

Host department: Bristol

Project Title: Co-prescribing of medications associated with dependence, withdrawal effects and poly-drug overdose: a mixed methods study within general practice in the UK.

Proposed supervisory team:

Names and areas of expertise to be included

- **Dr Jenny Scott**, [lead supervisor] Senior Lecturer (pharmacist), University of Bristol: *opioid addiction, drug related deaths and pharmacy practice; qualitative methods supervision.*
- **Dr Anita McGrogan**, Senior Lecturer (epidemiology & statistics), University of Bath: *pharmaco-epidemiological studies using CPRD datasets; vulnerable populations; quantitative analysis.*
- **Dr Maria Theresa Redaniel**, Senior Lecturer (Health Services Research and Epidemiology), University of Bristol: *expertise using CPRD datasets; quantitative analysis; mental health.*

Potential for cross consortium networking and educational opportunities:

This project will help strengthen pharmacy related research and build cross-disciplinary links between pharmacoepidemiology (AMcG), pharmacy practice (JS) and epidemiology (MTR). It aligns with CAPC priorities to grow academic collaboration with non-medical healthcare departments in the Southwest. The student will gain mixed methods research skills relevant to understanding prescribing practice.

Project description:

Background

In recent years there has been increased concern around the prescribing of medications associated with dependence and withdrawal. These medications include opioids, benzodiazepines and gabapentinoids^{1,2}. One particular concern is polypharmacy, because annual statistics show combinations are implicated in rising numbers of deaths^{3,4}. Implicated opioids may be pharmaceuticals to manage pain, opioid substitution therapy (OST) e.g., methadone or illicit drugs like heroin. Although caution is advised on co-prescribing benzodiazepines and gabapentinoids alongside opioids, including to people who misuse opioids, anecdotally this is known to occur. This project will determine the scale of co-prescribing of these medications, including to those with a known history of opioid misuse. Contributing factors will be explored in depth, to help inform opioid stewardship (OS) interventions for use in general practice. OS is coordinated interventions designed to improve, monitor, and evaluate the use of opioids, to protect and improve health.

Aim 1. To determine levels of co-prescribing of opioids, benzodiazepines and gabapentinoids in adults in the UK and to determine the extent and variation in adverse outcomes for these medications, including in people with a history of opioid misuse.

Aim 2: To understand co-prescribing of opioids, benzodiazepines and gabapentinoids in depth and identify targets to modify prescribing behaviour to build into an OS intervention.

Objectives

1. To describe the frequency, doses, and length of prescribing of opioids, benzodiazepines and gabapentinoids in adults in the UK.
2. To describe the characteristics of and, nature of co-prescribing and co-morbidities in patients who are co-prescribed these medications.

3. To determine the incidence of and risk factors for death, fatal overdose, non-fatal hospitalisation, and all cause admission to hospital in those co-using these medications compared with those who do not co-use.
4. To compare prescribing in subgroups of interest:
 - a) people with a history of opioid dependence vs those without,
 - b) people in receipt of OST vs people not in receipt of OST.
5. To explore contributing factors identified in Obj 1-4 in depth to inform greater understanding of what underpins them and identify targets to modify prescribing behaviours in general practice.

Methods

Objectives 1-4:

An observational retrospective study using data from the Clinical Practice Research Datalink (CPRD) Aurum data to form a cohort of adults newly prescribed opioids, benzodiazepines or gabapentinoids. This group will be matched to a healthy comparator group who do not receive these medications. The full cohort will be followed over time from the point of their first prescription until they die, stop contributing data to the study or until the end of the study period (2010-2022). Patient outcomes will be identified along with the use of healthcare, co-prescribing and comorbidities that may have an impact on outcomes. Analyses will take into account the type of medication prescribed, changes in prescription and prescribing patterns, dose, and any combinations of therapy as well as the length of time these are prescribed for.

Objective 5:

A qualitative interview study with prescribers in general practice, to give greater depth to understanding the findings from Obj1-4. Analysis will take a reflexive thematic approach, informed by behaviour change theory (COM-B/TDF), to understand prescriber practice and to identify modifiable targets to build into a future opioid stewardship intervention.

Impact

This study has the potential to inform the development of OS interventions for general practice, to reduce polypharmacy opioid-related deaths. OS is gaining international application as an approach to reducing harm and ensure appropriate prescribing, including in the UK.

Training and development provision by host:

Formal training: By month 3, a bespoke needs assessment will be conducted. Sources of training include Short-courses at University of Bristol (e.g. Introduction to Qualitative Methods, Writing a Journal Paper); Bristol Medical School Graduate Studies programmes (1/2 days): Library induction and literature searching; Introduction to EndNote; Quality papers; Patient & Public Involvement (ARC West). University of Bristol IT courses. Formal course(s) on Stata or R; SQL; statistical modelling e.g. rates and survival analysis, logistic regression; and qualitative analysis will be undertaken.

Informal training: JS will provide guidance on qualitative methods, research ethics and PPIE. MTR will provide guidance on quantitative methods, analysis of CPRD data, AMcG will provide guidance on algorithms for CPRD data checking and cleaning analysis. Attendance at CAPC Medicines & Prescribing Team meetings and seminars within PHS provide additional opportunities.

PPIE: Bristol's Medicine & Prescribing research group has an established PPI group that will be approached to support the project, paying attention to EDI and vulnerable group representation. JS can recruit additional PPIE members with lived experience of substance dependence if required.

References:

1. National Institute for Health & Care Excellence, 2022. Medicines associated with dependence or withdrawal symptoms: safe prescribing and withdrawal management for adults, [NG215]. London: NICE.
2. HM Government, 2020. Opioids: risk of dependence and addiction Drug Safety Update 14(2): September 2020: 1.
3. Office for National Statistics, 2022. [Deaths related to drug poisoning in England and Wales: 2021 registrations](#). Newport: ONS.
4. National Records of Scotland. [Drug-related Deaths in Scotland in 2021](#). Edinburgh: NRS.