

THE S-O-S INITIATIVE—STOP OVERDOSE SAFELY

S-O-S Study: UNODC-WHO multisite implementation study on community management of opioid overdose including the use of naloxone for preventing overdose deaths

THE FACTS

Opioid overdose is a growing global concern and every year on 31 August, many people around the world commemorate the International Overdose Awareness Day. An estimated 62 million people globally used opioids in the year 2019 according to the United Nations Office on Drugs and Crime (UNODC) estimates (UNODC, 2021) and opioid overdose is among the leading causes of avoidable death among people who inject drugs (Degenhardt & Hall, 2012; Mathers et al., 2013). Access to evidence-based treatment, including medication-assisted therapy, helps prevent drug-related deaths and improve the health and well-being of people with opioid use disorders. According to the latest UNODC World Drug Report (2021), on a global average, only one in eight people in need of treatment have access to it.

Naloxone (N-allylnoroxymorphone) has been used in opioid overdose management for over 40 years, with minimal adverse effects beyond the induction of opioid withdrawal symptoms. It is a semisynthetic competitive opioid antagonist with high affinity for the μ opioid receptor. It rapidly displaces most other opioids from opioid receptors, and if given soon enough, it will reverse all clinical signs of opioid overdose. It can be administered by a variety of routes including intravenously, intramuscularly, subcutaneously and intranasally. It carries no potential for abuse, although high doses may lead to the development of opioid withdrawal symptoms. Although naloxone is on the WHO Model List of Essential Medicines, it is not always available on site when most needed. In line with the WHO guidelines on "Community management of opioid overdose", the UNODC-WHO Stop-Overdose-Safely (S-O-S) project delivered training on overdose management, including naloxone provision to potential first responders: people who use drugs, their peers and their family members.

Recommendations of WHO Guidelines on Community management of opioid overdose (2014)

1. People likely to witness an opioid overdose should have access to naloxone and be instructed in its administration to enable them to use it for the emergency management of suspected opioid overdose.
2. Naloxone is effective when delivered by intravenous, intramuscular, subcutaneous and intranasal routes of administration. Persons using naloxone should select a route of administration based on the formulation available, their skills in administration, the setting and local context.
3. In suspected opioid overdose, first responders should focus on airway management, assisting ventilation and administering naloxone.
4. After successful resuscitation following the administration of naloxone, the level of consciousness and breathing of the affected person should be closely observed until full recovery has been achieved.

CONCLUSIONS

The S-O-S project was successfully implemented in three Central Asian countries (Kazakhstan, Kyrgyzstan and Tajikistan) and Ukraine. Rapid distribution of take-home naloxone (THN) was achieved, with in excess of 14,000 potential opioid overdose kits distributed within the eight-month implementation phase. The kits were distributed to a variety of potential overdose witnesses, including those in key risk groups such as people who consume opioids.

The process evaluation clearly demonstrates the feasibility of S-O-S project implementation in different countries with different health systems, cultures, religions and drug markets.

The process evaluation also showed how the S-O-S project and its implementation was considered acceptable to stakeholders ranging from people who use drugs through to health and law enforcement officials. However, the implementation of the project was seen as more than merely acceptable, with reported benefits of participation described in the qualitative evaluation that match the impacts stated in other studies internationally (Olsen et al., 2017).

Table 2. Programme implementation measures for the S-O-S project across project countries

Program dimensions	Overall	Kazakhstan	Kyrgyzstan	Tajikistan	Ukraine
N Level III Trainers trained	224	110	54	20	40
N Witnesses trained	14,263	3,055	4,578	4,000	2,630
% female witnesses	24.9	20	27.5	23	33.3
% opioid consumers	70.2	79	89	73	86
% peers/family members	14.8	12	9	17	12
% health workers	9.8	9	2	10	2
N kits distributed	16,278	3,700	4,578	4,000	4,000
N Refill kits requested	1,328	776	422	537	115

The cohort study used to evaluate S-O-S impact showed the clearly positive results of the project in key domains. First, the S-O-S training delivered to participants in the study demonstrated that the benefits of the training, both in terms of attitudes towards opioid overdose and knowledge of the subject, across all participant groups. These findings are consistent with previous research on similar THN programmes (Dietze et al., 2018). Importantly, measures of knowledge of opioid overdose were almost perfect (near measure ceiling) at the follow-up to the training, with knowledge enhancement most evident among those showing the lowest knowledge at baseline.

The cohort study shows that overall the target of 90 per cent of programme participants using naloxone at witnessed overdoses was achieved across almost all countries. In almost all instances the victim was reported to have survived. These findings are important and demonstrate that implementation of the S-O-S intervention under the current delivery framework can have an impact on opioid overdose in the four study countries in line with stated WHO-UNODC targets.

S-O-S INITIATIVE

In order to promote the expansion of the community management of opioid overdose, the Stop-Overdose-Safely Initiative was launched by UNODC and the World Health Organization (WHO) at the 2017 Commission on Narcotic Drugs. In line with the WHO (2014) guidelines on "Community management of opioid overdose", this initiative aims to save lives by promoting access to naloxone and by training potential first responders (including peers and family members) in overdose management. It also aims to support Member States in their efforts to develop policy and legal frameworks for the community management approach to overdose. A further aim of this initiative is to mobilize and support people likely to witness an overdose in the community, with particular focus on people who use drugs, their peers and family members. The ultimate goal is to contribute towards reducing deaths caused by preventable opioid overdoses.

Figure 1. S-O-S 90-90-90 target



The S-O-S initiative supports people likely to witness an overdose in the community, with a focus on people who use drugs, their peers, as well as family members with take-home naloxone (THN) programmes that include training, provision of naloxone and linkage with treatment services. Moreover, it encourages broad partnerships between national governments, regional organizations, research institutes, civil society, interested funding agencies and other entities to work towards the 90-90-90 global implementation target, set by the initiative as a joint point of reference (figure 1).

Table 3. Training impacts indexed by pre-post change among cohort study participants

Measure	Improvement PWID n=1125	Improvement Non-PWID n=521
OAS score change (mean):		
Total	9*	14*
Competence	6*	9*
Concerns	3*	5*
Readiness	0	-1*
BOOK score change (mean):		
Total	2.1*	4.9*
Opioid knowledge	0.4*	1.3*
OD knowledge	0.8*	1.8*
OD response	0.9*	1.8*

Note: * p<0.05.

The cohort study was not designed to specifically measure carriage of naloxone by potential witnesses, although this is noted as a key parameter in WHO-UNODC targets and considered a part of the so-called naloxone cascade of care (Tobin, Clyde, Davey-Rothwell, & Latkin, 2018). Low rates of naloxone carriage, such as those observed in this study have been previously noted (Tobin et al., 2018). Future work should examine whether alternative measures of naloxone access can better capture naloxone availability for opioid overdose response than the carriage measure used in the current study.

Table 4. Follow-up THN measures among cohort study participants with a history of injection drug use by country

Measure	Total (n=1388) % (95%CI)	Kazakhstan (n=341) % (95%CI)	Kyrgyzstan (n=349) % (95%CI)	Tajikistan (n=356) % (95%CI)	Ukraine (n=342) % (95%CI)
Witness overdose since baseline	34.2 (32.1-37.1)	49.8 (44.6-55.2)	32.4 (27.7-37.5)	19.9 (16.1-24.4)	36.6 (31.4-41.8)
Overdose response (at witnessed overdose)	(n=479)	(n=170)	(n=113)	(n=71)	(n=125)
Used naloxone at witnessed overdose (95% CI)	89.1 (86.0-91.6)	89.4 (83.8-93.2)	89.4 (82.2-93.9)	100 (90.5-99.8)	82.4 (74.7-88.2)
Victim survived	98.3 (96.6-99.2)	98.8 (95.3-99.7)	100 (90.5-99.8)	98.6 (90.5-99.8)	95.9 (90.6-99.8)
Other program variables					
Still have naloxone from enrolment	64.7 (62.2-67.2)	45.2 (39.9-50.5)	52.7 (47.5-57.9)	88.8 (85.0-91.2)	71.4 (66.4-75.9)
Carried naloxone past three days	36.5 (33.9-39.1)	25.0 (20.7-29.9)	14.0 (10.8-18.1)	88.7 (84.9-91.6)	16.6 (13.0-20.9)

Although the S-O-S implementation study was not intended to measure the impact of THN distribution on opioid overdose mortality in the four countries, it nevertheless demonstrated high rates of naloxone usage at witnessed overdoses. Extrapolation of the naloxone use figures from the cohort study (31 per cent) to the entire S-O-S project sample of 14,263 would suggest that the implementation may have resulted in naloxone administration by as many as 4,388 individuals. Modelling work from British Columbia suggests that there is "one averted death per 11 [95% CRI = 10-13] THN kits used". If this figure can be generalized to the settings of the S-O-S project, it would then suggest that some 398 lives may have been saved.

S-O-S MULTISITE PROJECT

Within the framework of the UNODC-WHO S-O-S initiative, an "S-O-S multisite project on community management of opioid overdose including the use of naloxone" was designed to demonstrate the feasibility and public health impact of the implementation of an opioid overdose intervention in low- and middle-income countries, specifically in Kazakhstan, Kyrgyzstan, Tajikistan and Ukraine.

In line with the WHO (2014) guidelines on "Community management of opioid overdose", the project aimed to prevent opioid overdose by promoting access to naloxone and the training of potential first responders in overdose management and thereby evaluate its feasibility and impact. The ultimate goal is to contribute towards reducing deaths due to preventable opioid overdoses.

Evaluation of the S-O-S project was undertaken through a mixed-methods study, comprising a process evaluation, qualitative data collection and a cohort study. The project intervention was rolled out at a city level, with at least one participating city per country. The intervention included two major components: (1) a short (15-30 min.) training on opioid overdose recognition and response including overdose management with the use of naloxone, and (2) the supply of a specially designed THN kit.

Specific objectives of the project included the following:

1. Train up to 4,000 potential opioid overdose witnesses in each participating country in opioid overdose prevention and management, including the use of naloxone
2. Distribute THN kits to trained potential overdose witnesses
3. Identify implementation barriers and facilitators
4. Evaluate the effectiveness of training and naloxone distribution and its impact on overdose response
5. Consider any other impacts where possible

The project involved four main phases conducted over 2016-2021 as shown in table 1. A description of each phase is provided below.

Table 1. Phases and timelines related to the S-O-S project

May-December 2016	January 2017-June 2019	June 2019-July 2020	July 2020-July 2021
ASSESSMENT PHASE	PREPARATORY PHASE	IMPLEMENTATION PHASE	EVALUATION AND DISSEMINATION PHASE
<ul style="list-style-type: none"> Governmental support Key-stakeholders' meetings Study protocol development Identification and engagement of national counterparts 	<ul style="list-style-type: none"> Situational analysis/site visits/legal reviews Finalization of study protocol Ethics approval(s) for the study Development of training materials Trainings of national partners 	<ul style="list-style-type: none"> OOD training and dissemination of naloxone Finalization of data collection Monitoring and evaluation 	<ul style="list-style-type: none"> Data analysis Development of national and international reports Dissemination of results Assuring sustainability and scale up

FUTURE DIRECTIONS

While opioid overdose management and prevention programmes involving THN have become available in many countries, they are still lacking in settings with fewer resources (Strang et al., 2019). The S-O-S project has demonstrated that a community management approach to opioid overdose can be successfully implemented in low- and middle-income countries in line with WHO recommendations. Future replication studies in other low- and middle-income countries would be beneficial, and interest has been expressed to UNODC and WHO by countries not currently participating in the project.

More advanced study designs (such as randomized controlled trials and analysis of data from routinely collected health data) aimed at systematically demonstrating the impact (including in terms of lives saved) of the community management approach to opioid overdose in low- and middle-income countries would be desirable. Improved measurement of naloxone carriage should feature in these studies.

However, reliable data on opioid overdose incidence remain limited globally, meaning the number of overdoses is likely to be underreported at national levels. Improved measurement of overdose in national and regional health data reporting systems as well as the broader development of drug information systems is needed.

The sustainability of the community management approach to opioid overdose, including the use of take-home naloxone, remains a challenge even in countries currently participating in the S-O-S project. The implementation of the current project was focused on the city level and, given the positive outcomes, scale-up to a country level with a strong evaluation component would be desirable.

While naloxone is on the WHO Model List of Essential Medicines (WHO, 2019), not under international control and available for affordable prices, access remains challenging in many jurisdictions. Naloxone is often not continuously registered at national level and has usually been purchased under emergency medication import frameworks and is not available for over-the-counter

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MAJOR ACHIEVEMENTS

As far as UNODC and WHO are aware, this is the first time that the feasibility of take-home naloxone schemes could be systematically evaluated and demonstrated in low- and middle-income countries.



FURTHER INFORMATION

Summary Report - UNODC-WHO Stop-Overdose-Safely (S-O-S) project implementation in Kazakhstan, Kyrgyzstan, Tajikistan and Ukraine:

Web story: [QR code]

A Film about Life: [QR code]

CONTACT:

For further information on the S-O-S Initiative and for countries interested in joining the study with their own resources, please contact:

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purchase in many countries. These issues present major barriers to the procurement of this life-saving medication in the community. Relatively simple national actions and positive policy developments could play a significant role in increasing access to naloxone. For example, this was observed as a positive unintended consequence of the S-O-S project when Ukraine amended its legislation making naloxone an over-the-counter medication.

WHO and UNODC recommend the use of a range of treatment options for opioid dependence in the "International Standards for the Treatment of Drug Use Disorders" (UNODC/WHO, 2020). Opioid agonist maintenance treatment (with medicines such as methadone and buprenorphine) offers the strongest evidence of effectiveness and cost-effectiveness. Further options include psychosocial treatment and support, and pharmacological treatment with opioid antagonists. WHO and UNODC support countries in their attempts to improve the coverage and quality of treatment programmes for opioid dependence and to introduce them where they do not already exist.

In the framework of the UNODC-WHO Programme on Drug Dependence Treatment and Care, UNODC and WHO will continue working with Member States to provide technical assistance in line with the Sustainable Development Goal target 3.5 on strengthening the prevention and treatment of substance abuse, including narcotic drug abuse and the harmful use of alcohol. This includes the implementation of existing guidance documents and technical tools, such as the WHO/UNODC International Standards for the Treatment of Drug Use Disorders (UNODC/WHO, 2020). Moreover, the S-O-S training package and materials will be made available for training on emergency management of opioid overdose with THN.