **Overdose**
  - **Overdose mortality**
  - **Cost to lives ratio**

Scenarios

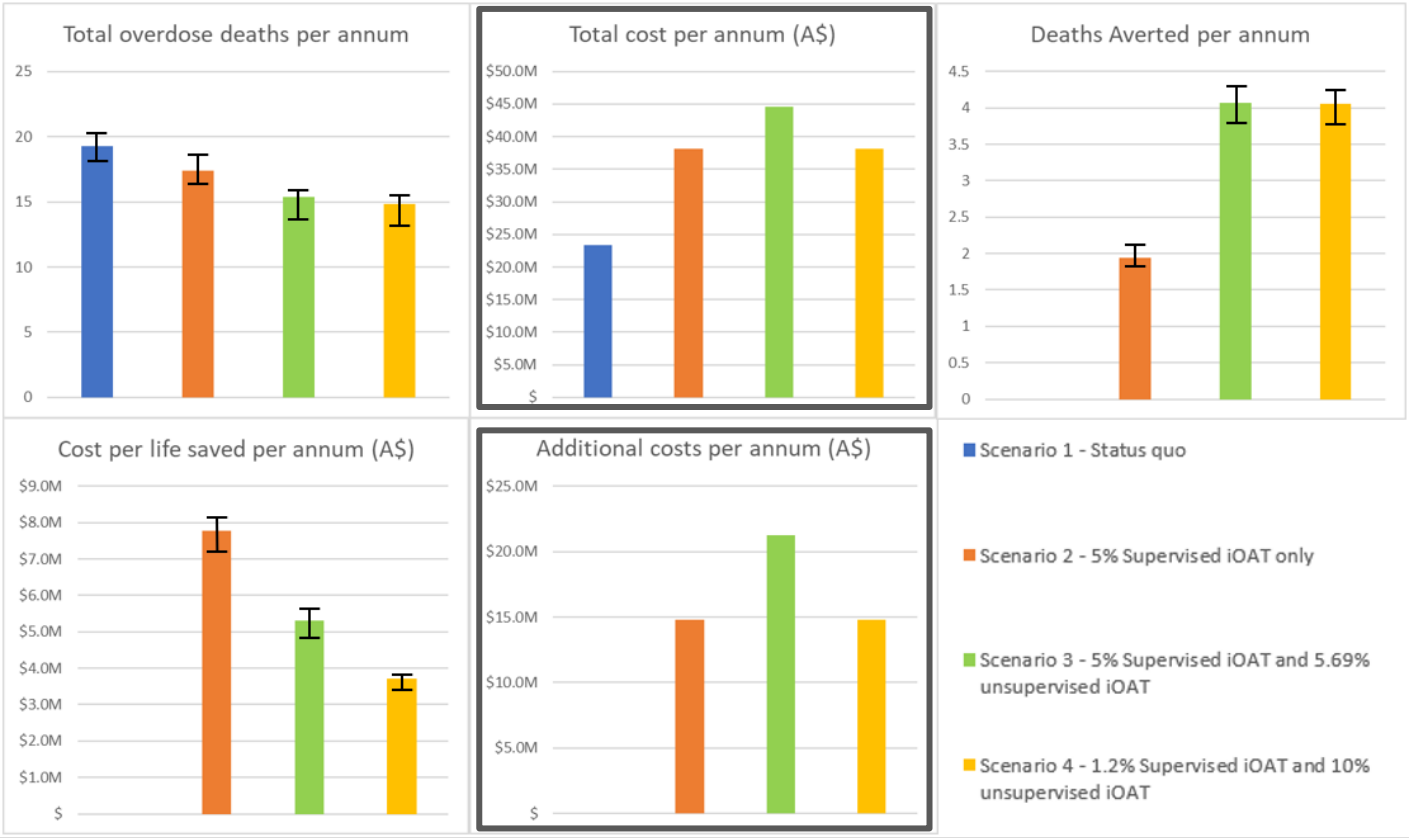
1) OAT only (status-quo)
2) Investment in supervised iOAT only (5% supervised iOAT)
3) A mix of supervised iOAT and unsupervised iOAT based on willingness to enter supervised versus unsupervised treatment (OAT + 5% supervised iOAT + 5.69% unsupervised iOAT)
4) The same resource allocation as scenario 2 but with a mix of supervised and unsupervised iOAT (OAT + 1.2% supervised iOAT + 10% unsupervised iOAT)

LET'S TAKE SUPERVISED IOAT FOR EXAMPLE



SCENARIO 3: OAT + 5% supervised iOAT + 5.69% unsupervised iOAT

RESULTS



- Within a population of 10,000 people over a 1-year period…
- Scenario 1 had **52.0%** of population on treatment with an average cost of **A$ 4,488** per person on treatment per annum
- Scenario 2 had **57.0%** of population on treatment with an average cost of **A$ 6,692** per person on treatment per annum
- Scenario 3 had **63.0%** of population on treatment with an average cost of **A$ 7,106** per person on treatment per annum
- Scenario 4 had **63.2%** of population on treatment with an average cost of **A$ 6,035** per person on treatment per annum

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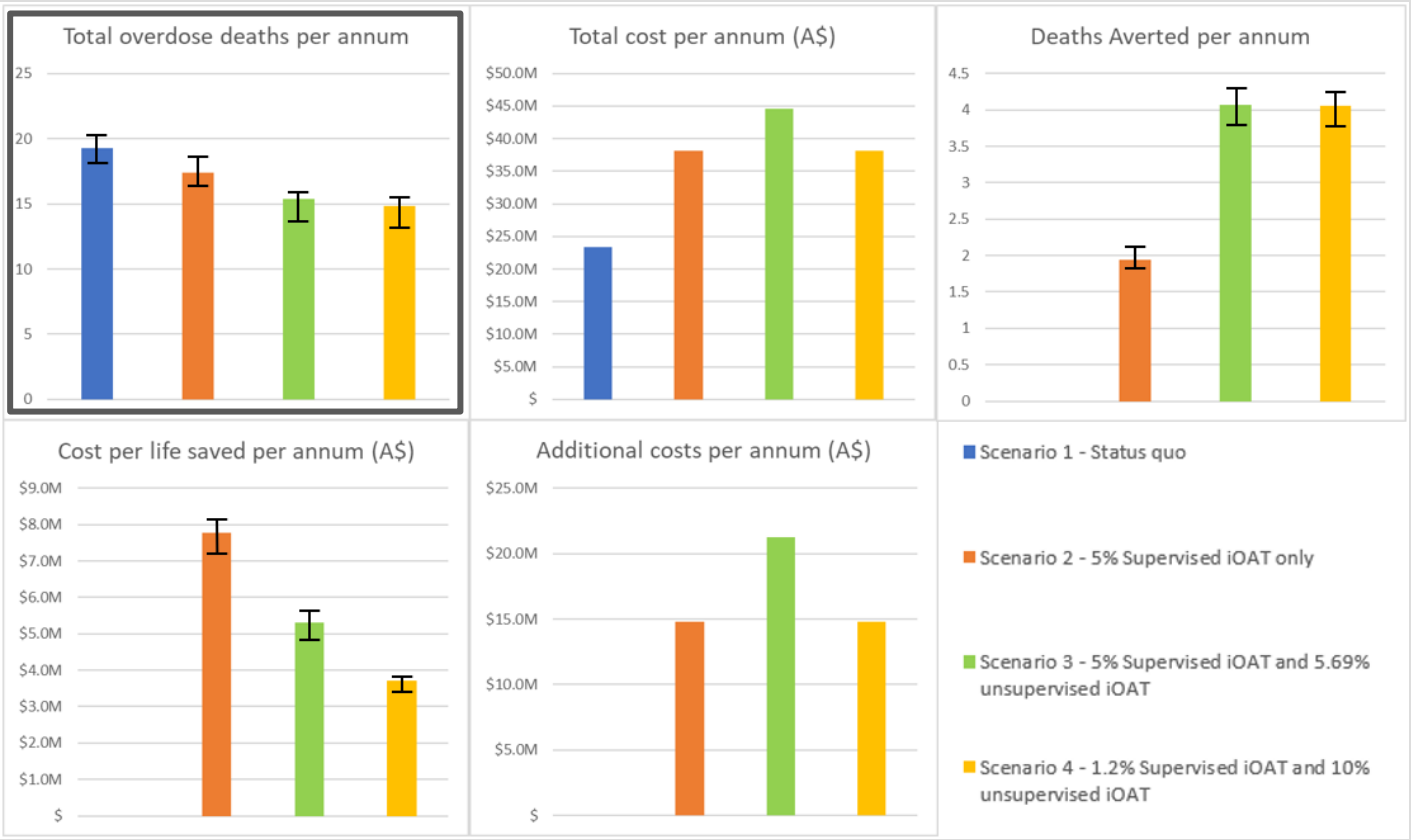
RESULTS



- Scenario 1 had **1655 overdoses** and **19 overdose deaths** per 10,000 people per annum
- Scenario 2 had **1534 overdoses** and **17 overdose deaths** per 10,000 people per annum
- Scenario 3 had **1384 overdoses** and **15 overdose deaths** per 10,000 people per annum
- Scenario 4 had **1349 overdoses** and **15 overdose deaths** per 10,000 people per annum

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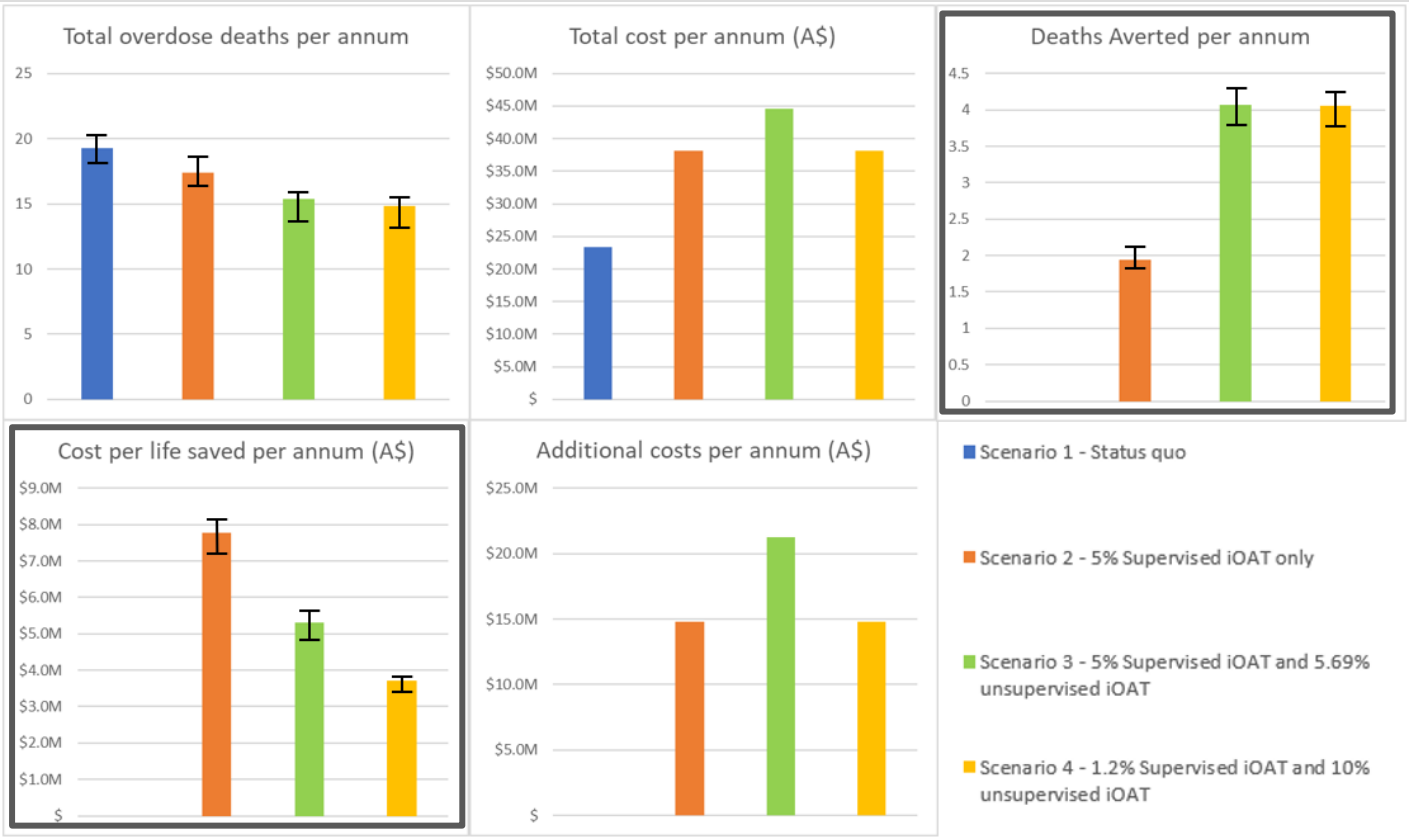
RESULTS



- Key findings:
- Scenario 3 and 4 demonstrated the **most additional overdoses** and **additional deaths averted** per 10,000 people per annum as there were no significant differences between the two scenarios
- Scenario 4 had the **lowest** cost per life saved per annum

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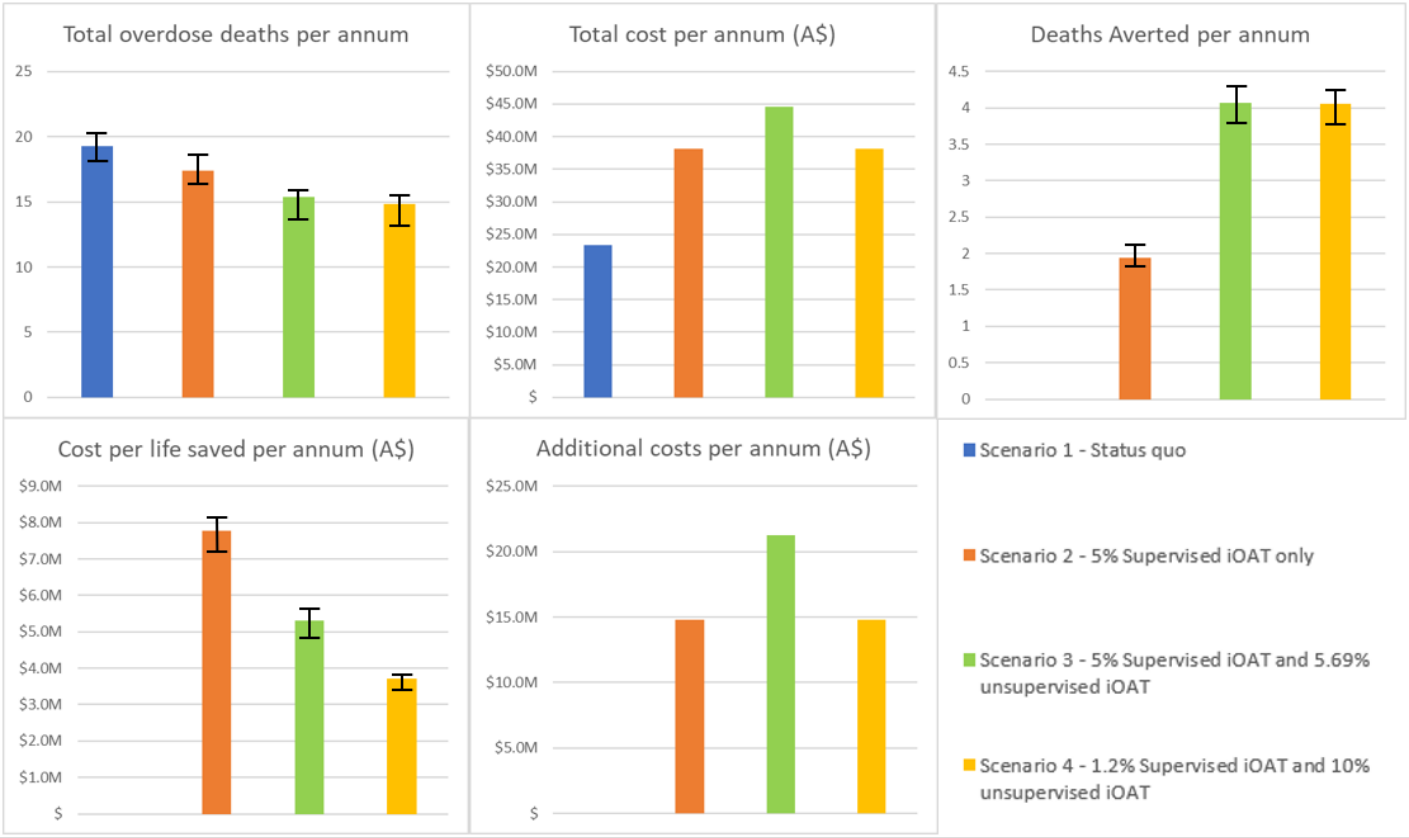
RESULTS



- SA for scenarios 3 and 4 determined that the parameters with the greatest influence on the main outcomes (deaths averted and cost per death averted) were:
  - Probability of overdose with co-use
  - Probability of a fatal non-witnessed overdose with co-use
  - Cost of iOAT

LIMITATIONS

There are several limitations to consider…

- Unable to identify reliable parameters of co-use for benzos and EtOH for overdose risk
  - Prioritize those with polysubstance dependence for supervised treatment places
- Clinic attendance model was most applicable to metropolitan settings
- Model does not consider additional benefits that treating opioid dependence
  - Crime, long term health outcomes, psychosocial impacts

IMPLICATIONS

- The **lowest average cost per person on iOAT treatment**, excluding the status quo, was seen with the greatest use of **unsupervised iOAT** without any negative impact on overdoses and overdose deaths
- While supervision may be adding more safety for clients compared to no supervision, the benefit from cost and coverage suggests upscaling unsupervised iOAT at a greater capacity may be more cost effective and represent no greater risk at the population level
- The introduction of supervised and unsupervised iOAT and subsequent **increased treatment coverage** to **have a greater impact on mortality** for countries like the United States and Canada that have much higher mortality rates compared to Australia
- *Bottom line:* Placing **most resources in upscaling unsupervised iOAT** may demonstrate the **greatest overall benefit** without additional cost

THANK YOU!

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