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Characterising Cocaine and Opioid poly drug use trends and drug related harms in Scotland 2015-2022

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*A dissertation submitted to the University of Bristol in accordance with the requirements of the degree of Master of Science by advanced study in Medical Statistics and Health Data Science in the Faculty of Health Sciences.*

*Population Health Sciences, Bristol Medical School, 08/2025*

**Author’s Declaration**

*I declare that the work in this dissertation was carried out in accordance with the*

*requirements of the University’s Regulations and Code of Practice for Taught Programmes*

*and that it has not been submitted for any other academic award. Except where indicated*

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**Plain Language Summary**

Scotland has one of the highest drug-related death rates in Europe. Many individuals who use opioids also use other drugs at the same time. One combination of concern is cocaine and opioids (C&O), because it can increase health risks. Cocaine can place strain on the heart and blood vessels, while opioids also can affect heart function. Cocaine, as a stimulant, can mask the sedative effect of opioids. When used together, they can lead individuals to take higher doses, increasing the risk of overdose or other serious problems.

This study looked at patterns of C&O dependence and related health harms in individuals in Scotland who were receiving opioid agonist therapy (OAT), a standard treatment for opioid dependence. We used data from national health records collected between 2015 and 2022. We included 37,409 individuals aged 15–64 with at least one OAT prescription. We compared individuals who used opioids only with those who also used cocaine. We focus on four health outcomes: drug-related deaths, all-cause mortality, non-fatal overdoses (where someone is taken to hospital but survives), and cardiovascular mortality.

We found that about 1 in 5 individuals (21.6%) receiving OAT also used cocaine. This group was more likely to experience a non-fatal overdose than individuals who only used opioids, even after accounting for differences in age, sex, region, and accommodation status. The highest overdose risk was in young men aged 15–34. However, individuals with C&O dependence had a lower rate of cardiovascular mortality compared with those using only opioids. Once all other factors were considered, there was no difference in the risk of drug-related deaths between the two groups.

Across all groups, older age, homelessness, and living in certain areas (such as Tayside) were linked to higher risks of death. Men generally had higher risks of cardiovascular death than women, especially in the middle-aged and older groups.

These results suggest that social care providers should take age, gender into account when designing services. Solving accommodation and regional problems is also important for reducing drug-related harm in Scotland.

**Abstract**

*Background*

Scotland has one of the highest drug-related mortality rates in Europe, with opioid dependence affecting over 1% of the adult population. Polydrug use, particularly concurrent cocaine and opioid (C&O) dependence, is increasingly prevalent among socially vulnerable groups, potentially exacerbating risks of overdose, cardiovascular harm, and premature mortality.

*Methods*

We conducted a retrospective cohort study using linked national datasets (2015–2022) to examine patterns of C&O dependence and associated harms among individuals aged 15–64 receiving opioid agonist therapy (OAT). Outcomes included drug-related deaths (DRD), all-cause mortality (ACM), non-fatal overdose (NFOD), and cardiovascular mortality (CVD). Poisson regression estimated incidence rate ratios (IRR), adjusting for age, sex, calendar year, region, and accommodation status.

*Results*

Among 37,409 OAT recipients, 21.6% had C&O dependence. C&O dependence had significantly higher NFOD rates (adjusted IRR = 1.68, 95% CI 1.61–1.75), particularly among males aged 15–34. No significant adjusted difference in DRD risk was observed between groups. C&O dependence had lower CVD mortality (adjusted IRR = 0.73, 95% CI 0.68–0.78), while age, homelessness, and residence in Tayside or Other NHS regions predicted higher mortality across outcomes. Interaction analyses revealed greater CVD risk in middle-aged and older males compared to females.

*Conclusion*

C&O dependence in OAT individuals is strongly linked to elevated NFOD risk, especially among younger men, but to lower CVD mortality compared with opioid-only. Targeted harm reduction, age and sex sensitive interventions, and strategies addressing homelessness and regional disparities are critical to reducing drug-related harms in Scotland.

**Background**

Scotland has consistently reported one of the highest drug-related mortality rates in Europe (1). In 2022/23, approximately 1.23% of the Scottish population aged 15–64 was estimated to be opioid dependence (2). In 2020, Scotland had the highest per capita drug-related deaths rate (DRD) in the European Union, with 245 deaths per million people, which was more than 3.7 times higher than the overall deaths rate of 67.1 deaths per million people in the United Kingdom and surpassed most international regions (3). Although opioid agonist therapy (OAT) remains the cornerstone of harm reduction strategies, an increasing amount of evidence indicates that a considerable proportion of individuals receiving OAT treatment are involved in polydrug dependence, especially cocaine. This is the reason for the persistently high drug-related deaths rate in Scotland, with approximately 90% involving opioids, which are often used in combination with benzodiazepines, gabapentinoids, cocaine and alcohol. Polydrug dependence, especially the simultaneous dependence on cocaine and opioids, has become an increasingly serious public health problem (1).

The rise in cocaine and opioids (C&O) dependence appears particularly acute among socially vulnerable populations, including individuals experiencing homelessness, unemployment or incarceration. These intersecting vulnerabilities create a syndetic pattern, where structural inequalities and substance use exacerbate each other (4). The HIV outbreak in Glasgow from 2015 to 2019 was associated with public injections of cocaine and opioid dependence, highlighting social marginalization, especially homelessness and street drug use. This shows that the accommodation status and the region interact with the evolving drug market to drive infectious disease clusters (5,6).

The demographic structure of the affected population has changed significantly. Among individuals who received OAT treatment in Scotland over the past five years, the opioid dependent population is aging. Between 2014/15 and 2019/20, the number of individuals aged 15-34 is estimated to have decreased by 5,100, while the number of individuals aged 50-64 has increased by 2,800 (7). In Scotland, the prevalence of opioid dependence has risen significantly among those aged 50–64, while rates have declined among younger groups (7). Older individuals on OAT are at greater risk of methadone‑specific mortality (methadone is a long‑acting synthetic opioid used in maintenance therapy), likely due to age‑related physiological changes (8).

Moreover, cocaine use is associated with substantial cardiovascular harm, affecting both vascular and myocardial integrity. Acute exposure can trigger coronary vasoconstriction, arrhythmias, myocardial ischemia and infarction, while chronic use has been linked to structural myocardial changes such as hypertrophy, dilated cardiomyopathy and myocarditis (9). These pathophysiological effects may be further compounded in individuals with concurrent opioid dependence. Stimulants such as cocaine can mask the sedative effect of opioids, which may lead individuals to increase the dosage of opioids to achieve the desired effect, thereby significantly increasing the risk of overdose and cardiovascular risks (10). Opioids themselves may interfere with cardiovascular function and pharmacological management, with potential interactions affecting medications commonly prescribed for cardiovascular disease (11).

In conclusion, the persistently high drug-related mortality rate in Scotland reflects the complex interaction among the changing patterns of substance use, social vulnerability and demographic changes among opioid dependent populations. Increasingly dependent on cocaine and opioid (C&O), especially in accept the OAT and marginalised in the elderly, poses a multifaceted challenge to public health. Understanding these dynamics and examining the connection between the dependence of cocaine and opioid (C&O) and drug-related harms is not only crucial for treatment strategies, but also for addressing the broader determinants of the health social structure that have sustained drug-related harms in Scotland for a long time.

**Methods**

*Data Sources*  
This study utilised linked national datasets from Scotland to characterise patterns of cocaine and opioid (C&O) dependence and associated harms between 2015 and 2022. The primary source of treatment exposure data was the Scottish National Prescription Information System (PIS), which records prescriptions issued by clinicians and dispensed by pharmacies. For this analysis, opioid agonist therapy (OAT) prescriptions were extracted for the period 2009–2023, with the study period restricted to 1 January 2015–31 December 2022. In this study, only calendar years were used instead of financial years. Key variables from PIS included the prescription payment date, a unique patient identifier (IAIN), date of birth, and the individual’s NHS health board of residence.

Data on drug misuse history were obtained from the Scottish Drug Misuse Database (SDMD) for 2015–2021 and its successor, the Drug and Alcohol Information System (DAISy), for 2021–2022. These systems record data about individuals coming to drug services for help, including personal information and the drugs used at the time of the visit. When the recorded substances include cocaine, crack cocaine or cocaine powder, we will determine that this person used cocaine.

Drug-related hospital admissions were identified from the national hospitalisation database, restricted to admissions where drug poisoning was recorded as the cause of admission. Non-fatal overdose (NFOD) events were defined as admissions with International Classification of Diseases, 10th Revision (ICD-10) codes T40.0, T40.1, or T40.3, corresponding to opioid, heroin and methadone drug-related poisoning.

Mortality data were sourced from the Scottish National Death Registry. Drug-related deaths were defined according to ICD-10 codes F11–F16 and F19 (mental and behavioural disorders due to psychoactive substance use, excluding alcohol and tobacco), X40–X44 (accidental poisoning), X60–X64 (intentional self-poisoning), X85 (drug-related homicide), and Y11–Y14 (poisoning of undetermined intent), when listed as a main underlying cause of death. All-cause mortality encompassed all deaths occurring during the study period, regardless of cause. Cardiovascular mortality was defined as deaths with a main underlying cause coded I00–I99.

*Study Design and Population*  
A retrospective cohort design was employed. The cohort comprised individuals aged 15–64 years who were resident in Scotland and received at least one OAT prescription between 1 January 2015 and 31 December 2022. Follow-up began at the date of the first OAT prescription within the study period and ended at the earliest of: (i) date of death, (ii) two years after the final OAT prescription (to capture ongoing risk after treatment cessation), or (iii) the end of the study period (31 December 2022).

The results of this cohort are as follows: from 53,100 individuals who received at least one OAT prescription from April 30, 2009 to March 31, 2023, 12,292 individuals without SDMD or DAISy records were excluded, leaving 40,808 individuals. Another 36 individuals aged 15 to 64 without an OAT prescription were excluded, and 321 individuals without an OAT prescription from 2015 to 2022 were also excluded. Finally, 42 non-Scottish residents or individuals lacking NHS board information were removed, and the final analysis cohort consisted of 37,409 individuals.

The results of this cohort are as follows: from 53,100 individuals who had received at least one OAT prescription between 30 April 2009 and 31 March 2023, 12,292 individuals without SDMD or DAISy records were excluded, leaving 40,808 individuals. A further 36 individuals without an OAT prescription at ages 15–64 were excluded, as were 321 individuals without an OAT prescription during 2015–2022. Finally, 42 non-Scottish residents or individuals with missing NHS board information were removed, resulting in a final analytical cohort of 37,409 individuals.

**Figure 1. Study Population Flow Diagram**

A diagram of a flowchart

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The participants were divided into two exposure groups. The first one is C&O dependence, individuals who have a history of cocaine use in the any record in SDMD or DAISy. The dependence of cocaine was determined based on the any records of substances reported during the research period, including cocaine, crack cocaine or cocaine powder. The second group consists only of opioid dependence, whose cocaine use is not recorded in any SDMD or DAISy records.

Covariates were measured at the annual observation period level and included calendar year, age group (15–34, 35–49, and 50–64 years), sex (male/female), NHS health board of residence (Greater Glasgow and Clyde (GGC), Tayside, or Other regions), and accommodation status (Homeless, Missing, Owned/Rented and Other). The accommodation situation in prison was classified under "Others" because we have no way to determine that this person remained in prison throughout the study cohort, and the relevant data may be incomplete.

*Statistical Analysis*

Descriptive analyses were first conducted to summarise demographic, clinical, and exposure characteristics of the cohort, stratified by drug dependence category (opioid-only vs. cocaine and opioid). Categorical variables were presented as counts and percentages.

Crude rates of drug-related deaths (DRD), all-cause mortality (ACM), non-fatal overdose (NFOD), and cardiovascular mortality (CVD) were calculated per 1,000 person-years (PY) for each exposure group across calendar years from 2015 to 2022. Person-time at risk was calculated for each individual from the date of cohort entry to the earliest of death, two years after the last OAT prescription, or study end. Rates were accompanied by 95% confidence intervals (CI) and plotted to illustrate temporal trends.

To evaluate the association between the exposure group and each outcome, a Poisson regression model with a logarithmic link function was fitted, using the natural logarithm of PY as the offset term. The unadjusted model only includes exposure variables (drug type). Then adjust the model to incorporate all potential confounding factors: age, gender, calendar year, residential board and accommodation status. The model results were expressed as an incidence rate ratio (IRR) with a 95% CI.

Potential effect modification by sex and age group was examined for each outcome by including an interaction term between sex and age group in the fully adjusted model, and likelihood ratio tests (LRT) were used to compare models with and without the interaction term. A statistically significant interaction was defined as p < 0.05.

**Results**

*Characteristics of the Study Cohort*

The final study cohort comprised 37,409 unique individuals aged 15–64 years who were resident in Scotland and had received at least one opioid agonist therapy (OAT) prescription between 2015 and 2022. Table 1 summarises the baseline demographic, clinical and exposure characteristics. Most individuals were male (68.3%), with females accounting for 31.7% of the cohort. The age distribution was skewed towards older adults, with 49.8% aged 35–49 years, 44.4% aged 15–34 years, and only 5.8% aged 50–64 years at the time of inclusion.

**Figure 2. Age Distribution of Opioid-Dependent Individuals**

A graph of a number of age distribution

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In terms of the drug dependence, 78.4% (n = 29,335) were classified as opioid-only dependence, while 21.6% (n = 8,074) met the definition for C&O dependence.

Indicators of drug-related harm showed that 14.9% of individuals experienced at least one non-fatal overdose (NFOD) during the observation period, while 8.7% died a drug-related death (DRD). All-cause mortality (ACM) occurred in 14.7% of the cohort, and cardiovascular mortality (CVD) accounted for 1.35% of deaths.

Accommodation status was dominated by the owned/rented category (72.9%), but a significant proportion were homeless (9.1%), living in other types of accommodation (8.9%), or missing accommodation data (9.2%). Geographically, the largest part of the cohort resided in Other NHS regions in Scotland (65.0%), followed by Greater Glasgow and Clyde (26.7%) and Tayside (8.3%).

**Table 1****. Characteristics of the Study Cohort**

|  |  |  |
| --- | --- | --- |
| **Characteristic** | **N** | **%** |
| **Total participants** | 37,409 | 100.0 |
| **Age group** |  |  |
| 15–34 years | 17,395 | 44.36 |
| 35–49 years | 19,536 | 49.82 |
| 50–64 years | 2,285 | 5.83 |
| **Sex** |  |  |
| Female | 11,855 | 31.69 |
| Male | 25,554 | 68.31 |
| **Drug dependence** |  |  |
| Opioid only | 29,335 | 78.42 |
| Opioid + Cocaine | 8,074 | 21.58 |
| **Accommodation** |  |  |
| Owned/Rented | 27,253 | 72.85 |
| Homeless | 3,394 | 9.07 |
| Other | 3,337 | 8.92 |
| Missing | 3,425 | 9.16 |
| **Region** |  |  |
| Greater Glasgow and Clyde | 9,987 | 26.7 |
| Tayside | 3,106 | 8.3 |
| Other NHS regions in Scotland | 24,316 | 65.0 |

**Table 2. Characteristics of Outcome**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Outcome** | **No Event** | **Event Occurred** | **No Event (%)** | **Event (%)** |
| **Non-fatal overdose** | 31,838 | 5,571 | 85.1% | 14.9% |
| **All-cause mortality** | 31,918 | 5,491 | 85.3% | 14.7% |
| **Drug-related deaths** | 34,169 | 3,240 | 91.3% | 8.66% |
| **Cardiovascular mortality** | 36,905 | 504 | 98.7% | 1.35% |

Figure 3 shows the annual proportion changes of the opioid only and C&O dependence groups in the cohort during the years 2015/16 to 2021/22. Since 2015/16, the proportion of opioid and cocaine dependence has shown a slight upward trend.

**Figure 3. Proportion of Opioid Dependent Individuals by Exposure Type**

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*Crude Rates of Outcomes*

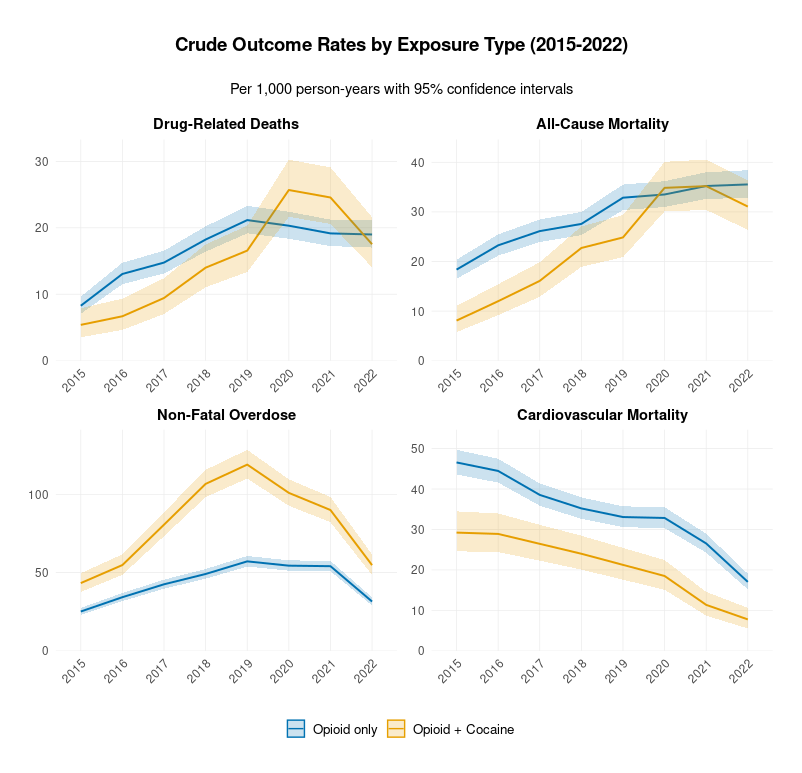
Crude event rates varied over time and between exposure groups (Figures 4). For drug-related deaths (DRD), individuals in the opioid-only group experienced a steady increase in rates from 2015, peaking in 2020 at just over 20 per 1,000 person-years, followed by a modest decline. In contrast, the initial DRD rate of the cocaine exposure group was lower, but it rose sharply in 2020, surpassing that of the opioid group, and then declined in the following years.

For all-cause mortality (ACM), rates increased in both groups throughout the study period. Opioid-only dependence consistently showed slightly higher mortality rates until 2020, after which the gap between the two groups narrowed.

In terms of non-fatal overdose (NFOD), the rate of cocaine exposure has always been significantly higher than opioid-only dependence. NFOD rates peaked at over 125 per 1,000 person-years in 2019 among the exposed group, then declined slightly but remained elevated throughout the remaining years.

Lastly, cardiovascular mortality (CVD) showed a overall downward trend in both groups. However, compared with C&O dependence group, the mortality rate of cardiovascular diseases in the opioid only group has always been relatively high.

**Figure 4. Crude Outcome Rates by Exposure Type (2015-2022)**



*Regression Analyses*

In unadjusted models, C&O dependence had lower DRD rates compared with opioid-only dependence (IRR = 0.91, 95% CI 0.84–0.99). After adjustment for age, sex, year, NHS board, and accommodation status, the association attenuated and was not statistically significant (IRR = 0.99, 95% CI 0.91–1.08). Higher DRD risk was observed among older participants (50–64 years: IRR = 1.60, 95% CI 1.41–1.81), residents of Tayside (IRR = 1.18, 95% CI 1.03–1.34), and those who were homeless or had missing accommodation data. DRD rates also rose almost monotonically across calendar years, from 1.51-fold in 2016 to 2.34-fold in 2022 relative to 2015 (2016: IRR = 1.51, 95% CI 1.26–1.82; 2022: IRR = 2.34, 95% CI 1.98–2.79, respectively)*.* No significant interaction between age and sex was detected (*p* = 0.29).

C&O dependence had lower ACM rates in unadjusted analysis (IRR = 0.81, 95% CI 0.75–0.87), but after adjustment, the association reversed slightly (IRR = 0.92, 95% CI 0.86–0.99). Mortality risk was higher in older age groups (50–64 years: IRR = 2.48, 95% CI 2.26–2.72), males, residents of Tayside, and those with homeless or missing accommodation. All-cause mortality likewise showed a steady year-on-year increase, peaking at 1.96-fold in 2021 compared with 2015 (2021: IRR = 1.96, 95% CI 1.75–2.22). No age-by-sex interaction was found (*p* = 0.13).

C&O dependence experienced substantially higher NFOD rates than opioid-only dependence in both unadjusted (IRR = 1.89, 95% CI 1.82–1.97) and adjusted models (IRR = 1.68, 95% CI 1.61–1.75). Risk was highest among younger participants, males, and residents of Tayside. Homelessness and non-standard accommodation were also associated with elevated NFOD risk, whereas owned/rented housing was protective. The model including the interaction between age group and sex showed a significantly better fit compared to the main effects model (Deviance = 23.37, df = 2, p < 0.001). When the interaction between age group and sex was added to the NFOD model, risk patterns showed notable modification by sex within age categories. Compared to the reference group (females aged 15–34 years), males in the 35–49 and 50–64 year groups had significantly lower relative risks of NFOD (IRR = 0.83, 95% CI 0.76–0.91; IRR = 0.72, 95% CI 0.62–0.84, respectively), despite the overall higher NFOD risk observed among males in the main-effects model. This suggests that the excess risk associated with male is most pronounced in the youngest age group, diminishing in older age categories.

C&O dependence had lower CVD mortality rates than opioid-only dependence (unadjusted IRR = 0.60, 95% CI 0.56–0.65; adjusted IRR = 0.73, 95% CI 0.68–0.78). Risk was strongly associated with age (50–64 years: IRR = 6.62, 95% CI 6.00–7.32) and higher among males and residents of Other NHS regions in Scotland. The interaction model showed a marginal improvement in fit (Deviance = 5.85, df = 2, p = 0.0537). For CVD mortality, inclusion of the age group × sex interaction indicated that males in the 35–49 and 50–64 year groups experienced higher risks compared to their female counterparts of the same age (IRR = 1.21, 95% CI 1.01–1.47; IRR = 1.29, 95% CI 1.05–1.58, respectively).

**Conclusion**

This retrospective cohort study of 37,409 individuals receiving opioid agonist therapy (OAT) in Scotland between 2015 and 2022 demonstrates that concurrent cocaine and opioid (C&O) dependence is associated with distinct patterns of drug-related harms compared with opioid-only dependence. C&O dependence experienced markedly higher non-fatal overdose (NFOD) rates, even after adjustment for demographic, region and accommodation status, indicating a sustained and significant burden of acute overdose risk in this group. Notably, elevated NFOD risk in men was concentrated in the youngest age group (15-34 years), whereas excess risk decreased in older men, highlighting important age-sex heterogeneity.

In contrast, C&O dependence is associated with a lower cardiovascular mortality rate (CVD), while there is no significant difference in adjusted drug-related deaths (DRD), which conflicts with our prior knowledge. The interaction analysis suggested that middle-aged and older males had higher CVD mortality compared to females of the same age, underscoring the importance of tailored cardiovascular risk monitoring in this subgroup.

Age, sex, region and accommodation status instability emerged as consistent predictors of adverse outcomes, with older age linked to higher drug-related deaths (DRD), all-cause mortality (ACM), and cardiovascular death (CVD) risk, and homelessness strongly associated with DRD and ACM. These findings reinforce the need for targeted harm reduction strategies for individuals with C&O dependence, particularly younger males at heightened NFOD risk and older males vulnerable to cardiovascular complications. Moreover, the persistent year-on-year rise in event rates from 2015 to 2022 underscores the urgency of implementing interventions. Addressing intersecting vulnerabilities—such as homelessness and regional disparities—will be critical to reducing the overall burden of drug-related harms in Scotland.

**Author Contributions**

My supervisors provided academic guidance in defining the study cohort, variables, and outcomes, and assisted in developing the corresponding code. My supervisors also offered suggestions on the selection of statistical models and the inclusion of interactions to ensure the rigor and efficiency of the methods. In addition, I received feedback on the presentation of results, including the choice and design of figures and tables. All data analysis, interpretation, and writing were conducted by the author.

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**Supplementary Material**

**Table 3. Poisson Regression Results**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Outcome / Model | Covariate | IRR | 95% CI | p-value |
| **DRD –** drug only | Intercept | 0.017 | 0.016–0.017 | <0.001 |
|  | drugpoly | 0.91 | 0.84–0.99 | 0.035 |
| **DRD –** fully adjusted | Intercept | 0.008 | 0.006–0.009 | <0.001 |
|  | drugpoly | 0.99 | 0.91–1.08 | 0.88 |
|  | age 35–49 | 1.39 | 1.26–1.53 | <0.001 |
|  | age 50–64 | 1.60 | 1.41–1.81 | <0.001 |
|  | sex (M) | 1.06 | 0.99–1.15 | 0.12 |
|  | 2016 | 1.51 | 1.26–1.82 | <0.001 |
|  | 2017 | 1.74 | 1.46–2.09 | <0.001 |
|  | 2018 | 2.21 | 1.86–2.62 | <0.001 |
|  | 2019 | 2.56 | 2.17–3.03 | <0.001 |
|  | 2020 | 2.73 | 2.31–3.23 | <0.001 |
|  | 2021 | 2.57 | 2.18–3.05 | <0.001 |
|  | 2022 | 2.34 | 1.98–2.79 | <0.001 |
|  | board (Tayside vs Greater Glasgow & Clyde) | 1.18 | 1.03–1.34 | 0.015 |
|  | board (Other NHS regions vs GGC) | 1.00 | 0.92–1.08 | 0.98 |
|  | accommodation (Missing vs Homeless) | 1.44 | 1.25–1.65 | <0.001 |
|  | accommodation (Other vs Homeless) | 0.80 | 0.68–0.93 | 0.004 |
|  | accommodation (Owned/Rented vs Homeless) | 0.62 | 0.55–0.70 | <0.001 |
| **ACM –** drug only | Intercept | 0.029 | 0.028–0.030 | <0.001 |
|  | drugpoly | 0.81 | 0.75–0.87 | <0.001 |
| **ACM –** fully adjusted | Intercept | 0.014 | 0.012–0.016 | <0.001 |
|  | drugpoly | 0.92 | 0.86–0.99 | 0.020 |
|  | age 35–49 | 1.49 | 1.37–1.61 | <0.001 |
|  | age 50–64 | 2.48 | 2.26–2.72 | <0.001 |
|  | sex (M vs F) | 1.08 | 1.01–1.14 | 0.016 |
|  | 2016 | 1.26 | 1.11–1.43 | <0.001 |
|  | 2017 | 1.42 | 1.25–1.61 | <0.001 |
|  | 2018 | 1.54 | 1.37–1.75 | <0.001 |
|  | 2019 | 1.79 | 1.58–2.02 | <0.001 |
|  | 2020 | 1.91 | 1.70–2.16 | <0.001 |
|  | 2021 | 1.96 | 1.75–2.22 | <0.001 |
|  | 2022 | 1.88 | 1.67–2.13 | <0.001 |
|  | board (Other NHS regions vs GGC) | 1.06 | 1.00–1.13 | 0.065 |
|  | board (Tayside vs GGC) | 1.18 | 1.06–1.31 | 0.001 |
|  | accommodation (Missing vs Homeless) | 1.42 | 1.28–1.58 | <0.001 |
|  | accommodation (Other vs Homeless) | 0.77 | 0.68–0.87 | <0.001 |
|  | accommodation (Owned/Rented vs Homeless) | 0.64 | 0.58–0.70 | <0.001 |
| **NFOD –** drug only | Intercept | 0.044 | 0.043–0.045 | <0.001 |
|  | drugpoly | 1.89 | 1.82–1.97 | <0.001 |
| **NFOD –** fully adjusted | Intercept | 0.046 | 0.041–0.050 | <0.001 |
|  | drugpoly | 1.68 | 1.61–1.75 | <0.001 |
|  | age 35–49 | 0.78 | 0.75–0.82 | <0.001 |
|  | age 50–64 | 0.70 | 0.65–0.75 | <0.001 |
|  | sex (M vs F) | 1.12 | 1.07–1.17 | <0.001 |
|  | 2016 | 1.35 | 1.22–1.49 | <0.001 |
|  | 2017 | 1.78 | 1.63–1.96 | <0.001 |
|  | 2018 | 2.18 | 2.00–2.39 | <0.001 |
|  | 2019 | 2.52 | 2.31–2.76 | <0.001 |
|  | 2020 | 2.32 | 2.12–2.53 | <0.001 |
|  | 2021 | 2.24 | 2.05–2.45 | <0.001 |
|  | 2022 | 1.35 | 1.22–1.49 | <0.001 |
|  | board (Other NHS regions vs GGC) | 0.99 | 0.95–1.04 | 0.78 |
|  | board (Tayside vs GGC) | 1.45 | 1.35–1.55 | <0.001 |
|  | accommodation (Missing vs Homeless) | 0.65 | 0.59–0.70 | <0.001 |
|  | accommodation (Other vs Homeless) | 1.15 | 1.08–1.23 | <0.001 |
|  | accommodation (Owned/Rented vs Homeless) | 0.47 | 0.44–0.49 | <0.001 |
| **CVD –** drug only | Intercept | 0.035 | 0.034–0.036 | <0.001 |
|  | drugpoly | 0.60 | 0.56–0.65 | <0.001 |
| **CVD –** fully adjusted | Intercept | 0.015 | 0.013–0.017 | <0.001 |
|  | drugpoly | 0.73 | 0.68–0.78 | <0.001 |
|  | age 35–49 | 2.55 | 2.32–2.80 | <0.001 |
|  | age 50–64 | 6.62 | 6.00–7.32 | <0.001 |
|  | sex (M vs F) | 1.20 | 1.13–1.27 | <0.001 |
|  | 2016 | 0.91 | 0.84–0.99 | 0.035 |
|  | 2017 | 0.76 | 0.70–0.83 | <0.001 |
|  | 2018 | 0.67 | 0.61–0.73 | <0.001 |
|  | 2019 | 0.60 | 0.54–0.66 | <0.001 |
|  | 2020 | 0.56 | 0.51–0.61 | <0.001 |
|  | 2021 | 0.42 | 0.38–0.47 | <0.001 |
|  | 2022 | 0.26 | 0.23–0.29 | <0.001 |
|  | board (Other NHS regions vs GGC) | 1.36 | 1.28–1.44 | <0.001 |
|  | board (Tayside vs GGC) | 1.17 | 1.05–1.29 | 0.004 |
|  | accommodation (Missing vs Homeless) | 1.25 | 1.12–1.40 | <0.001 |
|  | accommodation (Other vs Homeless) | 1.13 | 1.00–1.28 | 0.048 |
|  | accommodation (Owned/Rented vs Homeless) | 0.85 | 0.77–0.93 | <0.001 |

Reference categories: opioid only, age 15–34 years, female sex, calendar year 2015, Greater Glasgow & Clyde (GGC), and homeless accommodation. Outcomes: drug-related deaths (DRD), all-cause mortality (ACM), non-fatal overdose (NFOD), and cardiovascular mortality (CVD). IRR = incidence rate ratio; 95% CI = 95% confidence interval. All models use log(person-years) as offset.

**Table 4. Poisson Regression Results with Age-group × Sex Interaction terms for Non-fatal Overdose and Cardiovascular Mortality**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Outcome | Covariate | IRR | 95% CI | p-value |
| **Non-fatal overdose** | Intercept | 0.042 | 0.037–0.046 | <0.001 |
|  | drugploy | 1.68 | 1.61–1.76 | <0.001 |
|  | age 35–49 vs 15–34 | 0.88 | 0.82–0.96 | 0.002 |
|  | age 50–64 vs 15–34 | 0.89 | 0.78–1.01 | 0.086 |
|  | sex (M vs F) | 1.29 | 1.20–1.40 | <0.001 |
|  | 2016 | 1.35 | 1.22–1.49 | <0.001 |
|  | 2017 | 1.78 | 1.63–1.96 | <0.001 |
|  | 2018 | 2.18 | 2.00–2.39 | <0.001 |
|  | 2019 | 2.52 | 2.31–2.75 | <0.001 |
|  | 2020 | 2.31 | 2.12–2.53 | <0.001 |
|  | 2021 | 2.24 | 2.04–2.45 | <0.001 |
|  | 2022 | 1.34 | 1.22–1.49 | <0.001 |
|  | board (Other NHS regions vs GGC) | 0.99 | 0.95–1.04 | 0.79 |
|  | board (Tayside vs GGC) | 1.45 | 1.35–1.56 | <0.001 |
|  | accommodation (Missing vs Homeless) | 0.65 | 0.59–0.70 | <0.001 |
|  | accommodation (Other vs Homeless) | 1.15 | 1.07–1.23 | <0.001 |
|  | accommodation (Owned/Rented vs Homeless) | 0.47 | 0.44–0.49 | <0.001 |
|  | age 35–49 × sex M | 0.83 | 0.76–0.91 | <0.001 |
|  | age 50–64 × sex M | 0.72 | 0.62–0.84 | <0.001 |
| **Cardiovascular mortality** | Intercept | 0.016 | 0.014–0.019 | <0.001 |
|  | drugploy | 0.73 | 0.68–0.78 | <0.001 |
|  | age 35–49 vs 15–34 | 2.27 | 1.96–2.63 | <0.001 |
|  | age 50–64 vs 15–34 | 5.62 | 4.77–6.64 | <0.001 |
|  | sex (M vs F) | 0.99 | 0.84–1.18 | 0.94 |
|  | 2016 | 0.91 | 0.84–0.99 | 0.035 |
|  | 2017 | 0.76 | 0.70–0.83 | <0.001 |
|  | 2018 | 0.67 | 0.61–0.73 | <0.001 |
|  | 2019 | 0.60 | 0.54–0.66 | <0.001 |
|  | 2020 | 0.56 | 0.51–0.61 | <0.001 |
|  | 2021 | 0.42 | 0.38–0.47 | <0.001 |
|  | 2022 | 0.26 | 0.23–0.29 | <0.001 |
|  | board (Other NHS regions vs GGC) | 1.36 | 1.28–1.44 | <0.001 |
|  | board (Tayside vs GGC) | 1.17 | 1.05–1.29 | 0.004 |
|  | accommodation (Missing vs Homeless) | 1.25 | 1.12–1.40 | <0.001 |
|  | accommodation (Other vs Homeless) | 1.14 | 1.00–1.29 | 0.042 |
|  | accommodation (Owned/Rented vs Homeless) | 0.85 | 0.77–0.93 | <0.001 |
|  | age 35–49 × sex M | 1.21 | 1.01–1.47 | 0.043 |
|  | age 50–64 × sex M | 1.29 | 1.05–1.58 | 0.016 |

Reference categories: opioid only, age 15–34 years, female sex, calendar year 2015, Greater Glasgow & Clyde (GGC), and homeless accommodation. IRR = incidence rate ratio; 95% CI = 95% confidence interval. All models use log(person-years) as offset.