Pharmaceutical opioid use

An overview of some NDARC work (past, current and future)

Louisa Degenhardt

Acknowledgements

- **NDARC collaborators on some of the work described here**: Richard Mattick, Michael Farrell, Lucy Burns, Amy Gibson, Deb Randall, Jo Kimber, Briony Larance, Fiona Shand, Gab Campbell, Amanda Roxburgh, Sarah Larney, Emma Black, Stephanie Scott-Smith, Benjamin Phillips
- **External collaborators:** Nick Lintzeris, Robert Ali, Raimondo Bruno, Milton Cohen, Suzi Nielsen, Bradley Mathers, Adrian Dunlop, Rebecca Jenkinson, Wayne Hall, Tony Butler, Don Weatherburn, Matthew Law, Claire Vajdic, Andrew Grulich, Janaki Amin, Nancy White, Paul Dietze, Chris Doran, Deborah Zador, Devon Indig
- **NHMRC project grants** : #455451, #630531, #1005668, #1022522
- **NHMRC fellowships**: Louisa Degenhardt, Jo Kimber, Sarah Larney, Suzi Nielsen
- **Untied educational grants** from Reckitt Benckiser
- **Criminology Research Council** funding
- **Tasmanian Department of Health and Human Services**
- **United Nations Office on Drugs and Crime (UNODC), UNAIDS, WHO**

Background

- Pharmaceutical opioids have two primary indications
  - Treatment of pain: acute and chronic
  - As opioid substitution therapy (OST) for the treatment of heroin and other opioid dependence (considered “essential medicines”)
- There are a range of pharmaceutical opioids available in Australia and globally
  - These include morphine, fentanyl, pethidine, codeine, oxycodone (pain)
  - Buprenorphine and methadone most commonly used in OST (morphine, hydromorphine, diamorphine can also be used)

Background

- Opioids are strictly controlled globally
  - Including monitoring by the International Narcotics Control Board
- The norm is for opioids to be *less* available than is considered necessary to provide sufficient coverage for treatment of pain and use in OST
  - Countries typically appear to have an approach that sees restricted availability of these medications rather than using other ways of minimising harms
- Reviews have suggested that opioids in general, and OST specifically, are both far less available than required to ensure effective coverage
  - HOWEVER when opioids ARE made available, there are also risks

Aims

- Provide a quick global overview of opioid availability
- For OST, discuss:
  - Trends in NSW OST provision
  - Data on non-adherence, diversion and injection
  - OST-associated mortality risks and reductions
  - Harms among OST recipients: BBVs, cancer, mortality
  - Potential health, crime and cost savings for OST provision among those involved with the criminal justice system
- For opioids prescribed for pain, discuss:
  - Trends in Australian prescribing
  - Limitations in data on outcomes of prescribing and risks of adverse events; planned studies

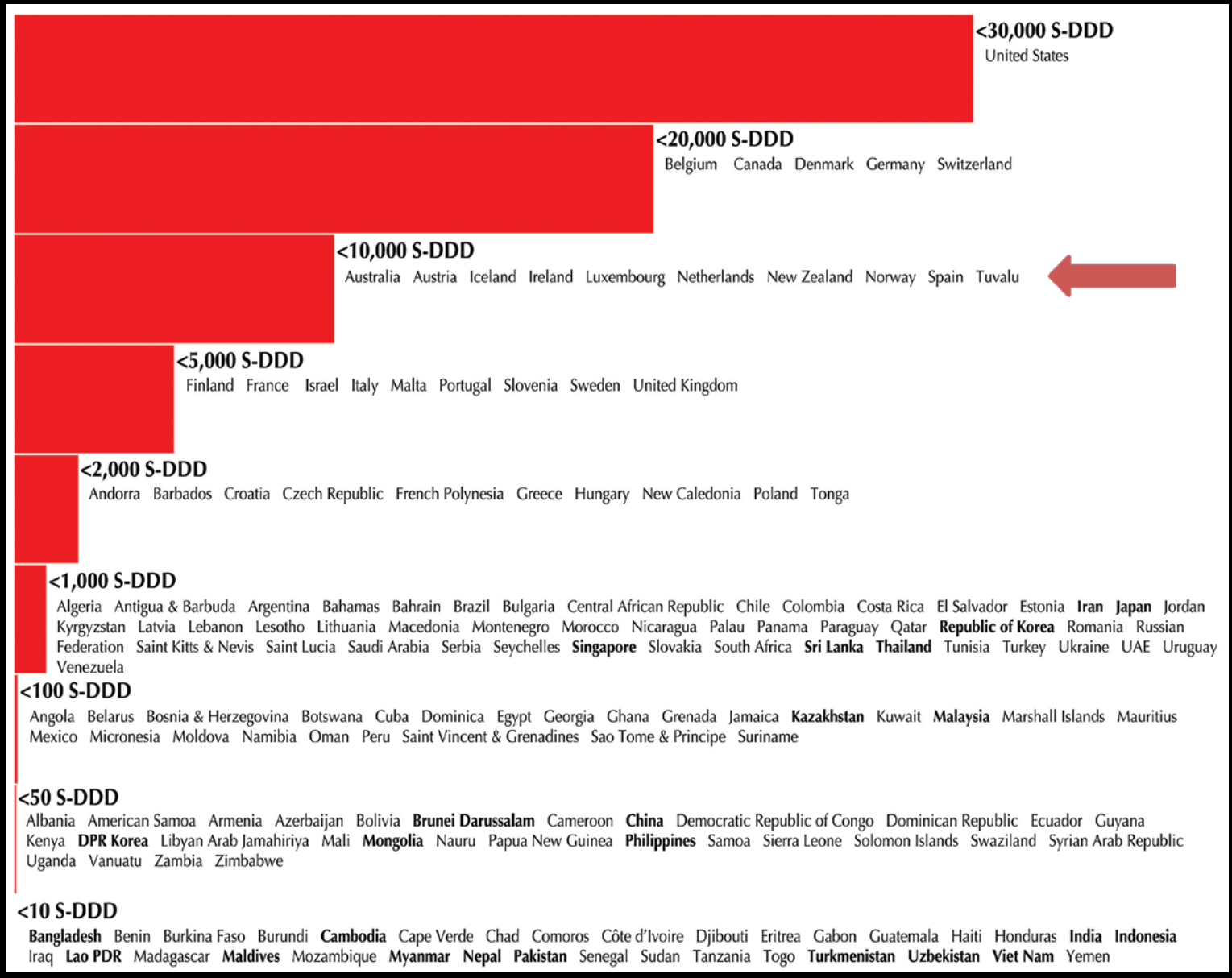
A brief global overview

Results from work for the Reference Group to the UN on HIV & Injecting Drug Use

CIs anytime 2007-2010: Louisa Degenhardt, Bradley Mathers, Richard Mattick, Alex Wodak, John Howard, Kate Dolan

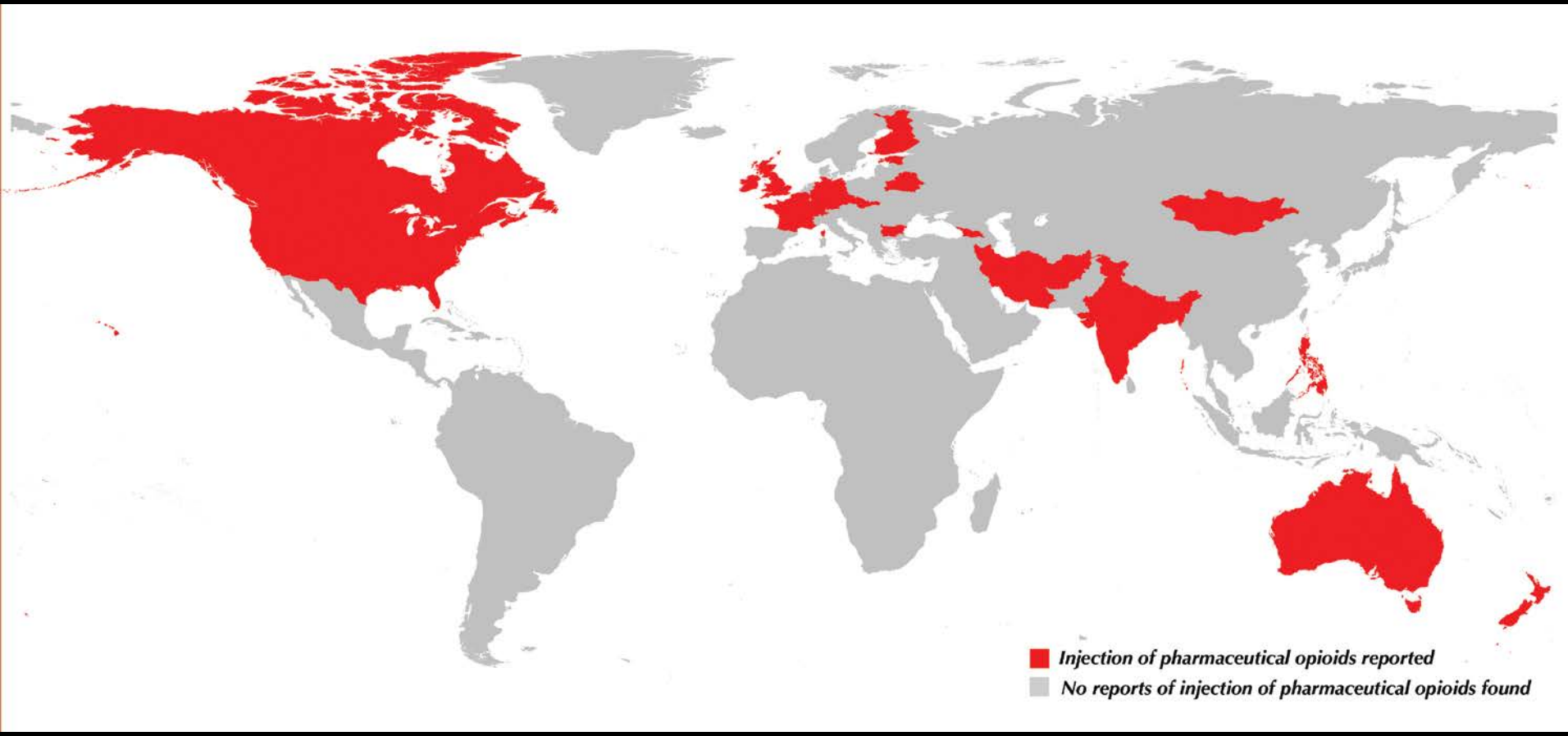
Other researchers: Benjamin Phillips, Anna Roberts, Hammad Ali

Global opioid consumption



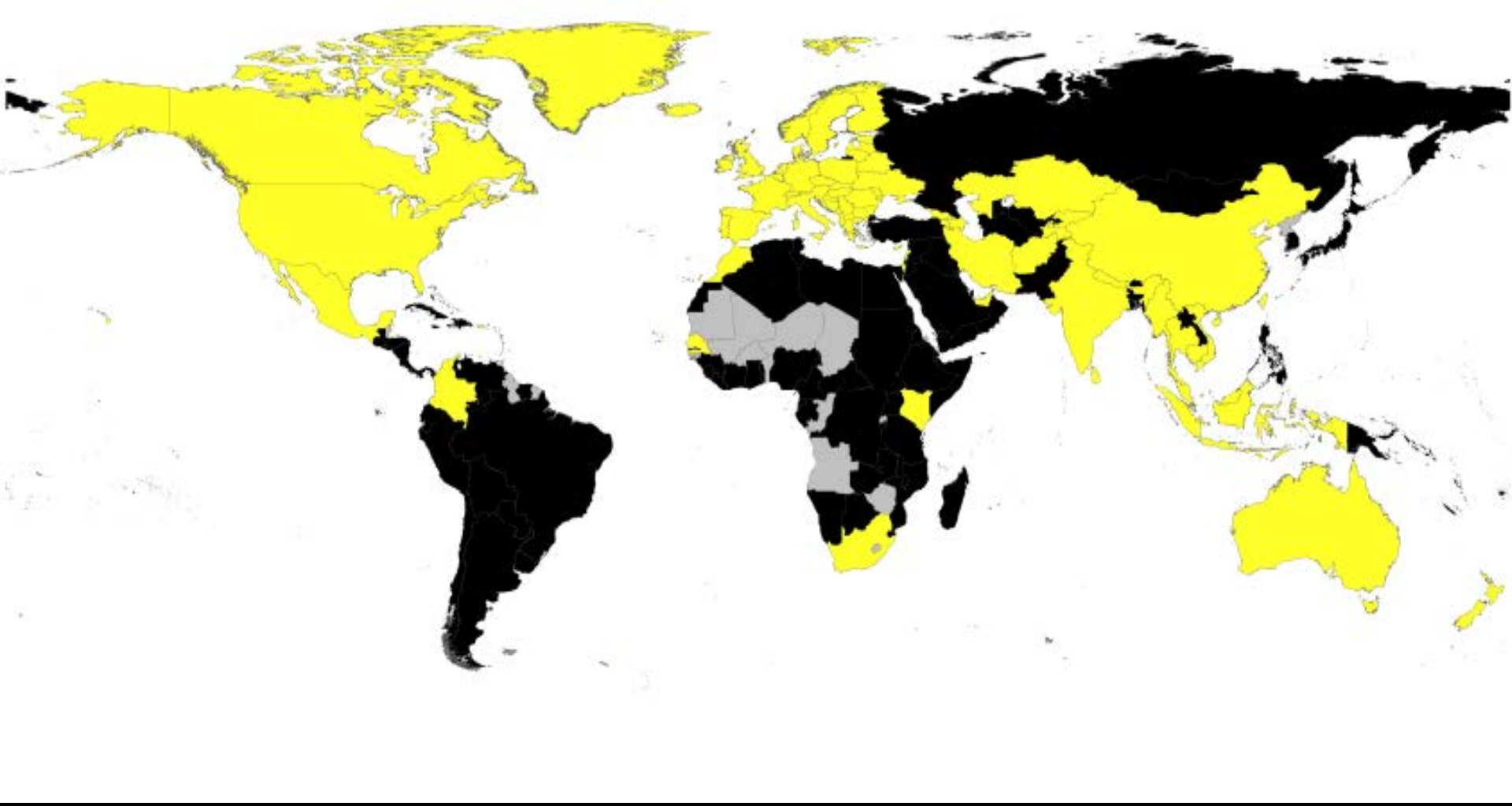
Reference Group to the UN on HIV and injecting drug use 2008

Pharmaceutical opioid injecting – where has it been documented?



Reference Group to the UN on HIV and injecting drug use 2008

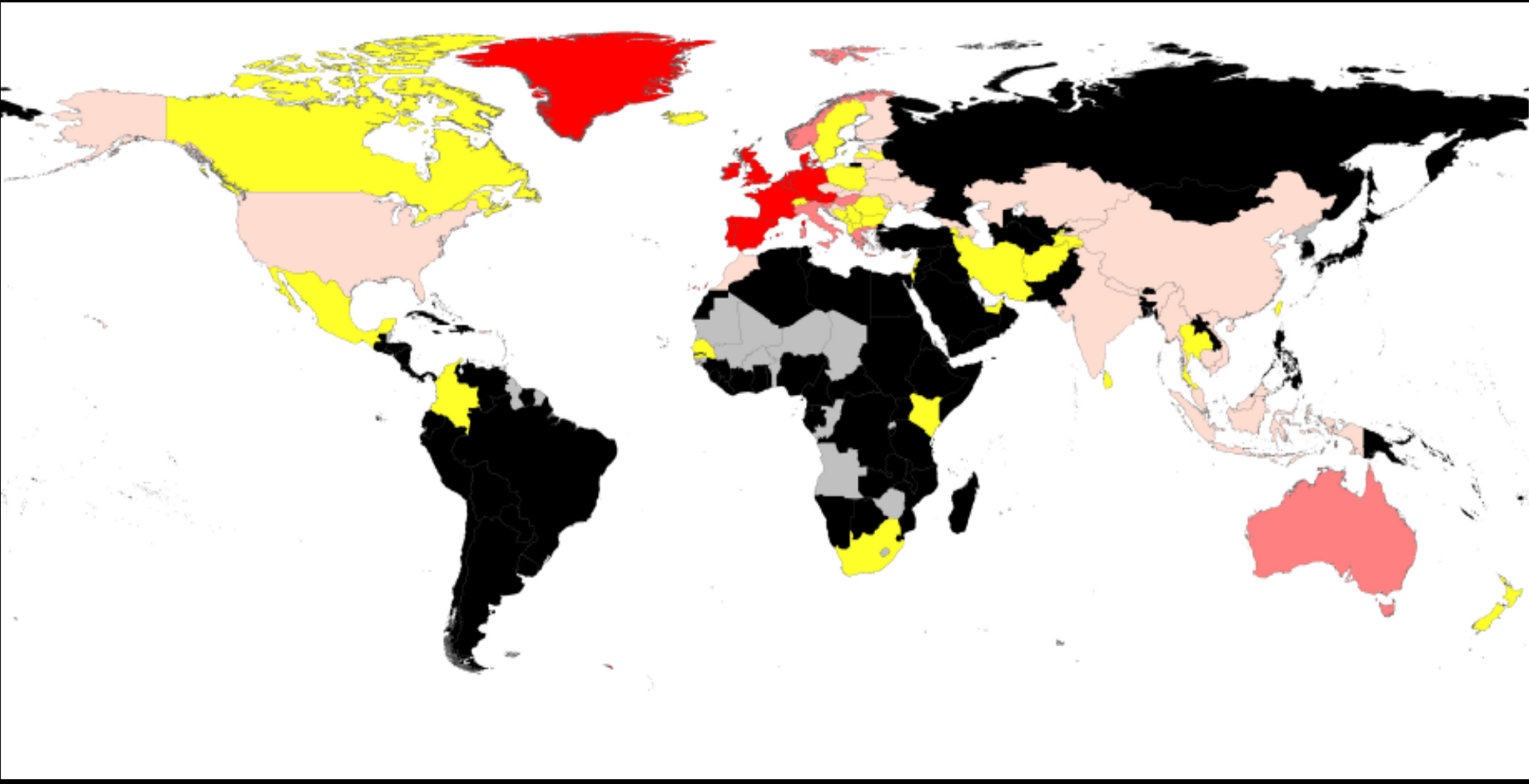
Opioid substitution therapy (OST)



Present in 75 countries

Absent in 76 countries where injecting occurs

Number of OST recipients for every 100 IDUs

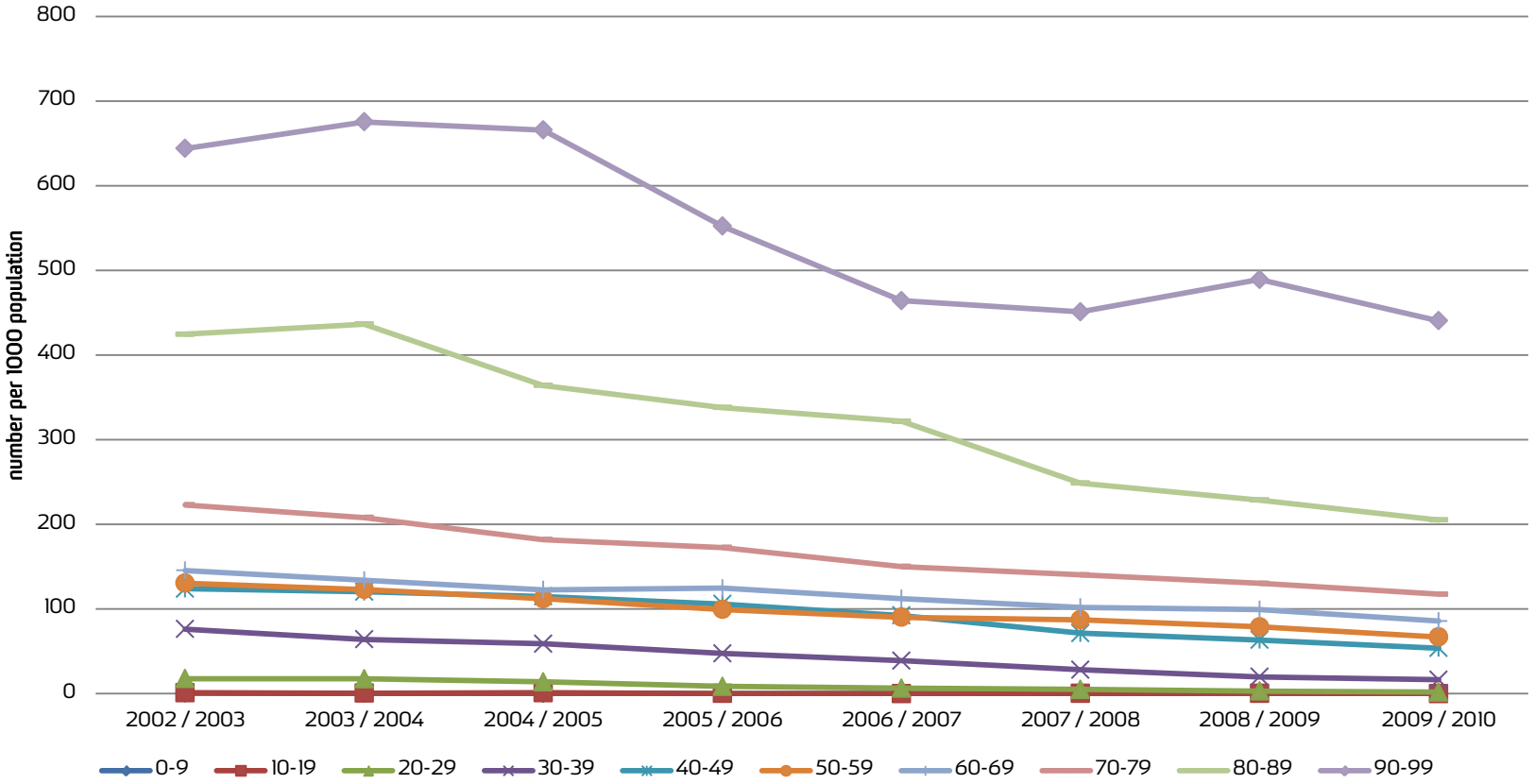


Globally, overall, only 8 people on OST (range 6-12) for every 100 IDUs

Recent Australian trends in general opioid prescribing (and some harms)

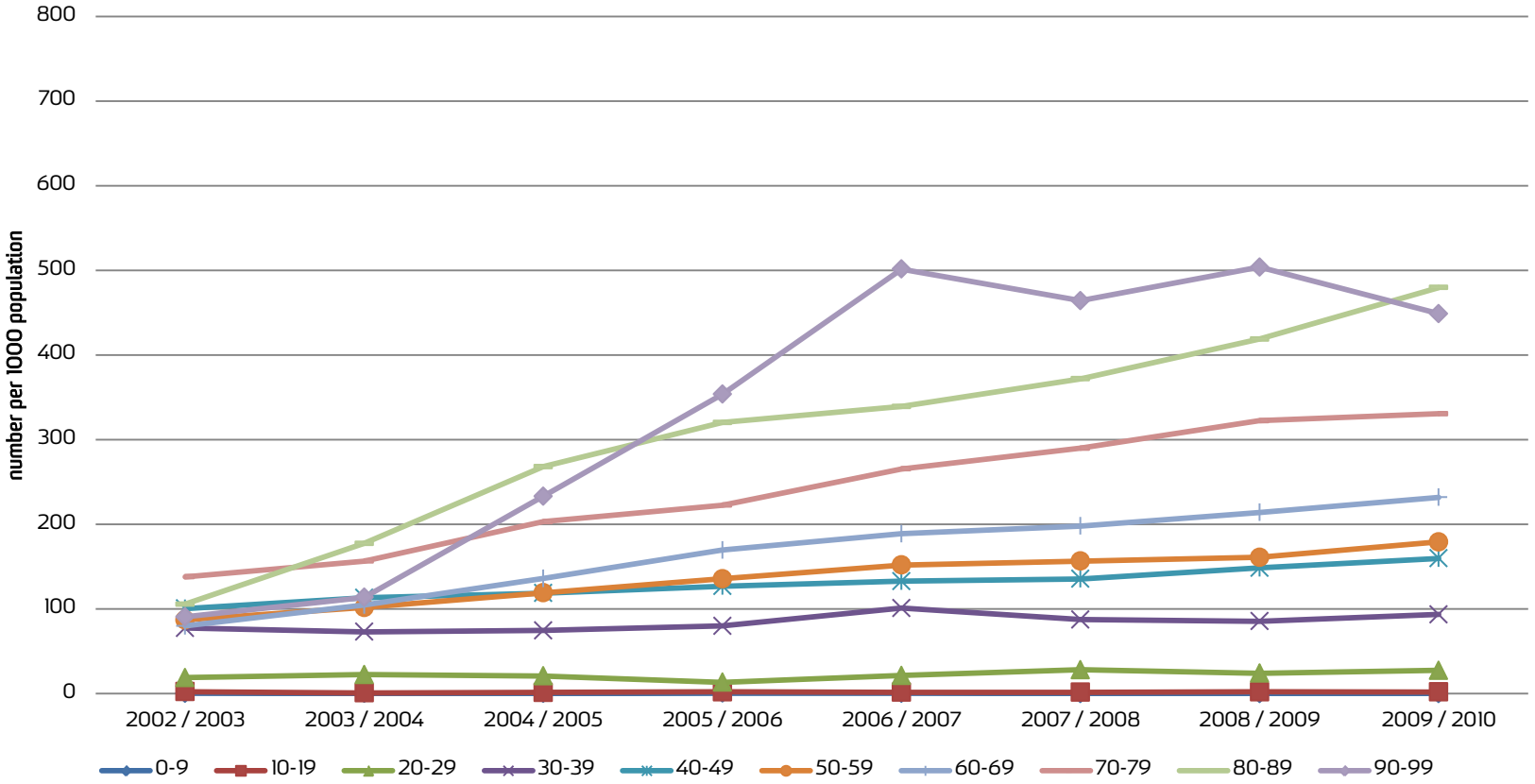
Morphine prescribing by age (per 1000 persons)

CIs: Richard Mattick, Fiona Shand, Louisa Degenhardt, Wayne Hall, Milton Cohen, Nick Lintzeris

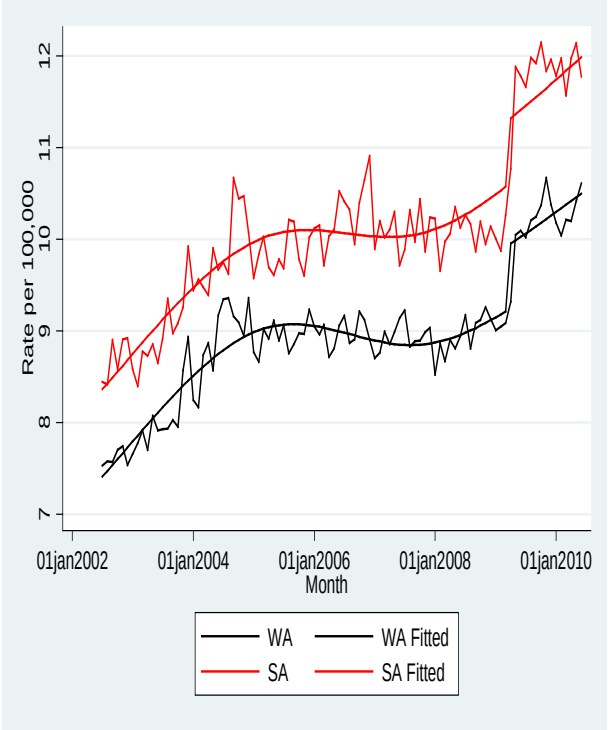


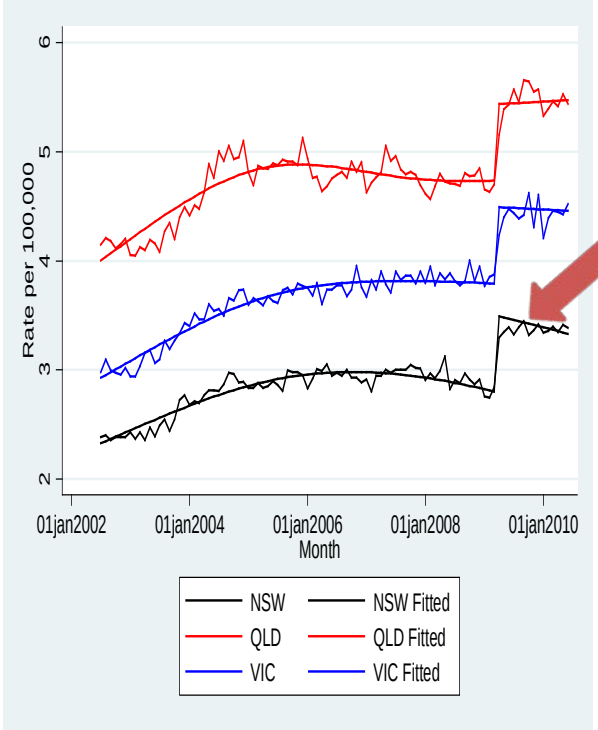
Oxycodone prescribing by age (per 1000 persons)

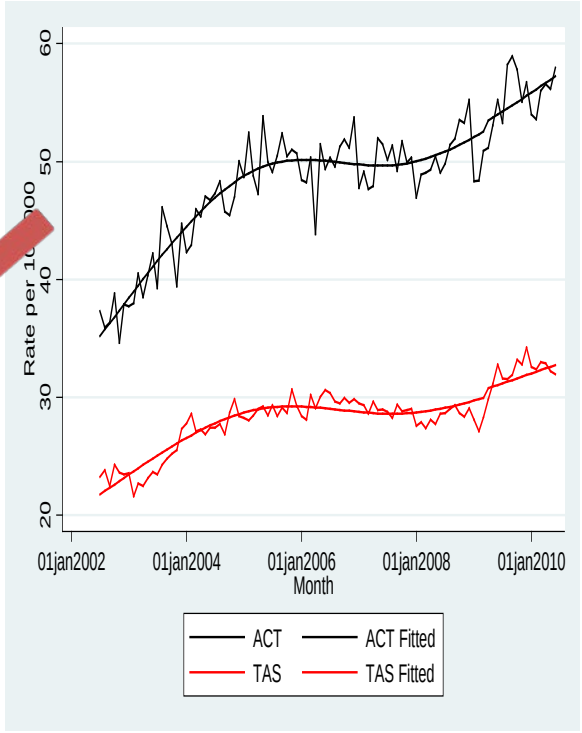
CIs: Richard Mattick, Fiona Shand, Louisa Degenhardt, Wayne Hall, Milton Cohen, Nick Lintzeris



Oxycodone prescribing by jurisdiction, 2002-2010

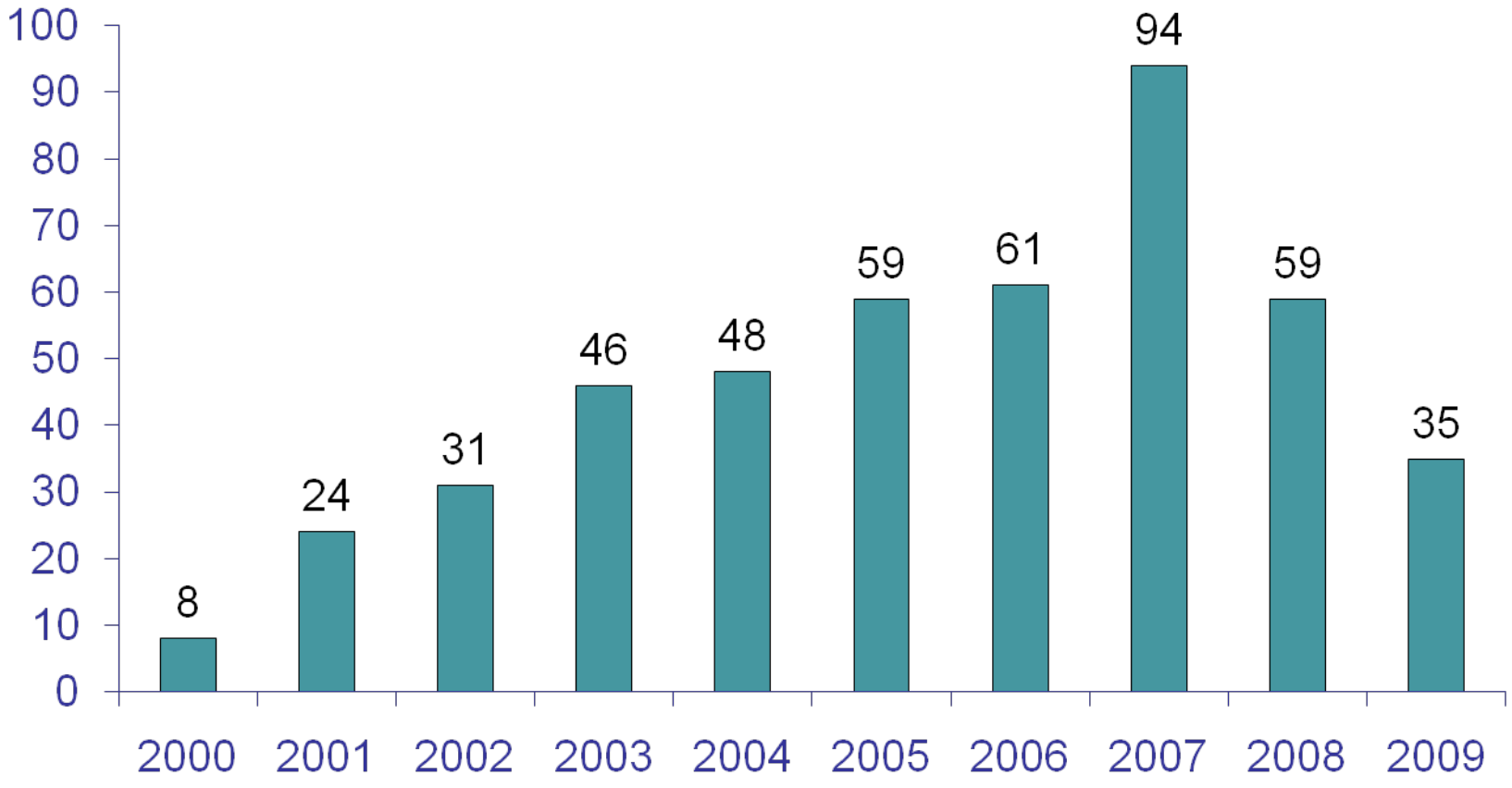






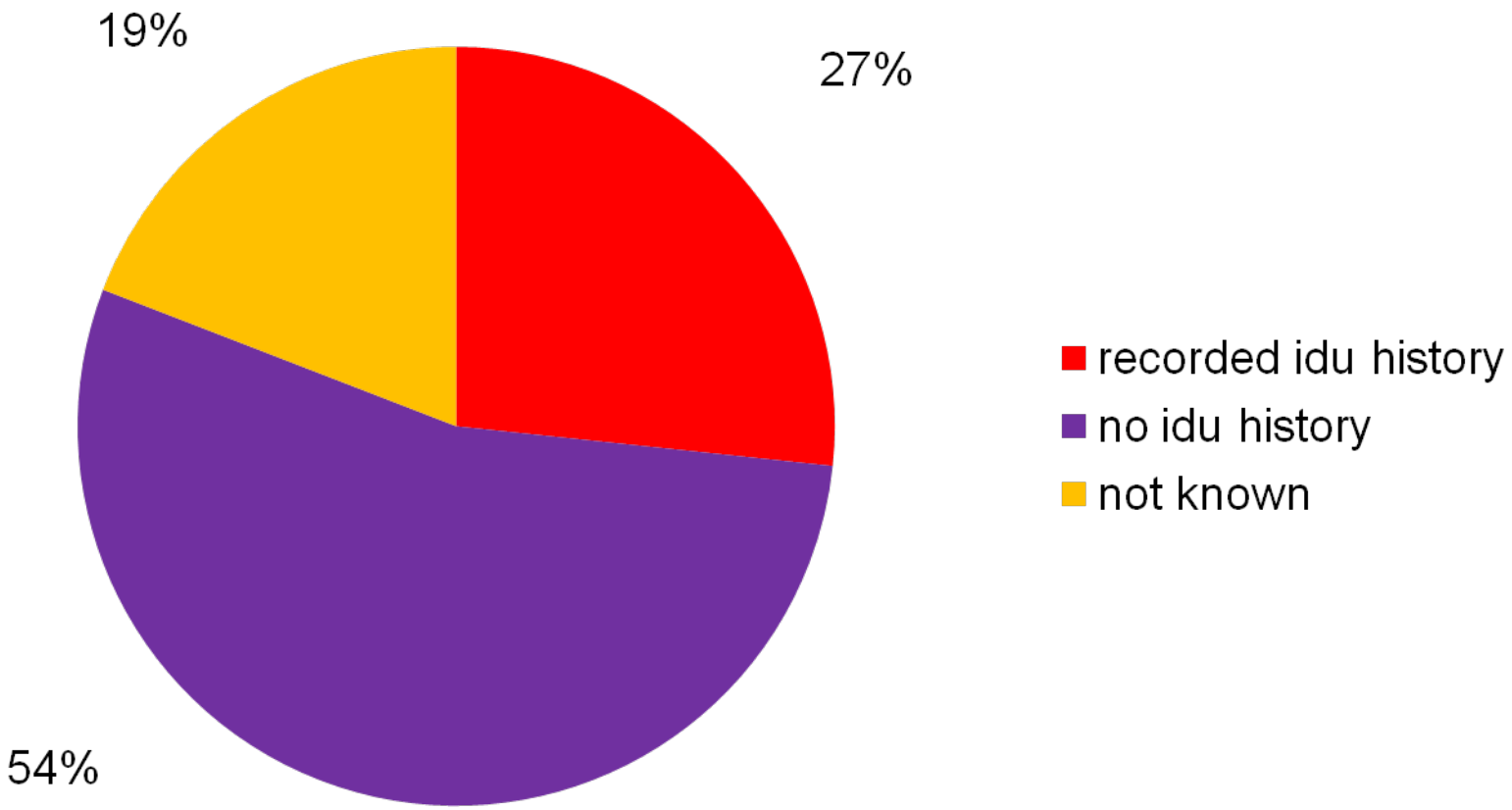
Oxycodone-related deaths

CIs: Amanda Roxburgh, Lucy Burns



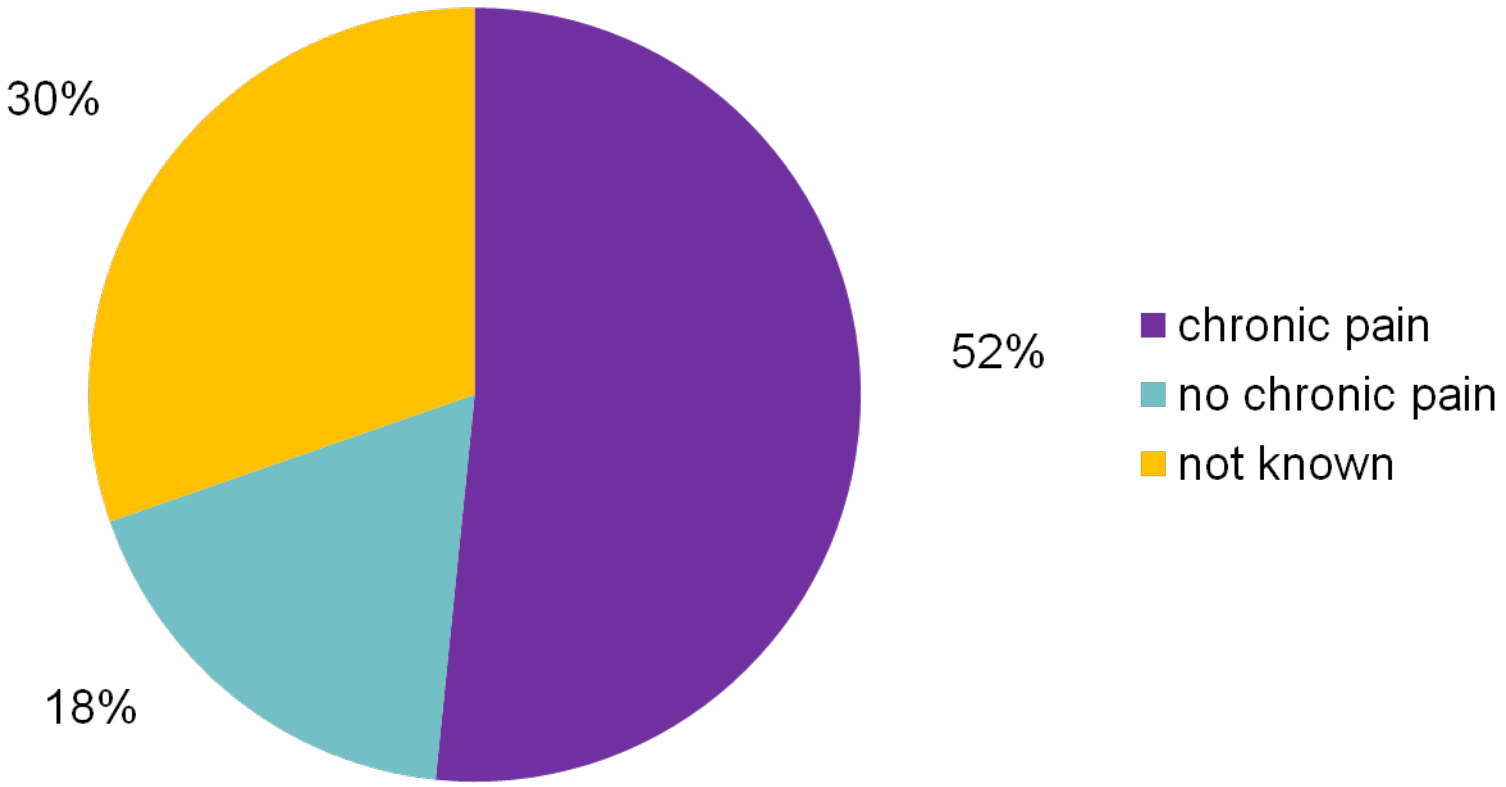
Source: National Coronial Information System, Victorian Institute of Forensic Medicine

Deaths by history of IDU



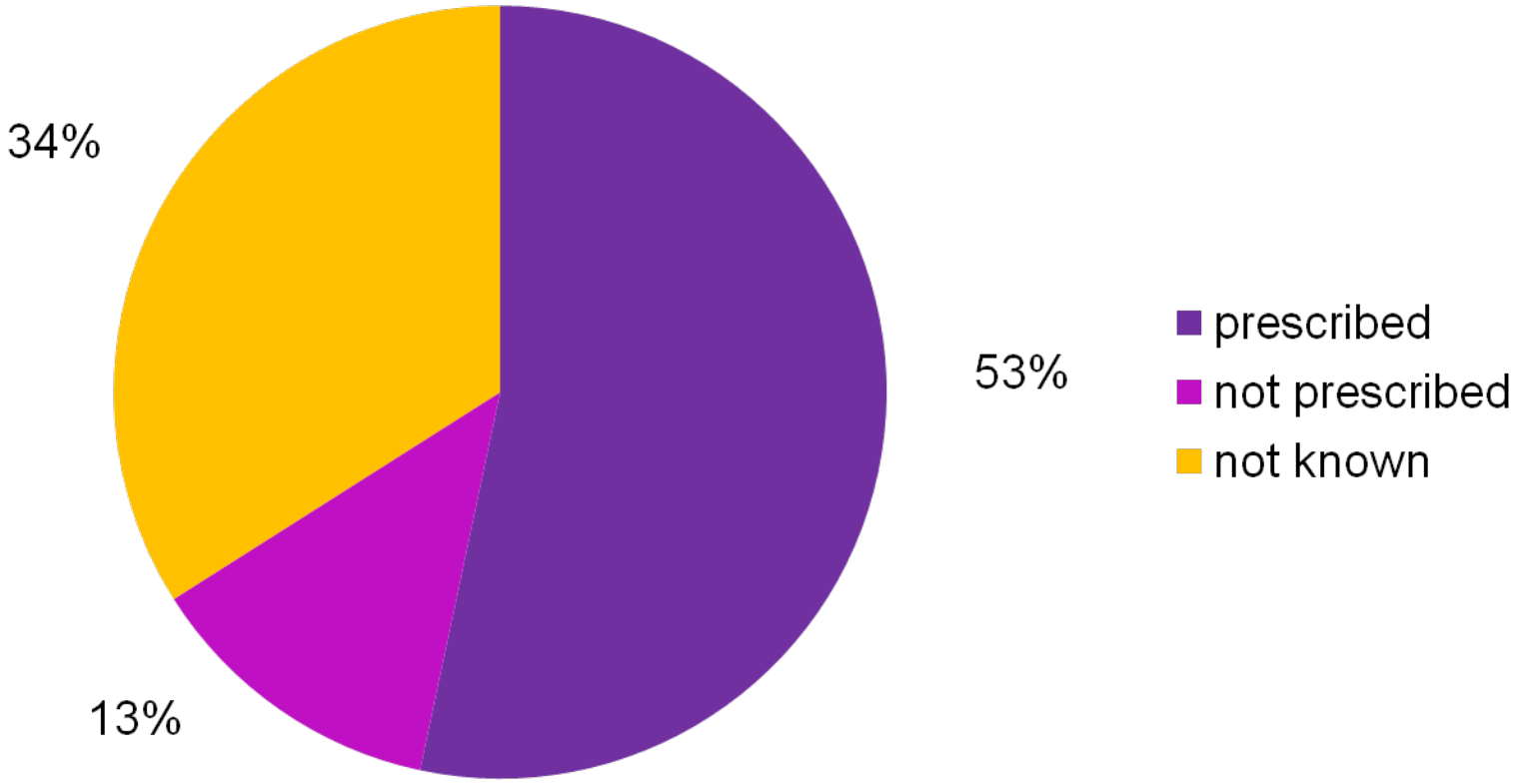
Source: National Coronial Information System, Victorian Institute of Forensic Medicine

Deaths by chronic pain status



Source: National Coronial Information System, Victorian Institute of Forensic Medicine

Deaths by prescribed medication



Source: National Coronial Information System, Victorian Institute of Forensic Medicine

OST in NSW: trends, benefits risks and the harms faced by opioid dependent people

Background

People who are heroin dependent have well documented increases in mortality across a range of domains

Some work has examined mortality in and out of treatment but these analyses have often been crude or lacking statistical power

Data linkage across an entire treatment programme presents an opportunity to consider risk in a more fine grained manner (although it lacks the detailed measurements that other methods of establishing cohorts have)

Aims

- Examine mortality among all person entering opioid pharmacotherapy in NSW between 1985 and 2006;
- A brief look at causes of death across time;
- Estimate risk during and out of treatment, and at “high risk” periods;
- Compare mortality risk for methadone and buprenorphine clients;
- Examine risk according to demographic and treatment variables;
- To estimate the number of lives and years of life that may have been saved due to provision of methadone and buprenorphine in NSW across this period

Overview: client entry and re-entry

N = 42,676 persons entered treatment during the period

N = 425,998 person-years (PY) of follow-up (FU)

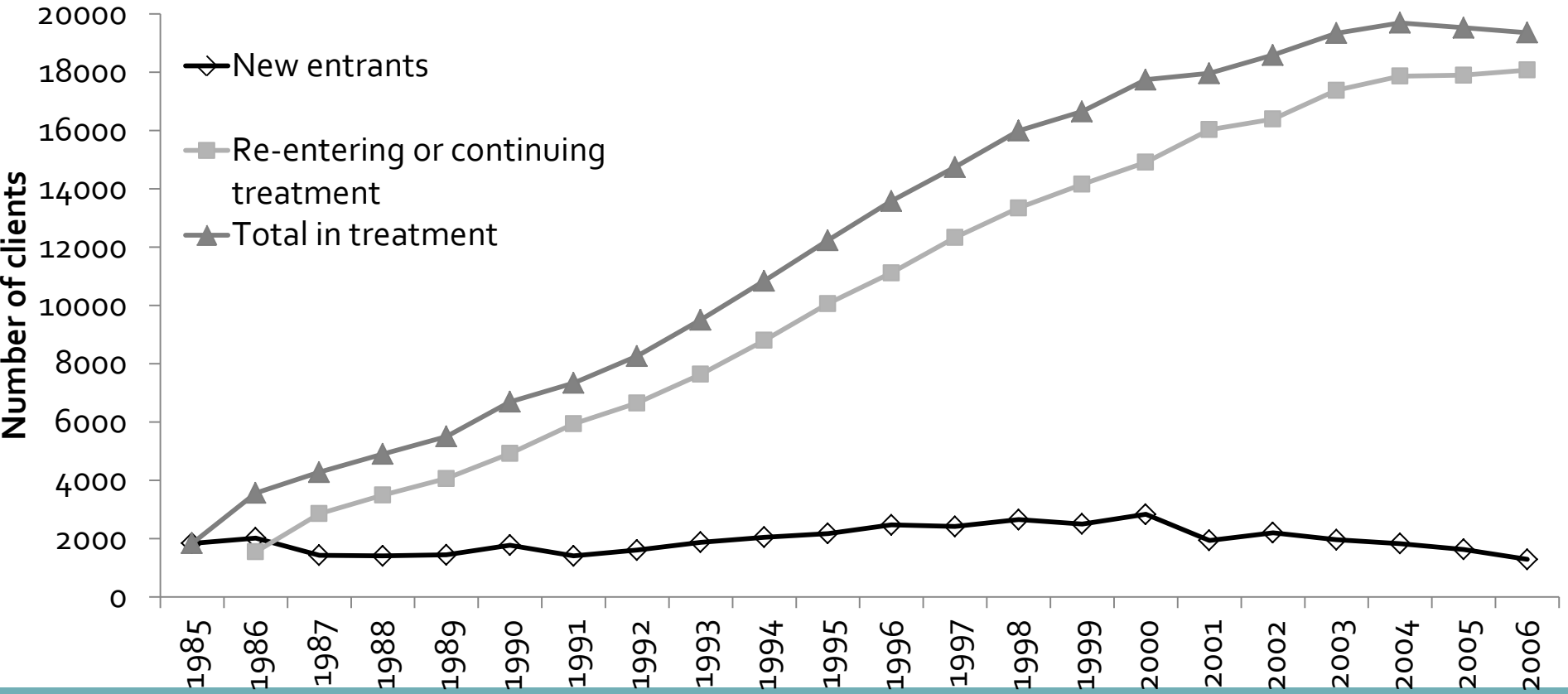
Average per client of 2.5 treatment episodes

Median length of treatment 198 days

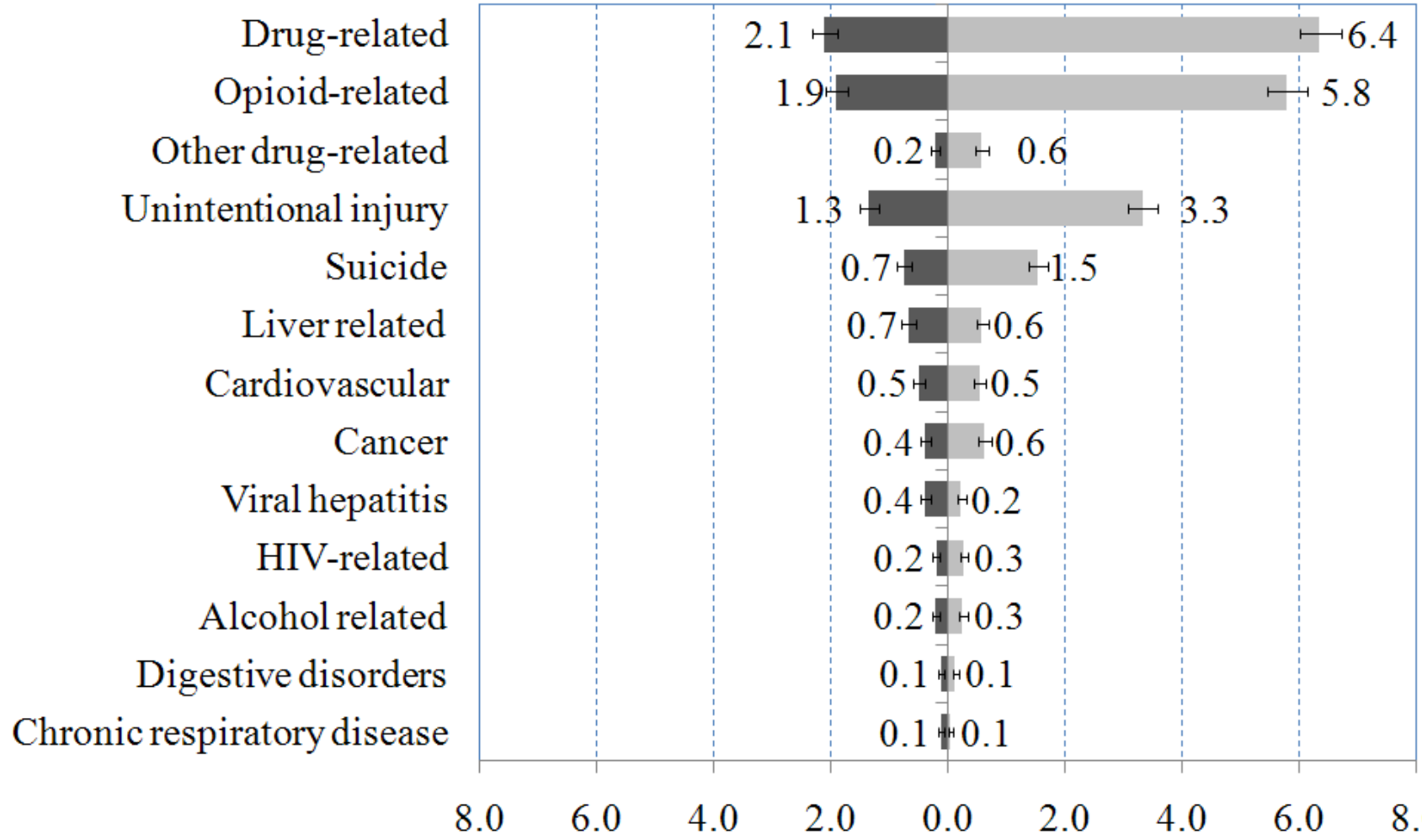
Buprenorphine introduced in 2001;

- retention shorter;
- more likely to switch between medications;
- more likely to have multiple episodes

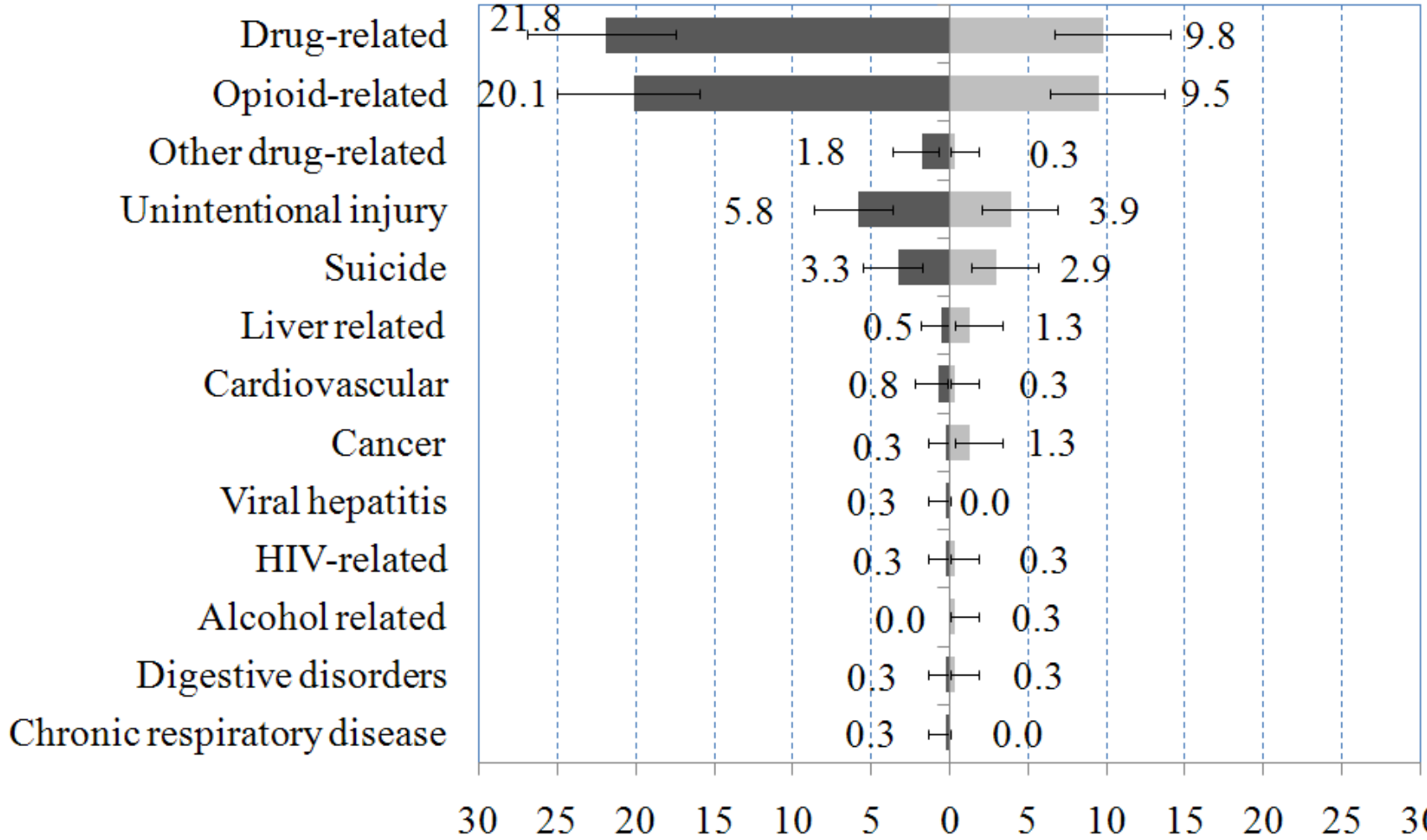
Numbers in opioid pharmacotherapy, NSW 1985-2006



Mortality due to specific causes, OVERALL in and out of treatment



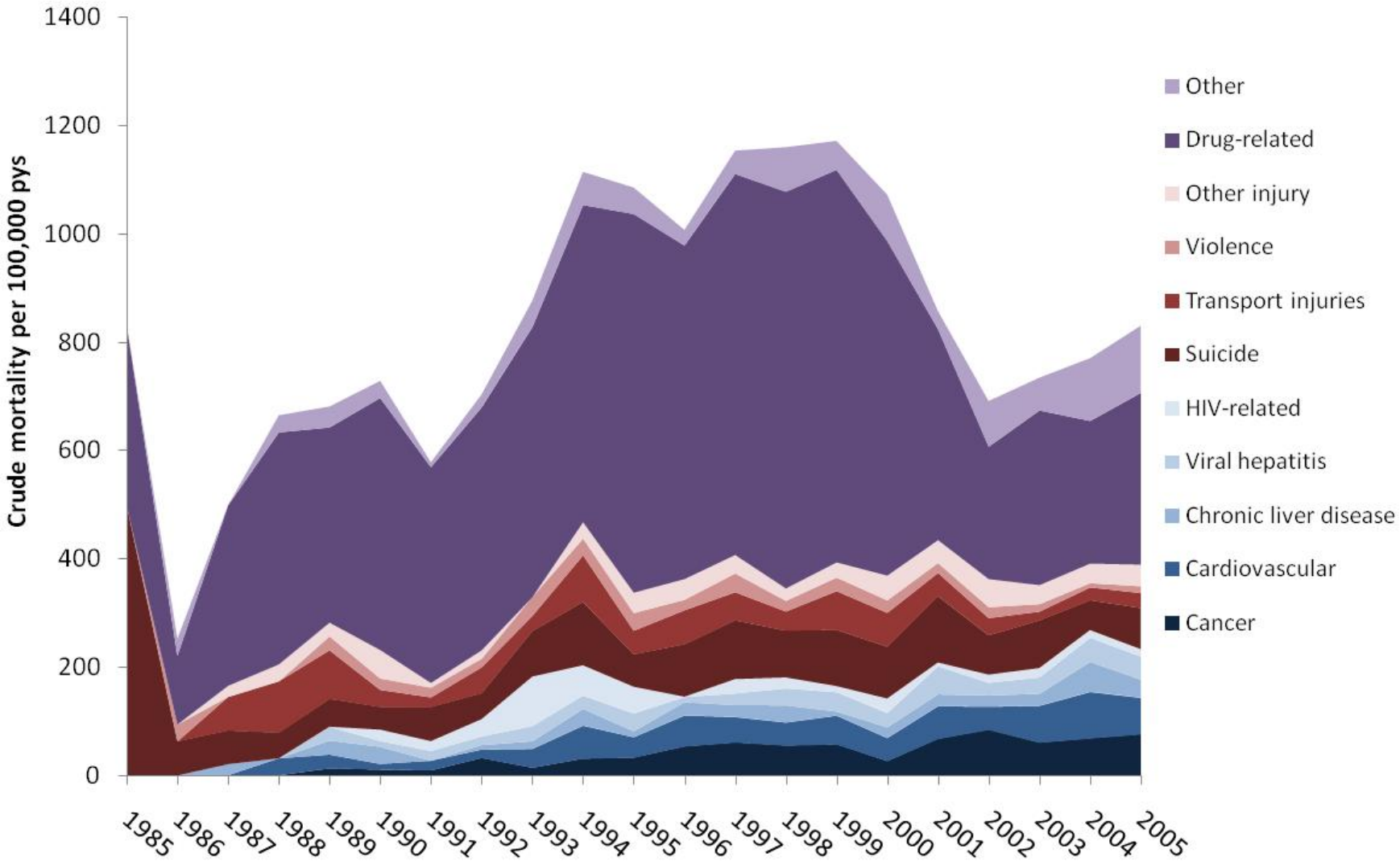
Mortality due to specific causes, FIRST 2 WEEKS in/out of treatment



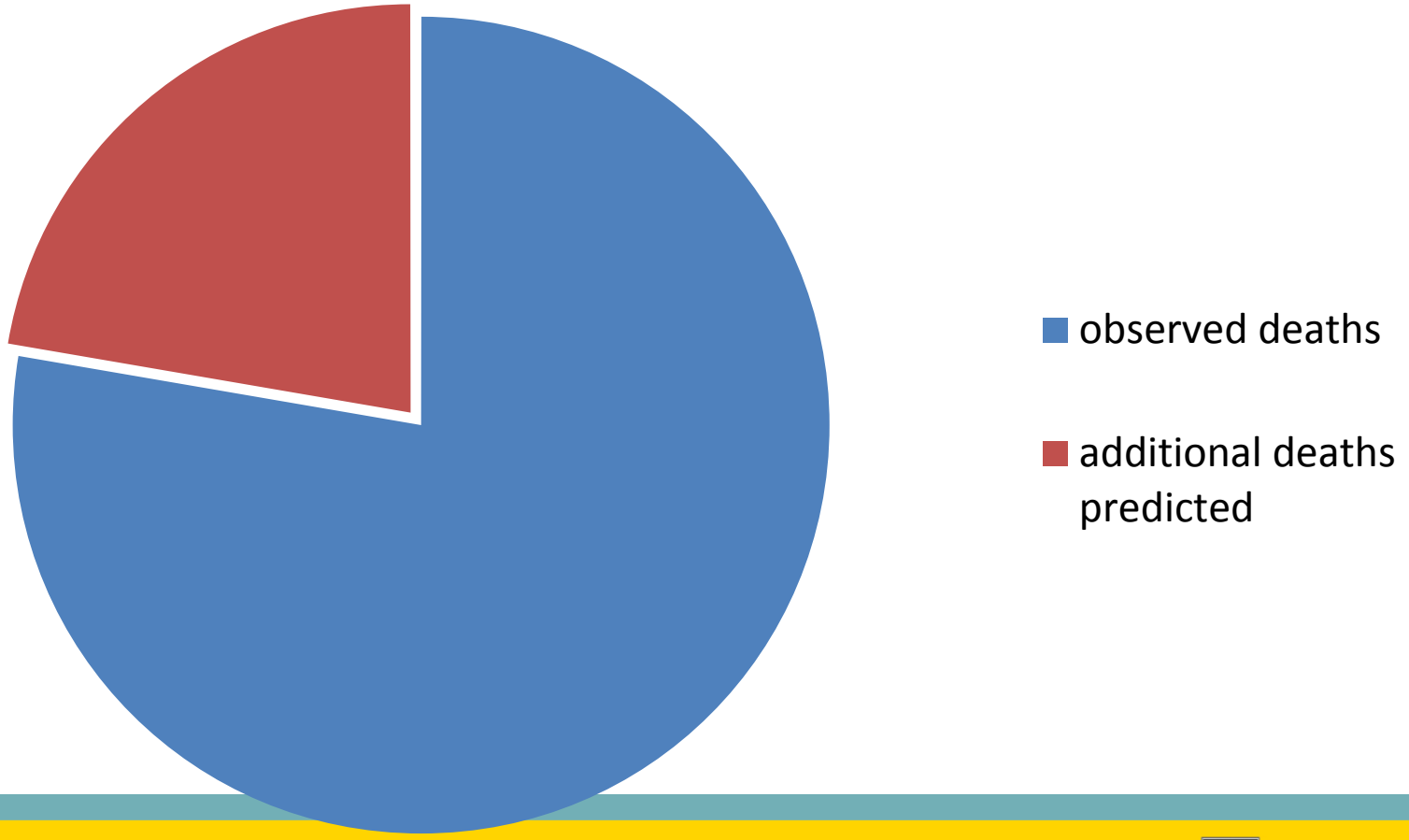
Comparing buprenorphine and methadone in NSW

- **Treatment patterns**
- *Burns, Randall, Hall, Law, Butler, Bell, Degenhardt, DAD 2009*
  - **Retention** poorer for buprenorphine; retention in ANY form also poorer
  - **Repeated episodes** greater for buprenorphine
  - **Switching medications** more likely among those beginning on buprenorphine
- **Mortality risk**
- *Jo Kimber, Louisa Degenhardt, Matt Hickman, analyses ongoing*
  - **Risk during INDUCTION** lower for buprenorphine than methadone
  - **Risk during REMAINDER OF TREATMENT** similar/slightly higher (drugs) for bup.
  - **Risk after LEAVING TREATMENT** higher for buprenorphine than methadone

Causes of mortality over time (CMR)



An additional 1130 deaths might have occurred without OST as provided (29% greater than observed number)

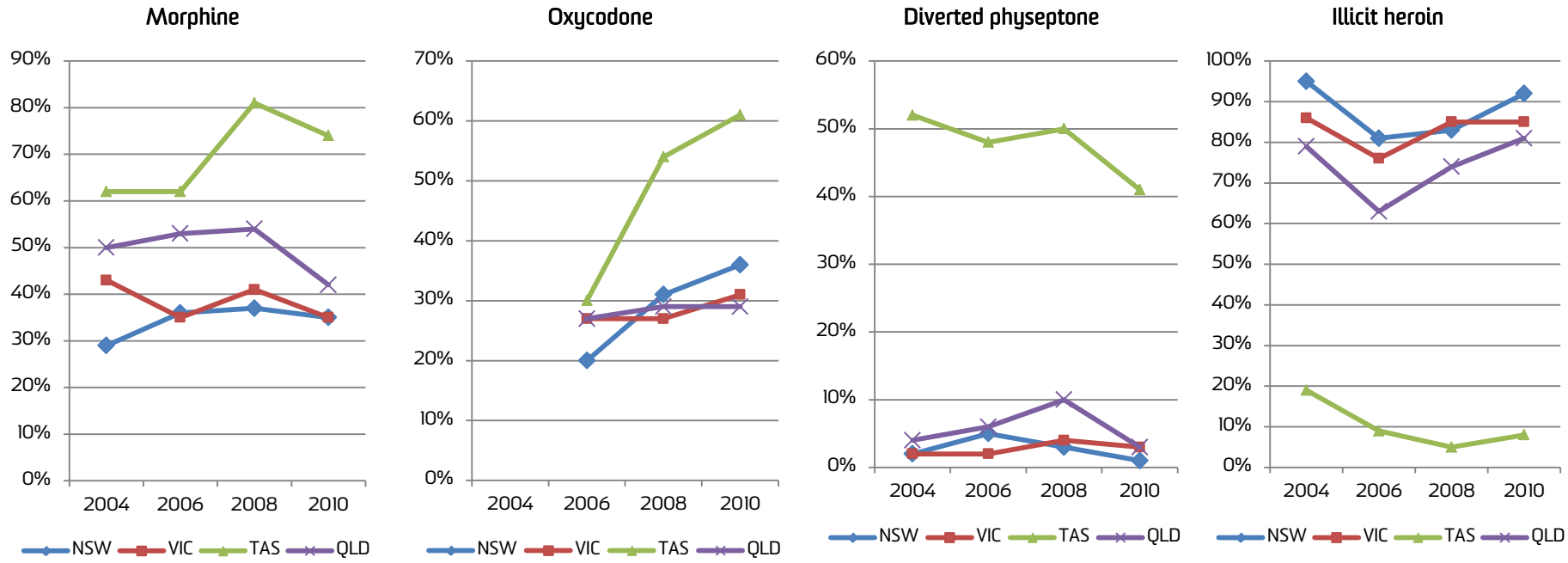


New work and work underway – linkage studies

- Cancer incidence among OST clients
- Hepatitis C, B and HIV notifications among OST clients
- Among OST clients, rates of court attendance, imprisonment, OST provision in prison, successful transfer to OST post-release, and impact upon recidivism, mortality and costs to the healthcare and criminal justic systems
- Postdoctoral work: Sarah Larney (Brown University)
- Jo Kimber – cross-national study of OST and mortality risk (UK, USA, Canada, Australia)

Non-adherence, injection and diversion of opioids

Proportion of people who inject drugs regularly who used opioids in the past six months, 2004-2010 (IDRS)



Monitoring of non-adherence to OST in Australia

CIs: Louisa Degenhardt, Briony Larance, Richard Mattick, Fiona Shand, Nick Lintzeris, Robert Ali, Rebecca Jenkinson, Paul Dietze

- Post marketing surveillance of buprenorphine-naloxone 2006-2008
  - Compared methadone, buprenorphine (Subutex), buprenorphine-naloxone (Suboxone) tablet
  - Availability, adherence, injection, diversion of each medication
  - FINDINGS:
    - Suboxone injected less frequently and by fewer overall
    - Subutex more frequently injected despite being less available
    - Methadone similar to Suboxone
  - **NEW WORK monitoring the introduction and uptake of the Suboxone Film product (2011-2013)**
    - Water-soluble “film” preparation
    - Designed to improve adherence to supervised doses
    - Extremely water soluble – unclear what will happen with takeaway doses

Aberrant behaviours scale development

CIs: Briony Larance, Richard Mattick, Louisa Degenhardt, Nick Lintzeris, Raimondo Bruno

Researchers: Emma Black, Rohan Holland, Adrian Dunlop

- N=400 chronic opioid patients from pharmacies, pain clinics and Opioid Substitution Treatment (OST) programs.
  - Self complete survey developed using the literature, key expert and advisory committee expertise.
  - Test-retest on 30 participants
- 1 item per 'aberrant' behaviour or related issue (38 items); participant rates each item, e.g. 'I have taken less of my opioid medication than was prescribed' - very often, often, sometimes, hardly ever, never
  - also asked 'Would you talk to your doctor about this, if he/she asked you about it?'
- Responses to the 38 opioid behaviour items analysed using exploratory factor analysis to develop a brief scale - aiming for 8 item scale

The use of pharmaceutical opioids for chronic pain

Background (continued)

- Increasing concern about the prescription of opioids for pain
  - ageing population?
  - better pain management?
  - greater problems with dependence?
  - diversion and injection of these medications?
- Question of how to measure risk and aberrant behaviour in pain patients

NHMRC project grant: two cohorts of opioid users

- **Chief Investigators-** Louisa Degenhardt (NDARC), Prof. Wayne Hall (University of Queensland), A/Prof. Milton Cohen (St. Vincent's Hospital, Pain Clinic), A/Prof Nick Lintzeris (USyd/SESIAHS), Dr. Suzi Nielsen (USyd), Dr. Raimondo Bruno, (UTAS), Dr Fiona Shand (NDARC), Prof. Michael Farrell (Director, NDARC)

- **Associate Investigators-** Prof. Richard Mattick (NDARC) and Briony Larance (NDARC)

- **Study coordinator-** Gabrielle Campbell

Prospective cohort: the POINT study: Pain and Opioids IN Treatment

Aim: Examine the long-term benefits and risks of opioid analgesics, and their predictors

Sample*:* 2,000 chronic non-cancer pain patients will be assessed as they begin treatment with opioid analgesics.

Proposed eligibility criteria*;*

- Suffering from chronic non-malignant pain (CNMP)
- Prescribed pharmaceutical opioids for CNMP
  - Prescribed pharmaceutical opioids for greater than 6 weeks and less than 6 months
  - Had not been prescribed pharmaceutical opioids for a period of three months or more in the 6 months prior
- IDU history not an exclusion, but primary pharmaceutical opioid use for OST due to heroin dependence not eligible

POINT study (2)

Proposed recruitment methods

- Recruitment through pharmacies (this includes those in the Pharmacy Guild and Chemist Warehouse), newspaper advertisements and the possibility of viral emails.

Procedure

- Baseline interview followed by three follow-ups over a two-year period. The follow-ups will occur at 6 months, 12 months and 24 months. The baseline interview will be conducted by interviewers over the phone, whilst the rest of the follow-ups will be self complete.

Outcomes

- **The Four "A's" of Pain Treatment Outcomes**
  - Analgesia
  - Activities of daily living (psychosocial functioning)
  - Adverse effects (side effects)
  - Aberrant drug taking (addiction-related outcomes)
- **Predictors of outcomes**
  - Mental health
  - Drug and alcohol use history (including parental substance use)
  - Child sexual abuse
  - Other medications
  - Other illnesses and disabilities

Retrospective cohort

Aim

- Examine trajectories of opioid analgesic prescribing for all people prescribed opioids in Australia using data linkage

Method

- The study will use national prescribing data from Medicare Australia and link it to Medicare data on health service utilisation, and mortality data.
- In New South Wales, the data will also be linked to the OST dataset and hospital admissions data.

Outcomes

- *Cessation* of use
- *Escalation of doses* greater than clinical recommended;
- Daily doses exceeding accepted clinical guidelines for maximum daily dosing
- "*Doctor shopping"*
- *Dependence* - transfer onto opioid substitution treatment (methadone or buprenorphine)

Discussion

- To summarise: there are multiple challlenges in this field – the juxtaposition of benefit to patients with clinical and population-level risks
- Increasing prescription for pain of some opioids requires new work to quantify and examine the magnitude of risks in an ongoing fashion
- Ongoing work to consider the risks of OST provision: adherence, injection, diversion and mortality
- Population-level linkage to examine risks that are difficult to study with small cohorts or clinical trials