

Real-World Use and Preferences of Emergency Seizure Medication in the Netherlands: A Dutch Survey of Patients and Caregivers

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Abstract

Objective:

Timely administration of benzodiazepine rescue medication remains the cornerstone in the acute treatment of prolonged seizures and seizure clusters. While international guidelines emphasize the importance of treatment within five minutes of seizure onset, real-world data on emergency medication use, especially in community settings, are limited. This study aims to explore the use, preferences, and perceived limitations of emergency medication among people with epilepsy in the Netherlands.

Methods:

An online survey was conducted among the community of EpilepsieNL, the national epilepsy foundation and patient organisation in the Netherlands. Individuals who had expressed interest in research ($n \approx 44,000$) were invited via email and social media between August 14th and 29th 2025. The survey collected data on the type, frequency, easy of use and limitations of emergency medication use.

Results:

A total of 1,244 respondents completed the survey, of whom 798 (64%) reported possessing emergency seizure medication. Of these, 78,7% used intranasal midazolam in a multidose format, 9,6% intranasal midazolam in combination with another formulation, 4,1% rectal diazepam, 4,4% intranasal single-dose midazolam, 2,6% oral clonazepam, and 0,5% buccal midazolam. While most users were satisfied with the way of their current way of administering their medication, practical limitations were reported, including spray malfunction, dosing uncertainty due to ictal movements, and shelf-life concerns. Despite these issues, 63% of users were unwilling to switch to another formulation, citing trust, familiarity, and perceived efficacy. The availability of emergency medication was also viewed as a key contributor to safety, autonomy and quality of life.

Significance:

These findings offer insights into emergency seizure medication use in the Netherlands. The strong preference for nasal midazolam multidose spray is influenced by healthcare guidelines and reimbursement policies. Our results underscore the need for individualized treatment options and equitable access to different formulations; to both multidose and single-dose intranasal midazolam formulations to ensure optimal seizure control, patient empowerment and social inclusion.

Introduction

Use of benzodiazepine rescue medications is the cornerstone in acute management of severe seizures and seizure clusters. There is evidence that early use of rescue medication helps to abort clusters, reduces emergency room visits, reduces status epilepticus and related mortality and sudden death in epilepsy (SUDEP) [1 and ref therein]. Current international and Dutch guidelines recommend administration of benzodiazepine rescue medication within 5 minutes of generalized tonic-clonic seizure onset to improve outcomes and reduce complications. In line with this, international and national health care guidelines provide clear protocols for early intervention, favoring non-intravenous routes such as intranasal midazolam or rectal diazepam in out-of-hospital settings [2,3]

Globally, the most commonly used rescue medications have included oral lorazepam (28.9%), rectal diazepam (7.8%), oral diazepam (7.0%), and intranasal midazolam (6.9%) [3]. In the United States, rectal diazepam was the first FDA-approved rescue therapy for increased seizure activity, and it has demonstrated both safety and efficacy in the treatment of acute repetitive seizures [4,5]. The most commonly reported side effect is transient lethargy [4,5].

There is growing evidence that patients, caregivers, and healthcare providers prefer non-rectal routes of administration due to practical, social, and psychological considerations, including personal dignity, privacy, and ease of use [5,6]. Consequently, alternative formulations and routes of administration have been explored, including buccal and intranasal midazolam. These non-rectal, non-intravenous options have shown comparable or superior safety and efficacy profiles, and they offer a significant advantage in terms of ease of administration, particularly in community or caregiver-administered settings [6,7].

Buccal midazolam is approved in Europe as a rescue medication for children aged between 3 months and 18 years [7]. Several studies have shown that buccal midazolam is as effective as, or even superior to, rectal diazepam in terminating seizures [8-12]. While generally well tolerated, buccal administration may be associated with an unpleasant taste and a theoretical risk of aspiration, although this has not been reported in clinical trials [5].

Oral clonazepam is widely used in the United States, Europe, and Latin America for seizure clusters. However, there is a notable lack of clinical evidence regarding its effectiveness in the acute treatment of seizure clusters in the community setting [13].

Intranasal midazolam has emerged as a serious alternative, with multiple studies confirming its effectiveness in aborting both prolonged seizures and seizure clusters [14-18]. Additionally, intranasal administration is associated with higher caregiver satisfaction and greater ease of use [16].

In a phase 3, double-blind, placebo-controlled trial involving 201 patients, the commercially available intranasal midazolam formulation demonstrated both efficacy and ease of use in the outpatient setting. Over half of the treated patients achieved rapid and sustained seizure control. The formulation was designed to closely mimic real-world use and was generally well tolerated, with side effects consistent with those expected from nasal drug delivery and obtained FDA approval in 2019 [16,18].

In the Netherlands, compounded intranasal midazolam in multidose spray format is widely used as rescue therapy in the community and caregiver setting since the early 2000s. Its introduction was based on clinical need. Although used off-label, the formulation became standard practice due to its practicality and favorable user acceptance. Formal national rollout occurred since 2012 [2], and peer-reviewed literature documenting the exact year of introduction is currently lacking. To date, no national data have been published on the real-world use of emergency seizure medication, including the types used, user satisfaction, or barriers to administration. We conducted the first national survey among the Dutch epilepsy community, examining current practices, preferences, and user experiences related to emergency seizure medication.

Method

EpilepsieNL, the Dutch organization supporting individuals with epilepsy, distributed a digital survey to a pre-consented database of 44,000 adult members interested in research. The survey link was shared via email and social media, and responses were collected anonymously between August 14th and August 29th 2025. Only respondents reporting possession or use of emergency medication continued beyond the initial screening question.

Survey items (Table 1) focused on medication type, frequency of use (categorized by 3-month intervals), satisfaction, and open-ended questions about limitations, preferences, and willingness to switch qualitative.

Descriptive statistics were calculated for frequency, type of medication, and satisfaction levels. Qualitative responses were categorized thematically. Due to small subgroup sizes for some formulations, inferential statistical comparisons were not performed.

	Question	Answer Options
1	Has a physician prescribed emergency medication for epileptic seizures?	Yes / No
2	For whom is the emergency medication prescribed?	For myself / For my child / For another family member / For a client
3	Which emergency medication has been prescribed?	Midazolam nasal spray (multi-dose) / Midazolam nasal spray (single-dose) / Buccal midazolam / Clonazepam / Stesolid rectiole
4	How often is the emergency medication used (on average)?	Never used (but available at home) / Once every three months / 2–5 times every three months / More than 6 times every three months
5	How easy is it to administer the current emergency medication?	Scale from 1 (very difficult) to 5 (very easy)
6	Do you experience any problems when administering the emergency medication, or do you encounter any challenges?	Open text field
7	What do you consider the most important feature of emergency medication?	Rapid effect / Ease of administration / Other, open tekst field
8	If your physician suggests a different route of administration, would you consider switching?	Yes / No
9	Why would you be willing to switch?	Open text field
10	Why would you prefer not to switch?	Open text field
11	This is the final question. Is there anything else you would like to share regarding emergency medication?	Open text field

Table 1: English translated items of the Emergency Medication Survey, presented in the order of questioning. The table includes all 11 questions used in the study, covering prescription status, indication, medication type, frequency of use, ease of administration, experienced problems, treatment preferences, and willingness to switch formulations.

Results

A total of 1,244 individuals completed the national survey. Of these respondents, 798 individuals (64%) reported currently possessing or using emergency seizure medication, while 446 (36%) indicated that they did not have access to or use such medication. The distribution for intended recipient for the prescribed emergency medication is given in table 2. For half of the responders the emergency medication is intended for the child 53%, 38% is intended for the person with epilepsy, 7% for another family member and 3% for a client.

Among those who reported having emergency medication, usage frequency varied considerably. Over half of the respondents (52%) indicated that they had never needed to administer their emergency medication. Meanwhile, 28% reported using it once every three months, 13% used it between two to five times per three months, and 7% reported more frequent use six times or more within a three-month period.

Recipient of emergency medication	n	%
for my child	419	53
for myself	301	38
for another family member	55	7
for a client	23	3
Total	798	100

Table 2. Distribution of emergency medication prescriptions by intended recipient. Among the 798 respondents who reported possessing or using emergency medication, the majority indicated that it was prescribed for their child (n = 419), followed by themselves (n = 301), another family member (n = 55), or a client (n = 23).

With respect to the type of rescue medication used, the vast majority of respondents (78,7%) reported using intranasal midazolam in a multidose spray formulation, making it the most commonly utilized option in this population. This was followed by 9,6% a combination of midazolam multi dose and another formulation, 4,1% rectal diazepam, 4,4% single-dose intranasal midazolam. A smaller proportion reported the use of oral clonazepam (2,6%), while only 0,5% reported using buccal midazolam. These data are summarized in Figure 1 on the next page.

There are small differences in distribution of use of type medication in frequency of administering emergency medication. Only 4 responders use buccal midazolam, 4 users use the single dose unit nasal midazolam and 4 users use rectal diazepam in the > 2-5 and 6 timed emergency medication in three months. In the group that never uses it or only once in three months, the amount of people using single dose nasal midazolam is 31 en 27 of rectal diazepam, see table 3 on the next page.

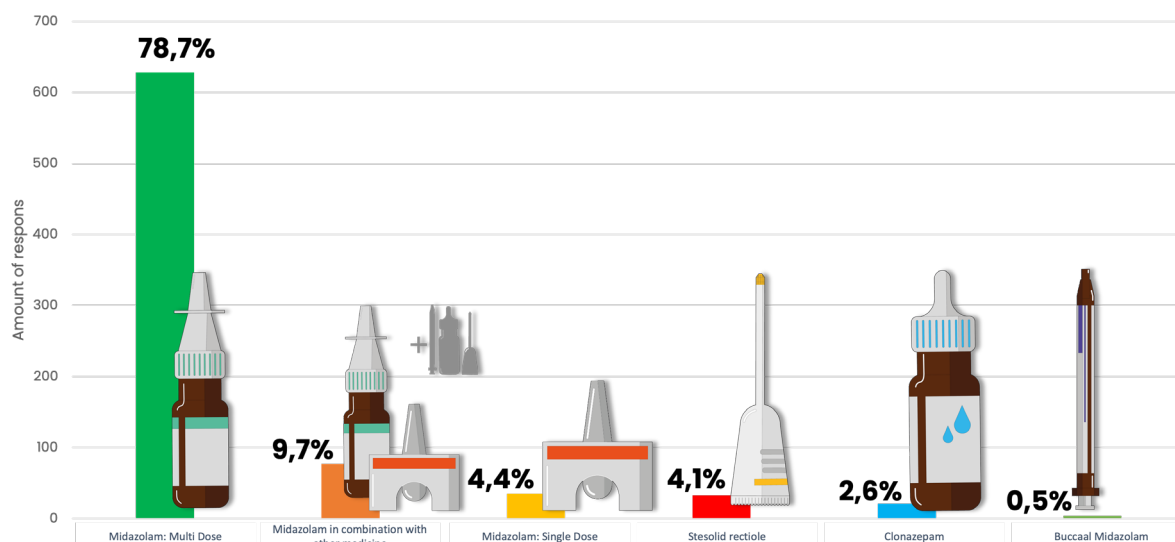


Figure 1: Preference of emergency medication in % in the Netherlands. The amount of responders are given per type of formulation on the y-axis. The calculated % per formulation is given in the legends. 100% represent the 798 individuals possessing emergency medication.

N, Usage of medication	Buccal midazolam	Clonazepam	Midazolam multi dosering	Midazolam single dosering	Stesolid rectiole	Combi	Total
Have it in my possession but never used it	2	8	359	21	10	15	415
Once in three months		3	168	10	17	21	219
2-5 times in three months	2	5	72	4	4	18	105
More than 6 times in three months		5	29		2	23	59
Total	4	21	628	35	33	77	798

Table 3: Frequency of emergency medication use by formulation type among respondents (n = 798).

This table presents the reported frequency of emergency medication use, categorized by type of formulation. Frequency was assessed and grouped as: never used, once, 2–5 times, or more than 6 times per three-month period. Respondents could only select one formulation. Buccal midazolam users (n = 4) are included for completeness but were not analyzed separately due to the small sample size.

Participants across all user groups reported generally high levels of satisfaction with their current route of administration for emergency medication (figure 2). Of the 798 individuals who reported using or possessing rescue medication, 44% rated their satisfaction as the highest possible (5 out of 5), while an additional

35% gave a rating of 4 out of 5. Only 7% of users expressed dissatisfaction, defined as a rating of 1 or 2. Satisfaction levels were broadly consistent across different medication types, although a slightly higher proportion of dissatisfaction was noted among users of rectal diazepam (table 4).

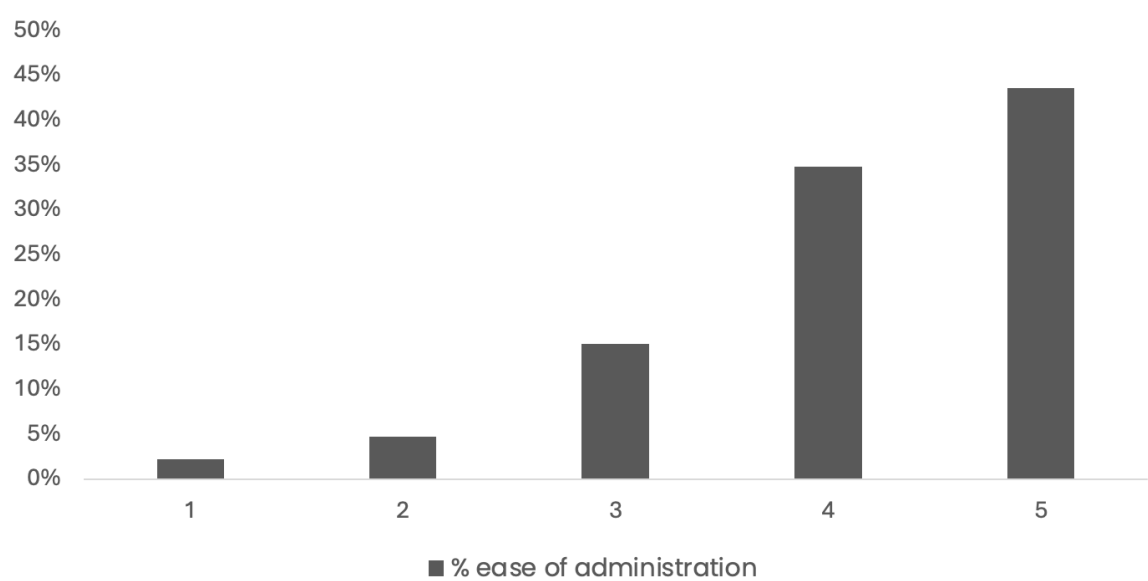


Figure 2: Overall Ease of use during administration of prescribed emergency medication among respondents (n = 798). This figure illustrates user-reported satisfaction levels of ease of use of their current administration route of emergency seizure medication, rated on a 5-point Likert scale (1 = very difficult, 5 = very easy). The majority of respondents reported high satisfaction, with minimal variation between different medication formulations. Only a small proportion (7%) indicated dissatisfaction (score 1 or 2).

Formulation	1	2	3	4	5	Total
Buccal midazolam	0%	50%	0%	0%	50%	100%
Clonazepam	0%	15%	31%	23%	31%	100%
Combi	2%	6%	11%	43%	38%	100%
Midazolam multi dose	2%	3%	15%	34%	46%	100%
Midazolam single dose	0%	7%	14%	21%	57%	100%
Stesolid rectiole	9%	4%	17%	39%	30%	100%
Total	2%	5%	15%	35%	44%	100%

Table 4: Ease of use during administration with emergency medication by formulation type (n = 798). This table shows the distribution of easyness of administrating scores across different emergency medication formulations, rated on a 5-point Likert scale (1 = not difficult, 5 = very easy) in %.

Despite the generally positive ratings, many respondents described practical limitations and challenges associated with the use of emergency medication. Open-text responses highlighted several recurrent themes. Availability of emergency medication, affordability, efficacy, comfort in usage also for children, severity of side effects, shelf life, easy to take along, perceived reliability of medication, recognizable package, ethical aspects, for instance not drawing attention from the public when administered are beneficial characteristics of emergency medication.

Without intending to cover all aspects, additional concerns mentioned were; the spraying technique doesn't work correctly, it is difficult to administer during a seizure due to movements, it is not always available due to medicine shortage in the Netherlands, shelf life and packaging wears out quickly, instructions are not clear, not easy to use. Several respondents expressed worry about potential side effects, the possibility of misuse, or dependency.

These insights suggest that while users are generally satisfied, real-world challenges can compromise the effectiveness or ease of use of emergency therapies.

Importantly, a recurring theme in both structured and open-ended responses was the significance of emergency medication beyond clinical effectiveness. Many respondents described their rescue medication as a critical element in maintaining autonomy, reducing anxiety about seizures, and enabling participation in daily life activities such as travel, work, or social events.

When asked whether they would be willing to switch to a different rescue medication if recommended by their neurologist (figure 3), 37% (n=269) of respondents answered affirmatively, while 63% (n=502) stated they would prefer to continue with their current formulation. In figure 3 an overview is given of the willingness to switch emergency medication.

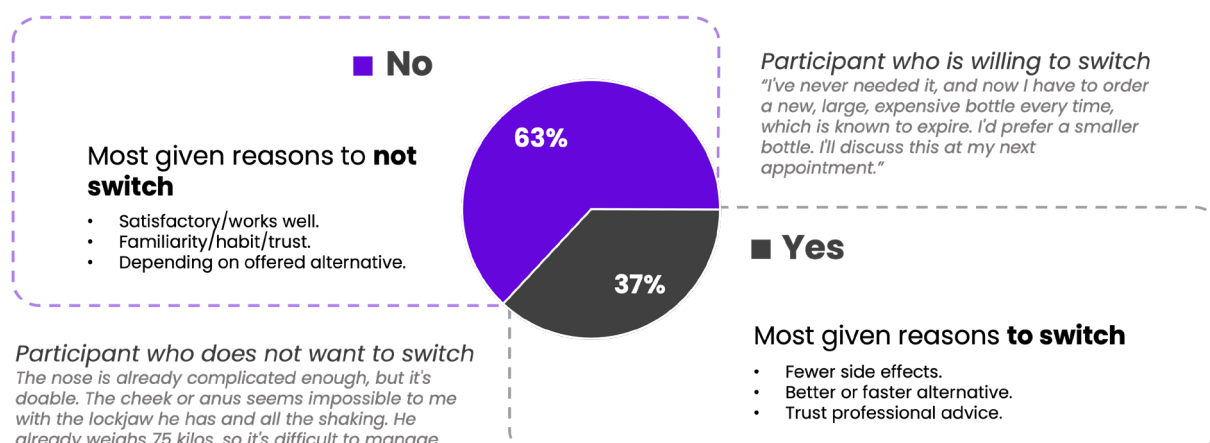


Figure 3: % willingness to switch emergency medication of a different formulation after prescription of a neurologists or epilepsy nurse (n=798).

Table 5 provides an overview, in percentages, of the 502 respondents who indicated that they were not willing to switch to a different formulation of emergency medication. Users of buccal midazolam were excluded from this analysis due to the small sample size (n = 8) and the fact that all buccal midazolam users expressed a willingness to switch. Below two illustrations of arguments given in the open text field.

Illustrative citation of a caregiver not willing to switch:

"The nose is already complicated enough, but it's feasible. The cheek or anus seems impossible to me during a seizure, with the lockjaw and all the shacking. He already weighs 75 kilo's, so difficult to manage"

Illustrative citation of a patient willing to switch:

"I've never needed it, and now I have to order a new large expensive bottle every time when it is expired. I'd prefer a smaller bottle. I'll discuss this at my next appointment"

Among the overall group unwilling to switch, the most frequently cited reason was confidence in the medical efficacy of their current medication (41%), followed by familiarity with and trust in the formulation they currently use (15%).

Clonazepam users were particularly resistant to switching, with 60% citing the perceived reliability of clonazepam's efficacy as the primary reason, and 40% pointing to prior negative experiences with alternative formulations.

The majority of respondents reported using intranasal midazolam in a multidose format. Among users of single-dose midazolam, the main reason for not wanting to switch was the ease of use associated with this particular formulation.

Reasons Noted:	Clonazepam	Midazolam multi dose	Midazolam single dose	Stesolid rectiole	Combi	Total
Familiarity/habit/trust	0%	16%	40%	0%	14%	15%
Easy usage current medication	0%	12%	20%	0%	0%	10%
Medical reasons/personal circumstances	0%	4%	0%	17%	9%	5%
Negative experience with alternatives	40%	6%	20%	33%	9%	9%
Satisfaction/works well	60%	39%	20%	17%	55%	41%
Depending on offered alternative	0%	15%	0%	0%	9%	12%
Other	0%	9%	0%	33%	5%	9%
Total	100%	100%	100%	100%	100%	100%

Table 5. Reported reasons for unwillingness to switch to a different emergency medication formulation among respondents (n = 502). Percentages reflect the distribution of cited reasons within the group unwilling to switch. Buccal midazolam users (n = 8) were excluded from this analysis, as all expressed willingness to consider alternative formulations.

Discussion

This study represents the first national effort to investigate the real-world use, preferences, and limitations of emergency seizure medication in the Netherlands. Although intranasal midazolam, particularly in a compounded multidose formulation, is commonly prescribed and widely used, no prior population-based data existed to support clinical or policy decisions. The present survey, conducted by EpilepsieNL in collaboration of the Dutch League against epilepsy, offers important insights into current practice, patient satisfaction, and unmet needs related to rescue medication for epilepsy.

Collecting such data is particularly timely, as ongoing policy discussions in the Netherlands concern the reimbursement of both single-dose and multidose intranasal midazolam. While emergency medication is reimbursed under existing health insurance schemes due to its critical role in preventing status epilepticus, hospitalization, and SUDEP, as outlined in various clinical guidelines [1-3], only the multidose formulation is currently covered in most cases. The single-dose unit, despite its potential advantages in ease of use and safety [16], is not routinely reimbursed, creating barriers to access for certain patient populations.

The use of intranasal midazolam in a multidose format is largely driven by compounding practices since the early 2000s and has become the standard of care in Dutch epilepsy centers and general hospitals. This practice contrasts with many other countries, where intranasal benzodiazepines were only more recently approved and commercialized [14,18]. In

our study, 83% of participants who reported using rescue medication indicated they used a nasal midazolam spray, confirming prior expectations about prescribing patterns in the Netherlands.

Despite widespread use, multidose formulations are not without limitations. Several respondents reported technical issues with the spray mechanism, such as inconsistent dosing or device failure during administration. These limitations are particularly problematic during ongoing seizures, when motor agitation and urgency may impair effective delivery. Previous studies, such as the GENS survey, have highlighted the importance of caregiver training and first-aid education in overcoming such barriers [19]; however, the challenges remain real and clinically relevant. In our findings, these concerns were echoed repeatedly in open-ended responses.

Notably, while the single-dose formulation was used by a smaller subset of respondents ($n = 35$), those who used it cited ease of administration and dosing accuracy as the primary advantages in consistence with previous findings [16]. This formulation may be especially suitable for individuals who use rescue medication infrequently, such as once every three months or less, assuming that it reduces complexity and minimizes the risk of incorrect dosing. Moreover, a single-dose unit potentially lowers the risk of habituation or inadvertent overuse by patients or informal caregivers.

In contrast, for more frequent users of rescue medication, the practicality of carrying fewer packages and the familiarity with multidose administration may outweigh these concerns. The preference for a specific formulation, therefore, may be linked to frequency of use, perceived reliability, and user experience. These findings may help guide shared decision-making in clinical practice.

Our results also shed light on user reluctance to switch between formulations. Among those who expressed unwillingness to change, key reasons included trust in the current medication's efficacy (41%) and familiarity with its use (15%). For users of oral clonazepam, resistance was particularly strong, with 60% citing perceived efficacy and 40% reporting prior negative experiences with alternatives. Interestingly, this trust-based reluctance to switch was not associated with significant differences in satisfaction scores between formulations, suggesting that psychological and experiential factors may play a larger role than objective efficacy in determining patient preferences.

Beyond pharmacological and practical considerations, a consistent theme throughout the responses was the importance of rescue medication in supporting autonomy and independence. Many respondents indicated that simply possessing a reliable emergency medication, regardless of frequency of use, reduced anxiety, enabled participation in daily activities, and increased their overall sense of safety. This perspective aligns with the broader goal of epilepsy care: to optimize not only clinical outcomes but

also quality of life. Access to appropriate emergency medication, therefore, should be viewed not merely as a medical necessity but as a critical component of patient empowerment and social inclusion.

This perspective raises further questions about whether similar attitudes toward emergency medication exist in countries with more restrictive policies or less liberal guidelines around caregiver administration. In the Netherlands, informal caregivers are legally permitted to administer intranasal midazolam following appropriate instruction, which likely facilitates its integration into standard care.

Globally, and particularly in Europe, timely access to emergency care is often limited due to policy barriers and a lack of awareness [19]. With the recognition of Rapid and Early Seizure Termination (REST) by the European Academy of Neurology [20], countries are beginning to adopt REST principles, as reflected in discussions at the Emergency Care Summit for European Patient organisation in Amsterdam 2025. The use and preference of emergency medication in the Netherlands may perhaps serve as an early indicator of future preferences in other countries.

Several limitations of the present study must be acknowledged. First, participation was voluntary and limited to individuals who had previously expressed interest in research, which may have introduced selection bias. Second, the survey was anonymous, and the representativeness of the sample cannot be confirmed. Although the first question excluded participants without emergency medication, it remains

unclear whether the sample reflects the broader population of people with epilepsy in the Netherlands. Additionally, only a small number of participants ($n = 35$) reported using single-dose midazolam, limiting statistical power for subgroup comparisons. Nonetheless, the overall sample size ($n = 1,244$) provides a robust foundation for descriptive analysis and policy considerations.

In summary, this national survey offers real-world insight into the use of emergency seizure medication in the Netherlands. Emergency medication was prescribed to 64% of respondents, and of these, a substantial majority (83%) used intranasal midazolam, predominantly in a multidose formulation. The choice between single- and multidose formats tends to be influenced by frequency of use and perceived ease of handling. Importantly, 67% of users indicated they were not willing to switch to another formulation.

Taken together, these findings underscore the medical, psychosocial, and policy-related importance of maintaining access to both multidose and single-dose intranasal midazolam formulations. Ensuring equitable reimbursement and availability is essential, not only to optimize seizure control, but also to support autonomy, reduce health disparities, and enhance the quality of life for people with epilepsy. These principles extend beyond the Dutch context and may inform broader international strategies in the provision of emergency epilepsy care.

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