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Research Paper

Increasing trend in accidental pharmaceutical opioid overdose deaths and diverging overdose death correlates following the opioid prescription policy liberalization in Norway 2010–2018

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ABSTRACT

Background: During the last decade, opioid prescription policies in Norway have been liberalised and pharmaceutical opioid (PO) dispensing has increased. Against this backdrop, we examined the trends in and the correlates of accidental overdose deaths attributable to PO in the period 2010-2018 in comparison with traditional heroin overdose deaths.

Methods: Accidental overdose deaths attributable to PO or heroin were identified through the Norwegian Cause of Death Registry (n = 1267) and cross-linked with population and patient registries. Overdose death correlates were examined using multivariable logistic regression.

Findings: The trend in accidental overdose deaths attributable to PO increased significantly from 2010 to 2018. Females, people aged 50 years or older, disability pension recipients and/or those with the highest net wealth had a greater risk of a PO vs. heroin overdose death, while those dying in public spaces, living in urban areas, having recent specialized drug treatment encounters, and/or criminal charge(s) had a lower risk. Among those with primary health care encounters, those with back problems and accidents and injuries had a greater risk of a PO vs. heroin overdose death, while those with a substance use disorder had a lower risk.

Conclusion: The increase in accidental overdose deaths attributable to PO coincides with the period of opioid prescription policy liberalization and an increase in PO consumption in Norway. The PO and heroin overdose deaths differed in terms of the associated sociodemographic characteristics, primary and secondary health care encounters, diagnoses, and criminal charges, indicating a need for additional interventions aimed at preventing PO overdose deaths specifically.

Introduction

Overdose deaths are on the rise and are a major public health concern in many western countries. The US, Canada, Australia, England, and Scotland have all experienced an upward trend in overdose deaths over the past decade (Chrzanowska et al., 2021; Hedegaard et al., 2021; National Records of Statistics, 2021; Office for National Statistics, 2021; Statistics Canada, 2021). The increase in these deaths has been associated with an increase in pharmaceutical opioid (PO) prescribing and consumption. In the US, the first wave of the opioid overdose epidemic followed increases in opioid prescriptions and consequently sales during the 1990s (Bohnert et al., 2011; Jenkins, 2021; Paulozzi et al., 2012; Paulozzi et al., 2006). Some parts of Canada have had the same experience as the US with an increase in PO prescribing and consumption, and a subsequent increase in PO overdose deaths (Fischer & Argento, 2012; Fischer, Gooch, Goldman, Kurdyak, & Rehm, 2014; Fischer, Jones, Urbanoski, Skinner, & Rehm, 2014). The increase in overdose deaths in England and Scotland does not appear to be related to opioid prescription practices (Kimber et al., 2019), but Australia experienced an increase in PO overdose deaths concurrently with an increase in PO prescriptions and consumption (Roxburgh et al., 2017). In some countries, but not all, liberal opioid prescription practices appear to contribute to increases in overdose deaths.

During the last decade, the Nordic country Norway, has experienced a liberalisation of its PO prescription scheme. In 2008, PO became reimbursable through the National Insurance Scheme if prescribed for chronic pain by a selection of specialist doctors (Norwegian Medicines Agency, 2020). The National Insurance Scheme is publicly funded and managed by the Norwegian Health Economics Administration (Norwegian Medicines Agency, 2016). In 2016, there was a further

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liberalisation whereby PO prescribed for chronic pain by general practitioners also became reimbursable (Norwegian Medicines Agency, 2020). At the same time, the health requirements for a driving licence were amended (Norwegian Directorate of Health, 2020). Individuals with chronic pain using short-acting opioids such as codeine/paracetamol preparations were prohibited from driving a vehicle for at least eight hours after intake, while those on a maintenance dose of long-acting opioids (max. 300mg OMEQ) such as oxycodone were permitted to drive except in the week following a dose increase. Patients eligible for short-acting opioids prescribed for chronic pain may therefore prefer a maintenance dose of long-acting opioids instead, to be able to drive a vehicle when needed. Concurrently with the implementation of these changes, there was an increase in the number of individuals receiving opioids on reimbursable prescriptions for the treatment of chronic pain (Odsbu et al., 2021). In 2009, there were 5568 users of opioids on reimbursable prescriptions (0.15% of the general population), while this increased to 18 443 users (0.45% of the general population) in 2019 (Odsbu et al., 2021). However, no study has examined the trend in accidental PO overdose deaths in Norway following these changes.

Furthermore, international studies have found a variation in overdose death correlates between different type of opioids (Jalal et al., 2018; Nechuta et al., 2018; Paulozzi et al., 2009; Roxburgh et al., 2017; Visconti et al., 2015). This may indicate that PO overdose death correlates differ from other opioid overdose correlates. These differences might pose a challenge, as many of the most common overdose prevention interventions, such as opioid substitution treatment, take-home naloxone programmes, promotion of safer intake modes, safe injection and user facilities, and interventions following prison release and discharge from drug rehabilitation treatment, are tailored towards people who use illicit opioids such as heroin or who inject opioids. Current interventions may therefore be insufficient for preventing overdose deaths attributable to PO. If this is the case, there is a need for more knowledge to design interventions that also reach those at risk of PO overdose deaths.

The changes in PO prescription policies and the increase in PO consumption in the general population in Norway, provide a unique opportunity to examine the trend in and correlates of overdose deaths attributable to PO over the same period. We examined the trends in and the correlates of accidental overdose deaths attributable to PO in the period 2010-2018 in comparison with accidental overdose deaths attributable to heroin, which has been the predominant attribution for such deaths in Norway (Gjersing et al., 2013).

Method

Setting

Norway is a sparsely populated Nordic country with a population of 5.3 million (Statistics Norway, 2019). The country has an annual average of 271 fatal overdoses (Gjersing, 2021), and the number of people who inject drugs is estimated to be between 7400 and 10 500 (Amundsen, 2018). PO such as morphine, codeine and oxycodone were the most frequent causes of overdose death in 2020, followed by heroin and methadone (Gjersing, 2021). In 2015, there were no fentanyl deaths in the overdose deaths autopsied in Southern Norway, but in 2016, there were 10 such deaths and 12 in 2017 (Edvardsen et al., 2018). Polydrug findings are common in overdose deaths and the median number of drugs (excluding ethanol) per case was four in 2017 (Simonsen et al., 2020).

Design

This was a retrospective registry study including all accidental overdose deaths attributable to heroin or PO between 1.1.2010 and 31.12.2018 in Norway.

Study population

Cases were identified through the Norwegian Cause of Death Registry based upon their primary cause of death. The Norwegian Cause of Death Registry codes deaths according to the 10th revision of the International Classification of Diseases (ICD-10). All those with accidental overdoses attributable to PO or heroin as their primary underlying cause of death and who were 13 years or older at the time of death were included ($n = 1267$). The inclusion criteria were based upon an amended version of the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) definition of drug-induced deaths. The EMCDDA's definition of drug-induced deaths is where the underlying cause of death (the condition that initiated the process that lead to the death) is: (1) mental and behavioural disorders due to psychoactive substance use (harmful use, dependence, and other mental and behavioural disorders (F codes) due to opioids, cannabinoids, cocaine, other stimulants, hallucinogens or multiple drug use, or (2) poisonings (X and Y codes) that are accidental, intentional or of undetermined intent due to substances under the heading of narcotics (T40-0 to T40-9) or psychostimulants (T43.6) (EMCDDA, 2017). This definition only includes the primary underlying cause of death. This means that, although the majority of the included deaths are likely to be due to the intake of multiple substances (Simonsen et al., 2020), these additional substances are not accounted for when using this definition.

However, in the current study we were interested in the trend for 2010–2018 of accidental overdose deaths attributable to PO given the changes in prescription practices in this period. In Norway, overdose deaths have been predominately attributed to heroin (Gjersing et al., 2013), and heroin overdose deaths were therefore used for comparison. Consequently, we included "X42 accidental poisoning" or "X44 accidental poisoning" in combination with "T40.1 Heroin", "T40.2 Other opioids" or "T40.4 Other synthetic opioids". "T40.2 Other opioids" is an ICD-10 code comprising 19 opioids e.g., codeine, morphine, oxycodone, and oxymorphone, while "T40.4 Other synthetic opioids" is a ICD-10 code comprising 29 opioids e.g. alfentanil, buprenorphine, fentanyl, and pethidine. Although methadone tablets are reimbursable if prescribed for chronic pain, methadone is rarely prescribed for this condition in Norway, T40.3 methadone was therefore not included into our study population.

Data sources and variables

Individual-level data linkage between registries was achieved through utilization of Personal Identification Numbers (i.e., Social Security Numbers). These are assigned to all legal residents of Norway. In addition to the personal identification number provided for matching purposes, the Norwegian Cause of Death Registry provided the following variables: date of death, place of death, and primary cause of death (ICD-10 codes). Statistics Norway provided the following information: gender, age on January 1st of year of death, highest completed level of education, area of residency on January 1st of year of death, number of people in the household on January 1st of year of death, employment income in the year prior to year of death, disability pension in the year prior to year of death, social welfare benefits in the year prior to year of death and estimated net wealth in the three years prior to year of death. Additionally, Statistics Norway provided data for criminal charges (dates and underlying criminal offences) for the five years prior to death. The Registry for Control and Payments of Health Claims provided dates for primary health care encounters (general practitioners and emergency rooms) and the corresponding International Classification of Primary Care-2 (ICPC-2) diagnoses. The Norwegian Patient Registry provided dates for inpatient and outpatient secondary health care encounters in the 12 months prior to death. This information was provided separately for specialized drug treatment, specialized psychiatric treatment, and general hospitals.

Estimated net wealth consisted of the estimated (market) value of physical and financial assets on average over the three years prior to death, adjusted for inflation using a consumer price index. We used criminal charges as a proxy for criminal activity. However, not all criminal activity results in a criminal charge. To be able to detect at least some criminal activity, we assumed that we needed a study period longer than 12 months. An arbitrary five-year cut-off for criminal charges was therefore applied, assuming that a history of more than five years would not be as relevant to the youngest cases (11% of the cases were 25 years or younger).

The cause of death variables "T40.2 Other opioids" and "T40.4 Other synthetic opioids" were aggregated into a variable labeled "PO overdose deaths" with the responses: 0 = Heroin overdose death and 1 = PO overdose death. The Cause of Death Registry provided the following categories for the variable "Place of death": 1 = Private home, 2 = Other (public spaces, open air, at sea, during hospital transportation, abroad, prison, military), 3 = Hospital, 4 = Other health institution, and 5 = Unknown. "Age" was aggregated into the three categories: 1 = younger than 30 years, 2 = 30-49 years and 3 = 50 years or older. "Highest level of education" was aggregated into the following categories: 1 = Not completed or completed primary school, 2 = High school, and 3 = University/college. Area of residency was aggregated into the variable "Urban" with the two categories: 0 = living in an area with <50 000 inhabitants and 1 = living in an area with ≥50 000 inhabitants. Number of persons in a household was aggregated into the variable "One-person household" with the responses: 0 = No and 1 = Yes. Employment income was used as a measure for employment, and the variable was aggregated into the variable "Employed" with the responses: 0 = No employment income in the year prior to death and 1 = Employment income of more than zero in the year prior to death. The two variables "Disability pension" and "Social welfare benefits" were aggregated into the responses: 0 = No and 1 = Yes. Net wealth was aggregated into four percentiles based upon the total net wealth in a matched gender and age controlled general population (1 = 25%/2 = 50%/3 = 75%/4 = 100%). The dates from primary and secondary health care encounters were aggregated into the variables "At least one primary health care encounter", "At least one specialized drug treatment encounter", "At least one psychiatric treatment encounter" and "At least one general hospital encounter" with the responses: 0 = No and 1 = Yes. The dates of criminal charges were aggregated into the variable "At least one criminal charge in the past five years" with the responses: 0 = No and 1 = Yes. Among those with a primary health care encounter, we selected the primary diagnoses that have been linked to overdose deaths in previous studies (Khan et al., 2020; Ogle et al., 2012; Roxburgh et al., 2019; Toblin et al., 2010; Turner & Liang, 2015). The included diagnoses were "psychiatric diagnoses", "substance use disorder", "accidents and injuries", "problems in the neck, shoulder, arms and legs", "back problems", "alcohol abuse", "prescription drug abuse" and "general pain and muscular problems".

Statistical analyses

All statistical analyses were conducted in Stata 16.0. We estimated the rates for accidental overdose deaths attributable to PO and heroin per 100 000 population and used univariable linear regression analysis to test the trend in PO and heroin overdose death rates from 2010 to 2018.

Sample characteristics across all individual characteristics detailed in the paragraph above were presented for PO and heroin overdose deaths separately and compared using Chi-square statistics. We then estimated the likelihood of accidental overdose deaths attributable to PO as a function of place of death, sociodemographic characteristics, primary and secondary health care encounters, and criminal charges using multivariable (adjusted) logistic regression analyses. Accidental overdose deaths attributable to heroin were the reference group. The adjusted odds ratios (aOR) and 95% Confidence Intervals (CI) were reported. Among those with a primary health care encounter in the 12 months prior to death, we examined and compared diagnoses from these encounters between heroin and PO overdoses using Chi-square statistics. The likelihood of accidental overdose death attributable to PO was then estimated as a function of the diagnoses from the primary health care encounters, as well as the individual characteristics in the previous multivariable logistic regression model, excluding place of death.

Funding

The Norwegian Directorate of Health and the Institute of Public Health funded this study.

Ethics

The Norwegian Medical Ethics committee approved this study in October 2019 (2019/10154/REK sør-øst-B).

Results

2010-2018 trend

There were 1267 deaths where the primary underlying cause of death was accidental overdose attributable to PO or heroin in Norway between 2010 and 2018: 48.6% attributable to PO and 51.4% to heroin. Fig. 1 shows the proportion of these deaths shifting from heroin overdoses as the most common cause of death to PO overdoses in 2016 and onwards. The rate for accidental overdose deaths attributable to PO increased from 1.0 per 100 000 population in 2010 to 2.0 per 100 000 population in 2018 (Fig. 2). The trend in the PO rates was statistically significant (b = 0.13 95% CI 0.06-0.20), while the trend in heroin rates was not (b = -0.07 95% CI -0.18-0.05).

The Chi-square statistic was used to test for differences in sociodemographic characteristics. There were significant differences in place of death, gender, age, education, living in urban areas, living in a one-person household, recent primary and specialized drug treatment encounters, social welfare benefits, net wealth, and criminal charges (Table 1).

Table 2 shows the criminal offences underlying the criminal charges. A lower proportion among those that had died from a PO overdose had a criminal charge due to a drug offence (49.9% vs. 59.2%), property theft (41.6% vs. 57.6%) and other acquisitive crime (18.0% vs. 25.2%) compared to those that had died from a heroin overdose. There were no statistical differences in the other offences underlying the criminal charges.

PO vs. heroin overdose deaths

We examined PO overdose death correlates using multivariable logistic regression analysis (Table 3). Females, people aged 50 years or older, disability pension recipients and/or those with the highest net wealth were more likely to have died from a PO overdose. On the other hand, those dying in places other than private homes (e.g. public spaces, open air, at sea, during transport to hospital, abroad, prison, military), living in urban areas, having recent specialized drug treatment encounters, and having at least one criminal charge in the past five years prior to death were less likely to have died from a PO overdose.

Primary health care encounters and diagnoses

Primary health care encounters included general practitioner visits and visits to emergency rooms. Using the Chi-square statistic to test for differences in diagnoses from these encounters, we found significant differences in psychiatric diagnosis, substance use disorder, accidents and injuries, neck, shoulder, arm, and legs problems, back problems, and general pain and muscular problems (Table 4).

Table 1
Individual characteristics for those who died from accidental PO or heroin overdoses between 2010 and 2018 in Norway.

	PO overdose death (n = 616)	Heroin overdose death (n = 651)	Chi-square p-value
Place of death			
Private home	56.8% (350)	44.4% (289)	<0.001
Other[a]	17.5% (108)	31.0% (202)	
Hospital	11.4% (70)	5.5% (36)	
Other health facilities	3.1% (19)	2.3% (15)	
Unknown	11.2% (69)	16.7% (109)	
Female	31.7% (195)	16.3% (105)	<0.001
Age			
< 30 years	17.9% (110)	25.0% (163)	<0.001
30-49 years	44.3% (273)	57.6% (375)	
≥50 years	37.8% (233)	17.4% (113)	
Level of education			
Not completed or completed primary school	59.5% (359)	68.3% (431)	0.005
High school	32.2% (194)	24.7% (156)	
University/college	8.3% (50)	7.0% (44)	
Urban area[b,c]	38.7% (237)	55.2% (359)	<0.001
One-person household[b]	57.1% (352)	62.7% (408)	0.045
At least one encounter[d]			
Primary health care[e]	97.4% (600)	94.8% (617)	0.016
General hospitals	75.2% (463)	74.5% (485)	0.790
Specialized drug treatment	35.6% (219)	54.5% (355)	<0.001
Specialized psychiatric treatment	33.8% (208)	37.3% (243)	0.19
Employed[f]	29.0% (178)	28.3% (184)	0.770
Disability pension[f]	46.6% (287)	30.3% (197)	<0.001
Social welfare benefits[f]	39.4% (243)	55.3% (360)	<0.001
Net wealth[f,g]			
25%	60.6% (373)	71.1% (463)	<0.001
50%	13.8% (85)	14.7% (96)	
75%	13.5% (83)	10.1% (66)	
100%	12.2% (75)	4.0% (26)	
Criminal charges[h]	58.6% (361)	79.7% (519)	<0.001

[a] Includes public spaces, open air, at sea, during transport to hospital, abroad, prison, military etc.
[b] On January 1st of year of death.
[c] Municipality with ≥50 000 inhabitants.
[d] In the 12 months prior to death.
[e] General practitioners and emergency departments.
[f] Year before year of death.
[g] Estimated (market) value of physical and financial assets, average value over the three years prior to death adjusted for inflation using a consumer price index. The quartile values were based on a general population of the same age, gender and year of inclusion in the study (year of death for the sample).
[h] In the five years prior to death.Missing variables: 33 Level of education, 4 Urban area, and 4 Employed.

Table 2
Type of criminal offence underlying the criminal charges.

	POoverdose death n = 361	Heroinoverdose death n = 519	p value
Violation of the Medicinal Products Act	46.3% (167)	52.0% (270)	0.093
Drug offences[a]	49.9% (180)	59.2% (307)	0.006
Aggravated drug offences[b]	2.8% (10)	3.3% (17)	0.67
Property theft	41.6% (150)	57.6% (299)	<0.001
Other acquisitive crime	18.0% (65)	25.2% (131)	0.011
Vandalism	11.4% (41)	14.1% (73)	0.24
Substance use offence	57.1% (206)	63.2% (328)	0.067
Violence and abuse	29.4% (106)	33.5% (174)	0.19
Traffic offences	39.3% (142)	36.0% (187)	0.32
Public order and integrity violations	48.8% (176)	54.5% (283)	0.092
Sexual offences	1.4% (5)	1.9% (10)	0.54
Other offences	1.9% (7)	2.3% (12)	0.71

[a] Maximum 2 years incarceration.
[b] Maximum 21 years incarceration.Notes: The table shows being charged for an offence at least once during the past five years. This means that an individual can have several offences.

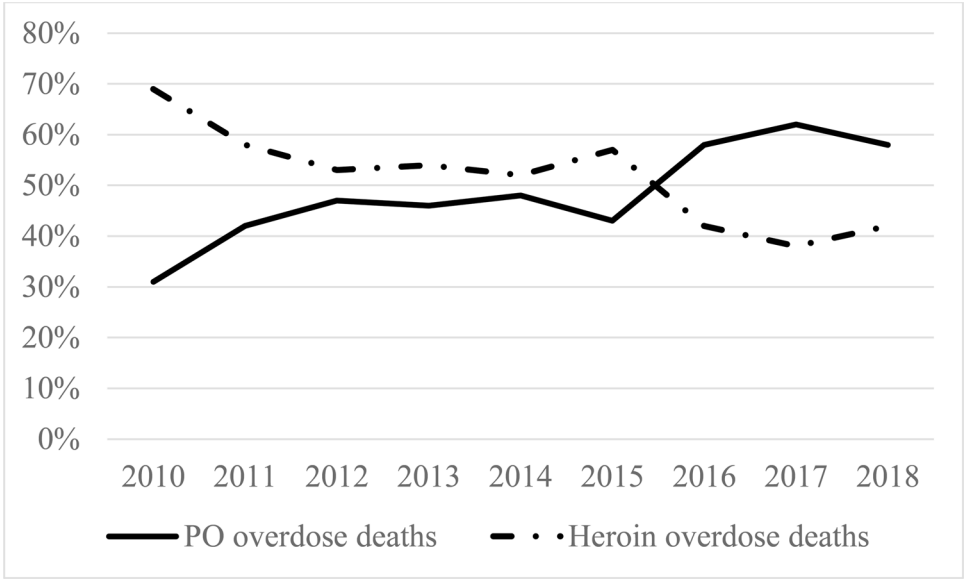

Fig. 1. Proportion of accidental PO (n = 616) and heroin (n = 651) overdose deaths between 2010 and 2018 in Norway.

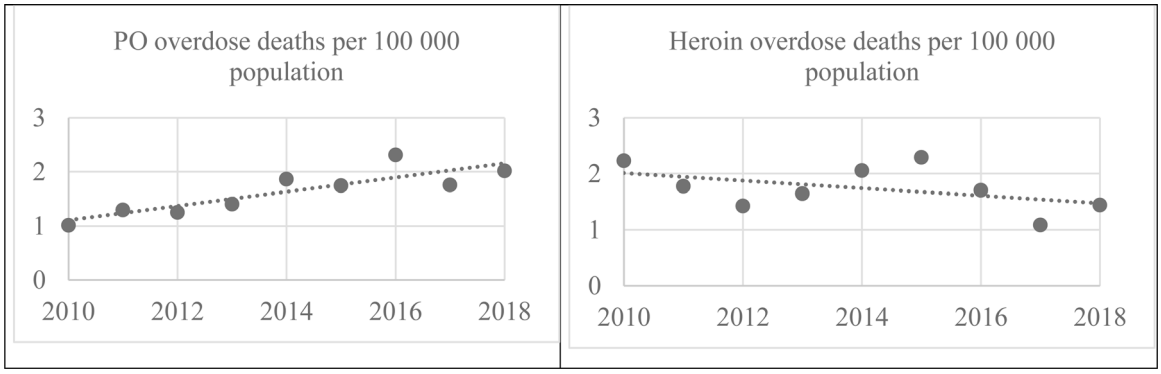

Fig. 2. Accidental PO and heroin overdose death rates. 2010–2018. Per 100 000 population 14 years and over.

Using multivariable logistic regression analysis among those with primary health care encounters, the likelihood of an accidental overdose death attributable to PO increased by 90% for those with back problems and 60% for accidents and injuries, while it was reduced by 40% for those with a substance use disorder (Table 5).

Discussion

There has been an increase in accidental overdose deaths attributable to PO coinciding with the period of opioid prescription policy liberalization (Norwegian Medicines Agency, 2020) and an increase in PO dispensing in Norway (Odsbu et al., 2021). Our findings show that those dying from PO and heroin overdoses differ greatly in sociodemographic characteristics, primary and secondary health care encounters and diagnoses, and criminal charges. This is in line with previous international studies which have found a variation in overdose death correlates between different type of opioids (Roxburgh et al., 2017; Jalal et al., 2018; Nechuta et al., 2018; Paulozzi et al., 2009; Visconti et al., 2015).

Overdose deaths in Norway have predominately been attributed to heroin (Gjersing et al., 2013). However, we found an increase in overdose deaths being attributed to PO over the study period and that there was a shift in 2016 from heroin to PO as the most common primary cause of overdose deaths. As outlined in the Introduction to the paper, two important changes in the opioid prescription scheme for chronic pain occurred in 2016. Firstly, opioids prescribed for chronic pain by general practitioners became reimbursable (Norwegian Medicines Agency, 2020). Secondly, the driving licence's health requirements for those prescribed opioids for chronic pain were amended in a manner that might have encouraged patients prescribed intermittent use of short-acting opioids such as codeine/paracetamol preparations to prefer a maintenance dose of long-acting opioids such as oxycodone instead (Norwegian Directorate of Health, 2017). These changes came in addition to the changes that occurred in 2008 whereby opioids prescribed for chronic pain by a selection of specialist doctors became reimbursable (Norwegian Medicines Agency, 2020). There is no doubt that these changes led to an increase in users of opioids on reimbursable prescriptions (Odsbu et al., 2021). However, we can only speculate whether these changes were also responsible for the increase in overdose deaths attributable to PO as we did not have access to prescription or dispensing data in this study.

On the other hand, the increase in overdose deaths attributable to PO occurring concurrently with the changes in the opioid prescription scheme is in line with international experiences (Bohnert et al., 2011; Imtiaz et al., 2020; Jalal et al., 2018; Jenkins, 2021; Paulozzi et al., 2009; Paulozzi et al., 2012; Roxburgh et al., 2017). It therefore seems unlikely that the increase in overdose deaths attributable to PO in Norway occurred solely by chance. Possibly, the changes in the opioid prescription scheme have led to an increasing number of patients dealing their prescribed PO in the illegal market; meaning that the increase in PO overdose deaths is due to an increase in non-medical PO use. On the other hand, it may also be that the increasing number of patients prescribed PO have led to the increase in PO overdose deaths. If this is the case, details such as diagnoses, dose, use over longer periods of time (persistent use) and concurrent prescribing of psychotropics will give a

Table 3
The likelihood of an accidental PO overdose death as a function of individual characteristics examined using multivariable logistic regression analysis (n = 1234). Accidental heroin overdose death was the reference category.

	PO overdose death aOR (95% CI)
Place of death	
Private home	1.0
Other[a]	0.5 [0.4,0.7]***
Hospital	1.4 [0.9,2.3]
Other health care facilities	1.3 [0.6,2.9]
Unknown	0.5 [0.4,0.8]**
Female	1.9 [1.4,2.6]***
Age	
< 30 years	1.0
30-49 years	0.8 [0.6,1.2]
≥50 years	1.6 [1.0,2.5]*
Level of education	
Not completed or completed primary school	1.0
High school	1.1 [0.8,1.4]
University/college	0.8 [0.5,1.4]
Urban area[b,c]	0.5 [0.4,0.6]***
One-person household[b]	0.8 [0.6,1.1]
At least one encounter[d]	
Primary health care[e]	2.0 [1.0,4.0]
General hospital	1.0 [0.8,1.4]
Specialized drug treatment	0.7 [0.5,0.9]**
Specialized psychiatric treatment	1.0 [0.8,1.3]
Employed[f]	1.3 [1.0,1.8]
Disability pension[f]	1.6 [1.2,2.2]**
Social welfare benefit[f]	0.9 [0.7,1.3]
Net wealth[f,g]	
25%	1.0
50%	0.9 [0.6,1.3]
75%	1.0 [0.6,1.5]
100%	2.3 [1.3,4.0]**
Criminal charge[h]	0.6 [0.4,0.8]**

[a] Includes public spaces, open air, at sea, during transport to hospital, abroad, prison, military etc.
[b] On January 1st of year of death.
[c] Municipality with ≥50 000 inhabitants
[d] In the 12 months prior to death.
[e] General practitioners and emergency departments.
[f] Year before year of death.
[g] Estimated (market) value of physical and financial assets, average value over the three years prior to death adjusted for inflation using a consumer price index. The quartile values were based on a general population of the same age, gender and year of inclusion in the study (year of death for the sample).
[h] In the five years prior to death.Notes: The adjusted model includes all variables in the table.*p<0.05, **p<0.005, ***p<0.001.

better indication of how to address this issue, especially since two studies have found higher dose and persistent and concurrent prescribing of psychotropics to be associated with opioid-related deaths in England (Chen et al., 2021; Chen et al., 2022). It is therefore vital to investigate these issues further before any decision to re-evaluate the current opioid prescription scheme.

In addition to the need for more knowledge regarding the associations between PO prescribing and overdose deaths, and a possible re-evaluation of the opioid prescription scheme, the differences in heroin and PO overdose correlates indicate a need for additional overdose interventions. While the risk of overdose death attributable to heroin is likely best addressed through well-documented overdose interventions such as take-home naloxone programmes and opioid substitution treatment (Mattick et al., 2009; McDonald & Strang, 2016), the risk of overdose deaths attributable to PO may need a different approach. This is because those that died from a PO overdose were less likely to have had a substance use diagnosis, less likely to have been in drug rehabilitation treatment and less likely to have received a criminal charge. Thus, it may be more difficult to identify and reach those at risk of a PO overdose than those at risk of a heroin overdose.

However, attending primary health care for accidents and injuries and back problems were diagnoses associated with overdose deaths attributable to PO relative to those attributable to heroin. This might indicate that at least some of those dying had been prescribed the PO that caused their deaths. In this case, one possible additional intervention to prevent PO overdose deaths would be to prescribe the antidote naloxone nasal spray concurrently with opioids for chronic pain. In addition to having the antidote available in the case of an overdose, this intervention might also raise awareness around the overdose risk from using opioids. Furthermore, this intervention might encourage patients to not use more than the prescribed dose and to refrain from combining their PO use with that of other psychoactive substances such as alcohol.

Unfortunately, we do not know the proportion of those who died from a PO overdose who had combined opioids use with that of other psychoactive substances such as alcohol prior to death. This study included cases based upon primary cause of death and the intake of multiple substances was not accounted for. We know, however, that polydrug findings are common in overdose deaths, and a Norwegian study from 2017 found that the median number of drugs (excluding ethanol) per case was four (Simonsen et al., 2020). It is therefore not unlikely that those dying from overdoses attributable to PO did so due to combined use with other psychoactive substances. Prescription and dispensing data will be able to uncover concurrent prescribing of psychotropics, but there is also a need for more details regarding the toxicology findings. If ethanol is commonly found in these cases, one intervention would be to educate patients in terms of the high overdose risk in combining opioid and alcohol use.

Particular caution following discharge from the secondary to the primary health care is also an intervention that may reduce the risk of an accidental overdose. Attending primary health care for accidents and injuries was one of the diagnoses that increased the odds of an overdose death attributable to PO rather than heroin. A Norwegian qualitative study found that patients received insufficient information regarding post-discharge opioid tapering and individually tailored follow-up plans following discharge from trauma centres with severe orthopaedic injury to primary health care (Finstad et al., 2021). If this finding is accurate, more care following discharge from secondary to primary health care in terms of opioid prescribing may possibly reduce the overdose risk for some individuals.

Even though some of those dying from an overdose attributable to PO were likely to have been prescribed opioids for chronic pain, our findings also suggest that some people who died of a PO overdose had a history of illicit drug use. In this study, 34% of those dying from a PO overdose were diagnosed with a substance use disorder from a primary health care encounter, and 36% had at least one recent specialized drug treatment encounter. Furthermore, as many as 59% of those dying from a PO overdose had at least one criminal charge in the five years prior to death. This was less than those dying from a heroin overdose, but it was still a sizable proportion of the PO overdose group. A lower proportion in this group had been charged with drug offences, property theft and other acquisitive crime compared to the heroin overdose group, but there were no differences for the other offences. This indicates that a sizable proportion of those dying from a PO overdose are PWUD who engage in criminal activity. Given that some of those dying from a PO overdose had similar characteristics to those dying from a heroin overdose, it is likely that they could be reached through traditional overdose interventions such as take-home naloxone programmes and opioid substitution treatment. However, prescription and dispensing data will enable us to examine if this population has also been prescribed the PO which they used and if there is a need to re-evaluate the opioid prescription scheme for PWUD as well.

Table 4
Diagnoses from primary health care encounters in the 12 months prior to death for those who died from accidental PO or heroin overdoses between 2010 and 2018 in Norway.

	PO overdose death (n = 600)	Heroin overdose death (n = 617)	Chi-square p-value
Psychiatric diagnoses	80.8% (485)	86.7% (535)	0.005
Substance use disorder	33.8% (203)	56.4% (348)	<0.001
Accidents and injuries	34.0% (204)	27.2% (168)	0.010
Problems in the neck, shoulders, arms and legs	26.0% (156)	20.7% (128)	0.030
Back problems	19.0% (114)	8.4% (52)	<0.001
Alcohol abuse	11.2% (67)	10.7% (66)	0.79
Prescription drug abuse	13.0% (78)	10.0% (62)	0.11
General pain and muscular problems	13.2% (79)	5.3% (33)	<0.001

Table 5
The likelihood of an accidental PO overdose death as a function of diagnoses from primary health care encounters in the 12 months prior to death examined using multivariable logistic regression analysis (n = 1188). Accidental heroin overdose death was the reference category.

	PO overdose death aOR (95% CI)
Psychiatry	1.0 [0.7,1.5]
Substance use disorder	0.6 [0.5,0.9]*
Accidents and injuries	1.6 [1.2,2.2]*
Problems in the neck, shoulders, arms and legs	0.9 [0.7,1.2]
Back problems	1.9 [1.3,2.9]*
Alcohol abuse	1.2 [0.8,1.9]
Prescription drug abuse	1.0 [0.6,1.4]
General pain and muscular problems	1.4 [0.9,2.3]

Note: The model is adjusted for male, age, education, urban, one-person household, in contact with general hospitals, drug treatment, psychiatric treatment, disability pension, social welfare benefits, net wealth, and criminal charges.
*p<0.005.

Limitations and strengths

This study used mortality data from the Cause of Death Registry and did not have access to autopsy reports. It was therefore not possible to access type of opioids causing the death within the ICD-10 codes "T40.2 Other opioids" and "T40.4 Other synthetic opioids". Using Cause of Death Registry data also meant we only had access to the primary underlying cause of death, while most of the deaths were most likely due to intake of multiple substances (Gjersing et al., 2013; Simonsen et al., 2020). In addition, we did not have access to data from the prescription database and we did therefore not have any information on the cases' prescription history. Such information could have indicated if the opioid listed as the primary underlying cause of death was legally or illegally obtained and also given us an indication of why the opioid was prescribed and from what setting (primary care, post-surgery etc). Furthermore, the diagnoses from the primary health care encounters should be interpreted with caution, given the inherent limitations of registry data including underreporting and misclassifications. This study only included those with a Norwegian personal registration number, which means that only legal residents were included. Also, the number of people in the household and home county must be interpreted with caution as those who were homeless or without stable living conditions might have been misclassified. Furthermore, the two variables "employed" and "disability pension" are only relevant for individuals of employable age. However, we reran the analyses for those aged 20 to 67 years and there were no changes to the main results.

On the other hand, information from the Cause of Death Registry was based upon autopsy reports in 94.3% of the included cases. This reduces the chances for misclassifications of deaths. The study had access to information from a wide range of public registries, and the majority (97-100%) of the information from these registries was complete. This means that this study was able to give a detailed picture of those who died from heroin and PO overdoses between 2010 and 2018.

Conclusion

There has been an increase in the proportion of PO overdose deaths coinciding with the period of opioid prescription policy liberalization and an increase in PO consumption in Norway. Our findings show that those dying from PO and heroin overdoses differ greatly in sociodemographic characteristics, primary and secondary health care encounters, and criminal charges. Because most of the traditional interventions in Norway are tailored towards preventing heroin overdose deaths, the differentiations between PO and heroin overdose deaths may indicate a need for interventions aimed at preventing PO overdose deaths specifically. However, our findings also highlight the need for a more detailed investigation into prescription and dispensing patterns, as well as toxicology findings, before additional interventions are designed and implemented.

Declarations of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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