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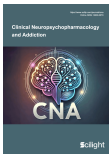

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Deaths Involving Gabapentin and Pregabalin, Scotland, 2000–2024: A Descriptive Account

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Abstract: Gabapentin and pregabalin, while prescribed for conditions like neuropathic pain and epilepsy, have shown increasing misuse, raising concerns about their potential for harm, especially with other central nervous system (CNS) depressants. This study describes the characteristics of deaths associated with gabapentin and/or pregabalin in Scotland from 2000 to 2024, using data provided by the National Records of Scotland. The analysis included socio-demographics, drugs implicated, and cause and manner of death. Out of 3813 deaths where gabapentin or pregabalin was listed in the Poison field, the number of deaths increased from 2008 to 2019, with a slight recovery in 2023 after falls in 2020 and 2021. The majority (65.6%) of deaths involved males, and the mean age at death was 43.0 years. Polypharmacy was common, with 98.9% of cases involving at least one other drug, typically opioids or benzodiazepines. Accidental poisoning was the most common cause of death (90.7%), with 4.7% attributed to suicide. There was no death involving a gabapentinoid on its own. Scottish trends in prescribing and deaths align with concerns about rising gabapentinoid misuse and associated harms across the United Kingdom. The findings underscore the risk of polypharmacy, particularly with CNS depressants, and highlight the need for cautious prescribing and greater awareness of the dangers of co-consumption.

Keywords: gabapentin; pregabalin; deaths; Scotland; characteristics

1. Background

Gabapentin (1(aminomethyl)cyclohexaneacetic acid) and pregabalin ((S)-3(aminomethyl)-5-methylhexanoic acid) are analogues of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), although they do not directly act on GABA receptors. Instead, these molecules possess a unique mode of action via the α2-δ subunit of the N-type calcium channel to modulate neurotransmitter release.

Gabapentin is an anti-convulsant medication. It is principally used to treat partial seizures and neuropathic pain, including pain caused by diabetic neuropathy, postherpetic neuralgia, and central pain. Off-label uses include treatment for anxiety disorders, bipolar disorder and sleep-related issues. Pregabalin is used as an anticonvulsant, analgesic and anxiolytic, treating a range of conditions including: epilepsy, fibromyalgia, generalised anxiety disorder, neuropathic pain, opioid withdrawal, etc.

Effects of gabapentin include calmness, relaxation and euphoria—and if snorted—a high similar to that produced by stimulants, whilst pregabalin can also cause a high or elevated mood [1]. However, the Advisory Council on the Misuse of Drugs (ACMD) also noted that "when used in combination with other depressants, they can cause drowsiness, sedation, respiratory failure and death" [1].

2. General Context on Gabapentinoid-Related Deaths

A scan of the literature relating to gabapentinoid deaths, i.e., fatalities involving these two prescription medications, reveals several dominant themes which are briefly outlined below to provide the broad context of the present study.

European population-based research shows an ever-rising growth in deaths involving gabapentinoids, especially pregabalin, over the past decade or so [2,3]. This general pattern, although varying in gradient and magnitude, parallels sharp increases in treatment demand, intentional drug overdoses, and general growth in harms from other drugs [3,4].

The rising numbers of such fatalities are occurring within an expanding burden of drug-poisoning deaths, though typically as part of polysubstance profiles rather than isolated agents. In turn, these patterns support the view that deaths involving gabapentinoids are best understood within drug ecosystems shaped by opioid availability, benzodiazepine co-use (including 'designer' agents such as etizolam), and local markets [5,6].

Both mechanistic and clinical warning signals emerge from observational studies and regulatory advisories about gabapentinoid co-administration with central nervous system (CNS) depressants, particularly opioids and benzodiazepines. The United States (U.S.) Food and Drug Administration's (FDA) 2019 class-wide label update explicitly warned of serious respiratory depression and fatal outcomes when gabapentinoids are co-used with opioids or other CNS depressants, or in people with underlying respiratory compromise [7]. in January 2025, the agency required new safety label updates for gabapentinoids, adding warnings on withdrawal (including neonatal withdrawal), and reinforcing respiratory depression risks when combined with other sedatives [8].

Clinical data support these concerns. A hospital case control study found that inpatients receiving opioids + gabapentinoids had nearly five-fold higher odds (adjusted OR ≈ 4.91) of opioid-related overdose (measured by naloxone administration) compared with opioids alone [9], again illustrating synergy in clinical practice. International pharmacoepidemiology also notes concerning high dose usage patterns: a French population study in 2025 identified cohorts of escalated pregabalin/gabapentin dosing, underscoring how exposure intensity may intersect with overdose risk, especially in polysubstance contexts [10]. Recently updated narrative and clinical resources describe dose-dependent respiratory interactions in multimodal pain regimens and emphasise structured tapering to mitigate withdrawal-related harms [11,12].

Prescribing trends and availability continue to shape risk, remaining central to understanding deaths. U.S. Medical Expenditure Panel Survey data show adult gabapentinoid use increased from 4.0% (2015) to 4.7% (2021), concentrated among older adults and those using other sedating medicines commonly used for chronic pain and mental health conditions—profiles associated with higher overdose risk in the presence of opioids [13,14]. In the Republic of Ireland, prescription and law-enforcement seizure data demonstrate rising pregabalin availability—both prescribed and illicit—alongside increasing post-mortem detection, especially among subgroups with heroin/methadone exposure and frequent co-detection with benzodiazepines and prescription opioids [4]. Collectively, these findings suggest that expansion of gabapentinoid use—partly as an alternative in the context of opioid-prescribing restrictions—has intersected with polysubstance patterns in ways that elevate population risk.

New evidence also refines understanding of self-harm risk around initiation and discontinuation of gabapentinoids. A large UK self-controlled case series found elevated self-harm incidence in the 90 days before initiation and a marked spike in the two weeks after discontinuation, while risk during treatment approximated baseline [15]. The authors conclude that gabapentinoids are unlikely to be directly causative of self-harm, but they stress proactive monitoring during initiation and especially after stopping therapy. These temporal dynamics align with the FDA's label updates highlighting withdrawal phenomena (including suicidal ideation warnings) and the need for cautious, structured tapering rather than abrupt cessation—particularly in populations with comorbid pain and psychiatric vulnerability [8].

Deaths involving gabapentinoids appear heavily context-dependent, amplified within opioid epidemics and less prominent in regions without widespread opioid misuse; they call for more rigorous, controlled work disentangling co-exposures and dose-response mechanisms of respiratory depression [5]. This perspective does not negate the accumulating signals of harm but frames them as emergent properties of drug ecosystems—where availability, prescribing norms, illicit markets, and comorbidities co-evolve.

In sum, recent evidence on gabapentinoids converges on six interlocking concerns: (1) rising mortality with pregabalin more often implicated; (2) high lethality of co-use with opioids/benzodiazepines; (3) polysubstance toxicology profiles in fatal overdoses; (4) sustained overprescribing/off-label utilisation; (5) self-harm risk concentrated around initiation/cessation windows; and (6) persistent evidence gaps regarding direct causality.

3. United Kingdom Context

In the United Kingdom (UK), gabapentin was first licensed as an anti-convulsant medication in 1993, with pregabalin first licensed in 2004 [16].

Historically, these molecules were regarded as having a low potential for misuse, but concerns about increasing reports of (recreational) misuse in Northern Ireland in 2014—against a background of growing UK prescribing of the drugs—led to the UK's ACMD undertaking a review of the potential harms associated with their misuse.

The ACMD [1] recommended that both drugs be (a) controlled as Class C substances under the Misuse of Drugs Act 1971; and (b) scheduled under the Misuse of Drugs Regulations 2001 (as amended) as Schedule 3 items (thereby avoiding any unintended restrictions and legitimate use on prescription). The Government accepted these recommendations and the changes came into effect on 1 April [17].

These changes appeared to have reduced the online availability with fewer websites offering these drugs for sale to potential UK purchasers, but they remained widely available for purchase via some online pharmacies without a prescription, at least up until June 2019 [18]. There were no material changes in the prescribing of gabapentin and pregabalin by General Practitioners in England in the two-year periods preceding and following the introduction of the above changes in April 2019 [19].

At the time of the ACMD's consideration of the existing evidence, the National Programme on Substance Abuse Deaths (NPSAD; now known as the National Programme on Substance Use Mortality or NPSUM) reported UK figures of 19 deaths where pregabalin had been implicated and 17 involving gabapentin in 2013; the following year (2014), the Office for National Statistics (ONS) registered 38 and 26 deaths, respectively, for England and Wales [1]. By 2023, these numbers had increased to 549 (10% of all drug poisoning deaths) and 137, respectively [20].

Northern Ireland data [21] highlighted pregabalin as the most frequently mentioned drug (n = 67; 40%) in 2023 drug-related deaths registrations (with 8 mentions of pregabalin) situating gabapentinoids within polysubstance fatalities rather than as solitary agents.

In Scotland, a systematic review synthesising 18 studies found gabapentinoid mentions in toxicology rising steeply since 2015 and contributing substantially to the national drug-death burden, including a jump from 2 to 367 gabapentinoid-involved deaths between 2008 and 2018 [6]. In 2023, 38% (n = 450) of all 'Drug Misuse' deaths in Scotland involved gabapentin and/or pregabalin [22].

The 2019 UK reclassification of gabapentinoids did not produce clear, sustained shifts in utilisation or mortality in segmental regression analyses extending through February 2025 in Scotland and Northern Ireland; cross-national differences appeared more sensitive to formulary guidance rather than legal status *per se* [23].

4. Study Rationale

In February 2024, the ACMD informed the then Home Secretary that:

> "*There has been concern around the increased prevalence of misuse of Gabapentinoids, such as Pregabalin. The ACMD is consequently looking to launch an updated harms assessment for Gabapentinoids, to review the position of these drugs under Class C drugs of the Misuse of Drugs Act 1971*" [24].

Providing an update to the new Home Secretary in March 2025 on this self-commissioned task in its current (2025) work programme, the ACMD stated it "aims to confirm if current controls of these medications are sufficient" [25]. It set up a working group with the aim of completing the review by the end of 2025.

The present study has its origins in an undertaking given by the authors, all members of the ACMD's Working Group on Gabapentinoids, to help fulfil this goal by collating and analysing information on UK fatalities related to gabapentinoids. Other members of the group focused on England and Wales, building on the work by Kalk et al. [26].

To complement this work, so that a nation-wide picture could be obtained, the present researchers decided to examine data made available to them by the National Records of Scotland (NRS) as part of the University of Hertfordshire's EU-MADNESS project (https://www.facebook.com/EUmadnessproject (accessed on 23 December 2025)). Furthermore, no previous research of this nature, i.e., an in-depth look at the characteristics of decedents and deaths involving gabapentinoids, has been undertaken relating to Scotland.

5. Aims and Objectives

The primary aim was to describe relevant characteristics of deaths associated with gabapentin and/or pregabalin in Scotland. The objectives were to examine specific aspects, including socio-demographics, drugs implicated, underlying cause and manner of death; and trends over time.

6. Methodology

The approach used here was that of a retrospective population-based observational study using routinely collected administrative mortality data.

The primary sources of information for this study are derived from Medical Certificates of Cause of Death (MCCD) and information from pathologists submitted to the NRS. Anonymised case-level data from NRS was supplied as an Excel dataset on 26 March 2025 to the lead author. The information provided covers all deaths registered from 2000 to 2023, for which gabapentin or pregabalin were reported as being involved. These data were supplemented by information for drug poisoning deaths registered in 2024, received on 3 October 2025. These were identified by a search of the 'Poison field' for 'gabapentin' and/or 'pregabalin'; relevant gabapentinoid cases were then extracted and added to the original NRS dataset.

The variables provided include:

- Flags created by NRS indicating cases where either molecule was included in the Poison field.
- Year and month of death;
- Socio-demographics—age at death (years), gender;
- Cause of death—text field;
- International Classification of Disease codes [27]—underlying cause of death and all codes;
- Poisons implicated as per pathologist;
- Substances also present in PM toxicology.

Pathologists have submitted Form ME4 to NRS in relation to deaths that have been registered since 1 January 2014 which includes, *inter alia*, answers to the following questions: "Based on the available evidence, what were the main drugs or solvents you believe were implicated in, or which potentially contributed to, the cause of death?" and "Please specify any other drug(s)/solvent(s) which were present, but which were not considered to have had any direct contribution to this death."[28] The introduction of this form will have led to a more consistent approach in the attribution of the involvement of substances in the cause of death over the period since the beginning of 2014. This followed a previous revision in 2008. There has also been a reduction in the number of centres undertaking toxicological investigations in Scotland over recent decades, thereby providing an increasingly standardised approach to recording and interpretation of toxicological information; for further details see the lead author's doctoral thesis [29]. Thus testing panels, forensic attention, and reporting norms could have changed over the period considered here. So, part of the rising trend in "mentions" of specific substances could reflect increased detection and recording rather than an actual change in underlying incidence.

Additional variables were created by the lead author to facilitate the analyses conducted. The analyses consist of frequencies, percentages and ratios. Statistical differences were assessed using the ratio of proportions, and the Mann-Whitney U Test for median ages. The results are presented as tables and figures. No attempt has been made here to examine potential causal relationships; these could be examined through record linkage studies (see Discussion).

7. Results

The earliest mention of gabapentin in the Poison field was a death in May 2008, whilst that for pregabalin was in February 2010. The earliest mention of both drugs was in February 2013.

7.1. Number of Gabapentinoid Mentions

The overall number of cases for 2000–2024 registrations fulfilling the above criteria (i.e., either gabapentin and/or pregabalin was listed in the Poison field) was 3813 (Table 1).

Table 1. Mentions of gabapentin and/or pregabalin in Poison field of drug poisoning deaths registered in Scotland, 2000–2024.

Mention of Gabapentin/Pregabalin	Number	Percentage
Gabapentin	1720	45.11
Pregabalin	2407	63.13
Gabapentin & Pregabalin	314	8.23
Gabapentin alone	28	0.73
Pregabalin alone	16	0.42
Only gabapentin & pregabalin	0	0.00
N	3813	100.00

The overall number of deaths involving gabapentin and pregabalin increased year on year from 2008 to 2019, followed by falls in 2021 and 2022 but with a modest recovery in 2023 (see Table 2). Much of this fall appears to be due to reduced numbers of gabapentin mentions, whilst pregabalin showed an increase in 2023.

Table 2. Number of mentions of gabapentin and/or pregabalin in Poison field, Scotland, 2000–2024.

Registration Year	Number of Mentions			
	Gabapentin	Pregabalin	Gabapentin & Pregabalin	Gabapentin and/or Pregabalin
2008	4	0	0	4
2009	2	0	0	2
2010	3	1	0	4
2011	11	1	0	12
2012	23	5	0	28
2013	51	13	1	63
2014	70	29	2	97
2015	104	40	10	134
2016	151	73	13	211
2017	152	131	24	259
2018	201	218	37	382
2019	195	276	31	440
2020	221	346	49	518
2021	156	335	29	462
2022	137	286	45	378
2023	135	352	45	442
2024	104	301	28	377
Total 2013–2024	1721	2407	314	3813

7.2. Age and Gender

The ratio of males to females (1.91:1) is lower than that for all drug poisoning deaths in Scotland during the period 2013–2024 (2.22:1). This is a statistically significant difference: $Z = -5.45$, $p < 0.001$. The ratio for Drug Misuse Deaths in 2024 was 2.20:1 [27].

The mean age of females is slightly higher than that of males (Table 3). A Mann–Whitney U test indicated no significant difference in median ages between males (n = 2502) and females (n = 1311), U = 1,592,406, $p = 0.14$. Similar differences are also true for the mean of all drug poisoning deaths in Scotland during the period 2013–2024 (male 43.70; female 46.31 years. By contrast, the mean age at death for both males and females using the Drug Misuse Definition in 2024 was lower (44.8 and 46.0 years, respectively).

Table 3. Age and gender.

	Number	%	Mean Age (Years)	Range	Standard Deviation
Male	2502	65.62	42.78	14–95	9.75
Female	1311	34.38	43.52	18–89	9.84
All	3813	100.00	43.04	14–95	9.78

7.3. Polydrug Deaths

There is at least one other drug listed in the Poison field (n = 3813; 100.0%). These are typically an opiate/opioid (methadone, heroin/morphine, etc.) or a benzodiazepine, especially ‘designer benzos’ (e.g., etizolam, bromazolam) or standard prescribed ones (e.g., diazepam), and to a lesser extent stimulants (e.g., cocaine, amphetamine). Antidepressants and antipsychotics are mentioned at much lower levels (Table 4).

Polydrug pharmacy is the underlying feature of gabapentinoid-related deaths; the mean number of number of drugs listed was 4.29 (range 1–11) see Table 5.

7.4. Cause and Manner (Intention) of Death

The most common underlying cause of death attributed to the gabapentinoid-related deaths registered during the period 2000–2024 was accidental poisoning, accounting for about 90.7% of cases (Table 6). About 4.6% were deemed to be suicide, with a further 3.2% regarded as of undetermined intent. A further 1% was attributed to “Mental and behavioural disorders due to psychoactive substance use”.

Table 4. Most common drugs listed with gabapentin and/or pregabalin in Poison field.

Drug Name	Number	Percentage
Heroin/morphine	1561	40.93
Methadone	2296	60.22
Buprenorphine	278	7.29
Oxycodone	101	2.65
Tramadol	268	7.03
Dihydrocodeine	546	14.32
Any opiate/opioid	3557	93.29
Etizolam	1632	42.80
Bromazolam	361	9.47
Flubromazolam	59	1.55
Diazepam	979	25.68
Alprazolam	264	6.92
Flualprazolam	45	1.18
Phenazepam	75	1.97
Any benzodiazepine	2816	73.85
Cocaine	1093	28.67
MDMA/Ecstasy	38	1.00
Amphetamine	124	3.25
Any stimulant	1163	30.50
Antidepressant	592	15.53
Antipsychotic	118	3.09
N	3813	100.00

Table 5. Number of drugs listed in Poison field where Gabapentin or Pregabalin was also listed in combination.

Number of Drugs	Number of Deaths	Percentage
1	44	1.15
2	343	9.00
3	893	23.42
4	1045	27.41
5	721	18.91
6	427	11.20
7	211	5.53
8	79	2.07
9	27	0.71
10	14	0.37
11	9	0.24
N	3813	100.00
Mean	4.29	

Table 6. Selected underlying causes of death.

ICD-10 Code	Description	Number	Percentage
	Mental and behavioural disorders due to psychoactive substance use		
F13.2	Sedatives/Hypnotics; dependence syndrome	1	0.03
F14.2	Cocaine; dependence syndrome	1	0.03
F19.1	Multiple drug use and use of other psychoactive substances; harmful use	1	0.03
F19.2	Multiple drug use and use of other psychoactive substances; dependence syndrome	34	0.89
Sub-total for ‘F’ codes		37	0.97
	External cause—Accidental poisoning by and exposure to noxious substances		
X40	Nonopioid analgesics, antipyretics and antirheumatics	3	0.08
X41	Antiepileptic, sedative-hypnotic, antiparkinsonism and psychotropic drugs, not elsewhere classified	628	16.47
X42	Narcotics and psychodysleptics [hallucinogens], not elsewhere classified	2815	73.83
X43	Other drugs acting on the autonomic nervous system	2	0.05
X44	Unspecified drugs, medicaments and biological substances	10	0.26
Sub-total for X40–X44		3458	90.69
	External cause—Intentional self-poisoning		
X60	Nonopioid analgesics, antipyretics and antirheumatics	5	0.13
X61	Antiepileptic, sedative-hypnotic, antiparkinsonism and psychotropic drugs, not elsewhere classified	52	1.36
X62	Narcotics and psychodysleptics [hallucinogens], not elsewhere classified	113	2.96
X63	Other drugs acting on the autonomic nervous system	4	0.10
X64	Other and unspecified drugs, medicaments and biological substances	1	0.03
Sub-total for X60–X64		175	4.59
	External cause—Event of undetermined intent		
Y10	Nonopioid analgesics, antipyretics and antirheumatics	1	0.03
Y11	Antiepileptic, sedative-hypnotic, antiparkinsonism and psychotropic drugs, not elsewhere classified	34	0.89
Y12	Narcotics and psychodysleptics [hallucinogens], not elsewhere classified	86	2.26
Sub-total for Y10–Y14		121	3.17
All underlying causes		3813	100.00

Note: Gabapentinoids are classed as “antiepileptics”.

The overwhelming majority (92.1%) of the deaths examined here were ascribed ICD-10 codes [30] that are usually deemed to capture accidental cases (Table 7). About 4.7% of cases were intentional (i.e., suicide) with the intention of the remainder (3.2%) being treated as undetermined. However, there is a difference in proportions between the two drugs. Deaths involving pregabalin are more likely to regarded as accidental and less likely to be deemed suicide or of undetermined intent. This difference is statistically significant: $p < 0.0001$ (95% CI: 3.9012% to 7.3536%).

Table 7. Selected manner (intentionality) of death.

Intention	ICD-10 Codes	Gabapentin		Pregabalin		Gabapentin/Pregabalin	
		Number	Percentage	Number	Percentage	Number	Percentage
Accidental	F11–F19; X40–X44	1533	89.13	2280	94.72	3511	92.08
Suicide	X60–X64	93	5.41	89	3.70	179	4.69
Undetermined	Y10–Y14	94	5.47	38	1.58	123	3.23
Total		1720	100.00	2407	100.00	3813	100.00

Note: The sum of the columns for the individual gabapentinoids will exceed that for the overall number of cases as some cases have both gabapentin and pregabalin implicated in them.

8. Discussion

The Medicines and Healthcare products Regulatory Agency (MHRA) Yellow Card Scheme [31] reports 116 fatal outcomes due to gabapentin in the period up to 18 October 2025, across the UK, the majority being male, or aged 30–59 years and resulting from Injury and poisoning. The corresponding characteristics for pregabalin are: total of 485, mostly male, or aged 20–59, resulting from injury and poisoning. These profiles tally with the results from the NRS data.

Unfortunately, comparisons with published statistics from the other UK sources on drug-related deaths—ONS and NISRA—are essentially limited to numbers of deaths registered.

8.1. Numbers of Deaths

The proportions of cases involving gabapentin and pregabalin were different between Scotland and England: gabapentin 47% vs. 30%, and pregabalin 61% vs. 76%, respectively. Both drugs were implicated in 8.3% of cases in Scotland, compared to 6.0% in England [26].

Whilst the first death involving gabapentin in Scotland was in May 2008, the NPSAD recorded a death in 2004 In England; similarly, the first pregabalin death in Scotland was in 2010; NPSAD report one case in 2006 [26].

In 2023, the number of deaths involving gabapentin (N = 136) and pregabalin (N = 359) accounted for 10.2% and 27.0%, respectively, of all drug poisoning deaths in (N = 1330) registered in Scotland [22]. For the period 2000–2023, the respective proportions were 7.9% (1606/20,396) and 10.3% (2092/20,396).

The drop in deaths involving gabapentinoids registered in 2020–2021, following a long period of increase, could be partially explained by the imposition of 'lock-down' during the COVID-19 pandemic with consequent delays in death registrations and investigations [28]. However, the pandemic does not appear to have affected the prescribing of gabapentinoids, access to them or related fatalities in Scotland [23]. As we have argued elsewhere, [32] 'lock-down' could have also limited access to illicit supplies.

ONS [20] first reported gabapentin involvement in a death registered in 1999. Registrations of such deaths were sporadic until 2010 when 4 were noted, they steadily rose to 133 in 2021, levelling off to 137 in 2023; a total of 931 have been registered to date. The first deaths involving pregabalin were registered in 2004, but the sharp rise in their numbers started in 2013 and peaking at 549 in 2023; a total of 2595 have been registered to date. Gabapentin and pregabalin have been implicated in 2.5% and 10.1%, respectively, of all drug-related deaths (N = 5448) registered in England and Wales in 2023.

The Northern Ireland Statistics & Research Agency (NISRA) first registered deaths involving gabapentin and/or pregabalin in 2013 [21]. Those for gabapentin peaked at 15 in 2019 and numbered 8 in 2023; a total of 62 deaths involving this drug have been reported. A similar pattern is observed for pregabalin, but at a greatly elevated level; a peak of 77 deaths registered in 2019, standing at 67 in 2023, with an overall total of 455 cases. Gabapentin and pregabalin have been implicated in 3.5% and 25.7%, respectively, of all drug-related deaths (N = 1771) registered in Northern Ireland in the period 2013–2023. The respective proportions for 2023 registrations were 4.7% (8/169) and 39.6% (67/169). In 2023, compared to the rest of the UK, Scotland had the highest proportion of deaths involving gabapentin and the second-highest proportion for pregabalin (after Northern Ireland).

The latest figures from the Republic of Ireland indicate that pregabalin was implicated in 18.4% (63/343) of deaths occurring in 2022 [33]. There was a 350.0% increase in the number of deaths involving pregabalin between 2013 and 2022, although the number peaked at 95 in 2020 [33].

At a slightly wider European level, the European Union Drugs Agency (EUDA) note that few countries submit data on drug-induced deaths involving gabapentinoids. The Agency reports that Finland reported 87 deaths in both 2022 and 2023, whilst increases across the same period were reported by Denmark (from 58 to 60 deaths) and Austria (from 54 to 71 deaths) [3].

Although there are reports of increased numbers of deaths where gabapentinoids were involved during the previous decade in the U.S., especially in relation to opioids [34,35], there are no published papers covering recent years. There is a dearth of up-to-date information on patterns in deaths involving gabapentinoids.

8.2. Socio-Demographics

The key NRS results here were that 65.4% of deaths involved males and that the mean age at death was 42.8 years.

Information from the most recent analyses of the Scottish National Drug-Related Deaths Database registrations provides some limited information on gender breakdowns, and information on individuals aged under 25 years for each index drug over the period 2009–2020 [36]. Secondary analysis of these data indicates that overall, males accounted for 61.2% of deaths where gabapentin was involved but 70.0% of deaths involving pregabalin; this finding is in line with NRS dataset results. Under 25 years accounted for 3.3% of deaths involving gabapentin, and 2.8% of deaths involving pregabalin. These low percentages are in line with the overall mean age of the NRS dataset being about 43 years.

Females outnumbered males in terms of the percentage of 2022 deaths involving pregabalin in the Republic of Ireland: 25.2% vs. 15.1% (n = 28 and 35, respectively) [33]. In the period 2000–2020, males accounted for 55.2% of the 887 deaths involving gabapentinoids in Australia, and the overall mean age at death was 45.7 years [37]; both these findings are in line with the findings for Scotland.

There are no contemporary breakdowns by age or gender for any other country that solely look at gabapentinoids. However, data for the U.S. suggests that mortality rates for gabapentinoids combined with opioids were higher for females up until 1999 [35].

8.3. Polydrug Deaths

The underlying feature of deaths involving gabapentinoids is polypharmacy, as is the case more generally with both drug poisoning and ‘Drug Misuse’ deaths in Scotland [22].

There were no instances in the NRS data of a gabapentinoid alone being implicated in death; in only two out of 3051 NPSAD/NPSUM cases was this the situation [26]. These findings are in line with findings reported from an examination of the European Medicines Agency’s ‘Suspected Adverse Drug Reactions’ Database [38]. Gabapentinoids taken on their own are relatively safe, although, very rarely, gabapentin on its own can cause severe respiratory depression [39].

Opiates/opioids were the most common class of other drug implicated in deaths involving gabapentinoids in both the NRS (93.7%) and NPSAD/NPSUM (92%) cases [26], in line with those reported for previous periods in Scotland (see above). Ciesluk et al. [6] noted that gabapentinoid use alongside other substances is evident from observational studies such the authors’ previous study on alprazolam-related deaths; pregabalin was found in 29.51% and gabapentin found in 18.3% of these cases [32]. A Scottish study found an elevated risk of drug-related deaths in those co-prescribed gabapentinoids and ‘Z-drugs’ [40]. Kalk et al. [26] found that 25.3% of deaths involving gabapentinoids reported voluntarily in England had been prescribed these drugs.

There is an emerging understanding of motivations for use of gabapentinoids with other substances. These reasons encompass a range of desired effects. Desired effects such as euphoria, muscle relaxation, pain reduction, sleep, and sensation of drunkenness have been obtained by using gabapentin with buprenorphine and other opioids, cocaine, and caffeine [41].

Co-used with opioids, gabapentinoids may enhance and/or lengthen the former’s effects, or even reduce the amount of them used to achieve the desired effects [42–48]. Enhancing the psychotropic effects of other substances has also been cited as a reason for pregabalin use [49]. The potentiation of methadone-derived euphoria has been mentioned as a motive for using gabapentinoids in Scotland [50]. Dealing with opioid withdrawal symptoms has also been a reason for co-using gabapentinoids [49].

However, most of the research published does not specify what motivations users of gabapentinoids, gabapentin and pregabalin have for co-use of particular classes of drugs (e.g., benzodiazepines, ‘Z’ drugs, etc.) or specific index drugs. Some of these studies are several years old and need replicating in the light of the changing world of synthetic opioids and designer benzodiazepines.

All deaths involving pregabalin (n = 63) in the Republic of Ireland in 2022 were polysubstance fatalities; the most common additional drugs implicated were diazepam (43), methadone (38), alprazolam (33), cocaine (22),

and heroin (20) [33]. The involvement of opioids, benzodiazepines and cocaine in deaths involving pregabalin mirrors the situation in Scotland and internationally.

The involvement of these drug classes in deaths is echoed in the U.S. [34,35] and Australia [37]; 99.8% of the Australian cases between 2000 and 2020 had other drugs present [37].

8.4. Underlying Cause and Manner of Death

Accidental poisoning accounted for about 91% of NRS deaths in terms of underlying cause of death compared to acute drug toxicity accounting for 93% and 95% respectively for NPSAD/NPSUM gabapentin and pregabalin cases [26].

In both Scotland and England, the overwhelming majority of deaths were deemed accidental or unintentional, respectively, there were some differences when broken down by drug. In both countries there was a higher proportion of pregabalin cases regarded as accidental/unintentional than for gabapentin: Scotland 94.6% vs. 89.3%, and England 91.3% vs. 85.4%, respectively. By contrast the proportions deemed suicide were higher for gabapentin than for pregabalin: Scotland 5.0% vs. 3.6%, England 9.7% vs. 5.3%, respectively.

There are no other recent studies that bear on intentionality. It should be borne in mind that ICD-10 categories and medico-legal determinations do not provide a direct insight into psychological intent and can vary by practice and circumstance. Such insights can really only be obtained through in-depth analysis of each case, using a technique such as a psychological autopsy. Readers should not infer that there are necessarily behavioural differences between gabapentin- vs pregabalin-involved deaths. Such differences may simply reflect classification practices, availability of information, case composition, etc. These aspects merit further investigation.

8.5. Relationship to Prescribing/Prescriptions Patterns

Although the NRS data do not capture information on the source(s) of drugs, including whether not they were prescribed to decedents, the latest report from the National Drug-Related Deaths Database provides some limited information on this aspect for 2019–2020 [36]. Prescribing of gabapentin or pregabalin within 90 days of death increased over time from 13% in 2012 to 25% in 2020. Over the same period, among people recently prescribed these drugs, the proportion of all drug-related deaths in which gabapentin and/or pregabalin was involved rose from 22% to 60%. In 2020, the proportion of cases where gabapentinoids had recently been prescribed and their presence at post-mortem was 80% compared to 36% where not prescribed. Over the time series combined, gabapentin or pregabalin prescriptions were more common among those prescribed Opioid Substitution Therapy (32%) than those not so prescribed (21%).

Ashworth et al. [51] reported that, at the UK level, “Gabapentinoids were commonly co-prescribed with opioids (60%), antidepressants (52%), benzodiazepines (19%), and Z-drugs (10%)”. Similar prescribing patterns have also been described in relation to opioids and benzodiazepines in Scotland during the same period [52]. Growing concern about the co-prescribing of gabapentinoids with other CNS depressants, especially opioids and benzodiazepines, led to research looking at the relationship between such prescribing and related mortality [52].

At a UK-level, *de novo* (or incident) prescribing of gabapentin peaked in 2016-17 before falling whereas incident prescribing of pregabalin peaked a year later (2017–2018). There was a similar upward trend in prevalent (or pre-existing) prescribing for these two drugs; gabapentin peaking in 2017–2018 and pregabalin in 2018–2019 [49]. Prescribing of both gabapentin and pregabalin was on an upward trajectory in both Scotland [52] and England [53]. This was also true for Wales, but even more so for Northern Ireland [54].

Despite the UK legislative changes which came into effect in April 2019, pregabalin and gabapentin prescribing and fatalities associated with their use continue to be at elevated levels in Scotland, as well as the rest of the UK.

The Republic of Ireland has also seen an increase in prescribing rates, especially for pregabalin, along with increased seizures of pregabalin by law enforcement agencies, with a commensurate increase in toxicology detections for both gabapentin and pregabalin [4]. An earlier Irish study found that being in receipt of treatment for problem drug use was associated with an increased odds of pregabalin-positive poisoning deaths for both males and females [55].

There are no other recent studies that examine these relationships; these merit further investigation.

8.6. Study Strengths and Limitations

While deaths involving gabapentinoids have been described in various literature, there is currently no published analysis focused on Scotland. This article provides the first detailed exploration of data on deaths

involving gabapentinoids in Scotland. This study provides a descriptive overview of such deaths in Scotland, informing research into prevention strategies.

There are two further strengths of this study: (a) coverage of all deaths registered in Scotland, whereas the NPSAD/NPSUM cases for England were submitted on a voluntary basis; and (b) NRS does receive some information on PM toxicology unlike its official counterparts in the rest of the UK, i.e., ONS and NISRA.

The study has limitations due to the nature of the information supplied via MCCDs or Form ME4. Unlike NPSUM, NRS do not receive information on: sources of the drugs, i.e., whether or not gabapentinoids were prescribed to decedents prior to death; whether acquired illegally; whether taken as directed or used non-medically; PM toxicology levels; past drug use, medical and psychiatric history; etc. It is impossible to know from MCCDs whether the accidental poisoning is from unintentional therapeutic errors/adverse drug reactions, or intentional misuse/abuse. The findings presented here should not be interpreted as an argument against appropriate gabapentinoid prescribing *per se*—indeed quite the reverse. One of the principal findings is that risk of death is focused in high-risk contexts/situations—such as co-use with other CNS depressants, especially opiates/opioids and benzodiazepines.

Not all deaths may be captured if gabapentinoids were not specifically tested for or mentioned. The data are also limited to deaths that reached the Procurator Fiscal and do not include non-fatal overdoses or misuse. These factors may underestimate the true burden of gabapentinoid-related harms, and prevents establishing clear correlations and patterns.

Finally, there may be further deaths that occurred in 2024 whose registration may not have yet been completed because of ongoing medico-legal investigations, such as Fatal Accident Inquiries, or the completion of toxicological analyses. Information from NRS indicates that a further 21 deaths that occurred in 2024 deaths had been reported by 30 June 2025 (personal communication to lead author, 3 October 2025).

8.7. Recommendations

Polypharmacy plays a key role in deaths involving gabapentin and pregabalin. With prescribing of gabapentinoids still at elevated levels across the UK, and many patients being co-prescribed opioids for pain relief, as part of an opioid maintenance programme or in OST, prescribers should be urged to act with caution in their prescribing habits. Furthermore, patients prescribed such drug combinations must be made more aware of the dangers of co-consumption; simply reading the patient information leaflet—if that even happens—is insufficient. Those taking gabapentinoids who have not been prescribed them also need to be informed/educated about the risks of polypharmacy—especially opioids and benzodiazepines—whether legal or illegal in origin.

Future studies should distinguish between prescribed and non-prescribed (diverted or non-medical) gabapentinoid use, as existing evidence suggests that risks are strongly shaped by the context of use [26,56,57]. While most patients prescribed gabapentinoids use them as directed [58], overdose risk is disproportionately observed in settings of non-medical or chaotic use, particularly in combination with opioids or other central nervous system depressants [7,48,59].

Further research is merited on understanding why particular combinations of gabapentinoids with other classes and specific drugs appeal to certain populations. The underlying cause of death and intentionality are also under-researched. The relationship between gabapentinoid prescribing patterns and deaths involving this class of drug warrant more examination.

In the Scottish context, more research should be undertaken, perhaps using the national drug-related deaths database [36] to examine some of the issues briefly outlined above; perhaps following the model followed by Kalk et al. [26].

9. Conclusions

This study presents some key analyses that can help inform the ACMD's review of its guidance on gabapentinoid harms.

Deaths involving the use of both gabapentin, but more especially pregabalin, are continuing to increase in number across the UK. The overwhelming majority of these involve other drugs, especially opiates/opioids and benzodiazepines. Both prescribers and consumers of gabapentinoids need to be more aware of the dangers of polypharmacy.

Further research in Scotland should consider a wider range of factors that may influence such fatalities, and attempt to undertake risk profiling looking at age, gender and other socio-demographics.

Author Contributions

J.M.C.: conceptualization, methodology, data curation, writing—original draft preparation, reviewing and editing; A.G. and F.S.: clinical assessment, writing—reviewing and editing. All authors have read and agreed to the publishing of the manuscript.

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Data Availability Statement

Under the EU-MADNESS agreement between the National Records of Scotland and the lead author, no data can be shared with third parties.

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Conflicts of Interest

The authors declare no conflict of interest. However, all three authors are members of the Gabapentinoids Working Group of the UK Advisory Council on the Misuse of Drugs (ACMD). J.M.C. was a member of the ACMD's Working Groups on Drug-related deaths (1999–2000 and 2016-7) and is currently a co-opted member of the Technical Committee (2016 to date) and NPS Committee (2009 to date). F.S. was a full member of the ACMD and its NPS Committee (2013-9); and is currently a member of the European Drug Agency NPS Advisory Group. A.G. became a full member of the ACMD in January 2025. The views expressed here reflect only the authors' views and not necessarily those of the ACMD or the authors' respective institutions.

Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

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