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Cohort linkage studies in England

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Addiction
RESEARCH REPORT
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Fatal opioid poisoning: a counterfactual model to estimate the preventive effect of treatment for opioid use disorder in England

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ABSTRACT

Aim A counterfactual model was used to estimate treatment services for opioid use disorder (OUD) in E OUD treatment episode data recorded by the English on opioid deaths recorded by the Office for National medical opioid users (aged 15–64 years; approximat (aged 15–64 years) treated for OUD in the study perio soning (opioid death). The opioid death rate [per 100 for study year, age group (15–24, 25–34, 35–64 yea ment', 'during treatment' and 'after treatment'. **Resul** deaths in the study: 741 during treatment (0.20 per PY; MRR = 3.76, 95% confidence interval (CI) = 3.1 95% CI = 1.64–2.41). By counterfactual estimation, deaths each year (95% CI = 702–1084). **Conclusion** shows that the English public treatment system for opi opioid-related poisoning. Counterfactual models of m itoring of substance use disorder treatment systems.

Keywords Counterfactual model, fatal opioid poi

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INTRODUCTION

The non-medical use of opioid drugs (particularly illicit oin) is associated with premature death in many cour (22–54 drug-related deaths per million population 15–64 in 2011 [1]). One per cent of the illicit opioid-u population dies each year, a rate 10 times higher tha general population [2,3]. Their most common cau death is acute opioid-related poisoning following accid overdose inducing respiratory depression, hypoventil and hypoxia [4]. Opioids are also frequently mention mortality records which describe violence, road traffic dents and long-term health conditions [5].

ADDICTION
RESEARCH REPORT
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Impact of treatment for opioid dependence on fatal drug-related poisoning: a national cohort study in England

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ABSTRACT

Aims To compare the change in illicit opioid users' risk of fatal drug-relate agonist pharmacotherapy (OAP) and psychological support, and investigate the criminal justice system (CJS) referral and treatment completion. **Design** N English National Drug Treatment Monitoring System and the Office for Natio Data were analysed using survival methods. **Setting** All services in Englan treatment for illicit opioid users. **Participants** Adults treated for opioid deper 151 983 individuals; 69% male; median age 32.6 with 442 950 person-ye outcome was fatal DRP occurring during periods in or out of treatment, with a injecting status and CJS referral. **Findings** There were 1499 DRP deaths [3. interval (CI) = 3.2–3.6]. DRP risk increased while patients were not enrolle (aHR) = 1.73, 95% CI = 1.55–1.92]. Risk when enrolled only in a psycholo OAP (aHR = 2.07, 95% CI = 1.75–2.46). The increased risk when out of tre 95% CI = 1.67–2.12), illicit drug injectors (aHR = 2.27, 95% CI = 1.97–2.62 use (aHR = 2.37, 95% CI = 1.90–2.98). **Conclusions** Patients who receiv dependence in England appear to be at greater risk of fatal opioid poisonin pharmacotherapy.

Keywords Drug-related poisoning, opiate dependence, opioid agonist treatment, residential treatment.

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INTRODUCTION

Non-medical use of opioid drugs is associated with a significant global burden of disease [1]. In the United Kingdom, 1% of the illicit opioid-using population dies each year [2,3]. More than half of these deaths are due to respiratory failure following accidental overdose [3–5].

Opioid agonist pharmacotherapy (OAP) is a community treatment for opioid dependence which aims to reduce heroin and other non-medical opioid use and associated harm. Using oral methadone or buprenorphine, well-delivered OAP manages the patient's physiological dependence, attenuates drug use cravings and facilitates access to health-care an randomized con retaining patier [6–8]. The Wo National Institu recommend OA for opioid dep buprenorphine withdrawal in c

Most develo psychological s dence. Guided previous clinica

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National record linkage study of mortality for a large cohort of opioid users ascertained by drug treatment or criminal justice sources in England, 2005–2009

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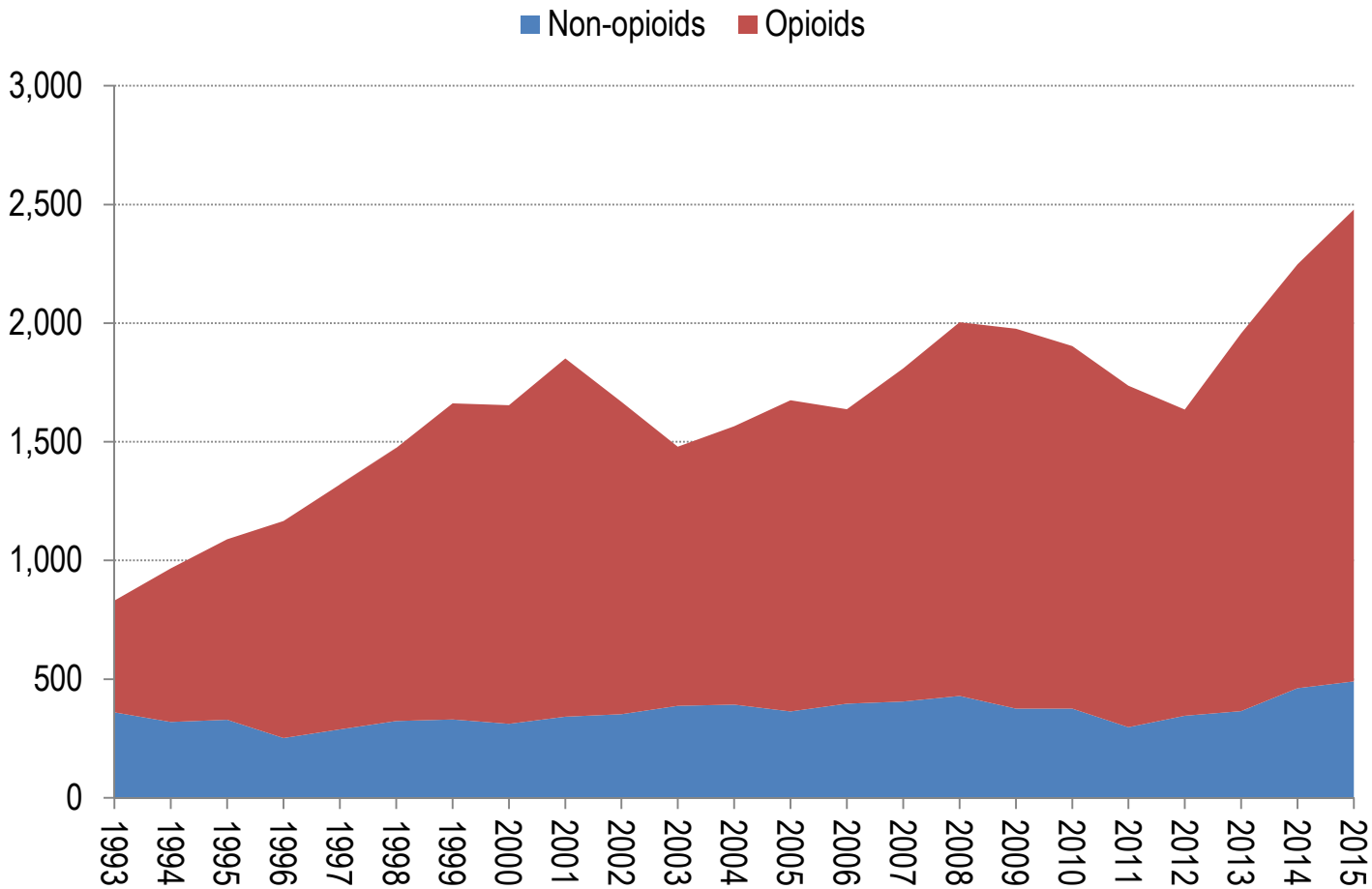
ABSTRACT

Background: Globally, opioid drug use is an important cause of premature mortality. In many countries, opioid using populations are ageing. The current study investigates mortality in a large cohort of opioid users; with a focus on testing whether excess mortality changes with age.
Methods: 198,247 opioid users in England were identified from drug treatment and criminal justice sources (April, 2005 to March, 2009) and linked to mortality records. Mortality rates and standardised mortality ratios (SMRs) were calculated by age-group and gender.
Results: There were 3974 deaths from all causes (SMR 5.7, 95% Confidence Interval: 5.5 to 5.9). Drug-related poisonings (1715) accounted for 43% of deaths. Relative to gender-and-age-appropriate expectation, mortality was elevated for a range of major causes including: infectious, respiratory, circulatory, liver disease, suicide, and homicide. Drug-related poisoning mortality risk continued to increase beyond 45 years and there were age-related increases in SMRs for specific causes of death (infectious, cancer, liver cirrhosis, and homicide). A gender by age-group interaction revealed that whilst men have a greater drug-related poisoning mortality risk than women at younger ages, the difference narrows with increasing age.
Conclusion: Opioid users' excess mortality persists into old age and for some causes is exacerbated. This study highlights the importance of managing the complex health needs of older opioid users.

1. Introduction

Illicit drug use, especially opioid addiction, is an acknowledged public health problem in most developed countries and a growing problem worldwide (Degenhardt and Hall, 2012; Degenhardt et al., 2004; Lim et al., 2013). Deaths due to illicit drug use are an important, increasing (Murray et al., 2013), and preventable cause of premature mortality (Bargagli et al., 2006). Recent global estimates suggest that the years of life lost due to illicit drugs are greater than for alcohol, because the former tend to occur at an earlier age (Degenhardt and Hall, 2012). In England and Wales, deaths directly attributed to illicit drug use (i.e., drug related poisonings) account for 12% of all fatalities between 16 and 40 years of age (Office for National Statistics Statistical Bulletin, 2013). The risk of a drug related poisoning is higher for males, drug injectors and those with concurrent depressant use (Davoli et al., 2007; Degenhardt et al., 2011; Merrall et al., 2012). A substantial, international body of evidence demonstrates excess mortality risk for many causes of

Number of drug related deaths: opioids vs. non-opioids: deaths registered: England & Wales: 1993-2015



Questions:

Published DRD statistics are helpful for some purposes, but tell us little/nothing about premature mortality ***risk*** and the effect of interventions to reduce risk:

1) DRD Risk (i.e. mortality rates) & risk factors

- Prevalence estimates (the denominator for risk) are too imprecise to assess rates/risk with necessary precision

2) The contribution of other (non-DRD) causes to premature mortality?

- Some evidence of excess mortality for additional causes of death (suicide, homicide, infectious disease, liver disease).[1–4]

3) Interaction between treatment and DRD risk

- To what extent does our treatment system reduce risk?

- Examination of risk requires a cohort approach.
- Also, to study non-poisoning drug user mortality (not otherwise ascertained).
- Very few studies have used adequate cohorts (too few participants, insufficient power).
- Most studies include only treated individuals: perhaps not representative for some purposes.

1- Merrall ELC, Bird SM, Hutchinson SJ. Mortality of those who attended drug services in Scotland 1996-2006: Record-linkage study. *Int J Drug Policy* 2012; **23**(1): 24–32.

2- Degenhardt L, Randall D, Hall W, Law M, Butler T, Burns L. Mortality among clients of a state-wide opioid pharmacotherapy program over 20 years: Risk factors and lives saved. *Drug Alcohol Depen* 2009; **105**(1–2): 9–15.

3 - Ghodse H, Oyefeso A, Kilpatrick B. Mortality of drug addicts in the United Kingdom 1967-1993. *Int J Epidemiol* 1998; **27**(3): 473–8.

4 - Crump C, Sundquist K, Winkleby MA, Sundquist J. Mental disorders and vulnerability to homicidal death: Swedish nationwide cohort study. *BMJ* 2013; **346**: f557

Drug Data Warehouse opioid user cohort: 2005-09

(n= 198,247): (extracted from substance user cohort of n=1,000,000)

Data source	Population	Opiate User Cohort Case Definition (aged 18-64 years)
Treatment (NDTMS)	Treatment clients receiving community or residential structured addiction treatment	Reporting a problem associated with opiate use at triage to treatment n=152k
Drug Test on Arrest (DTR)	Persons tested for opiates and cocaine metabolites by saliva sample, arrested following a "trigger" offence, or at police discretion.	Testing positive for opiate use n=55k
Arrest Referral	Persons assessed for referral to structured drug treatment following identification in a criminal justice setting, often following DTR	Reporting weekly or greater opiate use at assessment n=48k
Prison /Probation	Offenders assessed in prison, or whilst on probation, for needs and risks prior to sentencing, and at various points throughout their sentence.	Reporting weekly or greater opiate use at assessment n=40k

Outline:

- Main cohort (n=198k opioid users, 542k person-years)
  - Sub-cohort (n=152k *treated* opioid users, 443k person-years)
- 68k person years between age 45-64 years (uniquely informative)
- Linked to ONS mortality records: any cause of death, age 18-64 years (*355k deaths*): which people died, how, and when?
- 3,974 premature deaths (1,715 Drug Related Poisoning – **43%**)
  - (treated cohort: 3,503 deaths, 1,499 drug related)
- Analysis:
  - describe all-cause mortality amongst opioid users
  - identify common causes of death
  - identify demographic & behavioural risk factors (Cox regression)
  - investigate DRD association with treatment (Cox regression)

All Cause Mortality ….

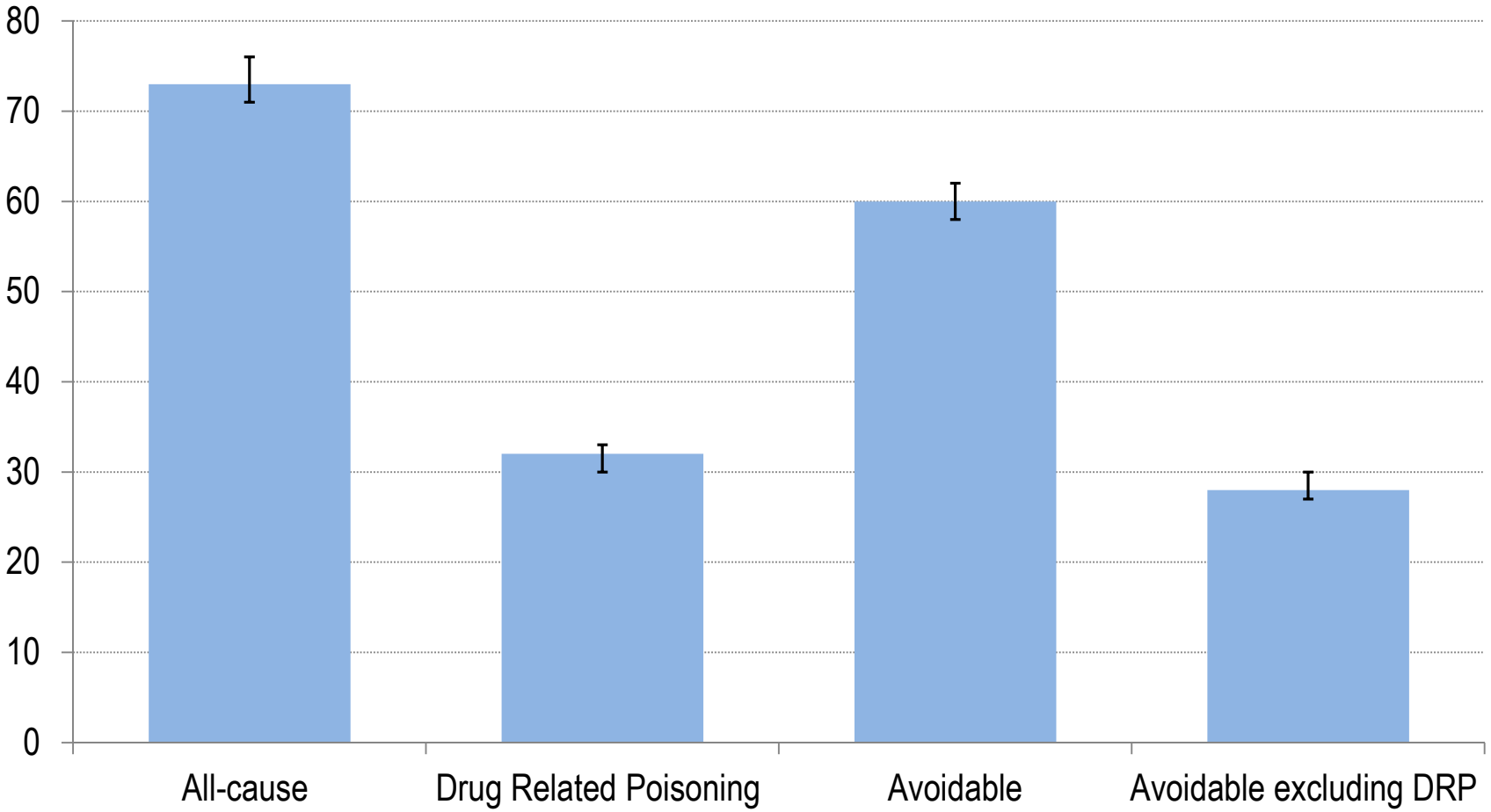
(Pierce, Bird, Hickman & Millar; 2015)

What is the extent of all cause premature mortality among (treated and untreated) opioid users?

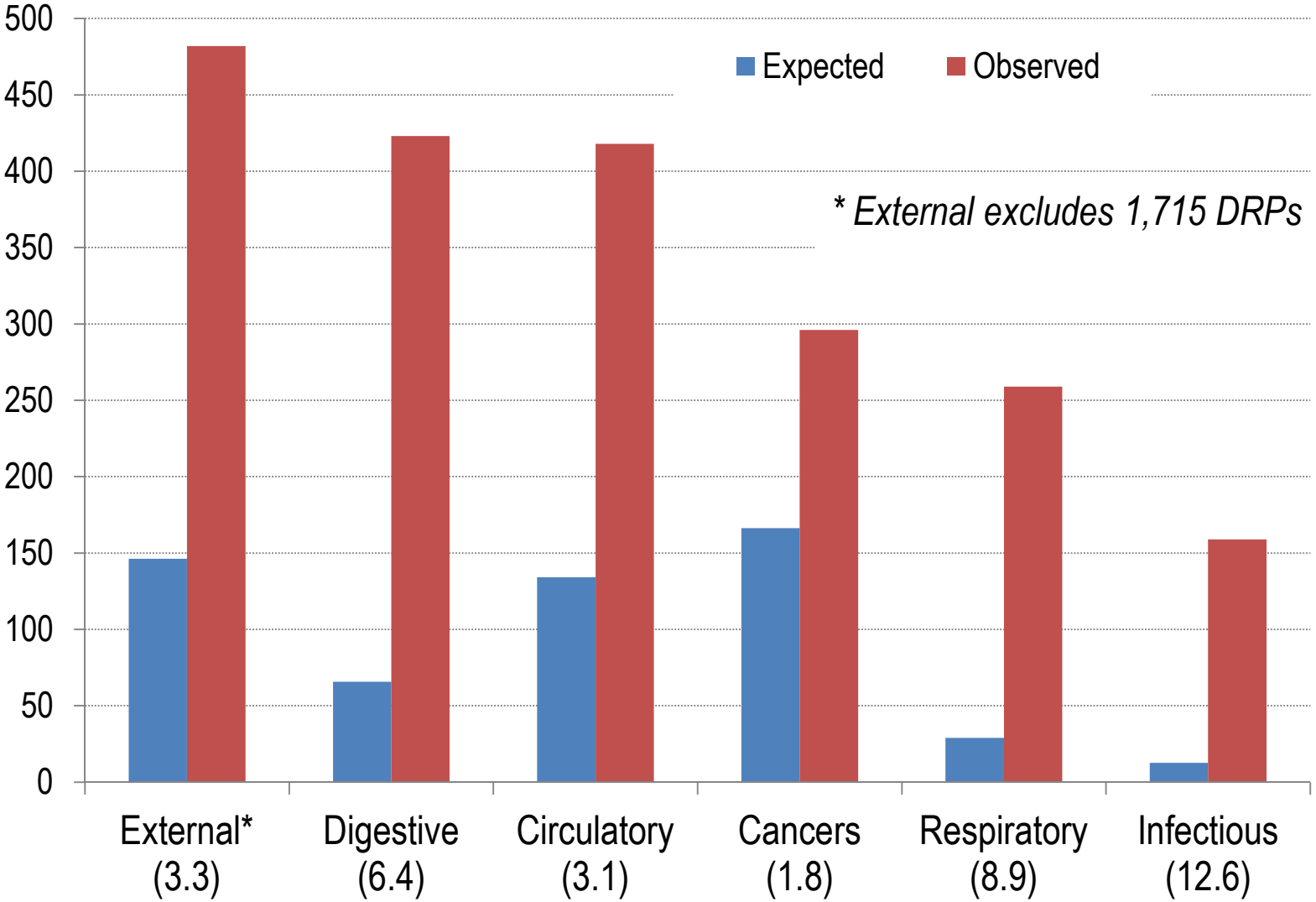
What are the common causes?

How much excess mortality is present in this group?

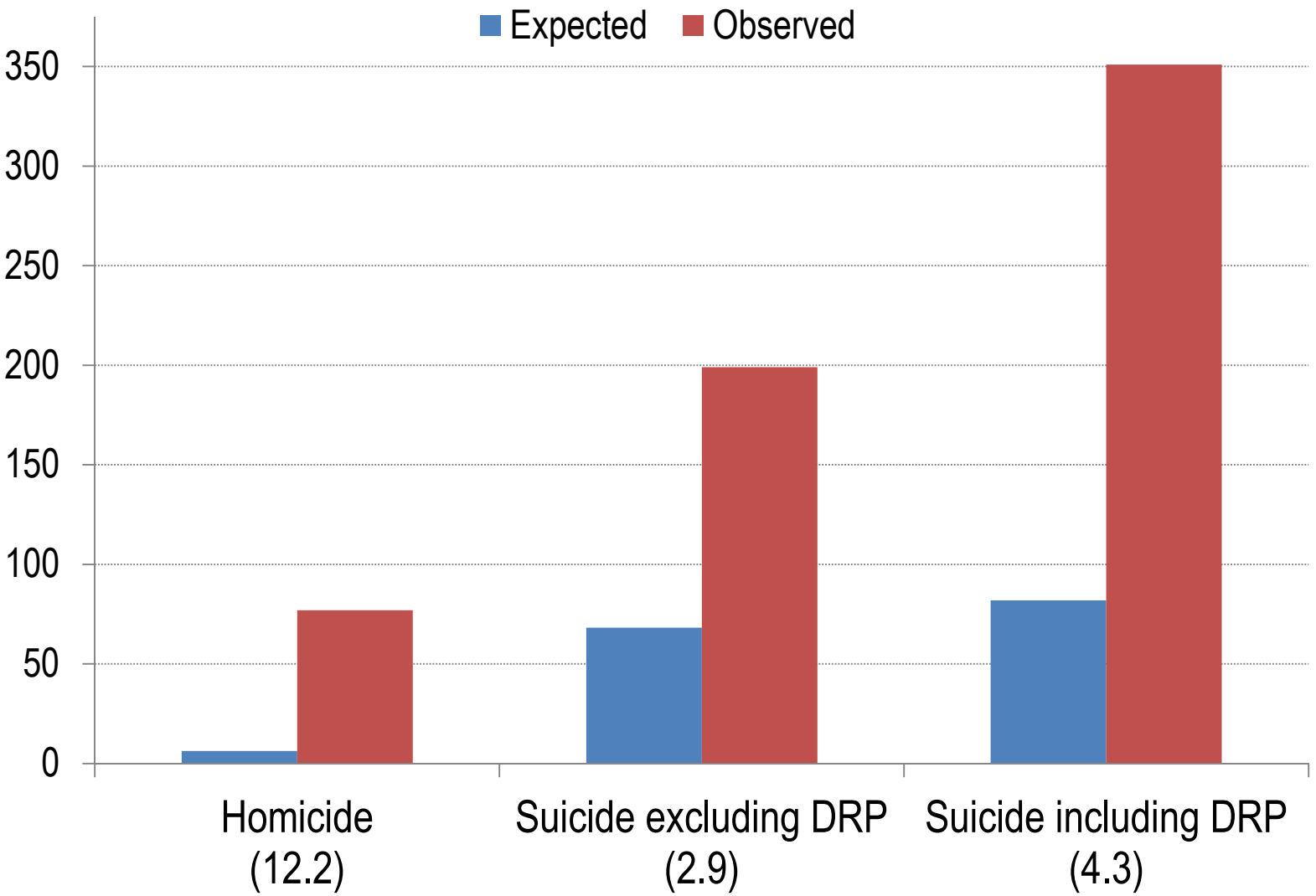
Opiate user cohort: Crude Mortality Rate per 10k person-years (n= 198,247)



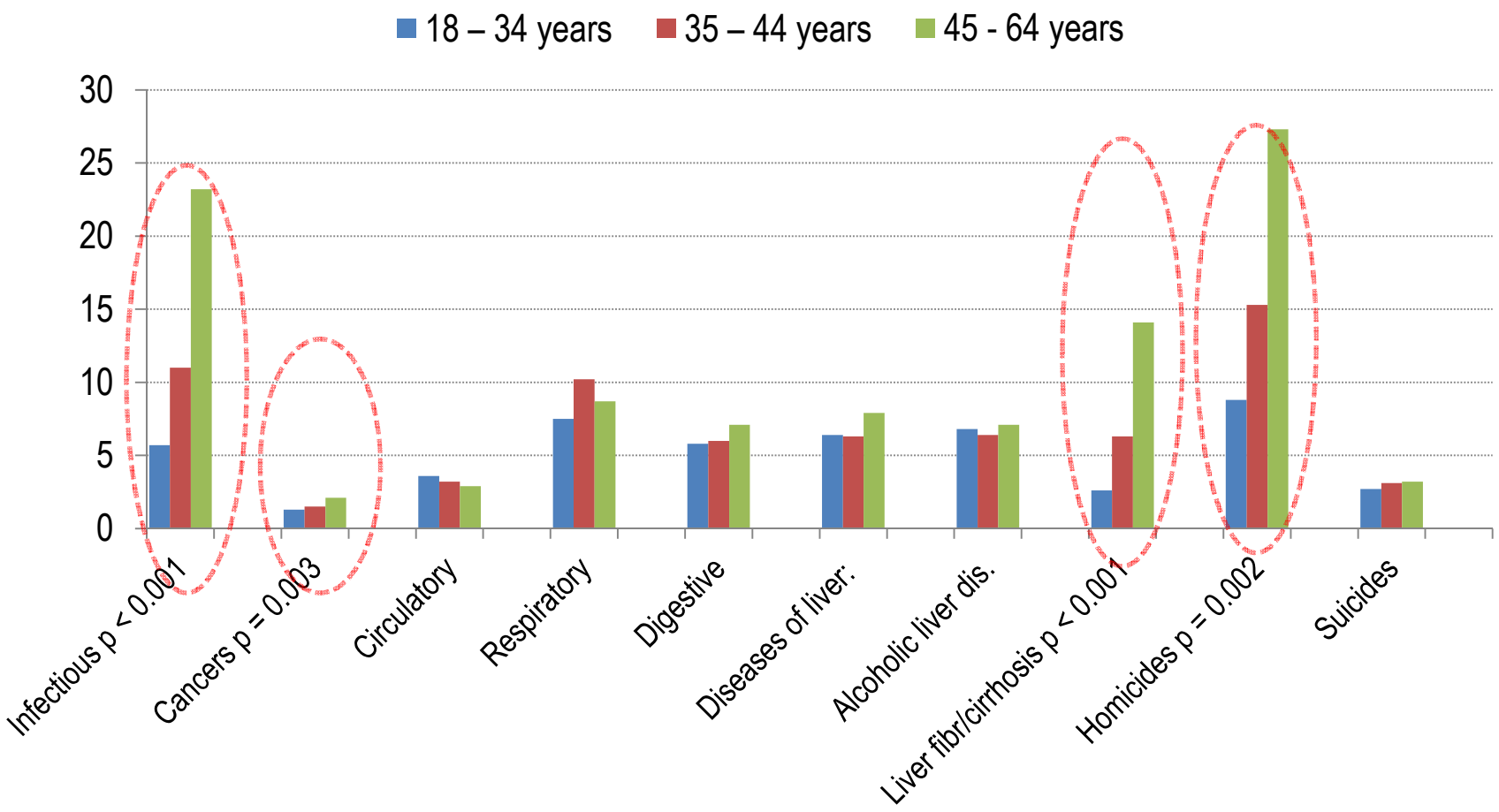
Opiate User Cohort: Expected vs. Observed deaths by cause (SMR) (n= 198,247)



Opiate User Cohort: Expected vs. observed *external* deaths by cause (SMR) (n= 198,247)



Opiate User Cohort: Standardised Mortality Ratio by cause and age (n= 198,247)



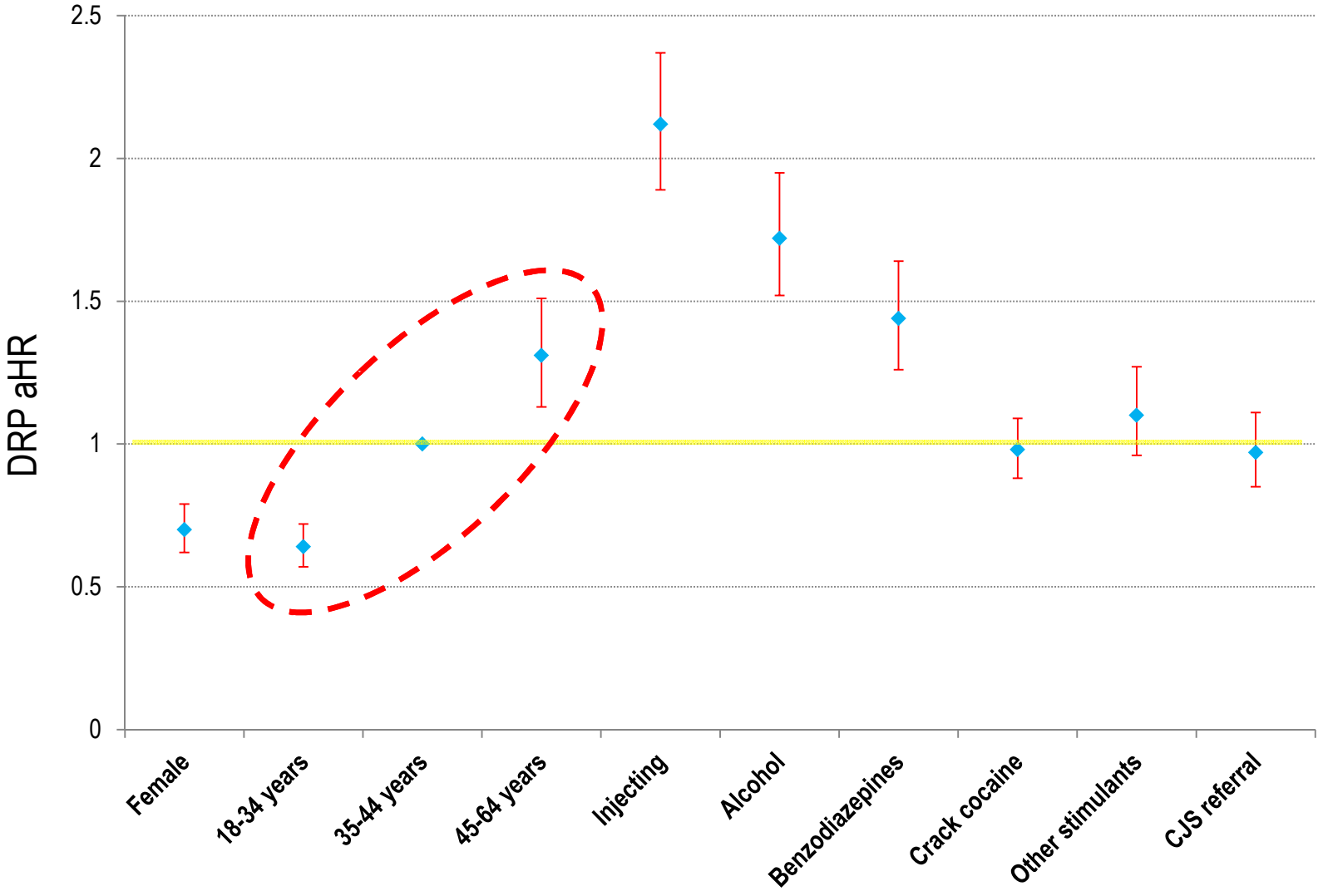
Drug Related Poisoning: treatment, and demographic & behavioural risk (treated sub-cohort) ….

(Pierce, Bird, Hickman, Marsden, Dunn, Jones, Millar; 2016)

To what extent do demographic & behavioural factors increase DRD risk?

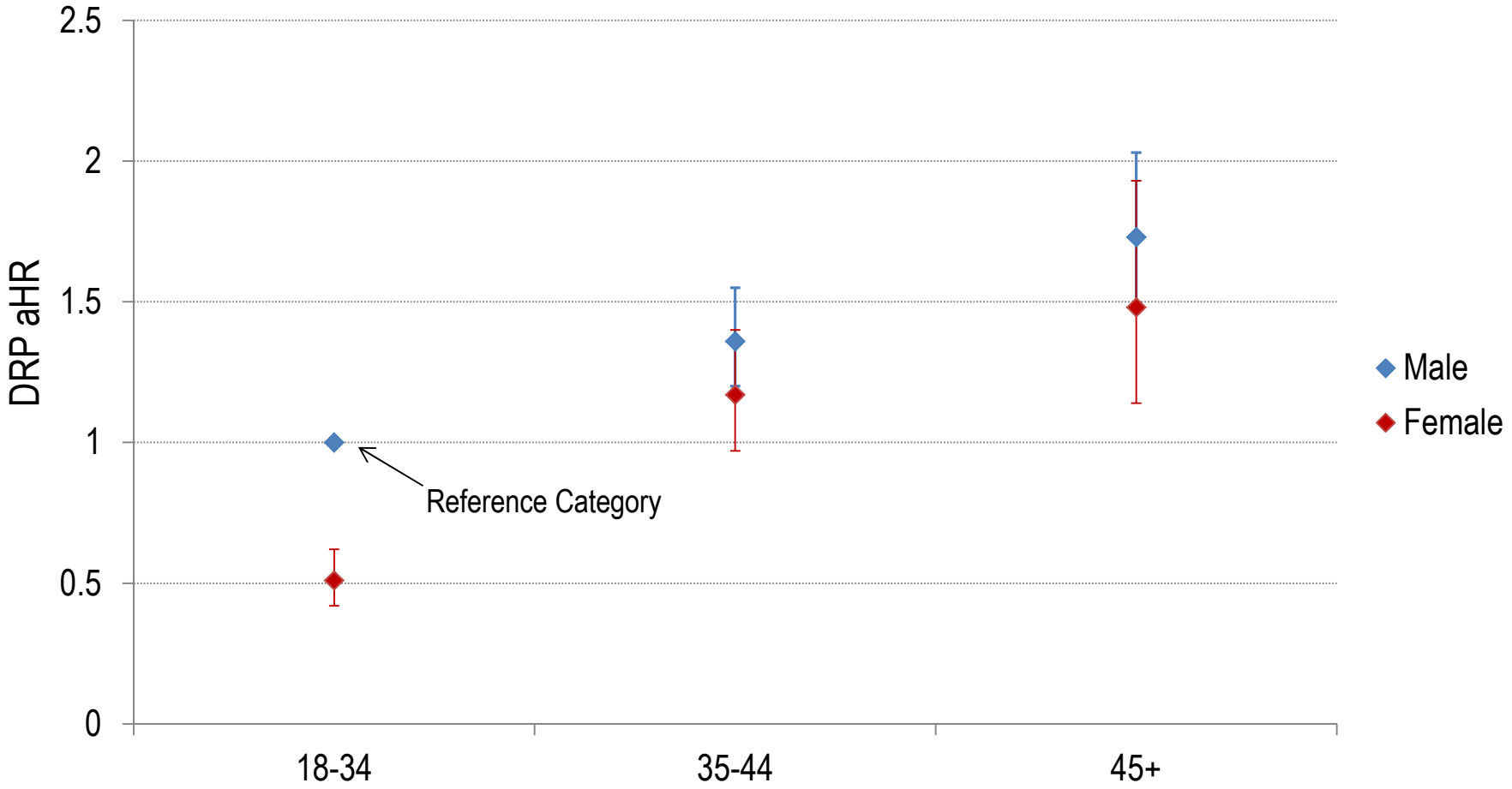
To what extent are different types of treatment associated with reduced risk?

Fatal DRP risk (aHR* & 95% CI) for demographic, behavioural, and referral covariates (n=151,983)

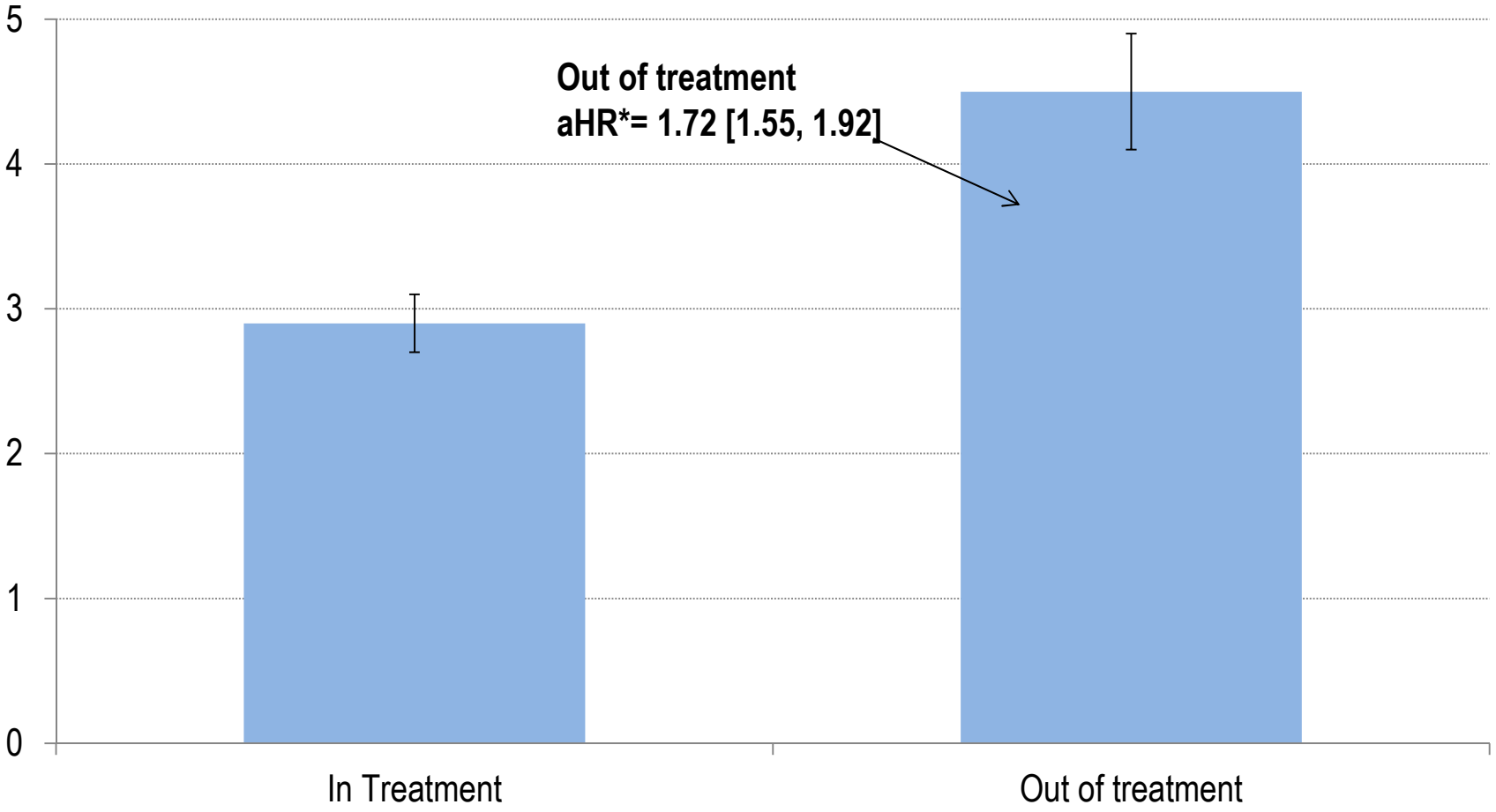


** adjusted for demographic and behavioural covariates & treatment status*

Fatal DRP risk (aHR & 95% CI) by Age & Gender (adjusted for behavioural risks) (n=151,983)

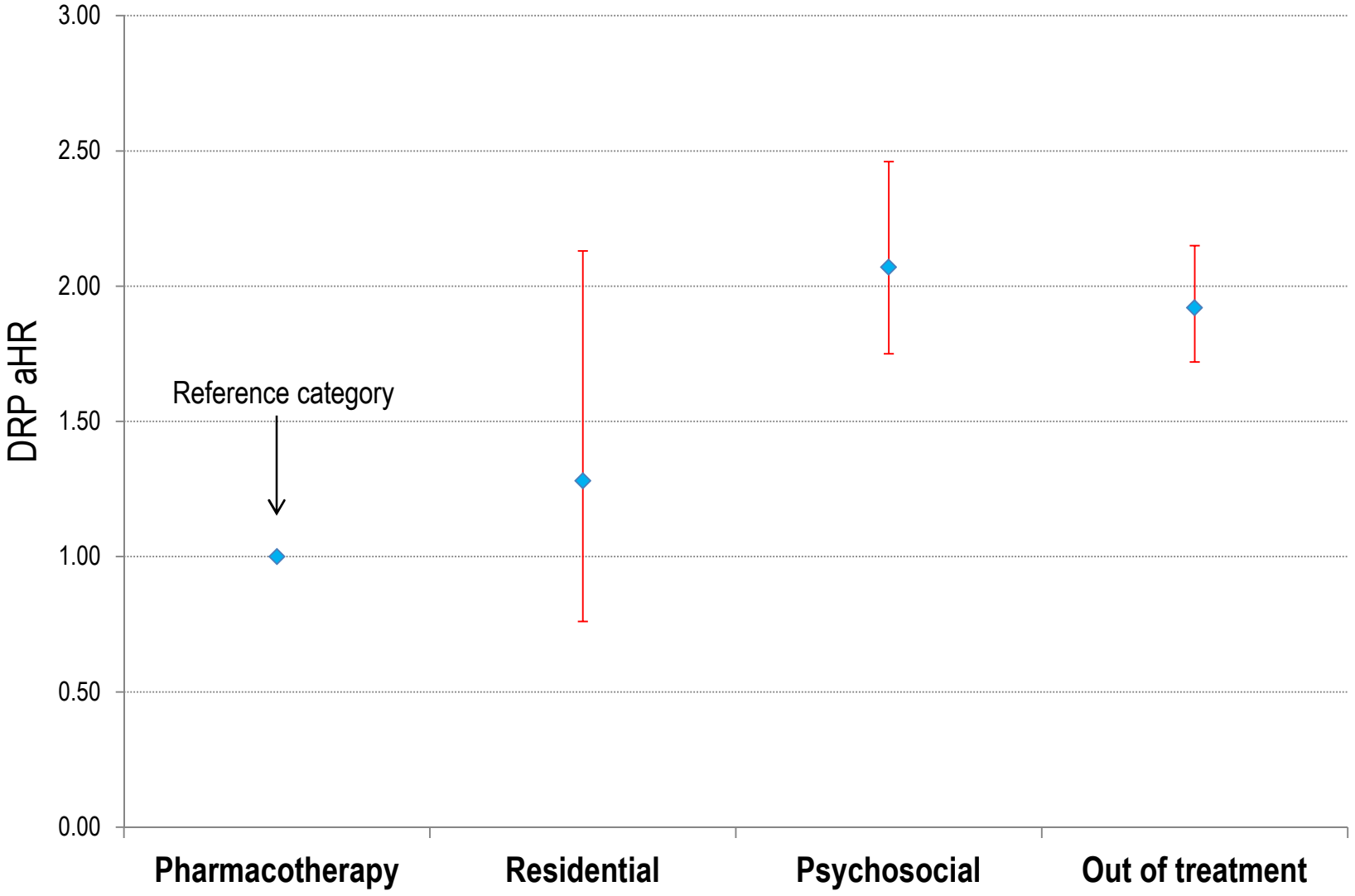


Treated Opiate User Cohort: Crude Mortality Rate per 1,000 person-years: In vs. out of treatment (n=151,983)



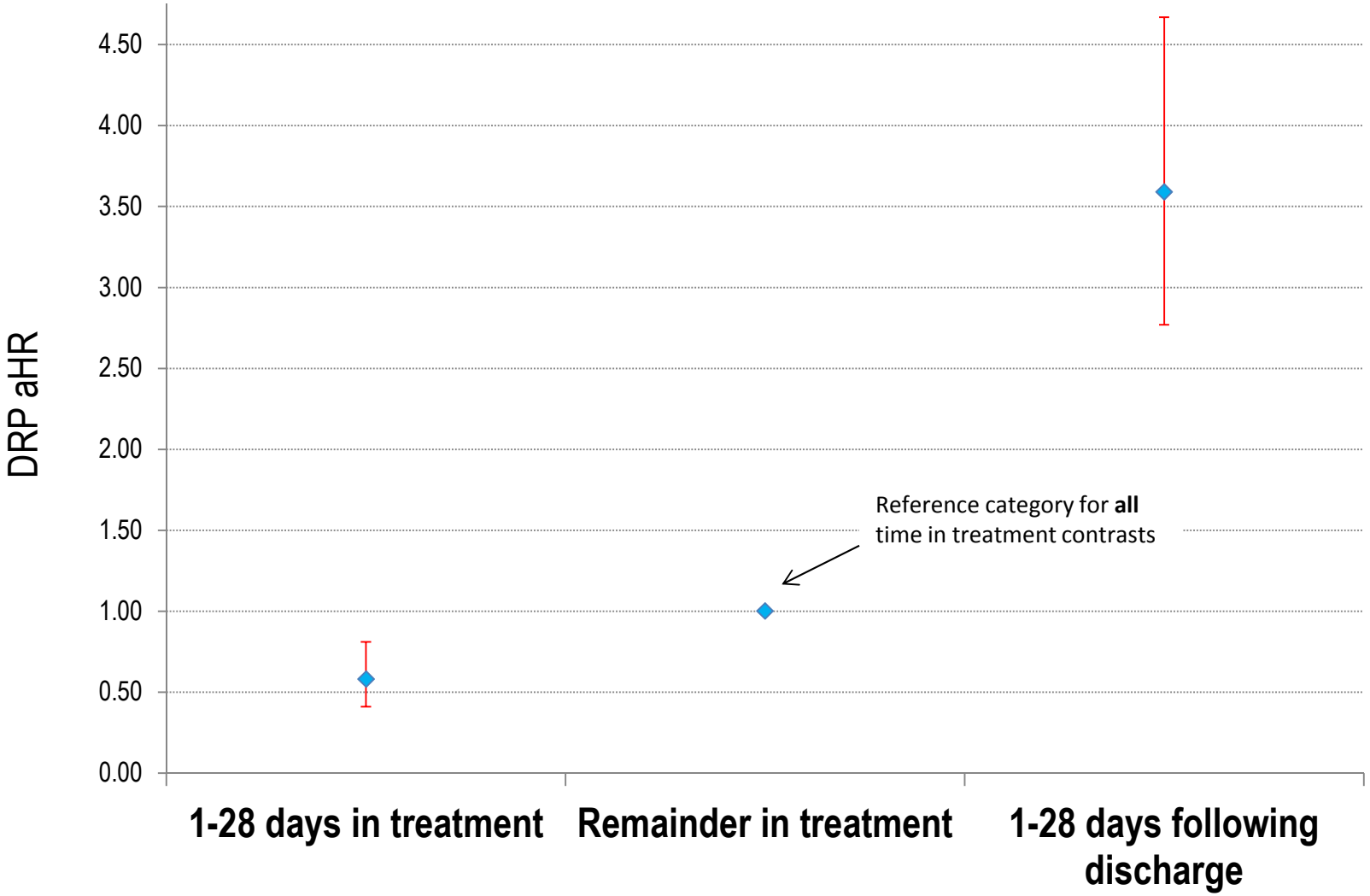
** adjusted for demographic and behavioural covariates*

Fatal DRP risk (aHR* & 95% CI) during specific intervention types (n=151,983)



** adjusted for demographic and behavioural covariates*

Pharmacotherapy: Fatal DRP risk and stage of treatment (aHR & 95% CI)



Counterfactual model, estimate the number of deaths prevented by treatment …

(White, Burton, Darke, Eastwood, Knight, Millar, Musto, Marsden; 2015)

Estimate how many deaths would occur in the absence of treatment.

Count how many actually occur.

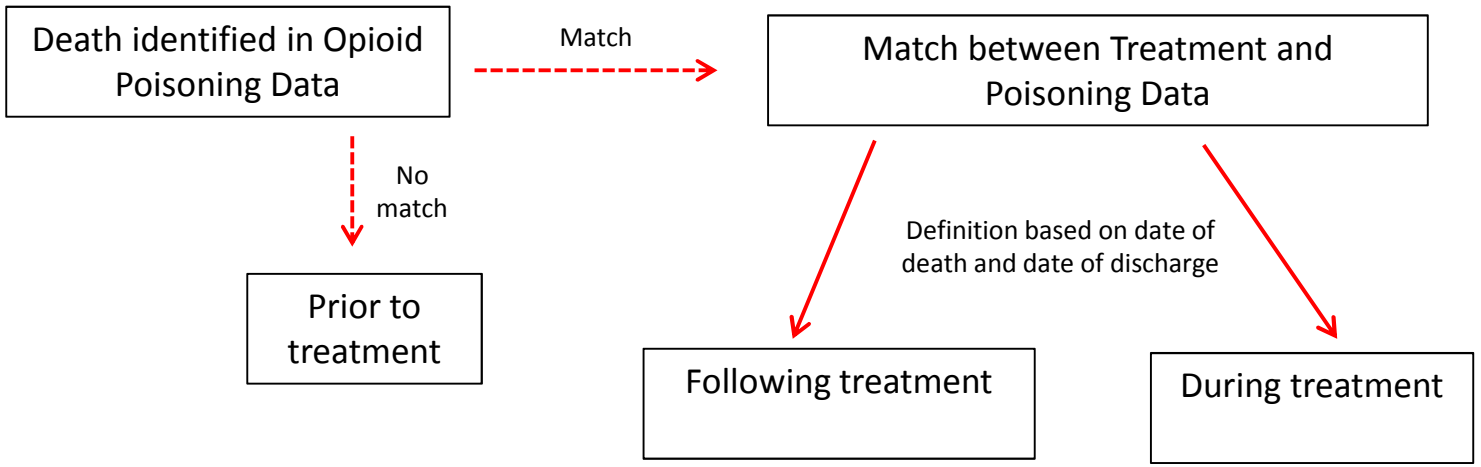
The difference between these = the number prevented.

Procedure:

- Database linkage: the treatment (n=221k) and opioid poisoning mortality databases were linked
- Calculate time spent: prior to, during and after treatment
- Subtract number treated annually (160k) from prevalent population (260k opioid users), assign remainder to “prior to treatment”
- Assign decedents according to treatment status: prior to (n=2722) / during (n=741) / after (n=268)

RB1

Methodology – fatal Opioid Related Poisonings



Data linkage of DPD and NDTMS based on attributor (initials, date of birth, gender) and region

Slide 20

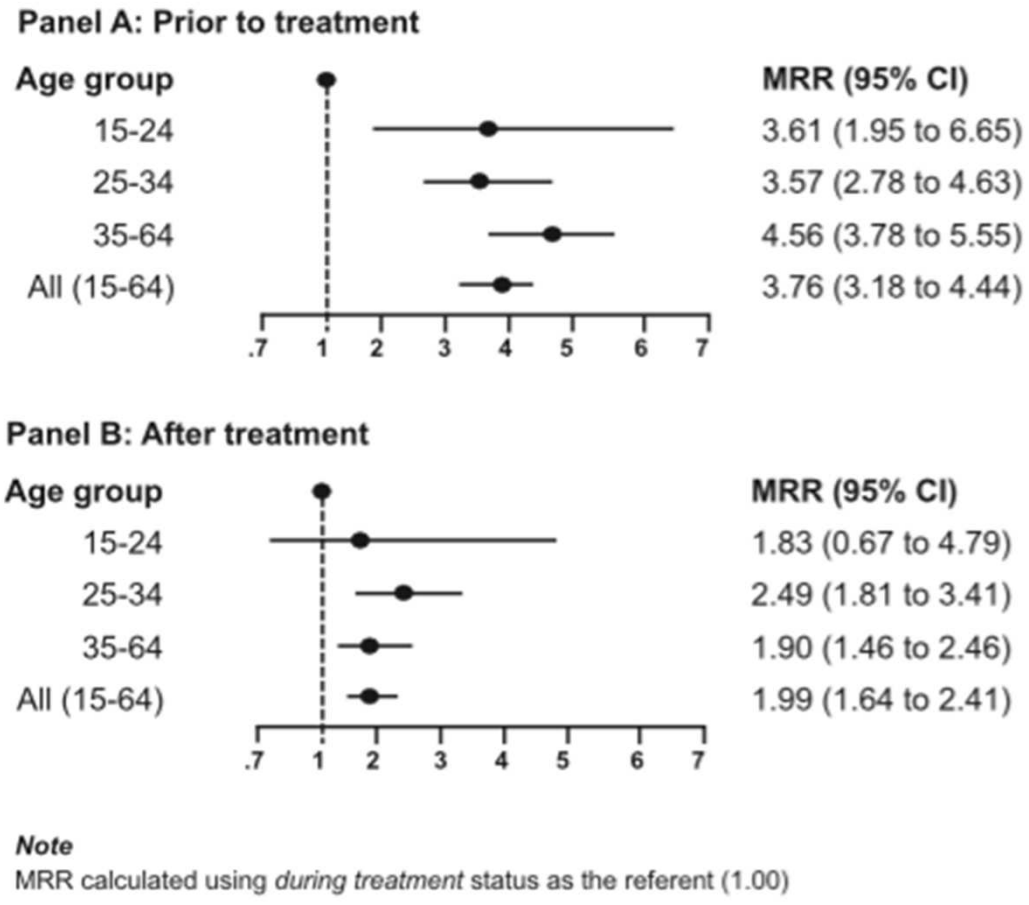
RB1 Martin - you will need to make reference to the fact that this was repeated for three years and aggregated - don't think it needs to be on the slides as long as it is explained clearly

Robyn Burton, 25/02/2014

Analysis:

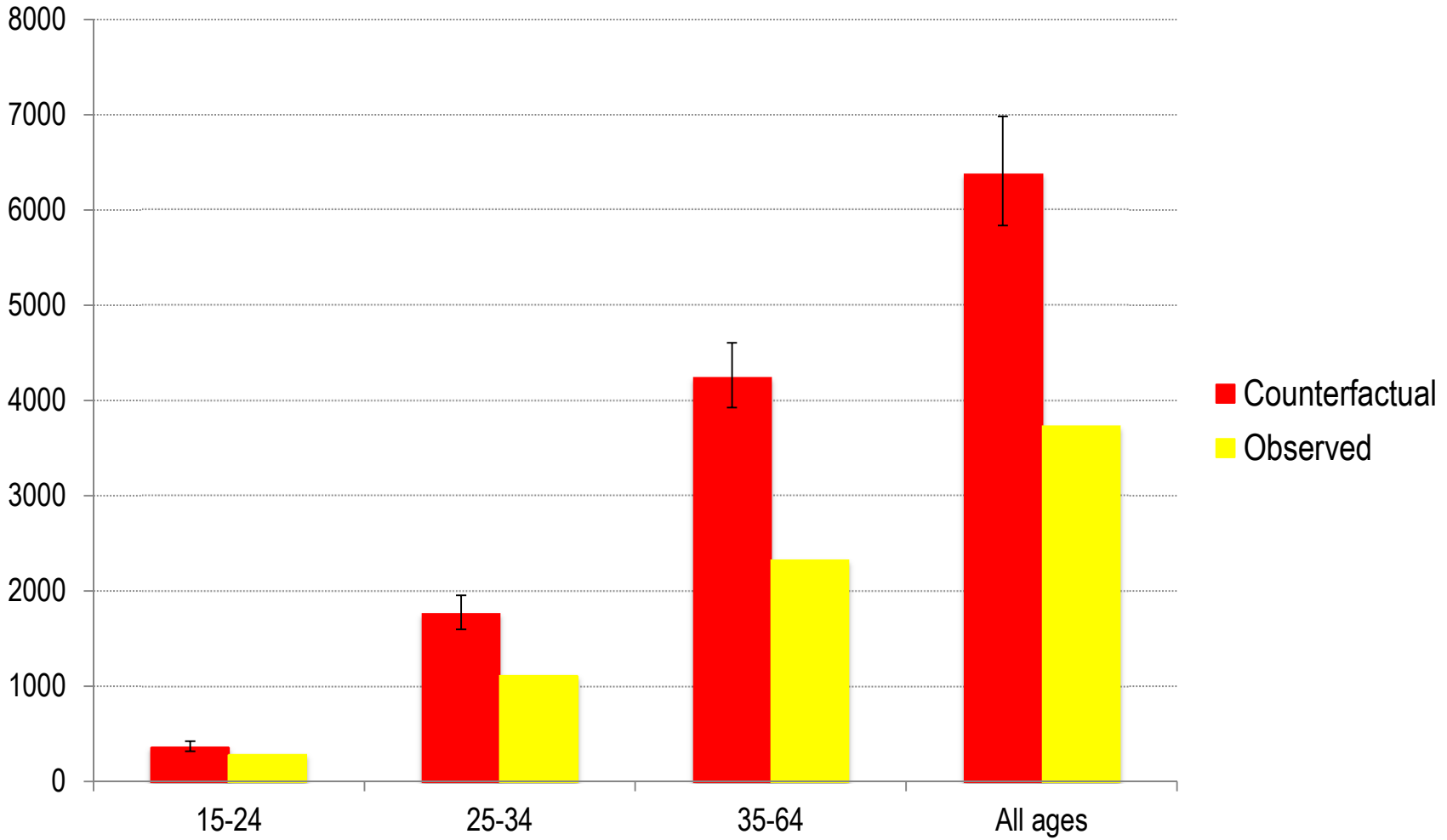
- Calculate number and opioid death rate in each treatment state & mortality rate ratio (in Tx as the referent)
- Prior to treatment rate applied to the prevalent population (the counterfactual estimate): *i.e.* the number of deaths which might occur in the absence of Tx
- Estimate the number of fatal opioid poisonings prevented by treatment (=counterfactual estimate minus number of deaths actually observed)

Mortality rate ratios (MRR) by treatment state and age:

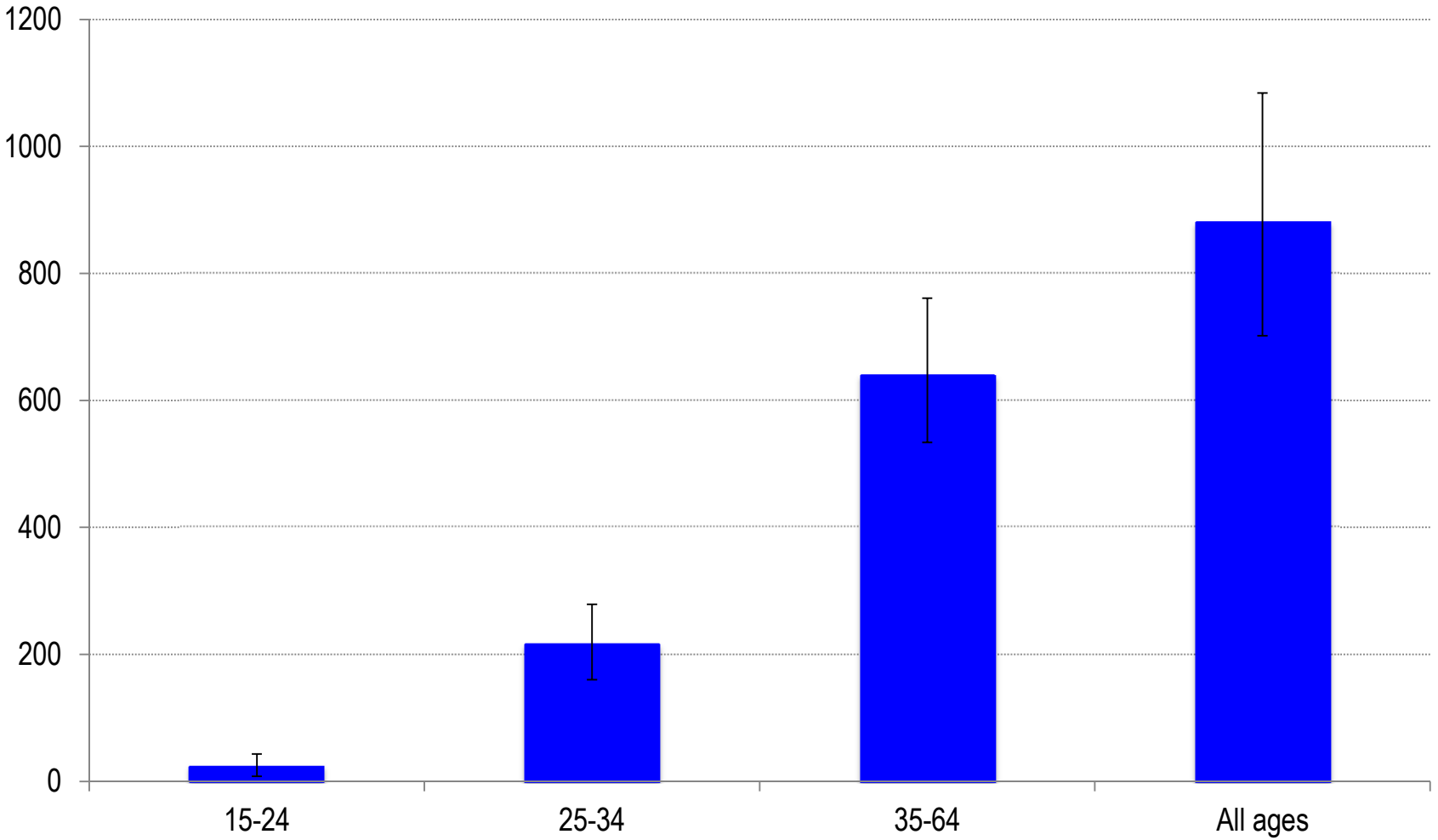


Note
MRR calculated using *during treatment* status as the referent (1.00)

Counterfactual estimate and observed number of opioid deaths (2008–11):

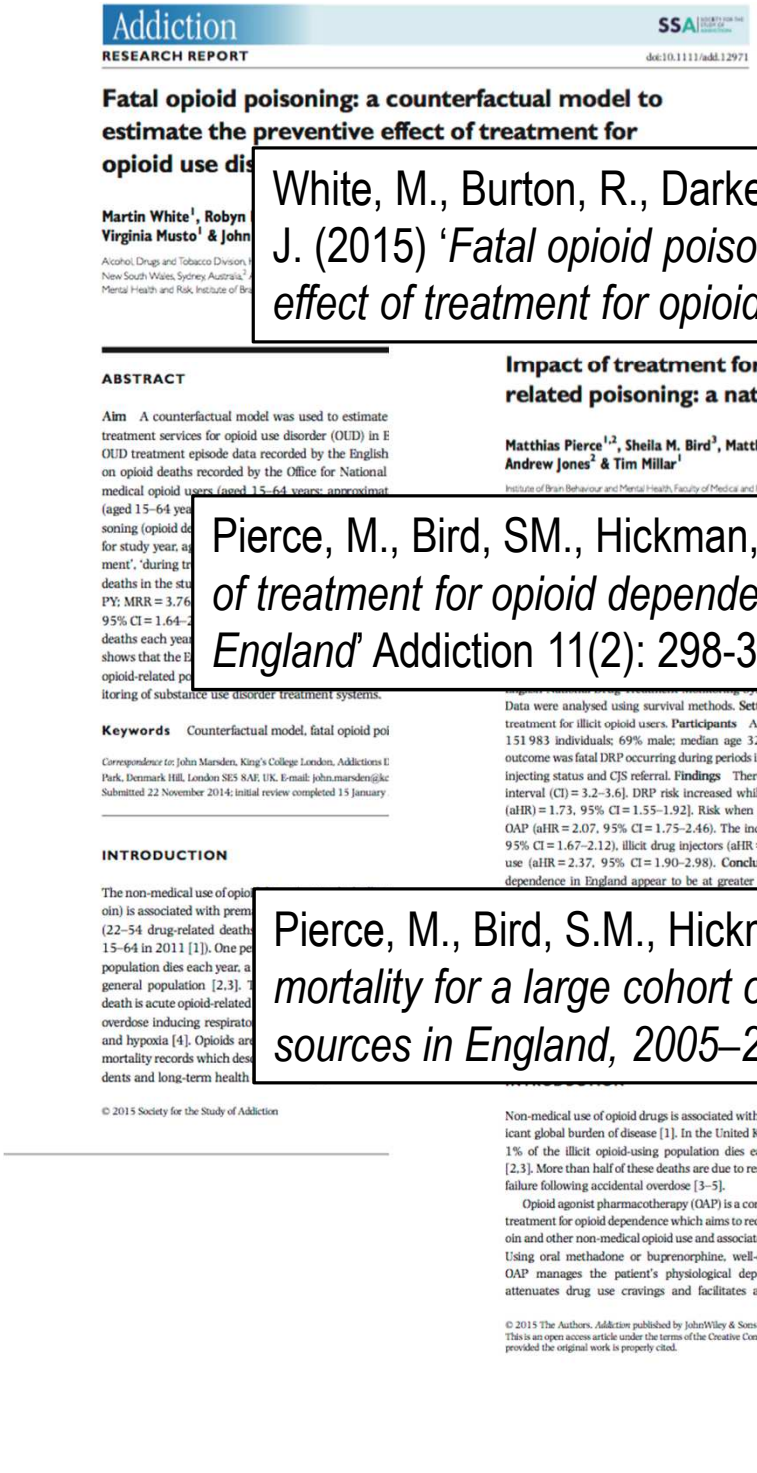


Estimate of number of opioid deaths that treatment prevented each year, by age (2008–11):



Considerations:

- Choose your cohort carefully. Clearly define case definition, restrict to those at risk of DRD. “Drug users” is too wide a definition. Opioid users the main risk group.
- Power is an issue, even for very large cohorts. Do you have sufficient participants available?
- Choose the setting carefully: is a (sole) treatment cohort appropriate?
- A focus on treatment *entrants* (TDI) is likely to introduce bias.
- Ensure that recruitment and observation are proximal: participants recruited many years ago may no longer be at risk.
- Strong (accurate) linkage mechanism is necessary. Weaker linkage *may* suffice when matching the most homogenous cohorts.
- Adequate censoring is required: participants who have died from liver disease are no longer available to die from an overdose.
- Covariate adjustment for in-out treatment status / behavioural risk / demographic risk (& time-update demographic & behavioural risk) may be desirable (but note power issue)
- Beware confounding by epoch: things change.



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Pierce, M., Bird, SM., Hickman, M., Marsden, J., Dunn, G., Jones, A., Millar, T (2016) '*Impact of treatment for opioid dependence on fatal drug-related poisoning: a national cohort study in England*' Addiction 11(2): 298-308

Pierce, M., Bird, S.M., Hickman M., & Millar, T. (2015) *'National record linkage study of mortality for a large cohort of opioid users ascertained by drug treatment or criminal justice sources in England, 2005–2009'* Drug & Alcohol Dependence, 146, 17-23