Using a Multi-Parameter Estimation of Prevalence (MPEP) model to estimate the prevalence of opioid dependence in Scotland

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Aims

- Increased drug-related deaths in Scotland facilitated the need for new prevalence estimates.
- Community of interest: people with opioid dependence aged 15 to 64 years, living in Scotland.
  - We wish to estimate the number of people with opioid dependence.
  - Specifically, estimate prevalence of opioid-dependence for each year between 2014/15 and 2019/20, stratified by *1.* sex (Females, Males), *2.* age group (15-34, 35-49, 50-64 years), and *3.* NHS Board (Greater Glasgow & Clyde, Lothian, Tayside, the Rest of Scotland).
- We used a Multi-Parameter Estimation of Prevalence (MPEP) modelling approach, previously implemented in England and New South Wales, to model adverse events among people with linked Opioid Agonist Therapy (OAT) prescriptions.

Simple Multipliers Approach

Assuming one wish to estimate the number of people who experience a specific event: n.

If the total population size is N, and the 'expected' proportion of the population with the characteristic of interest if π, then:

$$\widehat{n} = \pi \cdot N$$

Assumptions of *multiplier's approach*:

- All the events (n) occurred among the population of interest.
- We have a *good* (unbiased) estimate of the event rate ($\widehat{\pi}$).

MPEP Approach

- Observe a baseline cohort including everyone with the characteristic of interest — e.g. people receiving OAT.
- Estimate the event rate among those within the cohort.
- Given a number of events occurred among those not in the cohort, estimate the number of 'extra' people with the characteristic of interest.

Data

We used data from the Scottish Public Health Drug Linkage Programme (SPHDLP):

- administrative data on all individuals receiving OAT prescriptions in the community in Scotland,
- mortality data, and
- hospital admission data.

Baseline Cohort

We defined the *baseline cohort* (so-called *known or observed* population) of people with opioid dependence, for each financial year, as

- all people living in Scotland,
- aged 15 to 64 years,
- who received at least one OAT prescription during either the current or preceding four years.

Baseline Cohort

We estimated prevalence for the financial years 2014/15 to 2019/20.

- Prescription data from 1st April 2010 onwards was used.

Follow-up time was censored at the earliest of:

- 31st March 2020 (end of study period),
- date of death of any cause
- date of leaving Scotland, for those known to have left the country,
- the end of the financial year (31 March) lying between four and five years since OAT end date.

Coding 'on' and 'off' OAT within the baseline cohort

For each individual within the baseline cohort, all follow-up time was coded as 'on' and 'off' OAT.

Each individual can contribute to both the 'on' and 'off' OAT follow-up time.

Exact treatment (prescription) dates were not available, thus we approximated treatment start and end dates as follows:

- New treatment episodes commence 60 days before and end 12 days before the reimbursement date.
- Reimbursement dates with less than 62 days between them to be a continuous episode of treatment (i.e. follow-up time between these dates was coded as on treatment).

  Otherwise, the time between these two dates was coded as off-treatment.
- All remaining follow-up time was coded as off-treatment.

Adverse Events

Restrict the events modelled to only those that we're confident cannot occur outside of the population of interest (i.e. highly specific events)

> Perfect Specificity: The event never occurs within the rest of the population of interest (i.e. the event is completely specific)

Modelling events that are not specific to the population of interest could yield biased estimates of prevalence.

Mortality Data

We included accidental fatal drug-related poisonings where:

- ICD-10 code F11.2, F11.9 or X42[1] was reported as main underlying cause of death,
- toxicology reports indicated that heroin/morphine, methadone or buprenorphine was implicated in or potentially contributed to the death,
- the death did not occur among people who had been prescribed strong opioid analgesics on a long-term basis.

[1] F11.2: Mental and behavioural disorders due to use of opioids, with Dependence syndrome; F19.2: Mental and behavioural disorders due to multiple drug use and use of other psychoactive substances, Dependence syndrome; X42: Accidental poisoning by and exposure to narcotics and psychodysleptics [hallucinogens], not elsewhere classified (including heroin, methadone, morphine, opium).

Hospital Admissions Data

We included non-fatal drug-related poisonings that

- led to acute hospital admissions, and
- ICD-10 code indicating poisoning by opium, heroin or methadone (codes T40.0, T40.1, T40.3[2] in main or secondary position of the first episode).

[2] T40.0: Poisoning by narcotics and psychodysleptics, Opium; T40.1: Poisoning by narcotics and psychodysleptics, Heroin; T40.3: Poisoning by narcotics and psychodysleptics, Methadone

Data stratification

We stratified all data by:

- Age group: aged 15-34, 35-49, 50-64 years,
- Sex at the birth: Female, Male,
- Financial year: 2014/15, 2015/16, 2016/17, 2017/18, 2018/19, 2019/20, and
- NHS Board: Greater Glasgow & Clyde, Lothian, Tayside, Rest of Scotland.

resulting to $3 \cdot 2 \cdot 6 \cdot 4 = 144$ demographic groups.

Those within the cohort were further stratified by treatment status ('on' vs 'off' OAT).

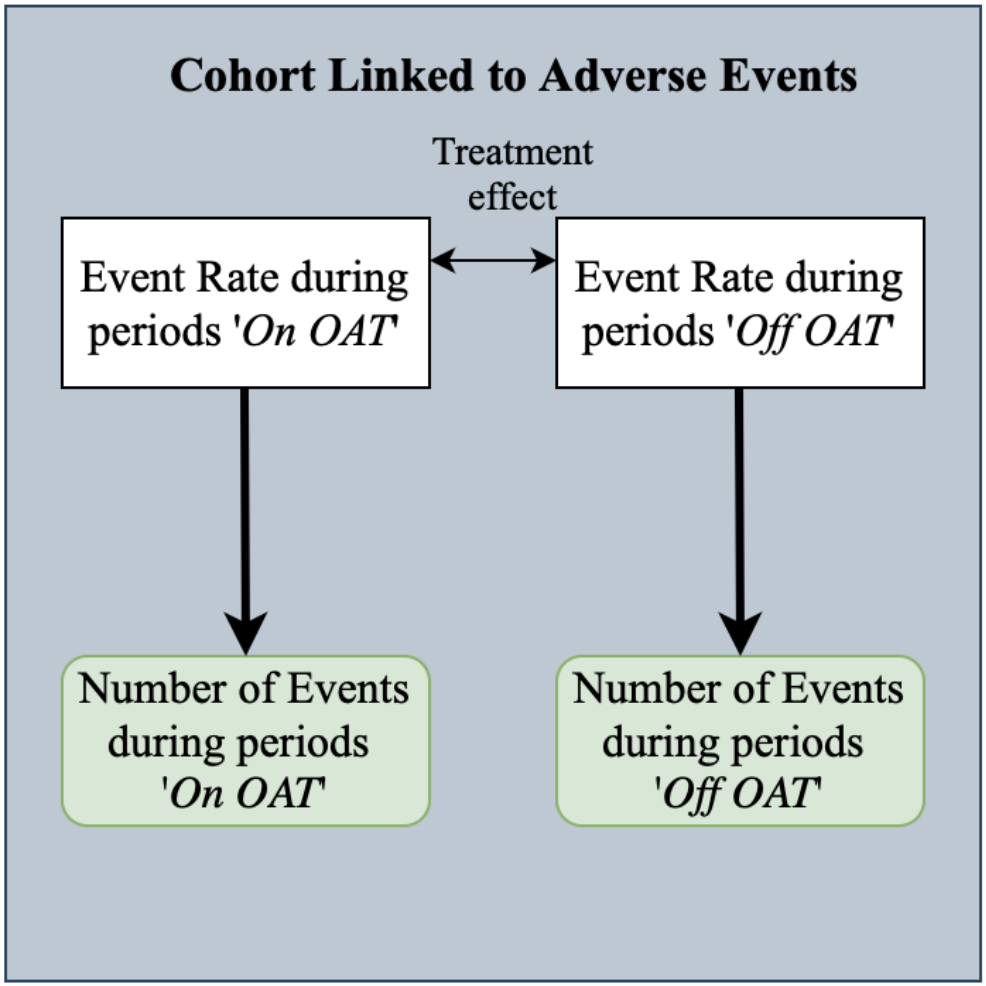
Model Assumptions: 3+1

1. The adverse events modelled are specific to the population of interest (people with opioid dependence).

   Any adverse event included in the model occurred among people with opioid dependence.

2. The baseline cohort includes everyone in receipt of OAT.
3. Everyone in the baseline cohort is opioid-dependent.

Modeling Adverse Events within the Cohort



Modeling Adverse Events within the Cohort

We modelled opioid-related deaths and hospital admissions within the baseline cohort using Poisson regression models, with follow-up time accounting for offset terms.

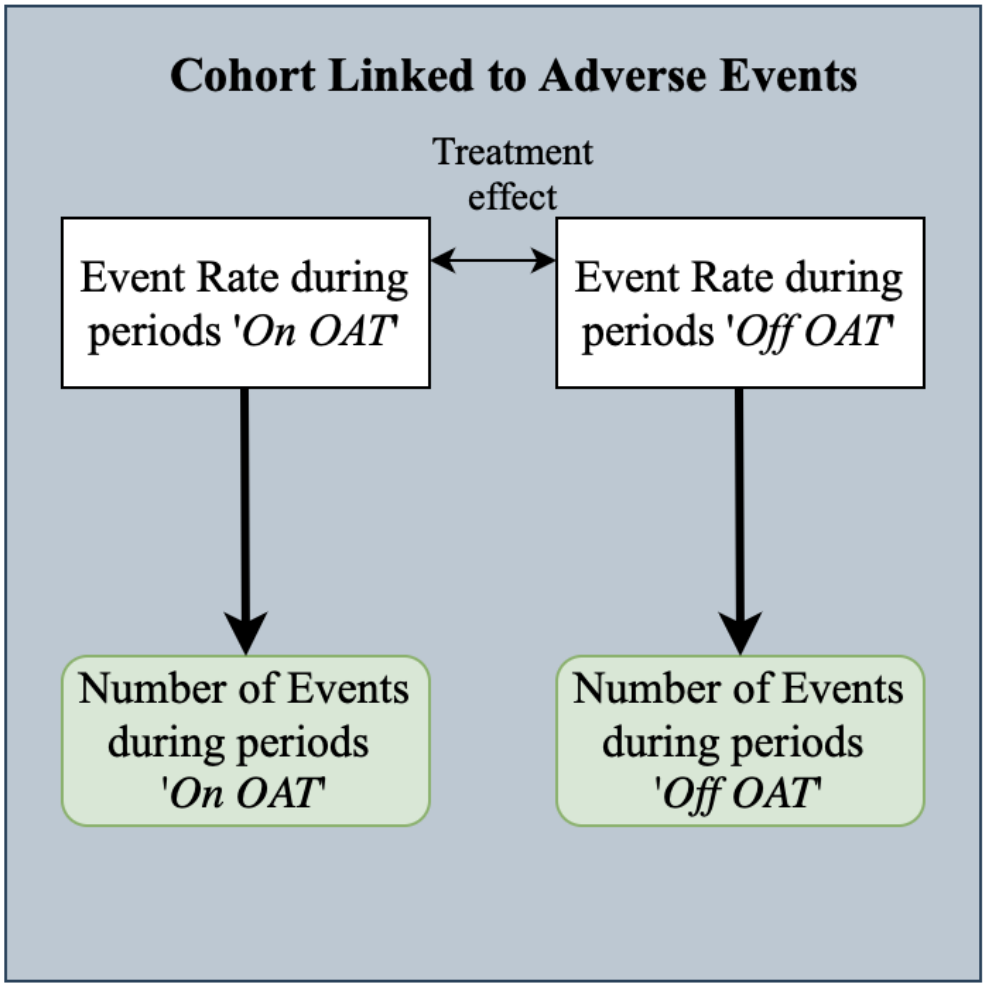
$$\#ofEvents \sim Poisson(\lambda^{on/off} \cdot pyr^{on/off})$$

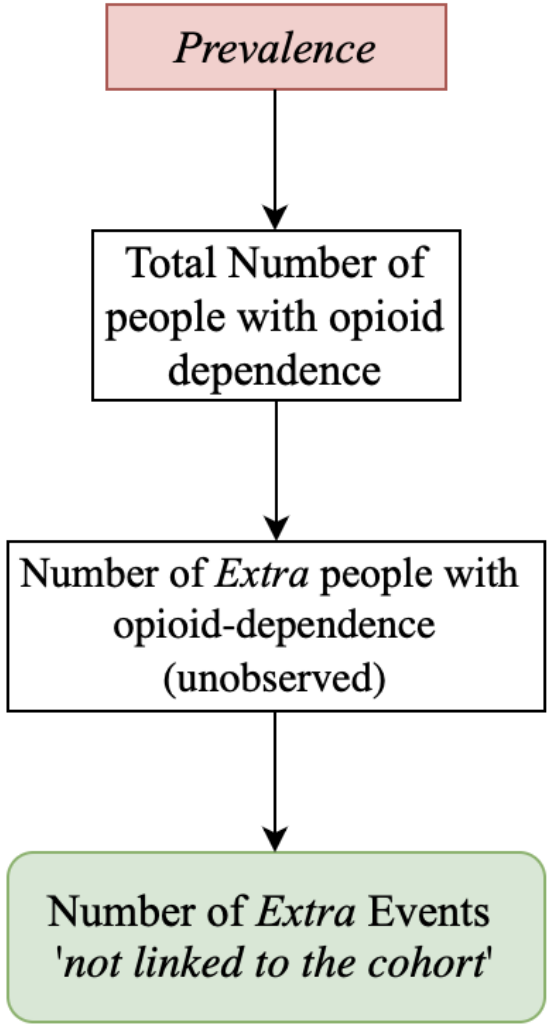
for each demographic (age-sex-year-region-treatment) group.

Interaction terms were included if supported by model fit statistics (i.e. DIC; models with lower DIC explain the data better).

- Selected models included all main effects plus the interaction terms year-by-treatment, region-by-treatment.
- Hospital admission rates model also included the interaction terms age-by-sex and year-by-region.

Modeling Approach





Model Assumptions: 3+1

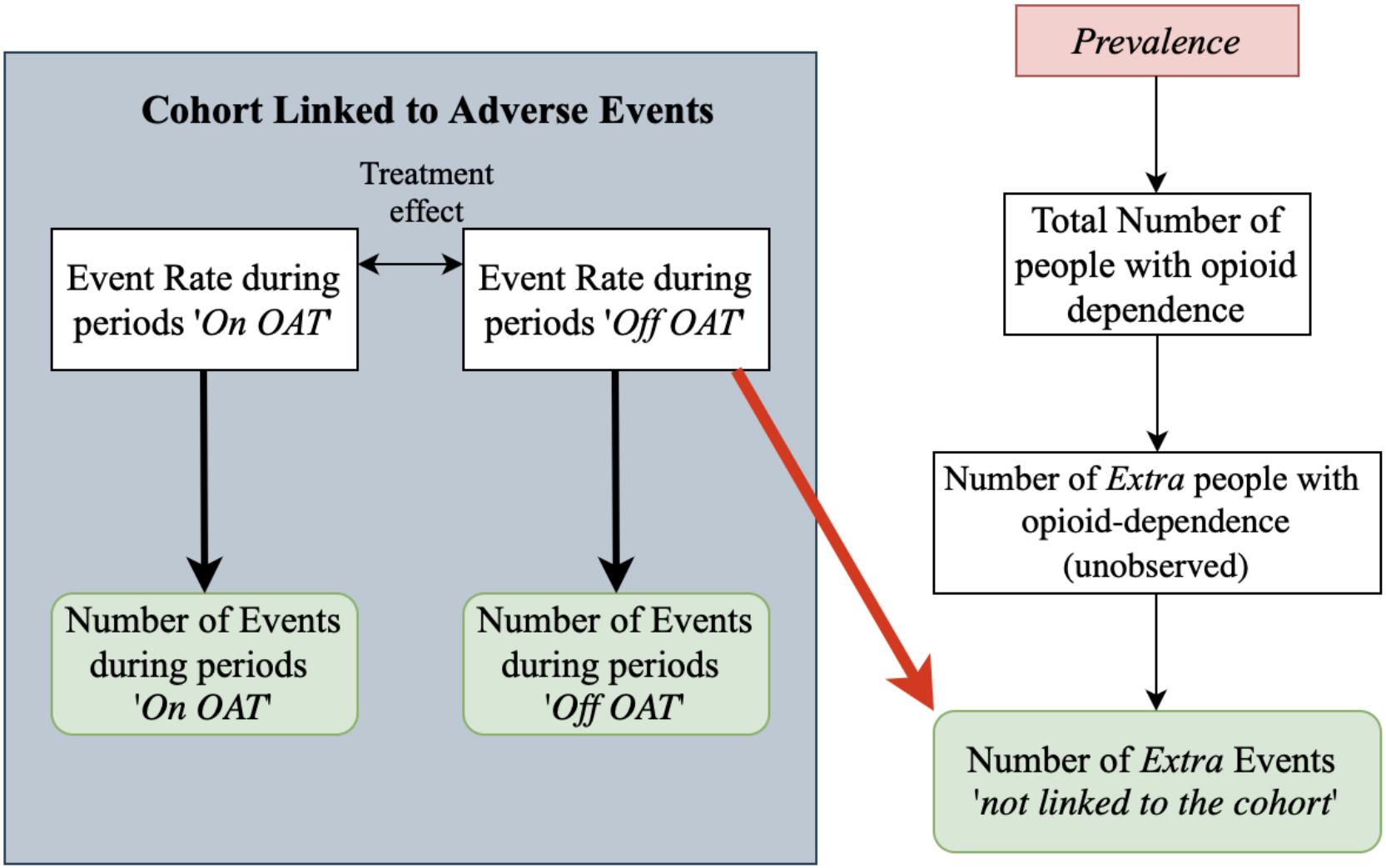
1. The adverse events modelled are specific to the population of interest (people with opioid dependence).

   Any adverse event included in the model occurred among people with opioid dependence.

2. The baseline cohort includes everyone in receipt of OAT.
3. Everyone in the baseline cohort is opioid-dependent.
4. Within each demographic group, rates of these adverse events among the unobserved part of the population are represented by and equal to the rates observed among the baseline cohort during periods not on OAT.

   $\Longrightarrow$ All adverse events occurring outside of this cohort were among people who were not currently receiving OAT.

Modeling Approach



Modeling Adverse Events outside the Cohort

The number of adverse events not linked to the cohort were also modeled using Poisson distribution.

Key assumption:

> We assumed that adverse events among those outside the cohort ('unobserved people with opioid dependence') occurred at the **same rates** (within each sex, age, year, region group) as among those observed in the cohort during time 'off' OAT.

As the (unobserved) person-years at risk is specified as a function of prevalence, prevalence was assumed to follow a linear regression model structure on the log-odds scale.

The Model

For events within the Cohort:

$$\#ofEvents \sim Poisson(\lambda^{on/off} \cdot pyr^{on/off}),$$

where

$$log(\lambda) = \beta_0 + TE \cdot TreatmentStatus + \sum_j \beta_j X_j$$

The Model

For events outside the cohort (extra):

$$\#ofEvents^{extra} \sim Poisson(\lambda^{off} \cdot pyr^{extra}),$$

where

$$pyr^{extra} = \overbrace{pyr^{died}}^{\text{time before death}} + \underbrace{\left(n^{extra} - pyr^{died}\right)}_{\text{number of extra people alive}} \cdot RMST\left[\lambda^{OCM}\right],$$

and $RMST\left[\lambda^{OCM}\right]$ is the 'restricted mean survival time' on the time interval (one year).

$$n^{total} = n^{cohort} + n^{extra}$$

$$n^{total} = prevalence \cdot Population$$

$$logit(prevalence) = \gamma_0 + \sum_j \gamma_j X_j$$

The Model — Modelling Interactions

- Interaction terms with *region* were modelled as Random Effects, e.g.

$$region - by - treatment \sim Normal(0, s.d.^2)$$

- Interaction terms with *year* were modelled as Random Walks, e.g.

$$\text{region-by-treatment}_1 = 0$$

$$\text{region-by-treatment}_{i,i>1} \sim Normal(\text{region-by-treatment}_{i-1}, s.d.^2)$$

- For the interaction term *year-by-region*

$$\text{year-by-region}_{1,j} = 0, \quad j \in \{1, 2, 3, 4\}$$

$$\text{year-by-region}_{i,j} \sim Normal(\text{year-by-region}_{i-1,j}, s.d.^2), \quad j \in \{1, 2, 3, 4\}$$

The Model — Prior Distributions

$$\beta_j \sim Normal(0, 100)$$
$$\gamma_j \sim Normal(0, 100)$$

$$\beta_j \sim Normal(0, 100), \gamma_j \sim Normal(0, 100)$$

$$\beta_0^{Deaths} \sim Normal(-4.6, 100) \Leftrightarrow MortalityRate_{baseline} \approx 10 per 1000 py$$

$$\beta_0^{Hosp} \sim Normal(-5.7, 100) \Leftrightarrow HospitalisationRate_{baseline} \approx 3.3 per 1000 py$$

$$\gamma_0 \sim Normal(-4.6, 100) \Leftrightarrow prevalence \approx 1\%$$

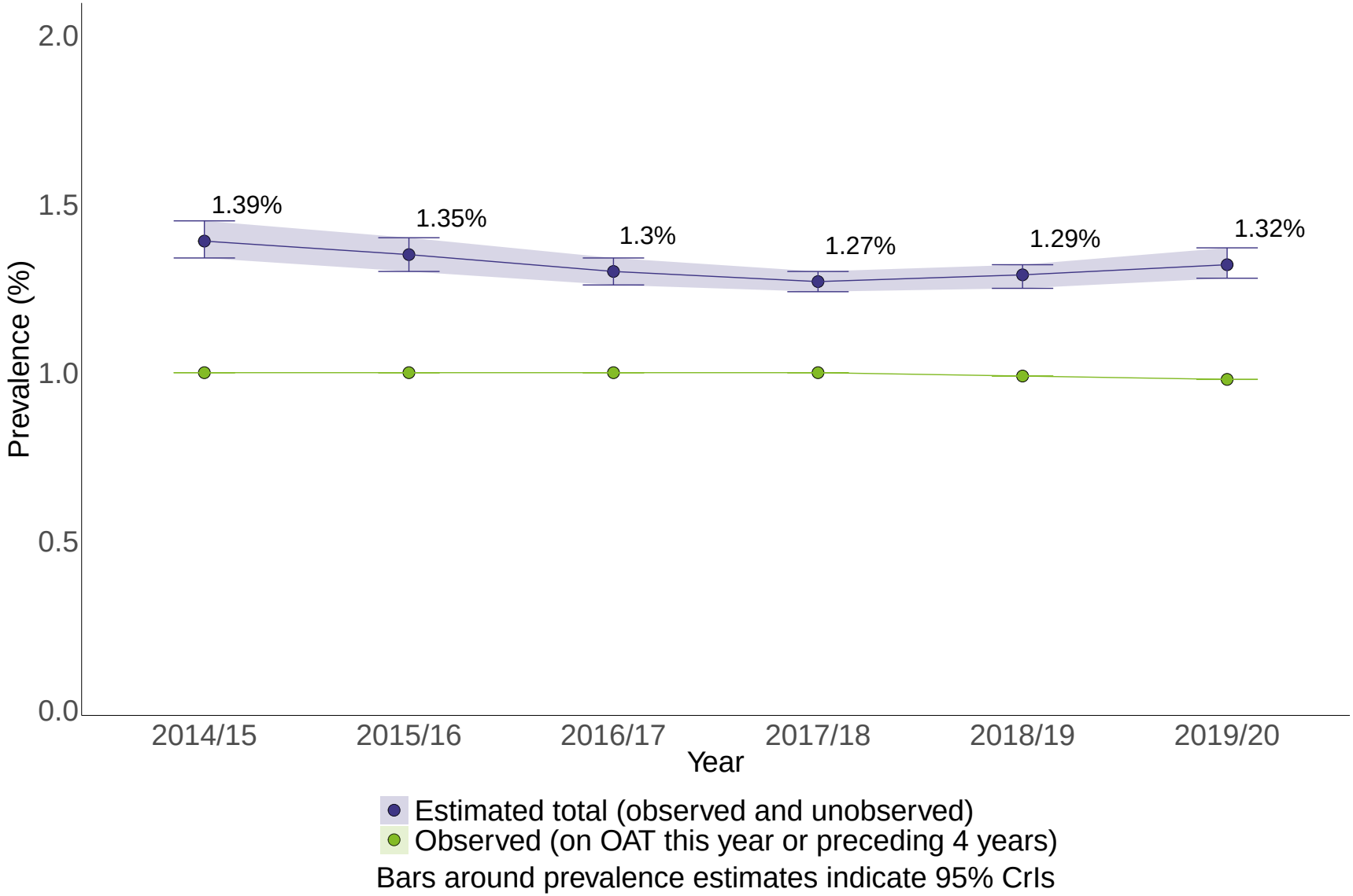
$$s.d. \sim Uniform(0, 3)$$

Results

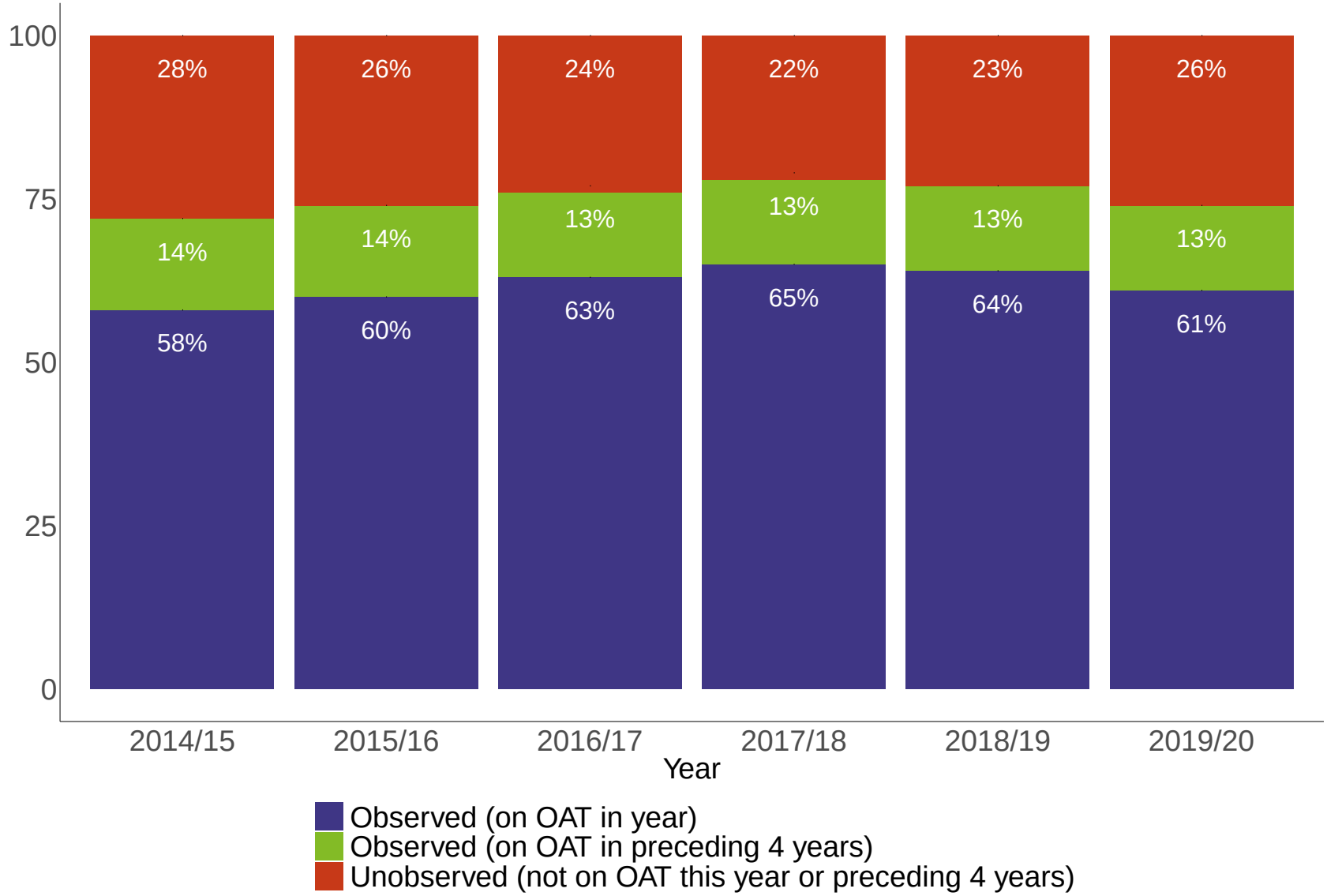
- All population size estimates have been rounded to the nearest hundred.
- Some line plots displaying prevalence estimates includes a line indicating the size of the baseline cohort as a percentage of the relevant general population.

  These lines represent 'lower bounds' for total prevalence, as they represent the population directly observed in the OAT data.
- Bar charts present the estimated percentage of people with opioid dependence that:
  1. received at least one OAT prescription during the year ('OAT exposure'),
  2. were among the observed baseline cohort,
  3. were 'unobserved'.

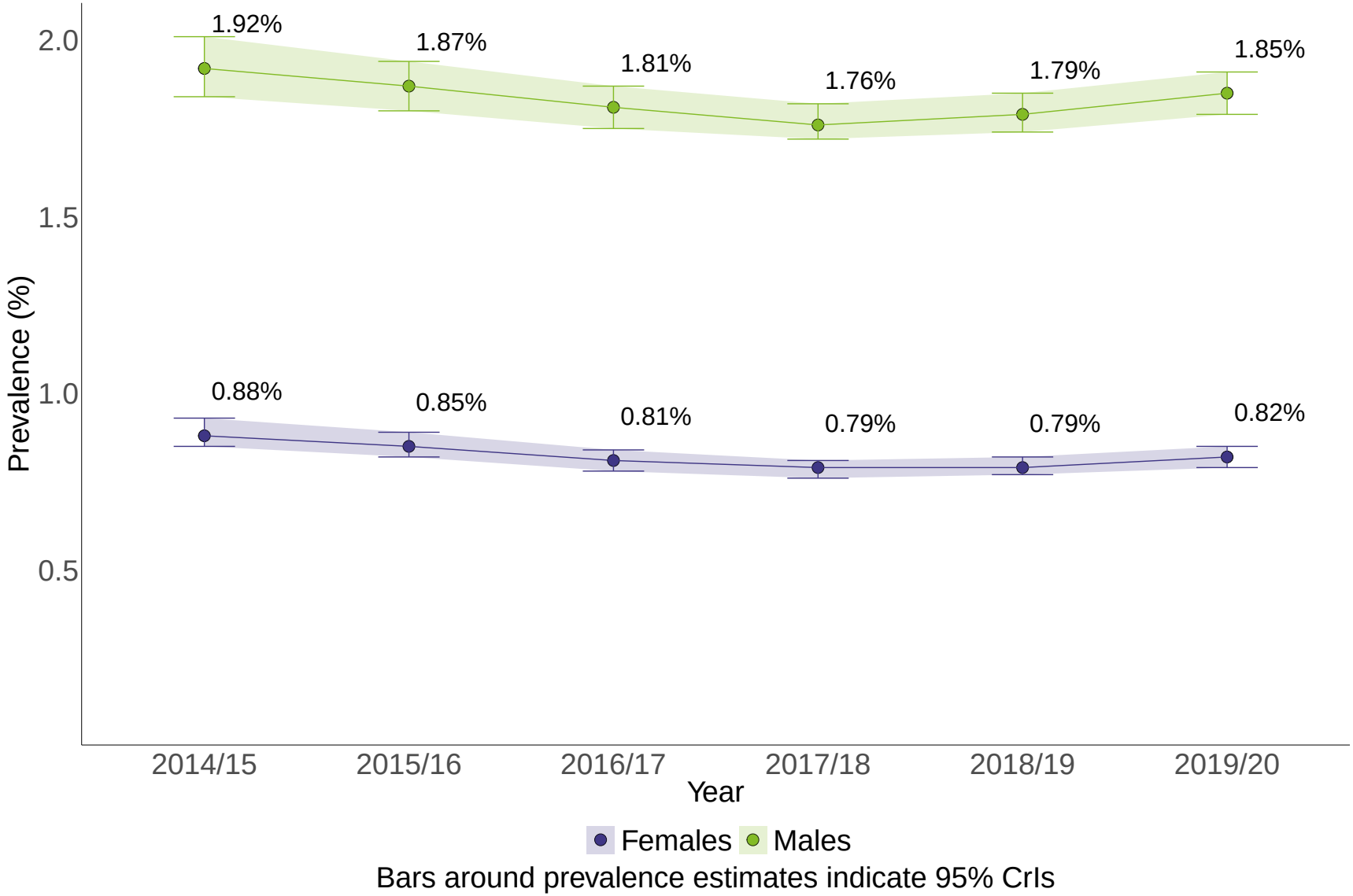
Estimated prevalence (%) of opioid dependence among the population aged 15-64 years in Scotland



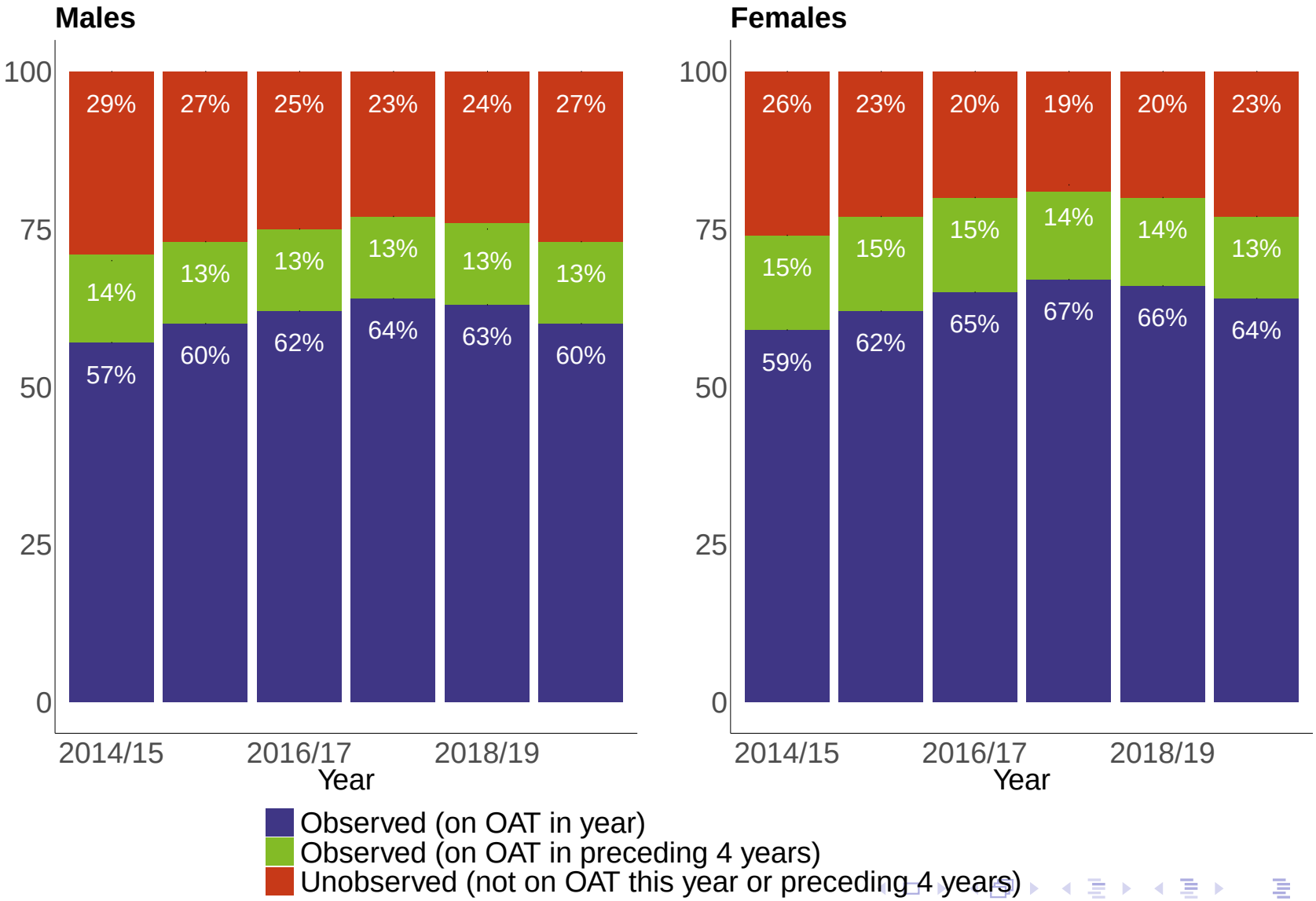
Estimated breakdown of treatment status for people with opioid dependence in Scotland



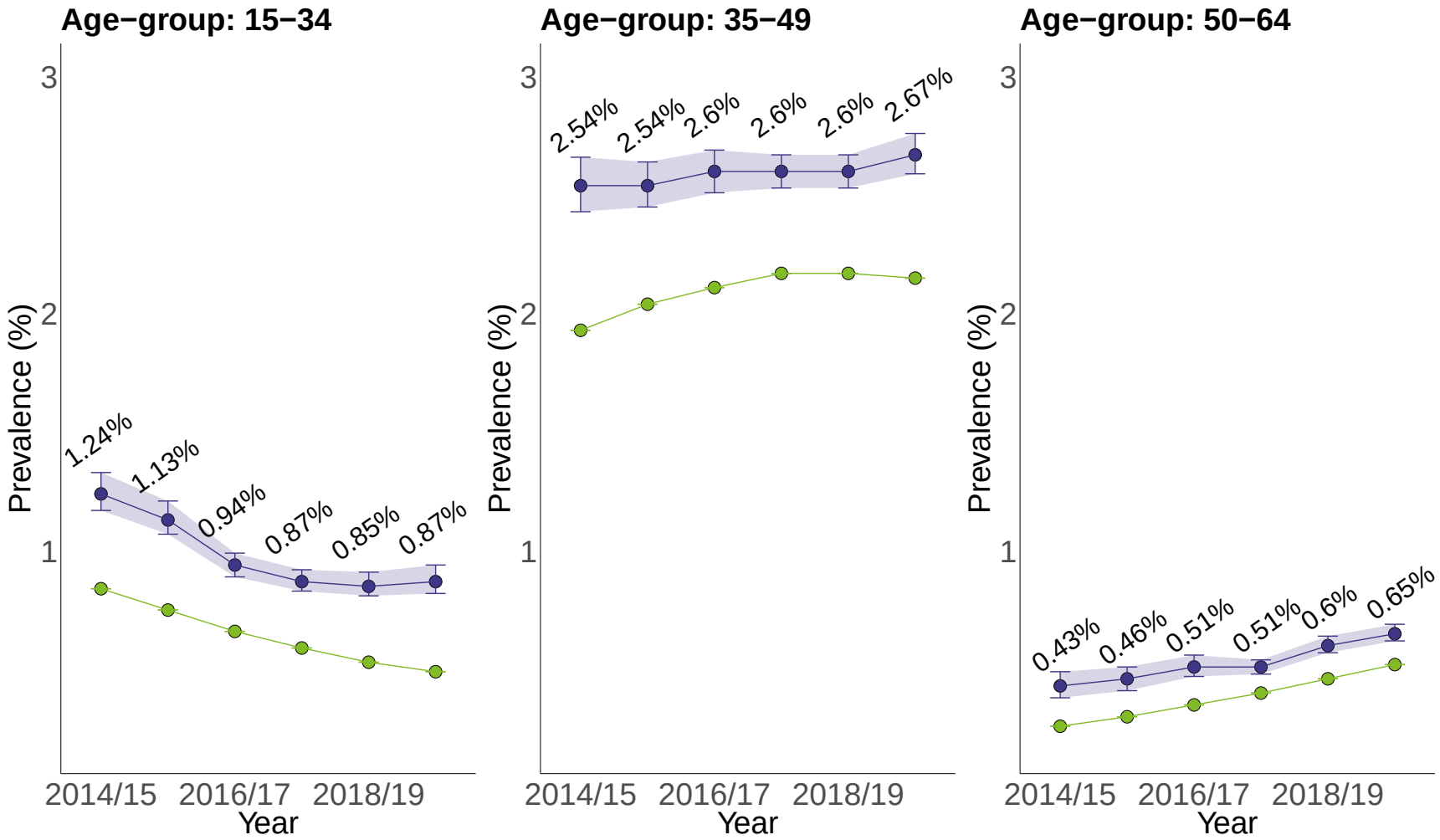
Estimated prevalence (%) of opioid dependence in Scotland by sex



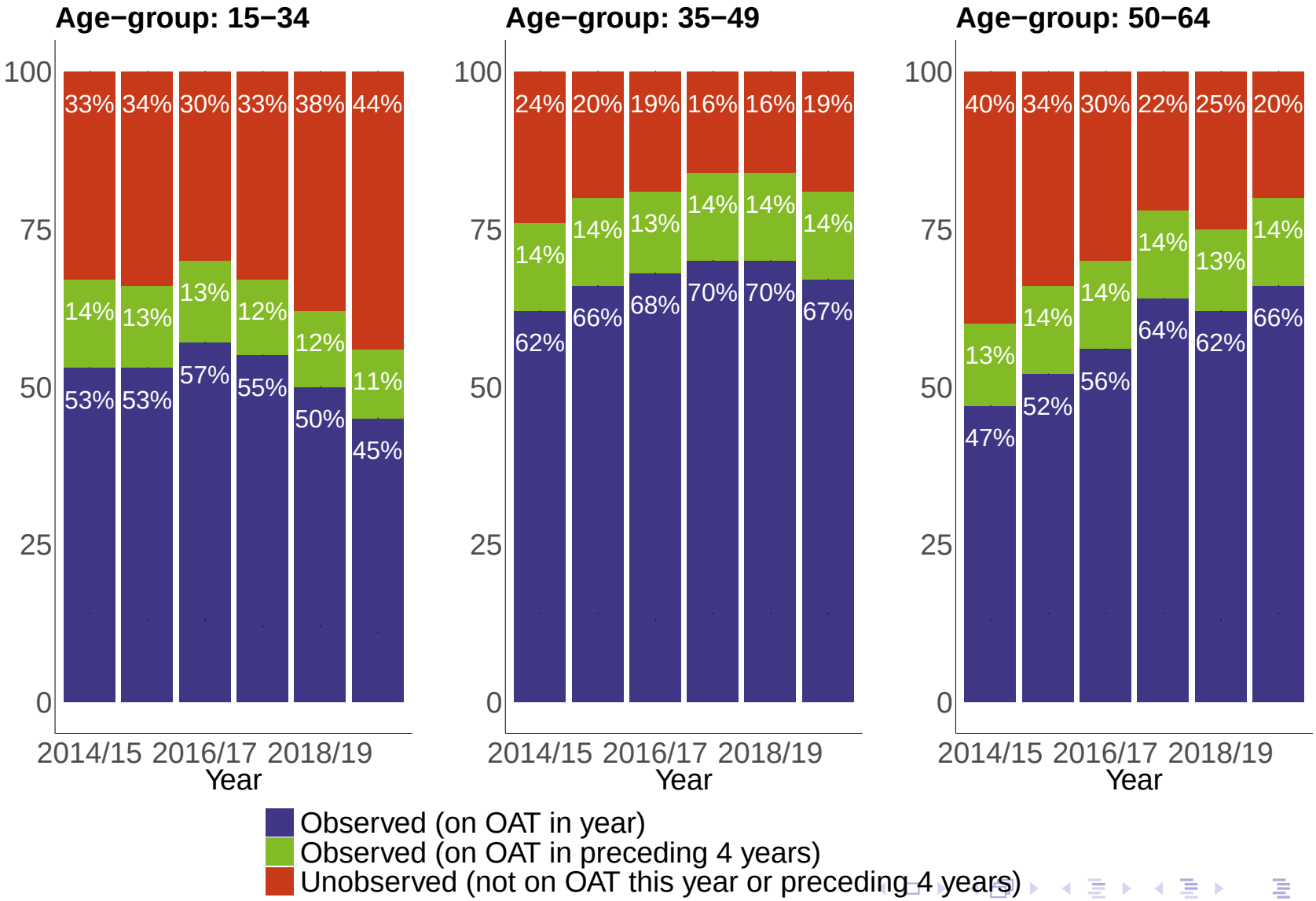
Estimated breakdown of treatment status for males and females with opioid dependence in Scotland



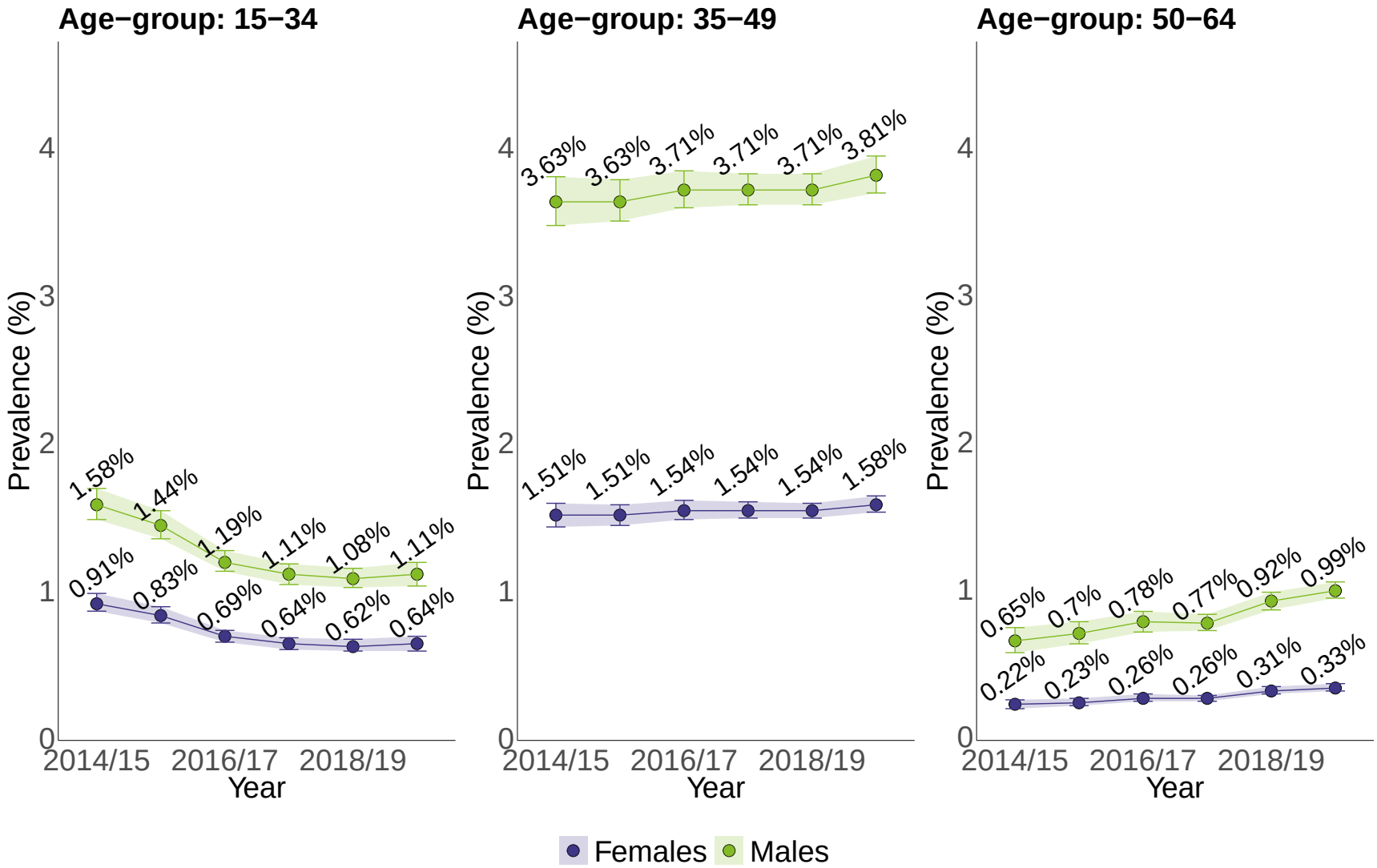
Estimated prevalence (%) of opioid dependence in Scotland by age group



Estimated breakdown of treatment status for selected age groups of people with opioid dependence in Scotland

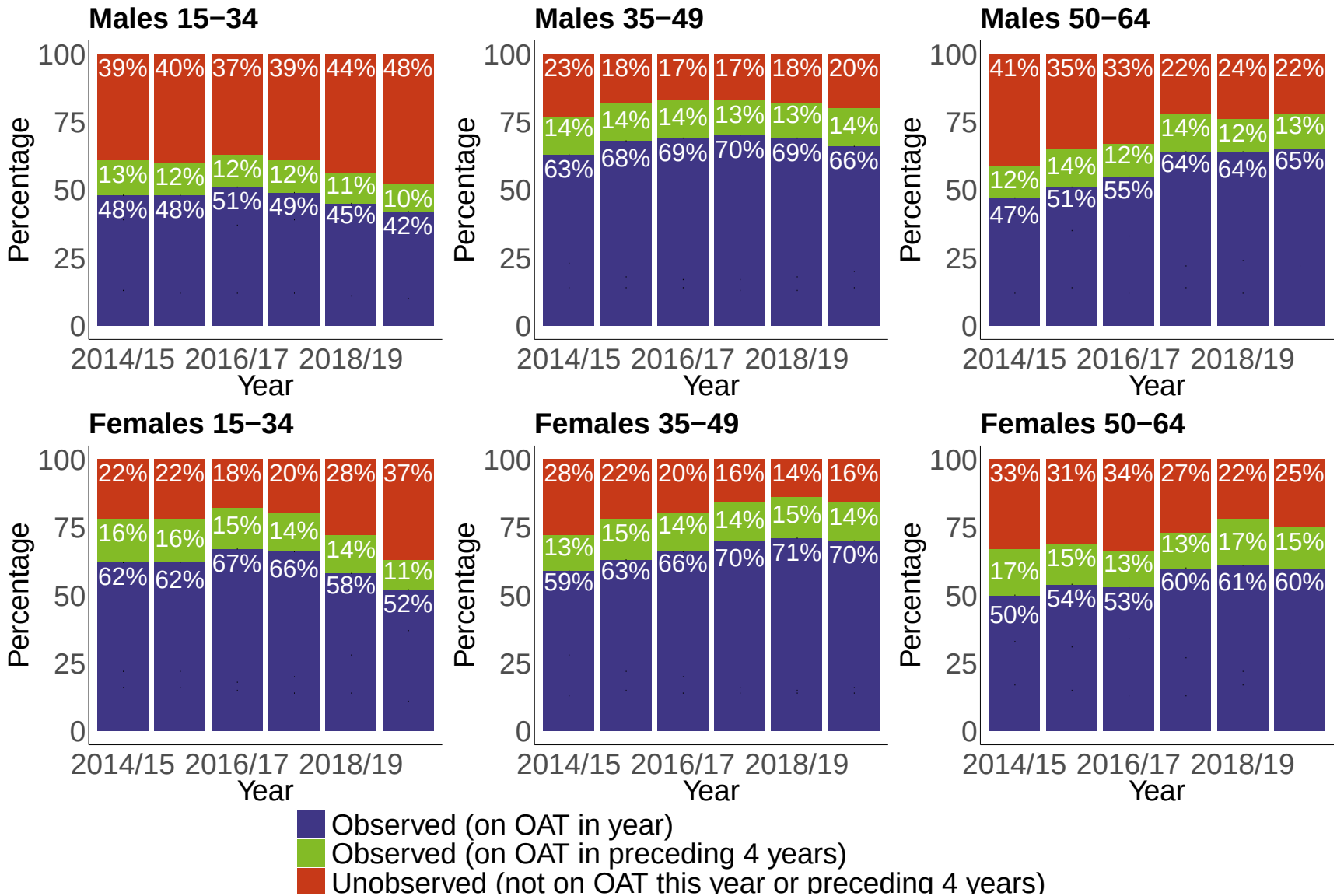


Estimated prevalence (%) of opioid dependence in Scotland by age-sex group

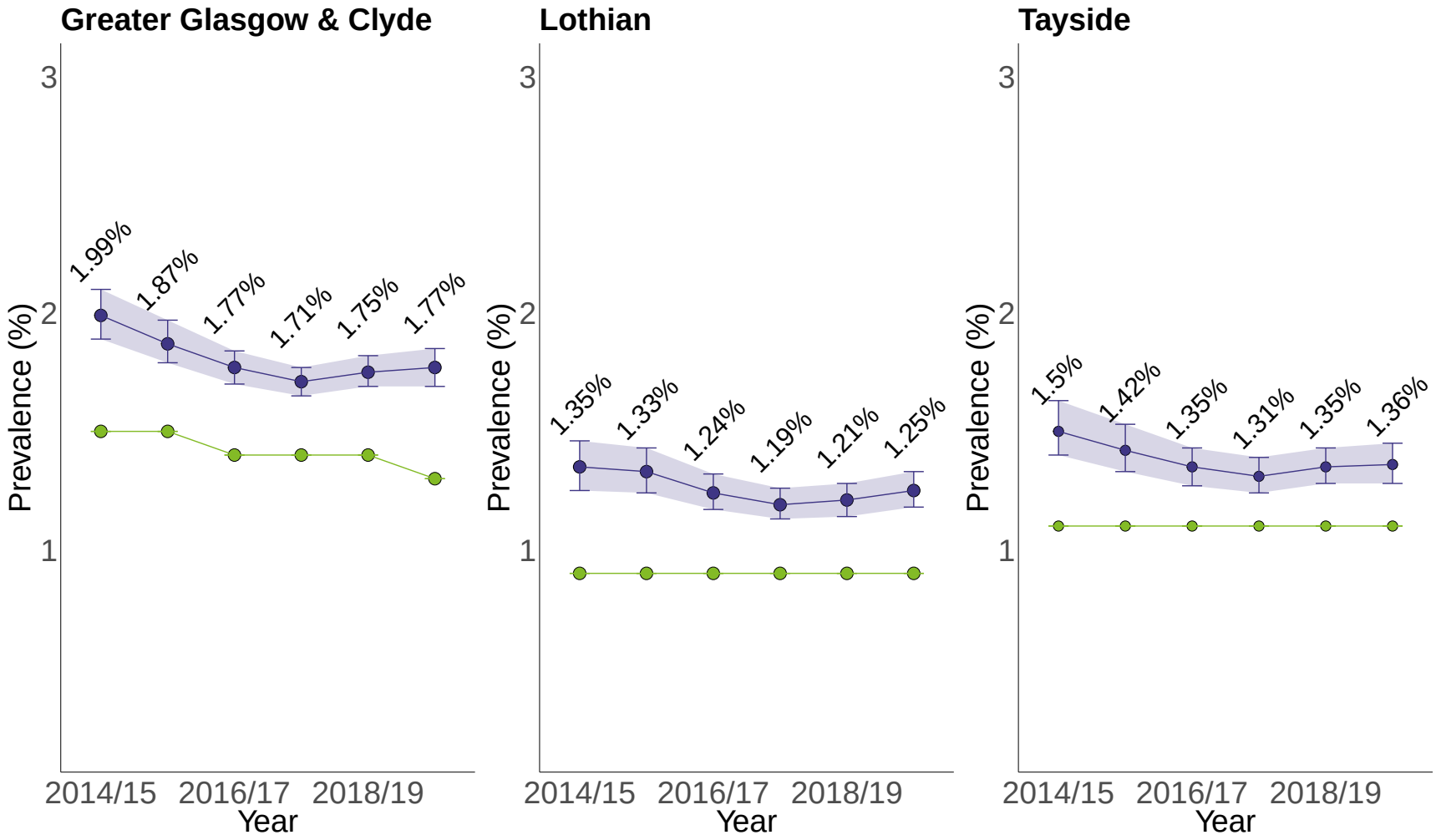


Bars around prevalence estimates indicate 95% CrIs

Estimated breakdown of treatment status by age-sex



Estimated prevalence (%) of opioid dependence for selected NHS Boards



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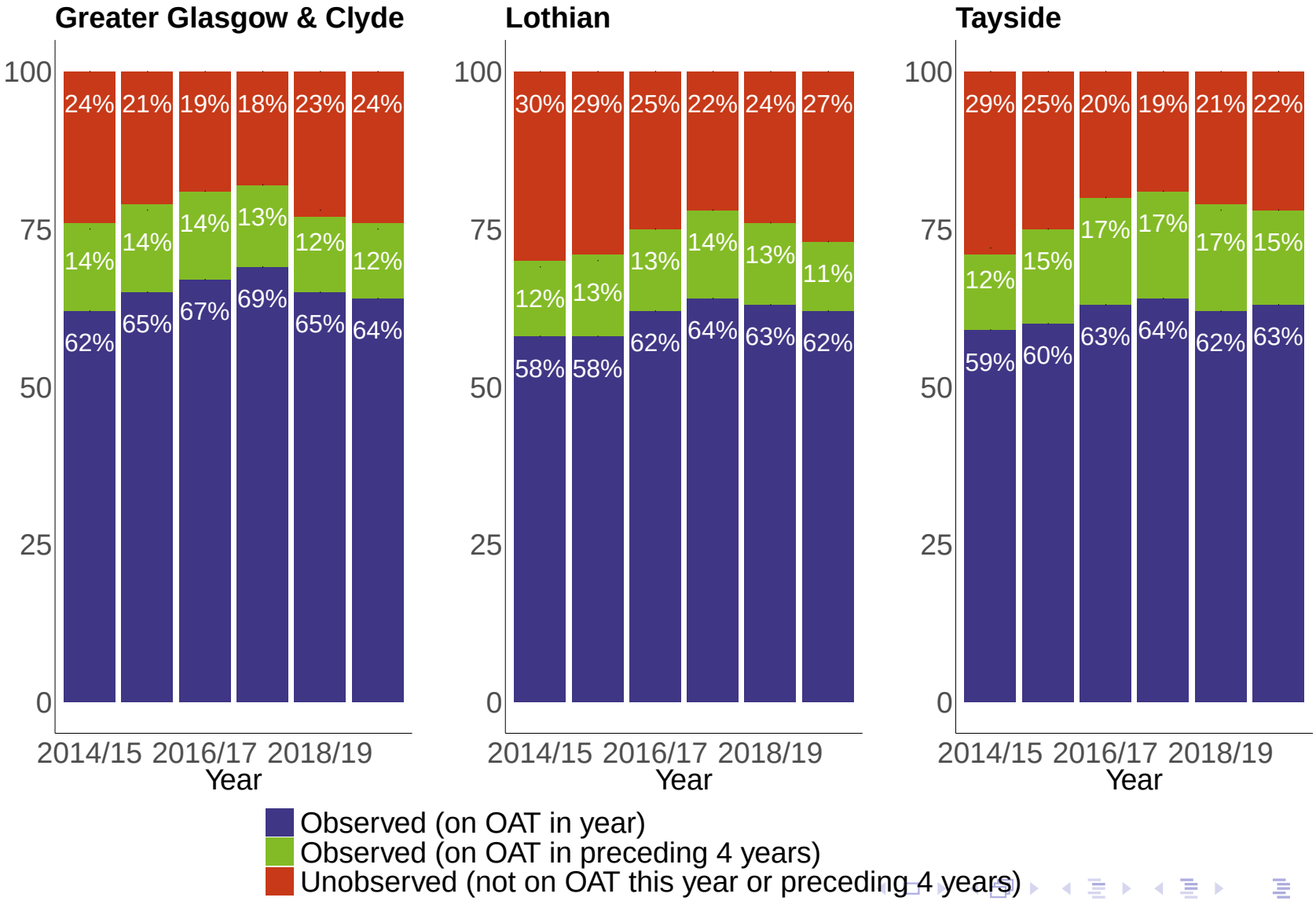

Any evidence of change or prevalence over the six-year period?

- There was weak evidence that overall prevalence fell slightly from 2014/15 (change −0.07%, 95%CrI −0.14% to 0.00%).
- The population of people with opioid dependence is ageing, with:
  - the number of people aged 15-34 reducing by 5,100 (95%CrI 3,800 to 6,400), and
  - the number aged 50-64 increasing by 2,800 (95%CrI 2,100 to 3,500) between 2014/15 and 2019/20.

Sensitivity Analysis

- Overall prevalence estimates using one data source (deaths only, or hospitalisations only) differed only slightly
  - maximum of 0.07% or 2,200
- Estimates of prevalence based on censoring baseline cohort follow-up time at 1-2 years since last OAT prescription, rather than 4-5 years, generated estimates that were slightly lower
  - by 0.1% or 3,000 people on average
- Results were robust to changing the mean values of prior distributions for intercept terms.
- Negative Binomial, rather than Poisson, for the regression models, had no effect on the width of credible intervals of the estimated prevalence, suggesting no evidence of overdispersion.

Summary

- The estimated prevalence in 2019/20 is 1.32% (95% CrI: 1.28% to 1.37%) of 15- to 64-year-olds.

	Mean	95% Credible Interval
Females	0.82%	0.79% to 0.85%
Males	1.85%	1.79% to 1.91%
15-34	0.87%	0.82% to 0.94%
35-49	2.67%	2.59% to 2.76%
50-64	0.65%	0.62% to 0.69%

Estimated Prevalence in 2019/20

- An estimated 61% of people with opioid dependence received opioid agonist therapy (OAT) at some point during the year, while 74% had received OAT at some point during the period 2015/16 to 2019/20.

Summary

- Our estimates are consistent with evidence on the number of drug-related deaths, non-fatal hospital admissions, and changes in the risk of drug-related deaths experienced by people with opioid dependence.
- MPEP builds on linkage between administrative databases which are increasingly available across Europe and beyond.
- MPEP is a flexible approach, adaptable to local settings and circumstances and builds in a test of consistency of information on size of known population and drug related harm.

Next Steps

We aim to expand the model to:

- Include more recent year (e.g. up to 2022/23);
- Estimate prevalence for more NHS Boards;
- Estimate prevalence for other types of drugs (e.g. cocaine);
- Replace the adverse event rates Poisson models with informative prior distributions.

Thank you!

Any Questions?

My team:

Dr Hayley E Jones

Prof Matt Hickman

Drugs Team, Public Health Scotland

Markoulidakis, Andreas, Hickman, Matthew, Andrew McAuley, Lee R Barnsdale, Nicky J Welton, Megan Glancy ... & Hayley E Jones. Prevalence of opioid dependence in Scotland 2015-2020: a Multi-Parameter Estimation of Prevalence (MPEP) Study. Addictions (2024).

This study was funded by the Scottish Government.

CHI Capture

- Data are linked on Community Health Index (CHI) number
  - a unique patient identifier used throughout health and care services associated with NHS Scotland.
- CHI numbers were available for between 75% and 81% of OAT prescriptions each year
- Variation in the proportion of OAT prescriptions linked to individuals (CHI capture) could affect
  - the size of the baseline cohort,
  - the classification of adverse events to observed/unobserved group.

Proportion of deaths with SDMD prescription

	On OAT	**Off OAT**	**Unobserved**
2014/15	66.7%	71.3%	39.0%
2015/16	77.5%	75.7%	32.5%
2016/17	69.5%	78.9%	43.4%
2017/18	74.9%	82.9%	41.7%
2018/19	80.5%	83.3%	41.0%
2019/20	78.7%	88.2%	50.5%