# A mixed-methods analysis of patient safety incidents involving opioid substitution treatment with methadone or buprenorphine in community-based care in England and Wales

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**Background and Aims**  Opioid substitution treatment is used in many countries as an effective harm minimization strategy. There is a need for more information about patient safety incidents and the resulting harm relating to this treatment. We aimed to characterize patient safety incidents involving opioid substitution treatment with methadone or buprenorphine in community-based care by: (i) identifying the sources and nature of harm and (ii) describing and interpreting themes to identify priorities to focus future improvement work. **Design**  Mixed-methods study examining patient safety incident reports involving opioid substitution treatment with either methadone or buprenorphine in community-based care. **Setting**  Data submitted between 2005 and 2015 from the National Reporting and Learning System (NRLS), a national repository of patient safety incident reports from across England and Wales. **Participants**  A total of 2284 reports were identified involving patients receiving community-based opioid substitution treatment. **Measurements**  Incident type, contributory factors, incident outcome and severity of harm. Analysis involved data coding, processing and iterative generation of data summaries using descriptive statistical and thematic analysis. **Findings**  Most risks of harm from opioid substitution treatment came from failure in one of four processes of care delivery: prescribing opioid substitution ($n = 151$); supervised dispensing ($n = 248$); non-supervised dispensing ($n = 318$); and monitoring and communication ($n = 1544$). Most incidents resulting in harm involved supervised or non-supervised dispensing ($n = 91$ of 127, 72%). Staff- (e.g. slips during task execution, not following protocols) and organization-related (e.g. poor working conditions or poor continuity of care between services) contributory factors were identified for more than half of incidents. **Conclusions**  Risks of harm in delivering opioid substitute treatment in England and Wales appear to arise out of failures in four processes: prescribing opioid substitution, supervised dispensing, non-supervised dispensing and monitoring and communication.

**Keywords**  Incident reporting, Health services research, opioids, patient safety, primary care, quality improvement.

## INTRODUCTION

Opioid substitution therapy is now used in many parts of the world and is an effective harm minimization strategy to treat opioid dependence. It reduces illicit drug use and the mortality associated with it [1–4]. With increasing demand for substitution therapies [5–7], it is important to evaluate the safety performance of these programmes [8].

The United Kingdom has community-based provision for opioid dependence [9–11]. There is a paucity of knowledge and understanding about the nature of patient safety incidents and related harm in those treatment programmes. With anticipated greatly increased numbers of people requiring these services in primary care settings around the world, patient safety will become a major concern [12]. The World Health Organization (WHO) have called on policymakers, health-system leaders and a range

of other stakeholders, including researchers, to design specific evidence-based programmes of action for improving the safety of medication practices and systems globally [13,14].

Our study explores the nature of patient safety incidents involving opioid substitution treatment with methadone or buprenorphine in community-based care settings. Our objectives were to:

1 Classify and quantify types of methadone- or buprenorphine-related patient safety incidents, and their underlying causes through application of coding frameworks to describe what happened, reported reasons why the incident occurred, harm outcomes and their severity.
2 Describe and interpret themes in reports and use this qualitative analysis to identify priorities to focus future improvement work.
3 Construct a driver diagram summarizing empirically identified ideas for systems improvement derived from objectives 1 and 2.

## METHODS

### Design

We undertook a mixed-methods study of people receiving either methadone or buprenorphine in community-based care programmes throughout England and Wales and whose treatment had been subject of a patient safety incident report. A patient safety incident is defined as: 'any unintended or unexpected incidents that could have, or did, lead to harm for one or more patients receiving health care' [15]. Such reports offer a lens to understand what happened and explore common patterns of reported reasons why the incident might have occurred [16]. To understand similarities and differences between incidents, we used detailed data coding and exploratory data analysis to identify the most frequent sources of incidents, coupled with a thematic analysis to identify themes about why such incidents occur and how they could be avoided in future care [17].

### Study population

We extracted data about patient safety incidents involving people receiving either methadone or buprenorphine from a national database of patient safety incident reports maintained by the National Health Service (NHS) in England and Wales; namely, the National Reporting and Learning System (NRLS). This is the largest repository of its kind world-wide, receiving more than 2 million patient safety incident reports every year [16]. When an incident occurs in England and Wales health-care staff are encouraged to complete a report about the incident, whether or not it resulted in patient harm [15]. Reports are anonymized and submitted by each organization to the national database,

where it undergoes further cleansing to ensure that all patient-identifiable information is removed.

A total of 272 884 patient safety incidents were reported by non-hospital community-based care settings (primary care, community pharmacies and other non-specialist services) between 1 January 2005 and 31 December 2015, which was the most recent available data set at the time of undertaking the analysis.

The study population comprised all patient safety incident reports in which methadone or buprenorphine had been used, as both of these have a strong evidence base for use as opioid substitution treatment and their use is recommended in England and Wales [2]. In the United Kingdom, drug users can receive opioid substitution treatment from community-based teams responsible for the induction and maintenance of prescribing [8]. A range of different models of drug treatment in primary care exist. A common approach is that a prescriber (e.g. general practitioner, nurse) with expertise in opioid substitution will provide a patient with a prescription that is dispensed at a pharmacy. Supervised dispensing is best practice for new patients prescribed methadone or buprenorphine. This requires patients to take daily doses under the eye of a professional and allows monitoring of compliance, progress and ongoing risk assessment [8].

Of the 3297 reports identified from free-text searches of the database for methadone or buprenorphine among all incident report categories (see Table 1), we manually reviewed all completed fields for each report and excluded reports that did not fit this category (see reasons for exclusion in Fig. 1). The resulting study population comprised 2284 patient safety incident reports.

### Measures

Each patient safety incident report requires the reporter to complete a form with structured categories about location, incident type, medication involved (if any) and the reporter's perception of severity of harm, along with free-text fields to describe what happened (IN07), why they think it happened (potential contributory factors: IN06) and how they think it could have been preventable (actions to prevent recurrence: IN10), the latter two of which are not mandatory for reporters to complete (Table 1).

### Data processing

Patient safety incident reports were analysed using a classification system aligned with the WHO International Classification for Patient Safety (ICPS) [18] and validated by a previous study of patient safety in primary care [17]. This includes four coding frameworks, each designed to capture a different aspect of the patient safety incident:

**Table 1** Data variables in the NRLS (example report).

| Category | Code name | Description | Example |
|---|---|---|---|
| RP01 | Unique ID | Numerical | 1 456 789 |
| RP02 | Care setting | Structured | Community pharmacy |
| RP05 | Local reference ID | Numerical | 3567 |
| RP07 | Trust organization code | Numerical | 0344 |
| PD01 | Patient age | Numerical | 84 |
| PD05 | Speciality | Structured | Primary care/community |
| PD09 | Clinical outcome | Structured | No harm |
| MD05 | Approved drug name | Unstructured | Methadone |
| IN01 | Date of incident | Date | 15/04/2013 |
| IN05 | Incident category | Structured | Medication |
| IN06 | Contributing factors | Unstructured | Lack of standard operating procedure for checking of prescriptions; patient factors (being late); staff work-load that day was high with back-to-back appointments |
| IN07 | Free-text description of incident | Unstructured | Client presented 1 hour late to appointment and was seen by keyworker only. Doctor agreed to sign prescription for methadone. However, wrong dose prescribed (20 instead of 40 ml) |
| IN10 | Re-occurrence prevention | Unstructured | Discussion around why incident took place, and agreement that staff should double-check prescriptions before asking doctor to sign. Agreement to develop standard operating procedure for double-checking of prescriptions |

NRLS = National Reporting and Learning System.
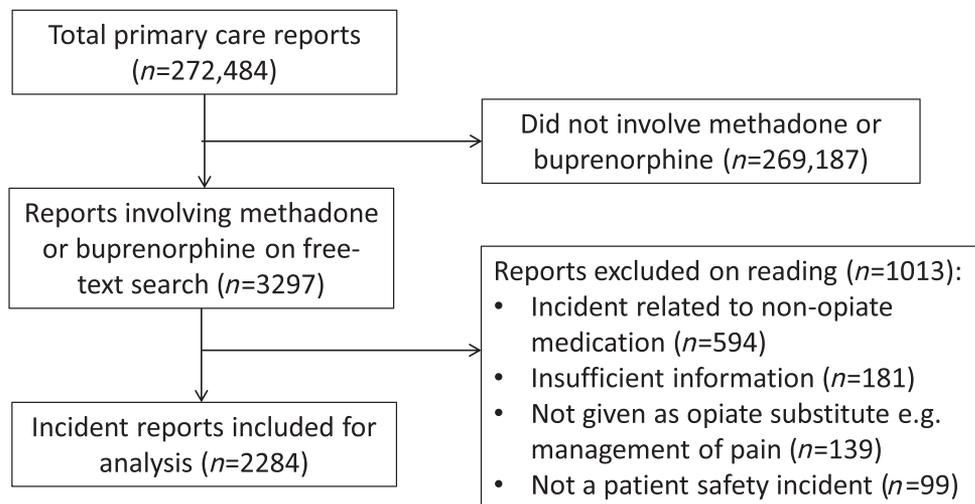


**Figure 1** Flow diagram of included and excluded incident reports

(a) incident framework to characterize the events leading up to the outcome (e.g. wrong dose of methadone prescribed);

(b) contributory factors framework to identify the human and systemic factors reported to underlie the incident (e.g. an inexperienced or locum pharmacist dispensing the drug);

(c) incident outcome framework (e.g. hospital admission); and

(d) severity of harm framework to characterize the level of harm of the outcome (defined as no harm, low, moderate or severe harm or death) classified in accordance with WHO definitions [18].

The coding frameworks were developed iteratively for use with methadone- and buprenorphine-related incidents using a constant comparative approach [19,20]. The analysis involved each patient safety incident report being assessed by two of the authors, who are clinicians trained in root cause analysis and human factors science (R.G., N. M.) to read the complete incident report, including the free text available in contributing factors (IN06), free text description of the incident (IN07) and actions to prevent

recurrence (IN10) (Table 1), and then select codes from the aforementioned frameworks which represent explicit statements made by reporters. No implicit judgements concerning what the reporter meant are made during coding. Each clinician was allocated approximately 50% of the total sample to code; further, to ensure the validity of coding throughout the process, each coder double-coded a random 20% sample of the other's reports. We calculated inter-rater reliability using Cohen's kappa ($\kappa$) coefficient. Cohen's $\kappa$ coefficient of inter-rater (coding) reliability was high for incident type ($\kappa = 0.70$) and moderate–high for severity of harm ($\kappa = 0.69$). Discrepancies were discussed at regular team coding meetings and resolved through discussion between four of the authors (R.G., N.M., H.W. and A.C.S.). Where an existing code was not available to represent the reported narrative, a new code was developed and added to the framework.

### Data analysis

We used an exploratory data analysis approach and produced quantitative data summaries of the most frequently reported incidents that were tabulated against severity of harm and contributory factors to identify categories for further exploratory analysis. Collections of inter-related codes were integrated into themes (R.G. and N.M.), and through wider team discussion we identified categories related to processes of care (R.G., N.M., A.C.S., H.W.). This iterative method and the evolving codes/themes/categories followed established qualitative research principles [19,20].

We have contextualized our findings through targeted literature searches and identified examples of existing interventions, initiatives or national guidelines in the highlighted priority areas. The mixed-methods analysis was integrated and synthesized in a driver diagram, an established quality improvement tool, to map potential exemplar interventions to priority areas for change [21].

### Institutional Review Board approval

Aneurin Bevan University Health Board Research Risk Review Committee judged the study as using anonymized data for service improvement purposes, and approved it on this basis (ABHB R&D Ref number: SA410/13). A protocol for this study was not pre-registered on a publicly available platform, and as such our findings should be considered, as intended, to be exploratory in nature.

## RESULTS

In our study of 2284 patient safety incidents involving opioid substitution (Fig. 1), methadone was the most commonly reported drug ($n = 1862$ of 2284, 82%), followed by buprenorphine ($n = 394$, 17%), then buprenorphine and naloxone used in combination ($n = 28$, 1%) (Table 2).

We identified four processes of care that were involved in most patient safety incidents involving methadone or buprenorphine; in order of decreasing frequency: non-supervised ($n = 1544$) and then supervised dispensing (i.e. daily supervision of new patients taking their prescribed methadone or buprenorphine to monitor compliance [8]) ($n = 318$), monitoring and communication ($n = 248$) and prescribing opioid substitution treatment ($n = 151$) (Table 3).

Incidents involving prescribing opioid substitution had the highest proportion associated with harm ($n = 14$ of 151, 9%), followed by monitoring and communication-related incidents ($n = 22$ of 284, 8%) and failures with supervised dispensing (24 of 318, 8%) (Table 3). Non-supervised dispensing had the lowest proportion resulting in harm (57 of 1544, 4%). Overall, 94% ($n = 2155$ of 2284) of incidents resulted in no harm, while 6% ($n = 129$ of 2284) caused harm to the patient (109 low harm, 20 moderate harm). There were no incidents identified resulting in severe harm or death.

Contributory factors could be identified in 75% of incidents ($n = 1721$ of 2284), with 40% of incidents ($n = 922$ of 2284) involving more than one identified contributory factor. The most frequently identified contributory factors were staff factors ($n = 1458$ of 2284, 64%)— for example, incidents due to attentional slips of action (such as being distracted or misread a concentration of medication) leading to dispensing the wrong dose of medication, followed by organizational factors ($n = 1010$ of 2284, 44%), such as poor working conditions with staff busy or overloaded by work leading to patient safety incidents during supervised consumption of methadone (Table 4). Other identified contributory factors included patient factors ($n = 205$ of 2284, 9%), medication storage and packaging ($n = 133$ of 2284, 6%) and equipment-related, e.g. information technology-related ($n = 47$ of 2284, 2%).

**Table 2** Medication types by severity of harm.

| Medication | Harm severity, N/n (%) | | | |
| --- | --- | --- | --- | --- |
| | No harm | Low | Moderate | Total N |
| Methadone | 1753 (94) | 93 (5) | 16 (1) | 1862 |
| Buprenorphine | 377 (96) | 14 (4) | 3 (< 1) | 394 |
| Buprenorphine/ naltrexone combination | 25 (89) | 2 (7) | 1 (4) | 28 |

**Table 3** Reported processes of care and related incidents by severity of harm.

| Process of care | Harm severity, N/n (%) | | | Total N (%) |
|---|---|---|---|---|
| | No harm | Low | Moderate | |
| Prescribing opioid substitution | 137 (91) | 10 (7) | 4 (3) | 151 (7) |
| Incomplete/inaccurate prescription | 54 | 7 | 0 | 61 |
| Wrong dose | 35 | 0 | 1 | 36 |
| Prescription unsafe or contraindicated | 9 | 1 | 2 | 12 |
| Incorrect number of doses | 7 | 0 | 0 | 7 |
| Incorrect strength of methadone liquid | 5 | 0 | 0 | 5 |
| Other | 27 | 2 | 1 | 30 |
| Monitoring and communication | 226 (91) | 19 (8) | 3 (1) | 248 (11) |
| Failure to stop dispensing | 67 | 4 | 0 | 71 |
| Prescription handling incidents | 52 | 10 | 0 | 62 |
| Duplicate prescribing | 50 | 2 | 2 | 54 |
| Failures in transfer of patient information | 20 | 0 | 1 | 21 |
| Inadequate medical record keeping | 17 | 2 | 0 | 19 |
| Other | 20 | 1 | 0 | 21 |
| Supervised dispensing | 294 (92) | 19 (6) | 5 (2) | 318 (14) |
| Wrong patient | 91 | 10 | 3 | 104 |
| Incorrect dose | 69 | 3 | 2 | 74 |
| Failure to supervise consumption | 55 | 1 | 0 | 56 |
| Incorrect formulation | 35 | 0 | 0 | 35 |
| Incorrect number of doses dispensed | 14 | 3 | 0 | 17 |
| Medication redirected | 7 | 0 | 0 | 7 |
| Other | 23 | 2 | 0 | 25 |
| Non-supervised dispensing | 1477 (96) | 59 (4) | 8 (< 1) | 1544 (68) |
| Incorrect dose | 339 | 22 | 3 | 364 |
| Incorrect number of doses | 294 | 7 | 0 | 301 |
| Incorrect formulation | 287 | 3 | 1 | 291 |
| Wrong patient | 203 | 9 | 0 | 212 |
| Dispensed against invalid prescription | 177 | 3 | 1 | 181 |
| Incorrect label applied | 59 | 1 | 1 | 61 |
| Incorrect medication | 50 | 7 | 2 | 59 |
| Other | 68 | 7 | 0 | 75 |
| Others | 21 (91) | 2 (9) | 0 | 23 (1) |
| Total | 2155 | 109 | 20 | 2284 |

## Prescribing opioid substitution

Most incidents ($n = 151$) related to prescribing opioid substitution (Table 3) were due to incomplete or inaccurate prescriptions ($n = 61$ of 151, 40%), prescribing the wrong dose of medication ($n = 36$ of 151, 24%) or unsafe or contraindicated prescribing ($n = 12$ of 151, 8%). Other incidents identified included prescribing an incorrect number of doses or specifying an incorrect strength of methadone liquid.

More than 40% of prescribing incidents involved attentional slips ($n = 63$ of 151, 42%) (Table 4). Poor communication between care providers led to 15% of incidents ($n = 23$ of 151), while 8% involved a failure to follow guidelines ($n = 12$ of 151), such as checking whether the patient was already taking opioids before prescribing methadone. Six reports described poorly designed prescription forms;

notably, prescribing forms not having space for specifying formulation of methadone.

Harm was experienced by 9% of patients ($n = 14$ of 151), with outcomes including missed doses of medications; repeated visits to or from health-care professionals; delayed management of their condition; and hospital admission. Four incidents were prevented from resulting in harm by a patient's intervention; for example, noticing they had been prescribed the wrong dose of medication.

## Monitoring and communication of treatment

Incidents relating to monitoring and communication of treatment were identified in 248 reports, such as failing to stop dispensing when appropriate ($n = 71$ of 248, 29%), typically involving not alerting the prescriber after a client has missed three daily doses to consider

**Table 4** Most frequent contributing factors with example by process of care.

| Contributory factor | Example of contributory factor | Process of care, N/n (%) | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| | | Prescribing opioid substitution | Monitoring and communication | Supervised dispensing | Non-supervised dispensing | Total, N |
| Staff factors | | 92 (6) | 103 (7) | 201 (14) | 1062 (73) | 1458 |
| Attentional slips during execution of a task | Prescriber misread previous prescription and prescribed incorrect dose | 76 | 55 | 158 | 840 | 1129 |
| Failure to follow protocol | Dispenser did not notify prescriber of missed doses | 12 | 41 | 32 | 172 | 257 |
| Others | | 4 | 7 | 11 | 50 | 72 |
| Organizational factors | | 77 (8) | 167 (17) | 145 (14) | 621 (61) | 1010 |
| Poor working conditions | Staff were overwhelmed by work and dispensed methadone to the wrong patient | 9 | 11 | 57 | 228 | 305 |
| Poor protocols/ procedures/policies | Pharmacy did not refer patients who had missed doses of methadone back to prescriber | 21 | 32 | 46 | 182 | 281 |
| Poor continuity of care | General practitioner unaware of medications prescribed by other services | 23 | 95 | 7 | 61 | 186 |
| Locum/agency staff | Locum pharmacist unfamiliar with patients and hence dispensed to the incorrect person | 5 | 19 | 29 | 126 | 179 |
| Others | | 19 | 10 | 6 | 24 | 59 |
| Patient factors | | 12 (6) | 44 (21) | 53 (26) | 96 (47) | 205 |
| Patient behaviour | Patient diverted methadone to another client | 8 | 38 | 40 | 86 | 172 |
| Others | | 4 | 6 | 13 | 10 | 33 |
| Medication storage/ packaging | Different formulations of methadone were stored in similar packaging and wrong formulation was dispensed | 0 | 4 (3) | 22 (17) | 107 (80) | 133 |
| Equipment, e.g. information technology-related | Methadone dispensing equipment dispensed the incorrect volume of methadone | 7 (15) | 0 | 4 (9) | 36 (77) | 47 |
| Other | | 8 (3) | 9 (3) | 36 (12) | 246 (82) | 299 |
| Total | | 196 | 327 | 461 | 2168 | 3152 |

re-titration as recommended [22]. Other frequent incidents were due to: prescription handling involving the loss of prescriptions by health-care staff or during transit between services ($n = 62$ of 248, 25%); duplicate prescribing ($n = 54$ of 248, 22%); failures in transfer of patient information between services ($n = 21$ of 248, 8%); and incorrect documentation of quantities of dispensed medication in pharmacy settings ($n = 19$ of 248, 8%).

More than one-third ($n = 95$ of 248, 38%) of incidents were due, at least in part, to poor continuity of care

between services; for example, after a failure of communication to halt a patient's previous prescriptions, resulting in the patient being able to draw duplicate prescriptions at separate pharmacies. Poor continuity of care due to poor information-sharing may also arise if a physician is unaware of prescriptions being provided by other services, allowing hazardous combinations of medications to be prescribed; e.g. simultaneous prescriptions of methadone or buprenorphine with benzodiazepines. Inadequate protocols or procedures resulted in 13% (32 of 248) of incidents;

for example, pharmacies lacking protocols for storing instalment prescriptions. Patient harm arose in 9% (*n* = 22 of 248) of incidents, with outcomes including delayed management, repeated visits to health-care professionals and hospital admissions.

### Supervised dispensing

Incidents during supervised dispensing were described in 318 reports, which included medication being dispensed to the incorrect patient (*n* = 104 of 318, 33%), dispensed at the incorrect dose (*n* = 74 of 318, 23%) and failures to supervise consumption of medication despite the prescription specifying supervised consumption (*n* = 56 of 318, 18%). Approximately half of incidents involved staff-related attentional slips (*n* = 158 of 318, 50%); these included the dispenser misreading the prescription. Other contributory factors identified include poor working conditions, patient behaviour and inadequate protocols or double-checking procedures.

In all, 7.5% (*n* = 24 of 318) of supervised dispensing incidents resulted in harm. These led to organizational inconvenience, including telephone calls or follow-ups to rectify or inform the patient or other service about the incident, repeated visits to health-care providers, repeated tests or additional treatment and hospital admission. In 18 of 318 (6%) reports, the patient identified that an incident had occurred and the patient prevented harm.

### Non-supervised dispensing

Non-supervised dispensing incidents involved dispensing incorrect doses of medication (*n* = 364 of 1544, 24%), supplying an incorrect number of doses (*n* = 301 of 1544, 19%) or the incorrect formulation of medication (*n* = 291 of 1544, 19%). Other incidents involved dispensing medication to the wrong patient (*n* = 212 of 1544, 14%) and supplying medication against an invalid prescription (*n* = 181 off 1544, 12%) for example, it had expired or was specified to begin at a later date.

Staff errors, notably attentional slips, were implicated in more than half of incidents (*n* = 840 of 1544, 54%), often involving staff becoming distracted or misreading prescriptions. Other staff factors include failing to follow dispensing protocol; for example, not double-checking dispensed medication against the original prescription or the use of temporary staff being unfamiliar with patients or local dispensing processes. Environmental and organizational factors which frequently contributed to incidents included poor working conditions, inadequate dispensing protocols and processes and inadequate medication storage or packaging, often involving storing different concentrations of methadone next to one another contributing to dispensing the wrong dose. Equipment-related problems involved staff inputting information incorrectly onto computer-aided

dispensing systems for methadone and buprenorphine or arising due to lack of machinery calibration.

In all, 4% (*n* = 67 of 1544) of non-supervised dispensing incidents resulted in patient harm. Outcomes for patients included repeated visits to or from a health-care professional; missed doses of medication; delays in treatment; admission to hospital; and requiring additional tests or treatment. Other types of harm included opioid withdrawal symptoms, such as pain, emotional distress, drowsiness, nausea and vomiting. Patients identified 64 incidents and prevented harm from occurring.

## DISCUSSION

From our analysis of submitted reports, risks of harm in opioid substitution treatments came from failure in one of four processes of care delivery: prescribing opioid substitution; supervised dispensing incidents; non-supervised dispensing incidents; and monitoring and communication activities.

Medication-related incidents are one of the largest sources of injury and avoidable harm in health systems world-wide. Despite being a tightly regulated service to prevent drug misuse [22], little is known about the occurrence of medication-related incidents within opioid substitution services. Even if a patient safety incident occurs in only a small proportion of cases, the challenges associated with the increasing prevalence of opioid dependence facing many nations [5–7] will multiply greatly the number of people needing and using such substitution therapies. As a result, many more people will be at risk of, and many more will be exposed to, the potentially harmful effects of medication-related incidents. Add to this the additional work-load pressures on already overstretched services [12,23], and another well-established incident-prone situation is created.

We believe that our study is the first to use patient safety data to explore sources of incidents and potential harm from opioid substitution therapies in community settings. We found that patient safety incidents involving methadone were nearly four times more commonly reported than those associated with buprenorphine. Compared to methadone, buprenorphine is consistently associated in the United Kingdom with lower rates of mortality, and prescribing data demonstrate that its popularity has increased from use in fewer than 20% of treatment episodes between 1998 and 2000 (83% methadone) to 41% between 2010 and 2014 (59% methadone) [24].

Understanding the reasons for unsafe care involving methadone and buprenorphine is essential to mitigating risk and strengthening systems to prevent future harm to this already vulnerable group of health-care users. Encouragingly, for the prospect of targeted prevention, we found that most incidents fell within one of only four processes

of care: prescribing, dispensing (whether supervised or unsupervised) and when undertaking monitoring and communication activities. Potential evidence-based interventions to address the failures in each of the four incident-prone processes of care exist.

Treatment decision-making and prescribing of methadone and buprenorphine for opioid addiction is complex and varies due to a diversity of patient factors, variability among clinicians (e.g. experience, speciality) and location of delivery (primary care, pharmacy, criminal justice settings) and the legal and regulatory position in the jurisdiction concerned [25,26]. Our data show that when incidents involving prescribing occurred, these had the highest proportion resulting in patient harm (14 of 151, 9%) and warrant targeted interventions to improve the safe provision of opioid substitution.

First, provider education could bolster compliance with legal requirements for prescribing opioids and reinforce protocols to reduce variability in prescribing—the American Hospital Association toolkit is a good framework to guide this process [27]; and secondly, the development of support for prescribers, such as electronic prescribing systems with inbuilt safety prompts to highlight patients at risk of overdose. Thirdly, the co-prescription of benzodiazepines is one that could raise a red flag to prescribers to promote safer prescribing. Fourthly, greater deployment of clinical decision support tools could promote adherence to prescribing guidelines [28–30], with safety prompts innovatively designed to mitigate the effects of 'alert fatigue' [31].

Action cannot rest with measures to ensure safer prescribing practice. Dispensing is also an important source of risk. Incidents involving non-supervised dispensing and supervised dispensing were the most frequently reported, but had the lowest proportion resulting in harm in our study. Nonetheless, due to the large number of reports, these constituted the majority of incidents resulting in harm ($n = 91$ of 127, 72%), and attention should also be focused on mitigating against the risk of dispensing incidents.

We found that dispensers of opioid substitution therapy often failed to contact the prescriber to obtain advice on whether to continue the supply despite three missed daily doses of methadone. Further, protocols and procedures for monitoring and communicating information about methadone use were inadequate. Poor information-sharing between different care providers during transitions of care led to duplicate prescribing. Centralized electronic recording systems could allow for safe prescribing, dispensing and monitoring of opioid substitution treatment, stop duplicate prescriptions and improve information-sharing between care providers through electronic transmission of prescriptions [32]. The existing evidence suggests that interventions could ensure careful induction (including

detailed assessment of opioid tolerance), rigorous monitoring and full stabilization during the first month of treatment due to higher mortality [33–35].

Where medication was dispensed to the wrong person during supervised or non-supervised dispensing, poor working conditions and patient behaviour (including redirecting medication to another person) were contributory factors. Safeguarding against diversion of prescribed opioids is vital for the development of safe opioid substitution treatment programmes [27]. Developing systems to incorporate rigorous identity checks, double-checking dispensed medication and introducing biometrics such as fingerprints or card reading are all possible strategies [36]. Medical-assisted therapy combines pharmacological treatment of opioid addiction with support services, such as psychosocial counselling, treatment for comorbid disorders and vocational rehabilitation to aid recovery [37]. Behaviour therapy appears to give better retention rates, but the evidence is not definitive because of a lack of long-term follow-up [38]. We have pointed to the role of the patient in identifying and preventing incidents. Existing evidence suggests that involving patients in decisions about treatment plans and educating them about risk of overdose (including the use of naloxone) could enhance patient–provider partnership working and compliance [2,27].

It is little surprise that we found incidents relating to the wrong formulation, dose or number of doses in the dispensing of methadone or buprenorphine, as these are prominent sources of medication-related harm in other fields of health care [39]. Complex incident reduction interventions using feedback and training could be effective in community pharmacies and could be adapted for dispensing methadone and buprenorphine [40]. For example, stocking multiple concentrations of methadone is a serious source of risk and could be eliminated [41]. Dispensing machines should be regularly calibrated and staff trained in their use to prevent this source of dispensing incidents. We have summarized our recommendations in the form of a driver diagram (Fig. 2).

*Limitations*

All incident reporting data, whether in health care or other high-risk industries, have the limitation of under-reporting of incidents as well as potential reporting bias [42]. They should therefore not be used to make estimates of incidence, nor to make geographical or institutional comparisons, in case variable reporting rates lead to spurious conclusions. These types of analysis of the patient safety incident data were not part of our study. When data are aggregated to national level, as we have done, bearing in mind these limitations, they can provide important insights into systemic factors underlying harm. As perceived contributory factors actions to prevent recurrence were not
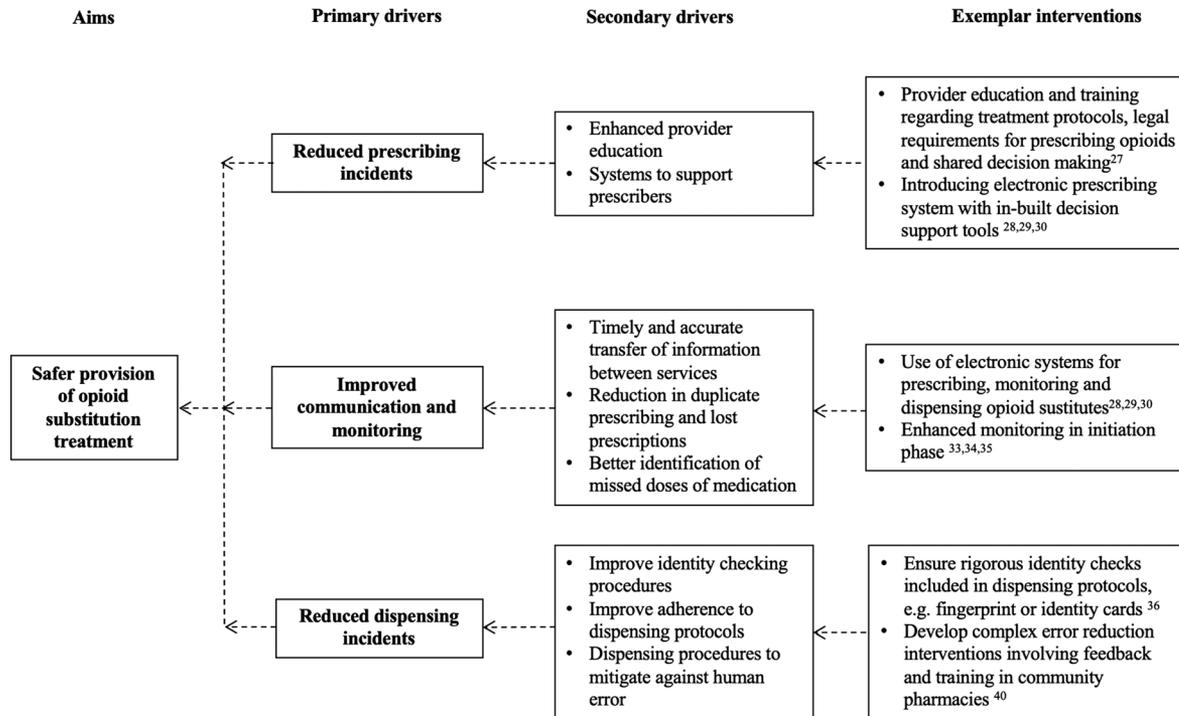
**Figure 2** Driver diagram summarizing recommendations to improve safe provision of opioid substitution treatment

mandatory fields, information in these fields was not consistently available, potentially limiting our findings. While our study team is not representative of all health-care professionals working within community settings, we were able to draw upon the expertise of different professional groups when required.

We were rigorous in minimizing the risk of observer bias. We double-coded 20% of incidents to ensure consistency of coding. We held regular coding meetings to discuss discrepancies. We maintained a clear audit trail recording coding decisions. Although none of the incident reports in our study population involved severe harm or death, many had the potential to be more severe or fatal. It is likely that people who had experienced severe adverse outcomes from opioid substitution therapy are more likely to present to emergency departments, and so incident reports from community-based clinics may not identify them. In the United Kingdom, some addiction services can be provided through third-sector services, such as charities, and these may be under-represented in our study. Further research using retrospective case reviews of patients' notes who have been involved in a patient safety incident could provide additional complementary insights and more detail into the prevalence, nature and severity of methadone- and buprenorphine-related harm.

## CONCLUSION

Addiction to opioids is a chronic disease, and sustainable strategies are needed to enable citizens to access high-value services and medications that ensure optimal health and wellbeing. Our study of patient safety incidents involving opioid substitution treatment with methadone or buprenorphine in community-based settings in England and Wales highlights risks from the delivery of services, and we highlight caution around prescribing practices, effective communication mechanisms for providers working across services and safe dispensing of potentially lethal medicines.

Priority areas for health-care systems world-wide to strengthen processes to mitigate against unsafe opioid substitution may include prescriber education, implementing and strengthening electronic prescribing systems to include transfer of prescriptions between prescriber and pharmacy, dispensing and monitoring systems, as well as specific procedural and educational interventions for pharmacy staff.

## Declaration of interests

None.

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