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Take-Home Naloxone Kits: Attitudes and Likelihood-Of-Use Outcomes from a European Survey of Potential Overdose Witnesses

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Keywords

Opioids · Opiates · Heroin · Overdose · Nasal · Naloxone · Carriage

Abstract

Background: Injectable naloxone is already provided as take-home naloxone (THN), and new concentrated intranasal naloxone is now being introduced in Europe. Despite evidence of the effectiveness and cost-effectiveness of THN, little is known about the attitudes of key target populations: people who use opioids (PWUO), family/friends, and staff. We examined the acceptability of different naloxone devices (ampoule, prefilled syringe, and concentrated nasal spray) across 5 European countries. **Objectives:** The aim of this study was to compare THN target groups (PWUO vs. family/friends vs. staff) in their past rates of witnessed overdose and THN administration (as indicators of future use), current THN device preference, and THN carriage on the day of survey.

Method: Cross-sectional survey of respondents (age ≥ 18) in addiction treatment, harm reduction, and recovery services in Denmark, England, Estonia, Norway, and Scotland. A purpose-developed questionnaire (59 items) was administered in the local language electronically or in a pen-and-paper format. **Results:** Among $n = 725$ participants, 458 were PWUO (63.2%), 214 staff (29.5%), and 53 (7.3%) family members. The groups differed significantly in their likelihood-of-future THN use ($p < 0.001$): PWUO had the highest rate of previously witnessing overdoses (352; 77.7%), and staff members reported the highest past naloxone use (62; 30.1%). Across all groups, most respondents (503; 72.4%) perceived the nasal spray device to be the easiest to use. Most reported willingness to use the spray in an overdose emergency (508; 73.5%), followed by the prefilled syringe (457; 66.2%) and ampoules (64; 38.2%). Average THN carriage was 18.6%,

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ranging from 17.4% (PWUO) to 29.6% (family members). **Conclusion:** Respondents considered the concentrated naloxone nasal spray the easiest device to use. Still, most expressed willingness to use the nasal spray as well as the pre-filled syringe in an overdose emergency. Carriage rates were generally low, with fewer than 1 in 5 respondents carrying their THN kit on the day of the survey.

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Introduction

Injectable naloxone is already provided as take-home naloxone (THN) in Europe, and licensed nasal spray products (“concentrated naloxone nasal spray”) have become available since 2018 [1, 2]. There is strong evidence for the effectiveness and cost-effectiveness of THN pre-supply to potential overdose witnesses, i.e., people who use opioids (PWUO), their family/friends, and staff in contact with PWUO [3–5]. Yet, little is known about the target groups’ attitudes toward different THN devices or their likelihood to witness overdoses. Data from Scotland [6, 7] and the USA [8] show low THN carriage rates (5–16%) among PWUO. This presents a central implementation challenge to community-based naloxone access in overdose emergencies, potentially reducing benefit from THN.

We thus surveyed potential overdose witnesses about their current attitudes and past experiences. We aimed to compare THN target groups (PWUO vs. family/friends vs. staff) in their:

1. Likelihood to use THN in future overdose emergencies. On the grounds that future behavior is best predicted by past behavior, we defined this as rates of past (a) witnessed overdoses and (b) THN administration
2. THN device preference (ampoules vs. concentrated nasal spray vs. pre-filled syringe), assessed as (a) perceived ease of use and (b) willingness to use in an overdose emergency
3. THN carriage rates

Materials and Methods

Eligibility

Adults (≥18 years) were asked to participate if they were (1) PWUO (current and former users, any treatment status), (2) their family members, or (3) staff working with PWUO. Individuals who could not effectively communicate with the interviewer due to intoxication or language comprehension barriers were excluded.

Table 1. Recruitment by country and participant group

Site (country)	PWUO	Family	Staff	Total (%)
London (England)	128	15	66	215 (29.7)
Copenhagen (Denmark)	132	14	49	195 (26.9)
Birmingham (England)	89	3	26	118 (16.3)
Narva and Tallinn (Estonia)	55	14	31	100 (13.8)
Glasgow (Scotland)	41	7	14	62 (8.6)
Bergen and Oslo (Norway)	13	0	28	41 (5.7)
Total (%)	458 (63.2)	53 (7.3)	214 (29.5)	725 (100.0)

Recruitment

Data collection occurred in 8 cities (see Table 1) across Denmark, England, Estonia, Norway, and Scotland via convenience sampling between April 2018 and June 2019, with PWUO and family being recruited from addiction treatment, harm reduction, and recovery services and staff from staff meetings. All were given a participant information sheet, alongside verbal summary, and could clarify questions with the interviewer before providing informed verbal (London sites) or written consent (all other sites).

Reimbursement

Only the Glasgow and Birmingham sites offered participating PWUO and the family a 5 GBP shopping voucher as compensation for their time.

Research Ethics

Ethics advice was sought locally. The Birmingham and Solihull Mental Health NHS Foundation Trust provided local approval (reference number: SE0123). All other sites waived the requirement for ethics review due to anonymized data collection (Copenhagen), recruitment outside NHS services (Glasgow), or the survey being conducted as quality improvement project (London, Estonia, Norway).

Measure

Interviewers (i.e., researchers or keyworkers) administered the purpose-developed questionnaire (translated from English into local languages for Denmark, Estonia, and Norway) in an iPad-based or pen-and-paper format. All responses were anonymous. The questionnaire took 10–15 min to complete and comprised up to 59 items (with skip patterns) covering the outcomes: history of witnessed overdose (yes/no), overdose rates (continuous), naloxone use (yes/no), THN daily carriage (yes/no), and THN device preference (see below).

Analysis

The data were analyzed in SPSS Statistics 25.0 (IBM, Armonk, NY, USA). The χ^2 test was conducted for categorical variables, and ANOVA was performed to compare group counts of witnessed overdoses. A *p* value below 0.05 was considered statistically significant. For measures of THN device preference, no inference statistics were calculated since responses were not mutually exclusive (e.g., “Which one(s) would you be willing to use in an overdose emergency?”).

Table 2. Demographics and outcomes by the participant group

	PWUO (n = 458)	Family (n = 53)	Staff (n = 214)	χ^2/F	p value
Age, n (%)					
18–24	8 (1.7)	2 (3.8)	7 (3.3)	–	–
25–44	259 (56.6)	11 (20.8)	124 (58.2)	–	–
45–64	175 (38.2)	30 (56.6)	80 (37.6)	–	–
65–84	9 (2.0)	10 (18.9)	2 (0.9)	–	–
Did not say	7 (1.5)	0 (0.0)	1 (0.5)	–	–
Gender, n (%)					
Female	119 (25.9)	33 (62.3)	140 (65.4)	105.1	<0.001
Male	333 (72.7)	19 (35.8)	73 (34.1)		
Did not say	6 (1.3)	1 (1.9)	1 (0.5)		
Overdose history, n (%)					
Witnessed overdose	352 (77.7)	27 (50.9)	119 (56.1)	40.754	<0.001
How many in the past 12 months	\bar{x} = 2.28 (SD = 5.04)	\bar{x} = 1.41 (SD = 2.19)	\bar{x} = 3.22 (SD = 5.49)	2.295	0.102
Naloxone use, n (%)					
THN prescribed/supplied	258 (56.8)	27 (51.9)	70 (34.7)	27.568	<0.001
Naloxone administered to others	88 (19.9)	4 (7.5)	62 (30.1)	15.463	<0.001
THN carriage, n (%)					
Carrying THN on day of survey	45 (17.4)	8 (29.6)	n/a	1.496	0.221
	PWUO	Family	Staff	Total ²	
THN – willing to use in OD emergency ¹ , n (%)					
Ampoules	177 (40.5)	16 (30.2)	71 (35.3)	264 (38.2)	
Prefilled syringe	282 (64.5)	34 (64.2)	141 (70.5)	457 (66.2)	
Nasal spray (single device)	303 (66.3)	41 (77.3)	164 (81.6)	508 (73.5)	
THN – easiest to use ¹ , n (%)					
Ampoules	47 (10.6)	12 (23.1)	7 (3.5)	66 (9.5)	
Prefilled syringe	138 (31.2)	16 (30.8)	39 (19.4)	193 (27.8)	
Nasal spray (single device)	292 (66.1)	39 (75.0)	172 (85.6)	503 (72.4)	

¹ Responses for THN device preference items (“Which one(s) would you be willing to use in an overdose emergency?”; “Which one(s) would be easiest for you to use?”) were not mutually exclusive. The sum of percentages may thus exceed 100%. ² Percentages are based on a total of 725 respondents (458 service users + 53 family members + 214 staff members).

Results

In the following sections, we report sample demographics and outcomes (see also Tables 1, 2). Results by country are provided as online supplementary material (see www.karger.com/doi/10.1159/000521197 for all online suppl. material).

Sample Demographics

A total of 725 respondents (425 male; 58.6%) were surveyed, of whom 458 (63.2%) were PWUO, 214 (29.5%) staff, and 53 (7.3%) family members of PWUO. Most respondents were recruited in London (209; 28.8%) and Copenhagen (195; 26.9%), followed by Birmingham (118; 16.3%), Estonia (100; 13.8%), Glasgow (62; 8.6%), and Norway (41; 5.7%).

Most PWUO (259; 57.4%) and staff (124; 58.2%) were of 25–44 years of age. Family members were mostly 45–64 year old (30; 56.5%). There was a significant gender difference across groups ($\chi^2(2, N = 718) = 105.1, p < 0.001$). Men were overrepresented among PWUO (333; 73.7%), whereas staff (140; 65.7%) and family members (33; 63.5%) were predominantly female.

Likelihood to Use THN in an OD Emergency

More than 3 quarters of PWUO had “ever witnessed an overdose” (352; 77.7%), which was significantly higher than for the other 2 groups ($\chi^2(2, N = 718) = 15.463, p < 0.001$). Most staff (119; 56.1%) and family members (27; 50.9%) had witnessed an overdose. The groups did not differ in past-year rates of witnessed overdoses ($F(2, 505) = 2.295; p = 0.102$), with on average 2.5 events per

respondent. Less than a tenth of family members (4; 7.5%) had “ever used naloxone to reverse an opioid overdose,” which was significantly higher in the other 2 groups ($\chi^2(2, N = 701) = 15.463, p < 0.001$). One in 5 PWUO ($n = 88$; 19.9%) and almost 1 in 3 staffers (62; 30.1%) reported THN use.

THN Device Preference

Willingness to Use in OD Emergency

Across groups, most respondents (508; 73.5%) were willing to use the nasal spray in an overdose, followed by willingness to use the prefilled syringe (457; 66.2%) and ampoules (64; 38.2%). Nasal spray preference was most pronounced among staff (164; 81.6%). The smallest difference in preference ratings was observed among PWUO, with little difference between the nasal spray (69.3%) and prefilled syringe (64.5%).

Ease of Use

Most (503; 72.4%) considered the nasal spray would be the easiest device to use, followed by prefilled syringes (193; 27.8%) and ampoules (66; 9.5%). Among PWUO, device preference was not associated with injecting status (ever; past 6 months).

THN Carriage Rates

No significant association was found between group and THN carriage ($\chi^2(1, N = 297) = 1.496, p = 0.221$). Among those supplied with THN, only few PWUO (45; 17.4%) and family members (8; 29.6%) reported carrying their kit on the day of the survey – equivalent to 18.6% (53/285) across both groups. Staff were surveyed during working hours and not asked about carriage.

Discussion

Our survey of potential overdose witnesses in 5 European countries has yielded 3 central findings. First, groups differed significantly in their experience of witnessing overdoses and using THN. Using past behavior as a predictor for future behavior, we found that PWUO had the highest likelihood of witnessing future overdoses, with >3 quarters having previously been present at an opioid overdose. Almost one-third of staff members reported past naloxone administration (i.e., the highest rate across groups). These findings suggest that PWUO and staff should be the primary target groups for THN distribution.

Second, THN device preference was less pronounced than expected. In an earlier Australian survey [9] which

preceded the development of a concentrated naloxone nasal spray, nearly 3 quarters of participating heroin users ($n = 99$) had preferred nasal spray to injection. Similarly, in our survey, almost 3 quarters of all respondents considered the nasal spray easiest to use and reported they would administer the spray in an overdose emergency. Nevertheless, over two-thirds of respondents stated that they would be willing to use the prefilled syringe in an emergency. These results highlight that both the concentrated nasal spray and prefilled syringe would seem suitable for layperson distribution. Nasal spray preference was more pronounced among family members and staff (see Table 2), suggesting that these groups may be more receptive to noninjectable devices – likely because they have less experience with injectable devices than PWUO.

Third, carriage rates were generally low, independent of the different THN supply rates (36–93%) in the survey countries (see online supplementary material). Less than a fifth of PWUO and family members (19%) had their THN kit available on the day of the survey, consistent with 5–16% carriage rates previously reported among PWUO in Scotland and the USA [5–7]. While local supply rates likely reflect the degree of THN implementation (incl. funding), the reasons for low THN carriage rates are poorly understood. Our findings highlight the need for emphasizing the importance of carriage during THN training to ensure naloxone access in overdose emergencies.

Our study is the first to assess naloxone device preference and likelihood to witness overdoses across different THN target populations. Notably, we managed to recruit over 700 respondents across 5 European countries, which strengthen the external validity of our findings. However, due to their limited presence at recruitment sites, family members ($n = 53$) were underrepresented in our sample, and the generalizability of their responses is unclear. Our use of convenience sampling may have produced a non-representative sample, with overrepresentation of male PWUO (333; 72.7%).

Further limitations include our cross-sectional design involving self-report data, which is inherently prone to social desirability and recall biases. Moreover, our survey was conducted before a concentrated nasal spray became commercially available in 3 survey countries (in Denmark and Norway, THN programs were already distributing concentrated nasal sprays, and an earlier device, i.e., 2 mg/2 mL multistep nasal sprays, was still in circulation but not included in the survey). Questions about device preference were thus mostly hypothetical and did not ad-

dress dosage or cost. Preliminary data on the prehospital use of a different concentrated nasal spray (i.e., a 4 mg/0.1 mL product) are available from the USA, reporting on 261 overdose cases [10]. Future research should use prospective designs to recruit cohorts of potential overdose witnesses who are provided different THN devices (e.g., concentrated nasal spray vs. prefilled syringe) and compare their carriage rates and experiences of THN use as well as post-overdose behavior (e.g., help-/treatment seeking).

Conclusion

The concentrated naloxone nasal spray was generally preferred, but prefilled syringes were also considered acceptable for use in an overdose emergency, especially among PWUO. Nasal spray may be particularly suitable for distribution to staff and family members, alongside tailored training.

PWUO were most likely to witness overdoses, but <1 in 5 were carrying their THN kit on the day of the survey. This highlights the need to promote naloxone carriage to maximize naloxone access and prevent overdose mortality.

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Statement of Ethics

The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. All participants provided informed verbal (London sites) or written consent (all other sites). Ethics advice was sought locally. The Birmingham and Solihull Mental Health NHS Foundation Trust provided local approval (reference number: SE0123). All other sites waived the requirement for ethics review due to anonymized data collection (Copenhagen), recruitment outside NHS services (Glasgow), or the survey being conducted as a quality improvement project (London, Estonia, Norway).

Conflict of Interest Statement

The authors Katri Abel-Ollo, Shabana Akhtar, Thomas Clausen, Ed Day, Helle Petersen, Andrew McAuley, Martin Sefranek, and Henrik Thiesen have no conflicts of interest to declare. In the past 3 years, Ed Day has taken part in research funded by Indivior and Mundipharma, but he has not received individual honoraria from any organization. Rebecca McDonald's and Sibella Bredahl's research posts at King's College London were partly supported by project-specific research grants to the university from Mundipharma to enable this project. Rebecca McDonald received conference-related travel funding and an honorarium from Improving Opioid Outcomes in the Treatment of Opioid Dependence (IOTOD) in 2018. Rebecca McDonald's employer (King's College London) has received a research grant from Mundipharma Research Ltd., for an observational cohort study of THN provision in Europe, on which Rebecca McDonald is partly employed (0.5 FTE). Separately, King's College London registered intellectual property on a novel buccal naloxone formulation, naming Rebecca McDonald as a coinventor. Rebecca McDonald worked as a consultant on community-based naloxone access in Central Asia and Eastern Europe for the UNODC (2016–17). In the past 3 years, Mike Kelleher has taken part in research funded by Indivior, Camurus, and Mundipharma. He has received honoraria from Indivior, Gilead, and Abbvie. John Strang, through his university, works with the pharmaceutical industry to identify new or improved treatments, and his employer (King's College London) has received grants, travel costs, and/or consultancy payments; this includes investigation of new naloxone formulations and has included work, within the past 3 years, with Accord Healthcare and Mundipharma (both of whom have naloxone products) including a multi-site observational prospective cohort study of recipients of different forms of THN (research grant support from Mundipharma Research Ltd). His employer (King's College London) has also registered intellectual property on a novel buccal naloxone formulation, naming John Strang as a coinventor, and he was earlier named in a patent registration by a pharmaceutical company regarding a concentrated nasal naloxone spray. John Strang worked as a consultant on community-based naloxone access in Central Asia and Eastern Europe for the United Nations Office on Drugs and Crime (UNODC; 2016–17). For a fuller account, see John Strang's webpage at <http://www.kcl.ac.uk/ioppn/depts/addictions/people/hod.aspx>.

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Author Contributions

Rebecca McDonald and John Strang conceived of the study and developed its design, oversaw data collection, and drafted the manuscript. Sibella Beidahl was involved in the design of the work, coordinated the acquisition and analysis of the data, and contributed to the drafting of the manuscript. Ed Day, Mike Kelleher, Andrew McAuley, and Martin Sefranek were involved in the design of the work, acquisition of the data, and critical revision of the manu-

script. Katri Abel-Ollo, Thomas Clausen, Helle Petersen, and Henrik Thiesen were involved in the design of the work; translation of the survey into Danish, Estonian, Norwegian, and Russian languages; the acquisition of the data; and the critical revision of the manuscript. Shabana Akhtar was involved in the acquisition of the data and the critical revision of the manuscript. All the authors have given the final approval of the version to be published agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its supplementary material files. Further inquiries can be directed to the corresponding author.

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