**REVIEW ARTICLE/BRIEF REVIEW** 



# Propofol misuse in medical professions: a scoping review Utilisation abusive du propofol dans les professions médicales : une étude de portée

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## Abstract

**Purpose** We aimed to describe the current literature concerning propofol misuse in medical professionals, specifically relating to the individual demographics of those misusing propofol and the outcomes of propofol misuse.

**Methods** We conducted a retrospective scoping review of the literature using a modified PRISMA approach. We used MEDLINE, EMBASE, and PsycINFO databases to identify relevant studies based on search terms. Studies describing individual medical professionals misusing propofol were included.

**Results** *Twenty-four articles describing 88 individual cases of propofol misuse were included for data charting and analysis. Anesthesiologists and certified registered nurse anesthetists were most commonly identified. Death was a common method of identification of misuse, while rehabilitation and death were common final outcomes associated with propofol misuse.* 

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Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, NY, USA **Conclusions** Despite knowledge of the pharmacokinetic and pharmacodynamic properties of propofol by those misusing this medication, death was a common outcome reported in the literature. Data related to long-term outcomes including re-entry to clinical practice or success of rehabilitation were limited.

## Résumé

**Objectif** Nous avons cherché à décrire la littérature actuelle concernant l'abus de propofol chez les professionnels de la santé, en particulier en ce qui concerne les données démographiques individuelles de ceux qui abusent du propofol et les issues d'un tel abus.

**Méthode** Nous avons réalisé une étude de portée rétrospective de la littérature à l'aide d'une approche PRISMA modifiée. Nous avons utilisé les bases de données MEDLINE, EMBASE et PsycINFO pour identifier les études pertinentes en fonction des termes de recherche. Les études décrivant des professionnels de la santé abusant du propofol ont été incluses.

**Résultats** *Vingt-quatre* articles décrivant 88 cas individuels d'abus de propofol ont été inclus pour la cartographie et l'analyse des données. Les anesthésiologistes et les infirmières anesthésistes autorisées certifiées ont été le plus souvent identifiés. La mort était une méthode courante d'identification de l'abus, tandis que la réhabilitation et la mort étaient des issues finales fréquemment associées à l'abus de propofol.

**Conclusion** Malgré la connaissance des propriétés pharmacocinétiques et pharmacodynamiques du propofol par ceux qui abusent de ce médicament, le décès était une issue fréquente rapportée dans la littérature. Les données relatives aux issues à long terme, y compris le retour à la pratique clinique ou le succès de la réhabilitation, étaient limitées. **Keywords** medical professionals · propofol · substance diversion · substance misuse

Diversion and misuse of a variety of anesthetic medications have been reported in medical professionals.<sup>1, 2</sup> Diversion can be defined as the channeling of a prescription drug to an unlawful channel of distribution or use,<sup>3</sup> and misuse can be defined as any medication use without a prescription or in ways not intended by the prescriber.<sup>4</sup> While many misused anesthetic medications are classified as controlled substances, the commonly used intravenous anesthetic agent propofol is not currently defined as a controlled substance by the United States Drug Enforcement Administration (DEA)<sup>5</sup> or the Canadian Controlled Drugs and Substances Act.<sup>6</sup> Propofol is, however, classified as a controlled substance in South Korea<sup>7</sup> and, in the USA, in Alabama, Georgia, and North Dakota.<sup>8</sup>

While opioids often receive the most attention regarding substance misuse by medical professionals, misuse of nonopioid medications including propofol, ketamine, and inhalational anesthetics has been described.<sup>9</sup> Increasingly, reports of propofol misuse are becoming more prevalent and should be given more attention.<sup>10, 11</sup> This is particularly true in cases of misuse by medical professionals with easy access to propofol. Due to the lack of accountability and oversight of propofol, diversion for misuse may be easier for medical professionals to obtain than for other commonly misused controlled substances such as opioids or benzodiazepines.<sup>12</sup> Additionally, the mortality rate associated with propofol misuse may be as high as 33%, even in persons with knowledge of the pharmacokinetics and pharmacodynamics of the medication.<sup>13</sup>

The reported rate of substance use disorder in medical professionals is 5.7%,<sup>14</sup> with some reporting that 10–15% of all medical professionals will misuse drugs or alcohol during their career.<sup>15</sup> As more emphasis is placed on wellness of medical professionals, consideration needs to be given to propofol misuse, particularly given its potentially fatal consequences. Identifying common themes in those misusing propofol, including baseline characteristics and outcomes, is vital in improving medical professional wellbeing.

In this scoping review, our aim was to describe the current literature regarding propofol misuse in medical professionals, specifically the individual demographics of the medical professionals identified as being involved with propofol misuse and the outcomes of those misusing propofol to identify gaps in knowledge and future areas for research.

# Methods

The methodology for this scoping review was developed using previously published guidelines by Arksey and O'Malley<sup>16</sup> based on a modified Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) approach for scoping reviews (PRISMA-ScR).<sup>17</sup> This process involves five stages for conducting a scoping review, which are described below. The PRISMA-ScR checklist can be found in the Electronic Supplementary Material eAppendix 1.

Stage 1: Identify the research question

To better evaluate propofol misuse by medical professionals, the research team developed the following research question: What individual characteristics of medical professionals misusing propofol are commonly reported in the literature and what are the reported consequences of propofol misuse?

# Stage 2: Identify relevant studies

A comprehensive search strategy was used with search terms including propofol, medication misuse, medical professionals, and addiction. A full list of search terms is available in ESM eAppendix 2. Searches were conducted on 29 November 2021 within the following databases: Ovid MEDLINE (1986 to November 2021), Ovid EMBASE (1986 to November 2021), and Ovid PsycINFO (1986 to November 2021). No article type restrictions were included to obtain broad search results from a wide variety of sources. Date restrictions from 1986 to present were used to reflect the period of clinical use of propofol. Because of limitations in translation services, the search was limited to articles written in English. Reference lists of the identified sources were reviewed to identify applicable sources not found in the initial search.

Inclusion criteria for the scoping review included reports on medical professionals misusing propofol. Exclusion criteria included discussions of laypersons misusing propofol, medical professionals misusing substances other than propofol, no full-text availability, and non-English language sources.

## Stage 3: Study selection

Two members of the research team independently screened publications for inclusion based on title and abstract review using a systematic review software (Covidence, Veritas Health Innovation; Melbourne, VIC, Australia). Sources deemed to be relevant by title and abstract review were screened for inclusion using a full-text review. Any disagreements were discussed until a consensus could be reached. A third reviewer was available to discuss disagreements that could not be resolved by the initial reviewers.

# Stage 4: Charting the data

After the full-text review, data were extracted from relevant sources. Extracted data included the article type, country of origin, year of report, profession, trainee status, sex, age, pre-existing psychiatric disorders, polysubstance use (use of propofol in addition to other substances), method of discovery, outcome, and if the misuse was associated with suicide.

### Stage 5: Synthesis of results

Analysis of identified articles including individual characteristics of medical professionals was conducted based on the previously listed data points to identify relevant themes.

## Results

Details of source selection are available in Fig. 1. Twentyone articles identified through database searches were deemed relevant to our research question, while three additional articles were identified through reference list review. Twenty-four articles were included for data charting and synthesis.<sup>10, 18–40</sup>

Data charting of the final 24 articles is available in the Table. Included articles were published between 1992 and 2021, with half of the included articles being published between 2007 and 2013 (n = 12). The most common article type was case reports (n = 17) focusing on single cases, but six included articles were case series reporting 2–25 cases of propofol misuse. One additional article meeting inclusion criteria was a survey study. Most included articles originated from Europe (n = 15), but most of the identified cases were from North America in two larger case series.

# Demographics

Of the identified articles reporting age of medical professionals misusing propofol, the median [interquartile range] age was 35 [29–43] yr, though discrete age data were only available for approximately half of the cases. The medical professionals' sex was approximately even when indicated (male, n = 33; female, n = 30), but was unknown in nearly one third of cases (unknown, n = 25).

No articles provided information on race or ethnicity of medical professionals misusing propofol.

#### Medical professional occupation

Twenty-two articles provided the medical professional occupation of 85 individuals. Medical professionals identified as misusing propofol most commonly worked within the field of anesthesiology as anesthesiologists (n = 42) or as certified registered nurse anesthetists (CRNAs; n = 16). Additionally, registered nurses (n = 12) and nonanesthesiologist physicians (n = 12) were also identified as misusing propofol in the literature. Nonanesthesiology physicians' specialties were surgery (n = 2), general practice (n = 2), critical care (n = 1), obstetrics (n = 1), emergency medicine (n = 1), radiology (n = 1) and unknown (n = 4). Figure 2 shows the full breakdown of medical professions. Only 22 of the identified cases involved trainees, but all 22 of the trainees identified as misusing propofol were noted to be anesthesiologists.

Previous psychiatric history/polysubstance use

Pre-existing psychiatric history was available in only 14 included articles spanning 59 cases. Pre-existing psychiatric disorder was noted in nearly half of the cases with available information (26 cases), but the information provided was limited in these articles. History of polysubstance use (use of substances in addition to propofol) was better reported in nearly all included articles, with one article providing partial data for identified cases. Overall, history of polysubstance use was reported in 72 cases and was present in most identified cases (n = 42).

#### Method of discovery/outcome

Data regarding method of discovery were available in 23 articles covering 48 cases, though these data were incomplete in one article. Among cases with a known method of discovery, death was most common (n = 38). Symptomatic intoxication (n = 6) and self-admission to rehabilitation (n = 4) were also noted methods of discovery.

Data regarding outcome of cases were available in all 24 articles, but one article included incomplete data on outcome, leaving known outcome data on 83 cases. Self-admission to rehabilitation (n = 42) and death (n = 41) were the most common outcomes. Of the 41 cases of death, association with suicide was reported in 31 cases. Suicide was associated with death in 13 cases. Information regarding subsequent recovery or resumption of clinical practice following rehabilitation was not identified.



## Discussion

Propofol is the one of the most common intravenous anesthetic agents used today. When administered by a trained professional, it is a safe and effective anesthetic agent, but self-administration can have devastating consequences. Our scoping review identified 24 articles reporting on individual characteristics of propofol misuse in 88 healthcare professionals over a 30-year period. While this may seem a small number given the amount of propofol in use worldwide during this period, it should be noted that these cases likely represent the tip of a large iceberg of unreported events. It is also likely that these reports represent a sample skewed toward prevalence in academic institutions where someone might be more likely to write a report. While it appears that the incidence of propofol misuse is increasing, without a clear understanding of either the real numerator or denominator involved, we cannot estimate a rate and our findings should be viewed in this context.

Given our search criteria, it is not surprising that individual case reports were the most common article type in this review. Despite this, much of the more robust data from the included articles came from multiple larger case series and a single survey study. This shows the need for larger studies to strengthen the understanding of medical professionals who misuse propofol and identify methods to identify and mitigate propofol misuse. Despite this need for additional data, future studies may be limited to the practical difficulties of measuring the impact of interventions to prevent propofol misuse due to difficulties in determining its true incidence.

Anesthesiologists and CRNAs represented the majority of identified articles and cases. Ease of access and familiarity with how it is used may explain why the rate of propofol misuse appears to be highest in this group of healthcare professionals. Other healthcare professionals with access and familiarity made up the second highest percentage group of medical professionals, which included registered nurses and nonanesthesiologist physicians in specialties such as critical care, surgery, and emergency medicine. The findings of this scoping review provide support to focus future prevention and recognition strategies on those working within the field of anesthesiology.

Previous studies investigating substances more generally<sup>11</sup> and propofol specifically<sup>10</sup> have suggested that trainees represent a larger proportion of medical professionals misusing these substances. Less than half of propofol misuse cases identified in this scoping review were in trainees, and all trainees identified were anesthesiologists. Though collation of the case reports, case series, and one survey study should not be used as a

reliable direct comparator with previous studies, we do recognize anesthesiology trainees as a high-risk population for propofol misuse. This finding suggests that propofol misuse may be more common in those out of training than previously believed and should be further investigated to truly understand the extent of this problem. Previous literature shows that the greatest risk for anesthesiologists and CRNAs developing addiction-related complications with misuse of anesthetic agents is early in their career.<sup>41</sup> Focus should therefore be on preventing healthcare professionals, particularly anesthesiologists, from misusing propofol early in their career.

Death was a commonly described outcome in cases of propofol misuse identified in the literature and was similar to findings in opioid misuse.<sup>42</sup> Most strikingly, this review found that death was a frequently reported method of discovery in cases of propofol misuse. Interpretation of this finding should be tempered as nearly half of all identified cases lacked a known method of discovery. Previous studies have shown mortality rates as high as 28% among anesthesiology attending physicians and 38% among resident physicians.<sup>10</sup> Induction doses of propofol can cause apnea more frequently than other anesthetic agents can, even opioids.<sup>43</sup> Rapid injection of propofol most commonly leads to death due to respiratory depression without ventilatory support and may also result in anoxic brain injury, aspiration pneumonitis, or cardiac arrest.<sup>30, 44</sup> When self-administered or administered outside the controlled medical setting, an induction dose of this medication may provide a lethal injection as shown in this review.

It is also important to note that death related to propofol misuse and known suicide were commonly reported, though data regarding suicide was not available for a portion of articles identified in this review. Suicide risk has been shown to be elevated in healthcare professionals,<sup>45, 46</sup> and particularly high-risk fields of medicine including specialties with access to propofol such as anesthesiology and general surgery.<sup>46</sup> While pre-existing psychiatric history was available in only 14 of the included articles, nearly half of the individuals in these articles had a preexisting psychiatric disorder. It is vital that all medical professionals remain vigilant and able to recognize colleagues with signs of depression or suicidality, particularly in those with access to drugs such as propofol, which is frequently used to facilitate suicide in this cohort.

There have been increasing reports of propofol misuse among medical professionals beyond the case reports and case series targeted by this scoping review. In a study including 11,666 attending physicians and resident physicians from 1990 to 1997 by Booth *et al.*, the calculated ten-year incidence of propofol misuse was 0.02%.<sup>47</sup> In a more recent study by Wischmeyer *et al.*, which included 20,865 attending physicians and resident physicians, the incidence rate increased five-fold to 0.10% during the period 1995–2005.<sup>10</sup> Most recently, Fry *et al.* surveyed the heads of 185 Australian and New Zealand departments of anesthesia and found that propofol was the most commonly misused drug, even when considering more traditionally misused substances such as opiates, benzodiazepines, and alcohol.<sup>11</sup> Due to this increasingly more common incidence of propofol misuse, it is important to recognize the misuse potential of propofol.

Compared with other commonly used anesthetic agents, propofol has a rapid onset of action for induction combined with rapid recovery,<sup>43</sup> making it an attractive target for diversion in the workplace setting. Individuals who have misused propofol reported self-administration of anesthetic or subanesthetic doses repeatedly throughout the day while still being able to function at a high enough level to avoid detection in between doses. So called "pro-napping" is associated with self-administration of a single bolus dose followed by rapid recovery and immediate return to work.<sup>48</sup> These reports of propofol misuse while on duty raise concerns regarding patient safety while being treated by medical professionals misusing propofol.

Similar to alcohol, benzodiazepines, and barbiturates, all of which have proven addiction potential, propofol acts on  $\gamma$ -aminobutyric acid type A (GABA<sub>A</sub>) receptors to enhance chloride currents.<sup>44</sup> The potentiation of GABA<sub>A</sub> receptormediated chloride currents by propofol occurs at low concentrations with direct activation of the GABAA receptor occurring with high concentrations of propofol.<sup>49</sup> Antagonizing the GABAA receptor blocks the action of propofol.<sup>50</sup> Both subanesthetic and anesthetic doses of propofol have been shown to increase the concentration of dopamine in the nucleus accumbens of rats, a main component of the mesolimbic reward process.<sup>51</sup> This is very similar to what occurs with alcohol and other recreational drugs that stimulate dopamine release in the nucleus accumbens and further enhance activation of neural networks associated with attention and reward behavior.<sup>52</sup> In a study conducted on baboons, these primates were shown to preferentially self-administer propofol, suggesting this medication also acts as a reinforcer.<sup>53</sup> In a more recent study evaluating patients undergoing propofol sedation during gastrointestinal endoscopy procedures, propofol induced euphoria in nearly half of patients enrolled.<sup>54</sup>

Although propofol isn't currently listed as a controlled substance throughout the USA or Canada, some institutions require propofol to be accounted for. Wischmeyer *et al.* showed that at 90 academic anesthesia programs (71% of programs in the study), the pharmacy did not securely store and account for propofol.<sup>10</sup> This study also showed that

more cases of propofol misuse were reported at programs without pharmacy control of propofol. While having stricter control on the supply of propofol in the hospital, even if propofol is not ultimately reclassified as a controlled substance (that is, treating propofol as a controlled substance) could potentially reduce the rate of diversion.

Through this scoping review, we identified several knowledge gaps regarding propofol misuse. One is the etiology for propofol misuse, an important point for identifying potential future mitigation strategies. Other gaps include the demographics of those misusing propofol, such as information on race, ethnicity, and socioeconomic background, which could be associated with propofol misuse. Another notable knowledge gap is related to reentry to clinical practice following propofol misuse. It is unknown if those misusing propofol successfully complete rehabilitation and are able to re-enter clinical practice within their previous subspecialty or within a new subspecialty. One identified study does provide a proposed framework for re-entry to clinical practice following propofol misuse,<sup>55</sup> but no data regarding success of this program exist. Similarly, no long-term follow-up of those who have undergone rehabilitation for propofol misuse has been reported, so it is unknown if rehabilitation prevents relapse or death. Additionally, the duration of misuse of propofol is unknown. Identifying how long those misusing propofol have been actively misusing may provide insight into opportunities to prevent diversion and misuse. Lastly, the success of potential training interventions or other prevention strategies is also unknown. While Wischmeyer et al. showed that pharmacy accountability of propofol was associated with a lower incidence of propofol misuse,<sup>10</sup> very little additional information related to training interventions or other prevention strategies exists, including outcomes related to propofol misuse in regions where propofol is listed as a controlled substance, such as South Korea, Alabama, Georgia, and North Dakota.

Future directions of research involving propofol misuse in medical professionals should address these knowledge gaps. An anonymous database of cases to better identify risk factors and outcomes associated with propofol misuse is one possible future direction. Care to make certain a database such as this maintains confidentiality and would not be reported to authorities or governing bodies would be imperative to limit stigmatization or discouragement from self-presenting for help. This database could help provide further insight into propofol misuse and outcomes through larger data analysis, similar to what has previously been done with the Malignant Hyperthermia Hotline.<sup>56</sup> Data from this database could be monitored over time to provide a more robust method for measuring success of

Authors	Publication year	Article type	Sample size	Profession	Age	Sex	Trainee status	Pre-existing psychiatric disorder	Poly- substance use	Method of discovery	Outcome	Death associated with suicide	Region
Follette JW, Fareley WJ	1992	Case report	1	Physician (anesthesiologist)	30	Male	No	Yes (depression)	Yes	Self- admission	Rehabilitation	N/A	North America
Ward CF	1992	Case report	-	Physician (anesthesiologist)	31	Male	No	No	Yes	Symptomatic	Rehabilitation	N/A	North America
Drummer OH	1992	Case report	-	Physician (radiology)	29	Female	No	Unknown	No	Death	Death	No	Oceania
Chao TC et al.	1994	Case report	1	Physician (unknown)	37	Male	No	Unknown	No	Death	Death	Yes	Asia
Soyka M, Shutz CG	1997	Case report	Н	Physician (general practitioner)	31	Male	No	Yes (depression)	No	Self- admission	Rehabilitation	N/A	Europe
Iwersen- Bergmann S et al.	2001	Case report	1	Nurse	26	Male	No	Yes (depression)	No	Death	Death	No	Europe
Crimele V et al.	2002	Case report	-	Certified registered nurse anesthetist	4	Female	No	Unknown	Yes	Death	Death	No	Europe
Roussin A et al.	2006	Case report	1	Certified registered nurse anesthetist	27	Male	No	Unknown	No	Death	Death	No	Europe
Kranioti EF et al.	2007	Case report	1	Physician (anesthesiologist)	38	Female	No	Unknown	No	Death	Death	No	Europe
Wischmeyer PE et al.	2007	Survey study	25	Physician (anesthesiology) $[n = 21]$ ; certified registered nurse anesthetist $[n = 3]$ ; anesthesia technician $[n = 1]$	Unknown	Unknown	Yes [ <i>n</i> = 16]	Yes [ <i>n</i> = 3; 9 known cases]; unknown [ <i>n</i> = 16]	Yes $[n = 7; 9$ known cases]; unknown [n = 16]	Death $[n = 7]$ ; unknown [n = 18]	Death $[n = 7]$ ; rehabilitation [n = 13]; unknown $[n = 5]$	Unknown	North America
Bonnet U et al.	2008	Case report	1	Physician (critical care)	30	Male	No	Unknown	Yes	Symptomatic	Rehabilitation	N/A	Europe
Riezzo I et al.	2009	Case report	1	Physician (anesthesiologist)	26	Male	Yes	Unknown	No	Symptomatic	Death	No	Europe
Klausz <i>et al</i> .	2009	Case report	1	Certified registered nurse anesthetist	42	Female	No	No	No	Death	Death	No	Europe
Koopmann A <i>et al</i> .	2011	Case report	1	Midwife	34	Female	No	No	No	Death	Death	No	Europe
Melliver M et al.	2012	Case series	7	Certified registered nurse anesthetist $[n = 2]$	Median = 40.5	Female $[n = 2]$	No [ <i>n</i> = 2]	No [ <i>n</i> = 2]	Yes $[n = 2]$	Symptomatic $[n = 2]$	Rehabilitation $[n = 2]$	N/A	North America
Bonnet U, Scherbaum N	2012	Case report	1	Physician (anesthesiologist)	30	Male	Yes	No	No	Self- admission	Rehabilitation	N/A	Europe
Colucci AP et al.	2013	Case report	1	Physician (anesthesiologist)	50	Male	No	Unknown	No	Death	Death	Yes	Europe
Mannocchi G et al.	2013	Case report	1	Unknown healthcare worker	Unknown	Male	No	No	No	Symptomatic	Death	No	Europe

Table Characteristics of included studies including charted outcomes relevant to the scoping review question

Table contin	nued												
Authors	Publication year	Article type	Sample size	Profession	Age	Sex	Trainee status	Pre-existing psychiatric disorder	Poly- substance use	Method of discovery	Outcome	Death associated with suicide	Region
Han E <i>et al.</i>	2013	Case series	6	Physician (unknown) $[n = 3]$ ; nurse $[n = 6]$	Median = 30	Male [n = 2]; female [n = 7]	No [ <i>n</i> = 9]	Yes $[n = 1]$ ; no $[n = 8]$	Yes $[n = 3]$ ; no $[n = 6]$	Death $[n = 9]$	Death $[n = 9]$	Yes $[n = 3]$ ; no $[n = 6]$	Asia
Hayashi T <i>et al</i> .	2013	Case series	6	Physician (anesthesiologist) $[n = 4]$ ; physician (surgery) $[n = 1]$ ; physician (general practice) $[n = 1]$ ; nurse $[n = 3]$	Median = 46	Male $[n = 7]$ ; female [n = 2]	No $[n = 9]$	Yes $[n = 2]$ ; no $[n = 6]$	Yes $[n = 8]$ ; no $[n = 1]$	Death $[n = 9]$	Death $[n = 9]$	Yes $[n = 8]$ ; no $[n = 1]$	Europe
Earley PH, Finver T	2013	Case series	22	Physician (anesthesiologist) $[n = 11]$ ; certified registered nurse anesthetist $[n = 8]$ ; physician (surgery) $[n = 1]$ ; physician (obstetrics) $[n = 1]$ ; dentist $[n = 1]$	Median = 40	Male $[n = 10]$ ; female $[n = 12]$	Yes $[n = 4]$ ; no [n = 18]	Yes $[n = 17]$ ; no $[n = 5]$	Yes $[n = 16]$ ; no $[n = 6]$	Unknown [ <i>n</i> = 22]	Rehabilitation $[n = 22]$	N/A $[n = 22]$	North America
Koroglu G, Tezcan AH	2015	Case report	-	Physician (emergency medicine)	29	Male	No	No	No	Self- admission	Death	Unknown	Middle East
Procaccianti P et al.	2017	Case series	0	Nurse $[n = 2]$	Median = 48	Male $[n = 1]$ ; female [n = 1]	No [ <i>n</i> = 2]	Unknown $[n = 2]$	No [ <i>n</i> = 2]	Death $[n = 2]$	Death $[n = 2]$	Yes $[n = 1]$ ; no $[n = 1]$	Europe
Gwiazda S et al.	2021	Case series	7	Unknown healthcare worker $[n = 2]$	Unknown $[n = 2]$	Male $[n = 1]$ ; female [n = 1]	No [ <i>n</i> = 2]	Unknown [ <i>n</i> = 2]	Yes [ <i>n</i> = 2]	Death $[n = 2]$	Death $[n = 2]$	Unknown $[n = 2]$	Europe

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interventions to prevent propofol misuse in medical professionals.

The limitations of this review should be recognized to minimize overinterpretation of our findings. We relied on reported cases in the literature, and it is possible that propofol misuse is under-reported for a number of reasons, limiting the impact of our review. Substance misuse in general still carries a significant stigma and data on death of a medical professional following an overdose of any kind are usually not publicly available. Suicide, for the same reasons, is also under-reported, and it is often difficult to distinguish between an intentional and unintentional propofol overdose because of the narrow therapeutic index of propofol. When propofol misuse causes death, there might be less inhibition (and more motivation) to publish the case reports, as opposed to when the victim survives and successfully enters treatment. Furthermore, we are unable to comment on duplicate reporting of propofol misuse between multiple articles identified because of the anonymous nature of these cases. It is possible that the same cases have been counted multiple times, particularly in articles with a case series design. Individual case reports seen in Table show no identifiable duplicate cases, but the possibility of duplicate cases should be considered when interpreting our findings.

## Conclusion

Propofol misuse by medical professionals exists and in the literature is most commonly reported in anesthesiologists and CRNAs. As death is a common reported result of propofol misuse, even in medical professionals who have knowledge of the pharmacokinetic and pharmacodynamic properties of the medication, areas for future study should focus on quantifying the significance of this problem and looking for ways to identify potential interventions for atrisk populations. Possible strategies include development of an anonymous database of medical professionals known to misuse propofol or expanding the scope of search to include public records such as from law enforcement, the national death index, or records from licensing agencies relating to suspension or termination due to substance misuse-related issues.

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