

# NATIONAL IMPLEMENTATION OF NALOXONE TRAINING COURSES AT DRUG TREATMENT CENTERS WITH SUBSTITUTION TREATMENT

2019-2022

SUMMARY AND RECOMMENDATIONS



April 2023

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## SUMMARY AND RECOMMENDATIONS

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## Preface

This report concerns the national project, "**Coordination of the Prevention of Opioid Overdose Deaths with Naloxone 2019-2021**" (extended until the end of 2022).

The project was initiated in 2019 and commenced in 2020. It is built upon the experiences of the overdose training concept "Red Liv," developed between 2010 and 2018, as one of the first projects for preventing opioid overdose deaths in Europe.

In Red Liv, a practical model has been developed to educate drug users in managing overdose cases through basic life-saving techniques and the administration of the antidote naloxone as a nasal spray. The project, in three phases, has investigated the relevance and viability of the concept in various municipal and NGO contexts.

Red Liv is structured with two levels of education, proven to be scalable from internal municipal to nationwide implementation. The first level is a trainer education program focusing on knowledge about opioid overdoses and treatment, as well as training others in overdose management. The second level involves training individuals who may encounter opioid overdoses in their daily lives to practically treat the overdose and seek assistance.

The dissemination of the Red Liv training method has occurred in later phases through a central unit developing trainer education and subsequently training local trainers. These trainers then educate drug users and others to be able to provide treatment, known as helpers. The method, known since the 1970s as the Train-The-Trainer model, is described further in this report<sup>1</sup>.

Similar to previous overdose projects, we have trained relevant personnel in overdose prevention using the morphine-blocking substance naloxone. Unlike before, we have not trained helpers but have focused on educating the trainer level in all Danish municipalities with substitution treatment, enabling these trainers to educate drug users at the municipal level.

The report is divided into two parts:

Part 1. The project's foundation, deliverables, data, and description of data collection.

Part 2. The practical implementation of the Train-The-Trainer concept's dissemination in Danish municipalities from 2020 to 2022.

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<sup>1</sup> The Train-the-Trainer method

Except for a brief section, no analysis of the biological and pharmacological aspects of overdose treatment has been conducted. The focus has been solely on the structural municipal landscape concerning substance abuse treatment, the dissemination of overdose training, and opportunities and barriers related to a future Train-The-Trainer model.

We would like to express our gratitude to the many leaders and employees in the municipalities who, despite isolation lockdowns and challenging conditions in general, provided facilities and time for the trainer education's 85 courses in 70 municipalities. Thanks to the management of the Center for Vulnerable Adults and Families for their willingness to support the project's implementation.

Last but not least, we must express our gratitude and remember the true key figure behind overdose training with naloxone, namely the chairman of the User Association of Active Drug Users, Jørgen Kjær, whom we lost in 2021. He is missed.



*Former Chairman of the Association of Active Drug Users, Jørgen Kjær. The first naloxone trainer in Denmark.*

Employees in the Red Liv Coordinating project:

Coordinator 2020 and 2021, Sine Lykke Bordorff, nurse, and M.A. in Social Work

Coordinator 2022, Iben Kiellberg, midwife, and M.Sc. in Health Promotion

Copenhagen, April 16, 2023

Henrik Thiesen, Chief Physician, Center for Vulnerable Adults and Families, Copenhagen City, Red Liv



## Summary

Red Liv has been developing lifesaving training in combination with the antidote naloxone since 2010. The project, initially anchored in Vesterbro, Copenhagen, has evolved over three phases to include both rural and urban municipalities. The use of naloxone as a nasal spray, coupled with training in identifying opioid overdoses and providing life-saving assistance, has been crucial throughout the development. The first cross-municipal project commenced in 2013, making it a decade of involvement for some municipalities in the naloxone training program this year.

Red Liv in Copenhagen Municipality has played a central role in developing the training concept and the use of nasal spray, initially as specially imported products and, since 2018, with fully developed and tested products tailored to drug users.

In November 2018, a supplement to the guidelines for doctors treating opioid-dependent patients with substitution treatment was introduced. According to the amendment, doctors were obligated to ensure that *"everyone in municipal treatment for heroin and other opioids misuse has the opportunity for a course in first aid and the use of the antidote naloxone, along with the provision of a naloxone kit."*<sup>2</sup>

In 2019, funds were allocated to a coordinating unit to support the development of training in municipalities with substitution treatment. In response to a request from the Danish Municipalities' Association (KL) to Copenhagen Municipality, Red Liv became the coordinating unit in January 2020.

The coordinating unit, supported by experiences from previous projects and in line with recommendations from prior Red Liv reports, differed from earlier projects. Notably, DUT funds were provided to individual municipalities, and there was no formal organization behind both the central and municipal units.

After a brief start-up and development phase in 2020, along with the identification of municipalities with in-house substitution treatment, the coordinating unit was affected by the Covid-19 pandemic, which made training activities impossible.

The first course was conducted on May 10, 2020, in Nykøbing Falster, and a total of 29 courses were conducted nationwide throughout the year. Despite periods of lockdowns and isolation requirements, there was relatively constant activity throughout the year. The courses are systematic sessions lasting 4

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<sup>2</sup> <https://www.sst.dk/-/media/Udgivelser/2017/Supplement-om-naloxon-til-vejledning.ashx>

hours, covering practical and theoretical elements of opioid overdoses. After the course, each trainer is capable of conducting a helper course for drug users, meeting WHO's standards for overdose treatment.

Local trainers have been supported subsequently by the coordinator, and some have been interviewed about the opportunities and barriers in establishing and conducting local courses. Unlike previous Red Liv projects, the coordinating unit has only been responsible for the trainer education and focused on supporting local development.

All municipal trainers are equipped with a package containing teaching materials and practical tools to conduct helper courses locally. They have had access to support and guidance from the coordinator throughout the project period.

In addition to the teaching package, everyone has been informed and practically assisted in the hands-on management of the course and involvement of the municipality's substance abuse doctor. Until April 2022, all helpers were appointed as the doctor's assistants in dispensing naloxone nasal spray, requiring a certain strict systematics in registration and handling of the spray.

2021 began with another Covid outbreak, but activity resumed from March. Throughout the year, efforts were made to strengthen internal cohesion in the municipalities, and many municipalities underwent a new round of trainer education.

During the year, various discussions were held to explore the establishment of a nationwide network to replace the coordinating unit. Several proposals are described in the chapter "Establishment of Structure for Naloxone Trainers," but typically, all proposals require active efforts from key individuals who are not immediately identifiable.

An intermunicipal network, at best, can maintain the current professional status, but there is no structure for training new trainers or upgrading knowledge. A functioning network requires persistent efforts. After an additional 39 trainer courses in 2021 and a total of 68 courses from May 2020 to December 2021, the coordinating unit was scheduled to cease operations at the end of 2021. However, it was agreed to utilize the available resources in an extension in 2022 if it was possible to hire a coordinator on a short-term basis.

In April 2022, new legislation was implemented that eased access to naloxone nasal spray for substance abuse centers. It is still prescription medication, but it can now be ordered for naloxone training programs by nurses, and the delegation obligation is replaced by handling instructions.

In May 2022, Red Liv was restarted with a new coordinator. In this part of the project, efforts were made to update teaching materials, train new trainers, and simultaneously upgrade those already trained in line with the new rules. In total, 17 courses were conducted in 2022.

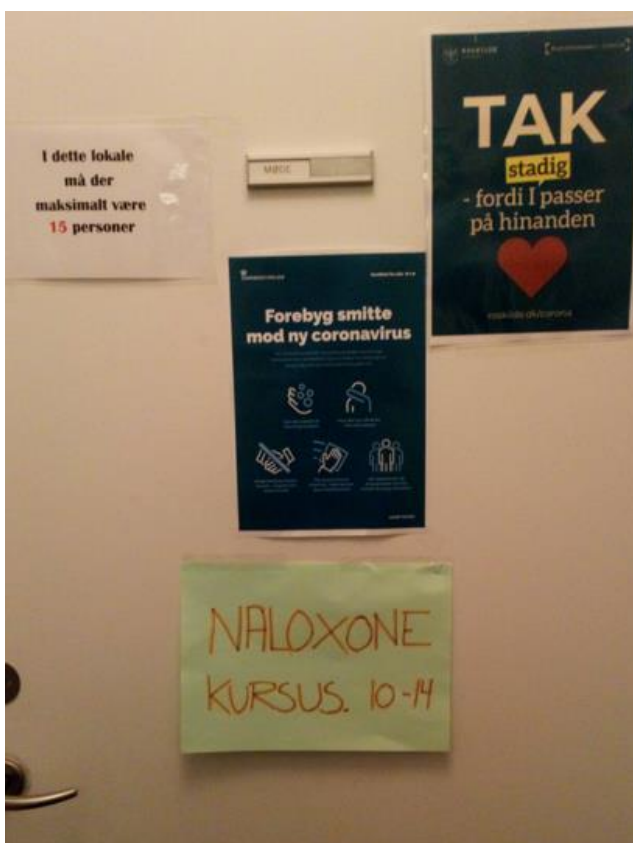
Originally, Red Liv committed to training 324 trainers in 50 courses. In the period 2020, 21, and 22, a total of 547 trainers were trained in 67 municipalities and by 5 private and regional providers of substitution treatment through a total of 85 courses nationwide.

Denmark currently has an extensive effort in municipalities compared to many other countries, but there is no retention of quality, and the 550 trainers cannot be supported. With good cooperation with management, some trainers can maintain their positions, but the helper training disappears with the employee. The idea of peer training is illusory except in very large municipalities.

Approximately 10% of trainers change jobs annually, and even under the current conditions with direct support, there is no consideration of handing over the function.

One municipality did not want further trainer courses in September-October 2022, as they had the 2 employees they wanted. In November, both had left the substance abuse center, and the municipality is now without trainer capacity as we could not conduct another course before the next closure.

Centre for Alcohol and Drug Research, in collaboration with Red Liv, has attempted to create an overview of the training of helpers in municipalities, but it is evident that, despite efforts to create a uniform registration model, different practices can easily arise in municipalities, resulting in uncertain registration of helpers.





## Background and Recommendations

### Background:

With this fourth version of the overdose training model Red Liv, the project has also gone through four phases, from a pilot study, through two implementation projects for urban and rural municipalities, to national coordination. Many countries in Europe have introduced naloxone training programs in the last 10 years, and Red Liv has, from 2010 onwards, inspired naloxone training programs in Norway and Sweden, which have evolved with sustained funding.

The coordinating unit has demonstrated that it is possible to quickly and simply establish a network of trainers, but the network is not self-sustaining. There is insufficient support from the leadership in most municipalities, not for negative reasons, but because there are many other tasks to be addressed, and employees are challenging to recruit and retain in many parts of the country. The substance abuse field is only a small part of the municipality's economy, and employees engaged in substitution treatment are often occupied with other responsibilities. With these limitations, it is unrealistic to imagine that a network functions, even locally, if there is no person responsible for ensuring its functioning – everyone's responsibility is no one's responsibility.

The recommendations from previous projects have been relatively consistent, with some being followed, and others losing relevance over time.

In Red Liv II, the recommendations included:

- **The model for prevention with Naloxone should be made permanent nationwide.**
- **The model for prevention should be made widely accessible.**
- **Educational initiatives should be flexible, accessible, and anchored in local structure and culture.**

These recommendations have largely been implemented in the current model.

Other recommendations arose with the introduction of new dispensing forms in 2018 and changes in legislation in 2022. Although the prescription status has not changed per se, nasal spray and its usage have been made more accessible.

- **Equipment for overdose treatment should be simplified to ensure correct usage.**
- **Overdose prevention should primarily, as far as possible, be done through nasal spray.**
- **The prescription requirements for Naloxone should be modified, and nasal spray should be made more accessible, possibly over-the-counter.**

- **Development of specialized Naloxone equipment for nasal spray for laypersons.**

In Red Liv III, some of the recommendations were:

- **Overdoses resulting from opioid use do not disappear and need to be addressed nationally.**
- **Prevention courses for opioid overdoses should be widely implemented.**
- **Broad education is necessary to reach a larger audience.**

Here too, the recommendations directly led to the model that is now implemented in municipalities.

All previous recommendations have also involved a coordinating unit to ensure quality and consistency in the overall national offering. The quality of resuscitation procedures is ensured by providing proper training to individual drug users, encompassing general methods and an understanding of overdose risks. Focusing solely on the administration of naloxone nasal spray is, in our opinion, a negative oversimplification of the problem.

This report demonstrates that a national naloxone training program can be relatively easily established and operated, but it is also vulnerable if central continuity is not ensured.

## Recommendations:

- 1. To ensure a continued high quality in the trainer corps, it is recommended that there is ongoing development and updating of educational materials.**
  - a) Materials should align with national legislation and international standards and be easily accessible for each trainer.
  - b) The trainer corps does not develop on its own but is experientially receptive to learning and information that improves the daily lives and health conditions of drug users.
- 2. It is recommended to continuously ensure a stable renewal of the trainer corps.**
  - a) A simple count of trained trainers shows that 13% have been replaced from May 2020 to October 2022.
  - b) Trainers who do not continuously maintain their skills tend to stop conducting courses, but ongoing updates and support can break this trend.
- 3. It is recommended to continue allocating funds for central coordination regarding the trainer network.**
  - a) It is still considered essential for the development and maintenance of consistent quality in overdose treatment nationwide that trainers undergo standardized and updated training. Training for general life-saving instructors is subject to stricter requirements and a high degree of systematicity. Allowing overdose treatment to be left to future peer training would be a step in the wrong direction.
  - b) Some municipalities have so few resources and staffing that it is not feasible to sustain the function without support.

4. **It is recommended that the trainer corps is also equipped to contribute to the prevention of overdose issues in other drug user groups beyond individuals in substitution treatment.**
  - a) Novel psychoactive substances (NPS) opioids and known painkillers seem to play a larger role in the future risk of opioid overdoses. This means that younger individuals, who may not necessarily perceive themselves as at risk, may come into contact with highly potent substances, putting them at high risk of overdoses and overdose deaths.
  - b) While heroin use is declining, other substances are more prevalent, and it has become more common to mix substances, posing a risk of opioid contamination. There are recurring stories of stimulant users overdosing on opioids because it is mixed with substances like cocaine, which is not perceived as particularly dangerous.
  
5. **It is recommended that the trainer corps be updated to participate in detecting NPS in a national 'sentinel network.' In that case, Denmark would be the first to have such a network.**
  - a) There is currently a spread of opioids in tablet form in recent years, both in Europe and anecdotally in Denmark, with the emergence of stronger opioids, such as Nitazenes, which in some cases can be stronger than fentanyl. The impact on the young population, who may not necessarily see themselves as high-risk users, is uncertain, and such information is not automatically reported from municipalities.
  - b) The experience from Red Liv indicates that local staff in substance abuse centers have a good understanding of local drug trends, but they have no place to share that knowledge. During the preparation of this report, we became aware of a case from Fredericia in 2016 where four deaths occurred due to fentanyl overdoses – information that was not conveyed to Red Liv III when it started later in the year.
  - c) Constantly, new opioids are under surveillance in the European early warning network EWS, and information to that network is currently retrospective in connection with accidents and poisonings. By involving a nationwide network, information could be incorporated into national and transnational action programs much earlier. d. Besides national surveillance, the trainer network can also contribute to faster regional information dissemination if a new type of substance or specific risk practice spreads.
  
6. **It is recommended that the registration of helpers and overdoses, if a central overview of developments is still desired, be significantly simplified, possibly in the form of an anonymized reporting app.**
  - a) In connection with previous versions of Red Liv, electronic reporting has been used, which has succeeded to some extent with a high degree of supervision and direct assistance to each trainer during registration. In the coordinating unit, we have experienced that the expansion of the previous projects to more than 10 times and involvement of a much more diverse group of municipalities has made the existing registration method unmanageable. By greatly simplifying the reporting procedure, almost real-time data could be obtained, supporting a sentinel function.
  - b) Registration in an app can be combined with geodata, without personally identifiable data, which can help facilitate voluntary registration and thus also registration of overdose treatment.



## Opioids and Overdose Situation in Europe and Denmark

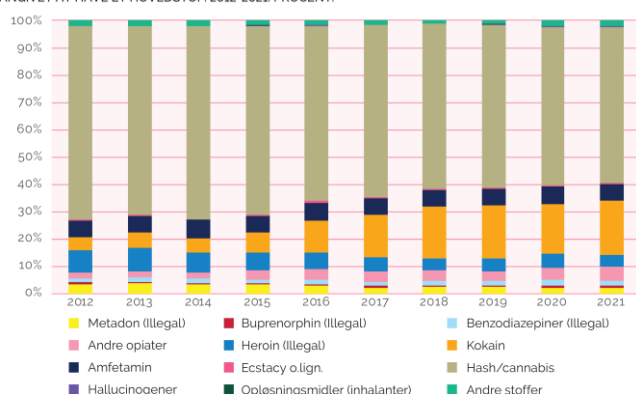
Overdose deaths represent the tip of an iceberg, with an estimated 2-4% of overdoses resulting in fatalities. The remaining 96-98% lead to unconsciousness and likely oxygen deprivation. The issue of non-fatal overdoses has been detailed in Red Liv II and III reports. While the number of people seeking treatment for opioid use has steadily declined over the past 20 years, there has been a consistent increase in hospital contacts due to opioid poisoning in the last decade, as reported in the Danish Drug Situation Sub-report 4, Health-Related Consequences<sup>3</sup>.

As mentioned, there is a general declining trend regarding heroin as the primary substance in treatment. When comparing all individuals in treatment with newly enrolled ones, the change is driven by a decrease in new enrollments with heroin as the primary substance. In contrast, there is a slight increase in the proportion of individuals using "other opioids."

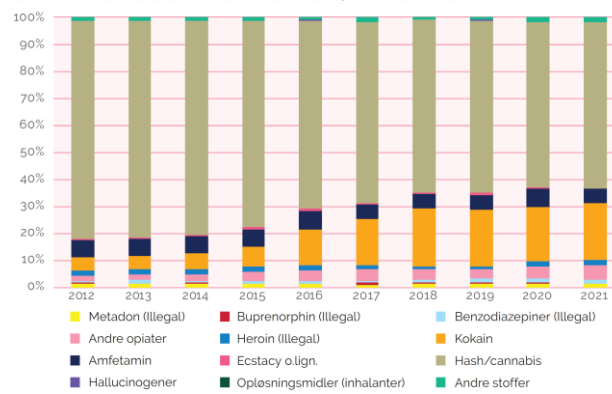
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<sup>3</sup> <https://www.sst.dk/da/Udgivelser/2021/Narkotikasituationen-i-Danmark---delrapport-4>

FIGUR 2.1 HOVEDSTOF BLANDT PERSONER INDSKREVET I BEHANDLING I DE PÅGÆLDENDE ÅR OG HAR ANGVIVET AT HAVE ET HOVEDSTOF. 2012-2021. PROCENT.



FIGUR 3.1 HOVEDSTOF BLANDT DEM, DER ER INDSKREVET I BEHANDLING, SOM HAR ANGVIVET AT HAVE ET HOVEDSTOF OG IKKE TIDLIGERE HAR VÆRET I BEHANDLING. 2012 - 2021. PROCENT.



Source: Substance Abuse Treatment – Demand and Availability. The Drug Situation in Denmark - Subreport 3, Danish Health Authority 2022.

There is no possibility to track the number of non-fatal overdoses unless the individuals who overdose are detected and admitted for acute treatment. Among injection drug users, there is often a desire to reach a state on the verge of overdose for an intense high, and therefore, an overdose that does not end fatally is likely not to be recorded. The biology of overdose is detailed in part 2 of the Red Liv III report.

Red Liv was originally established as a municipal/NGO collaboration between the Municipality of Copenhagen and the User Association of Active Drug Users. In all subsequent editions of Red Liv, there has been a focus on collecting both local and general knowledge about opioid overdoses and their treatment in various settings.

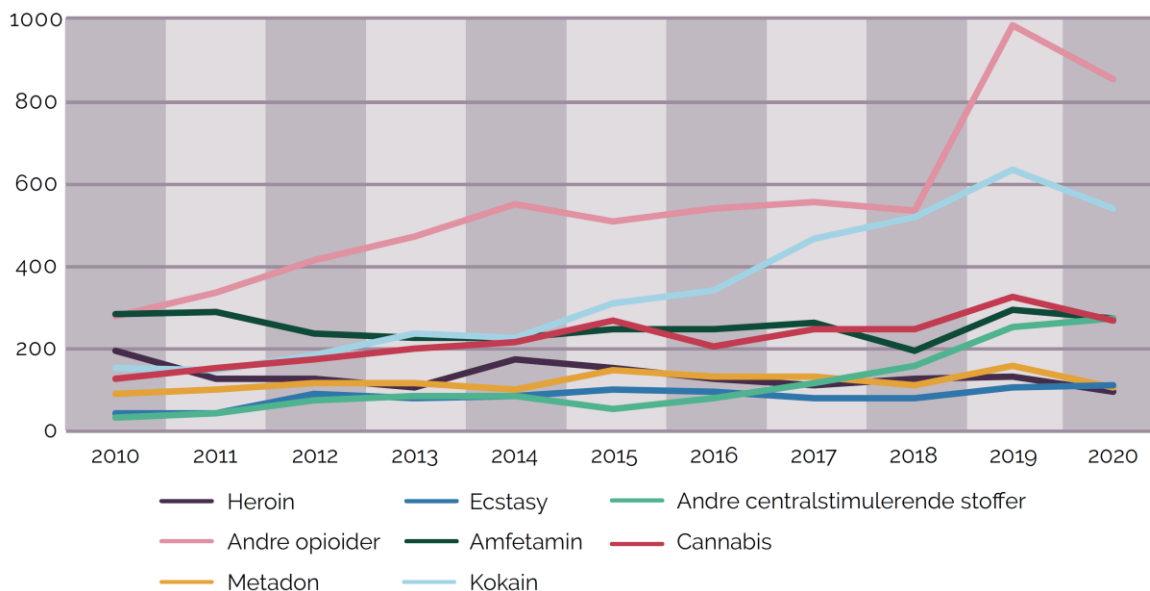
One way to assess the general drug situation and the use of opioids, in particular, is through the European<sup>4</sup> and Danish drug reports and the background knowledge contributed by Red Liv over the years. The issue with drug reports, in general, is that they are retrospective and only reflect the portion of individuals with substance issues who come into contact with health systems or the police, while the majority of substance use occurs in social environments and among regular users who have no intention or desire to encounter those authorities.

The closest one can get to a picture of non-fatal overdoses would be poisoning cases treated by healthcare professionals where the cause is known. The number of poisoning cases involving illegal substances and hospital contacts has remained stable for most groups throughout the 2010s, but for cocaine and other opioids besides heroin and methadone, there has been a stable increase until 2018, where there is a sudden rise in opioid poisonings. In the Drug Situation in Denmark - Subreport 4, reservations are made for

<sup>4</sup> [https://www.emcdda.europa.eu/publications/edr/trends-developments/2022\\_en](https://www.emcdda.europa.eu/publications/edr/trends-developments/2022_en)

changes in the registration method, but despite that, there is a stable increase in poisoning cases for these two types and a minor, upward trend for "other central stimulants."

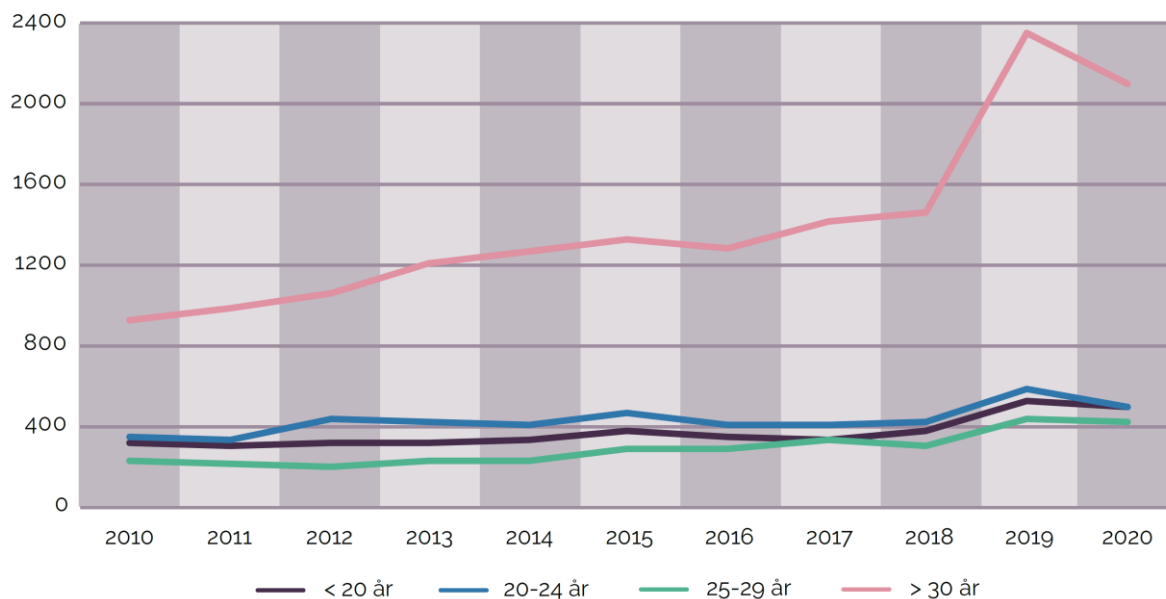
FIGUR 2.1. UDVIKLINGEN AF SYGEHUSKONTAKTER EFTER FORGIFTNINGER MED ILLEGALE STOFFER



Source: *The Drug Situation in Denmark - Subreport 4, Health-related Consequences. Danish Health Authority 2021.*

The age group that dominates the poisoning statistics is the >30-year-olds, and this group also appears to be experiencing a significant increase in poisoning cases in recent years. While there is indeed an increase in all age groups, it is particularly pronounced for the group over 30.

FIGUR 2.2. UDVIKLINGEN AF SYGEHUSKONTAKTER EFTER FORGIFTNINGER, FORDELT PÅ ALDERSGRUPPER



Source: *The Drug Situation in Denmark - Subreport 4, Health-related Consequences. Danish Health Authority 2021.*



Although the two curves 2.1 and 3.1 cannot be directly compared, the increase in opioid poisonings completely overlaps with the rise in individuals over 30 years old.

Individuals who experience poisoning with illegal substances typically constitute a much broader group than the known group of individuals in treatment for substance-related issues. Among individuals seeking treatment for substance-related problems, the proportion reporting illegal heroin and methadone has been consistently declining over the past 10-15 years.

While the increase in cocaine poisonings corresponds to a rise in treatment systems, there is no corresponding increase in opioids, which may be due to differences in injuries and addiction potential. In the end, the dynamics between the groups introduced to opioids, the types of opioids used, their sources, and who develops dependence and seeks treatment are not clear but influenced by various societal factors and generational differences interacting with each other.

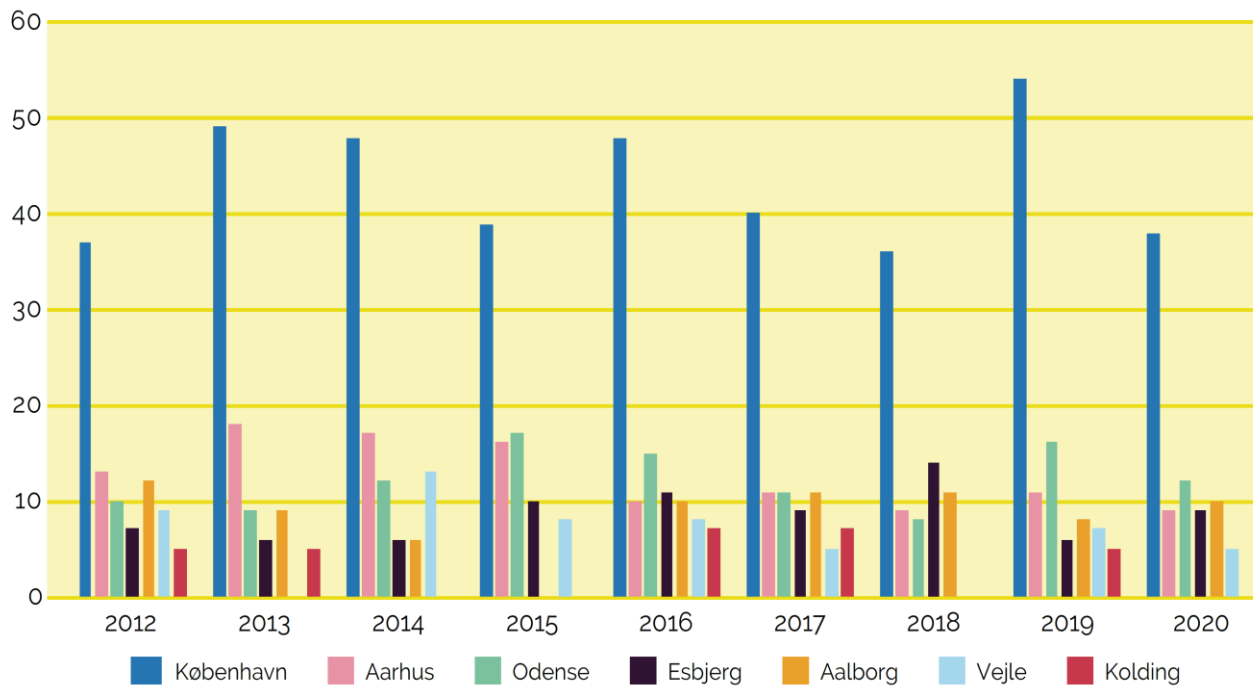
Among the total population using illegal substances of any kind, only a small proportion will develop dependence and escalating risk behavior. However, the risk of opioid overdose and poisoning is also significant among recreational users.

The closest one can come to a conclusion regarding the demographics of opioid use, poisonings, and overdoses is that there may not necessarily be a connection between the different groups, either temporally or in terms of individuals.

Among young users in treatment and anecdotally during Red Liv's training courses, there has been talk of opioid pill consumption for several years, mostly in rural communities but with increasing intensity. However, this has not manifested in overdose death statistics.

As a curiosity, it can be mentioned that overdose deaths in the City of Copenhagen have decreased in years when there has been an offer of a naloxone training program, while they have increased when the program is closed due to lack of funding.

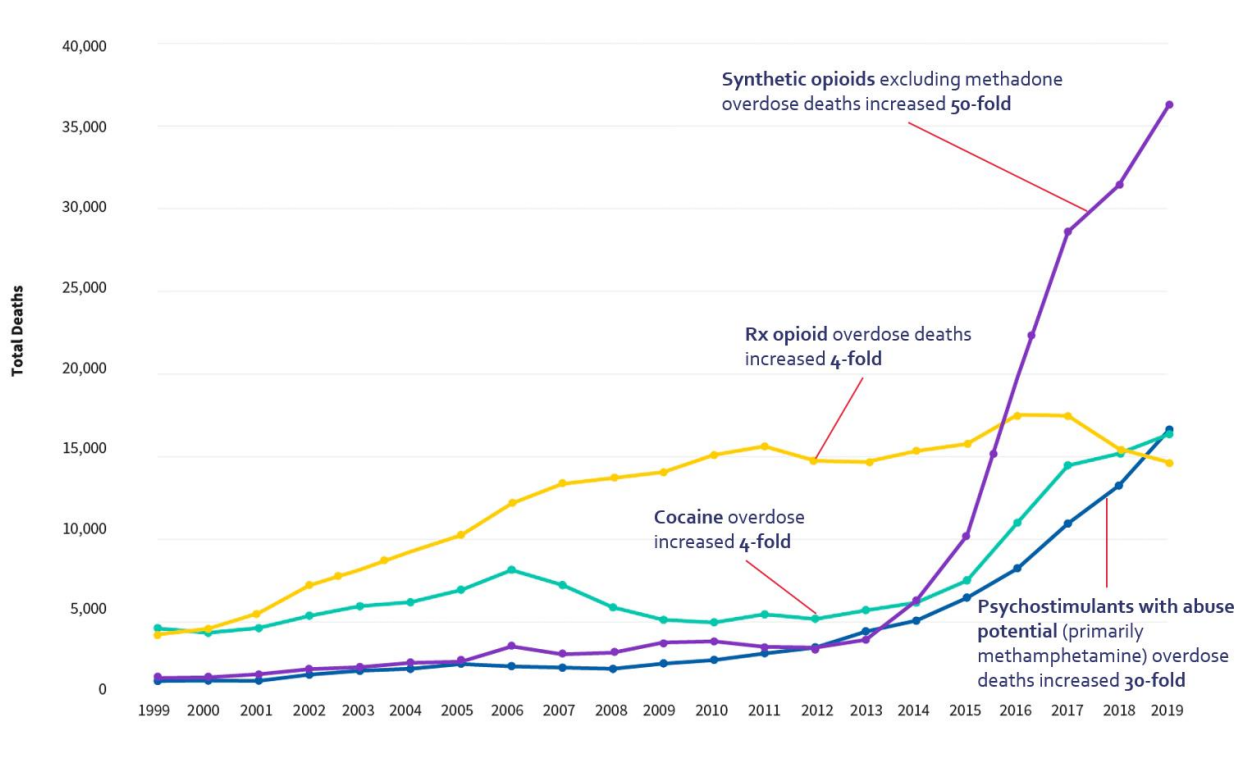
FIGUR 3. NARKOTIKARELATEREDE DØDSFALD FORDELT PÅ UDVALGTE KOMMUNER



Source: Drug-Related Deaths. Compilation and Analysis of Data for 2020. Danish Health Authority 2021.

## Fentanyls

The "overdose epidemic" in the USA has primarily been driven by the potent opioid fentanyl and stronger variants of fentanyl. The issues are described in detail in the Red Liv III report.



Source: National Vital Statistics System Mortality File<sup>5</sup>

The terrible development, which does not seem to have an end, has led to significant attention from our side regarding the situation. Since 2013, Red Liv has been trying to monitor whether there is an increasing incidence of opioids, especially the use of fentanyls, in municipalities involved in overdose rescue training. With an increased prevalence of fentanyls in the drug environment, there will be a need to upgrade the amount of naloxone available in these environments, and the risk of severe and difficult-to-treat overdoses will rise. In Red Liv's contacts with municipalities, we have not received information about strong opioids over the years, and beyond individual cases, we have not heard of a stable and increased use of fentanyl. This picture is supported by a stable number of overdose deaths in drug reports.

There has been occasional feedback from employees in municipal substance abuse centers about individual cases of ingestion of fentanyl patches, especially when smoked. Although fentanyls are very potent, there is

<sup>5</sup> <https://www.cdc.gov/nchs/nvss/drug-overdose-deaths.htm>

no recorded increase in overdose deaths associated with smoking, which could suggest that this practice is primarily seen in individuals already dependent on opioids.

It often happens that warnings are issued by the media based on local conditions and individual cases<sup>6</sup>, but in Red Liv, we have not observed a general development similar to the American one, probably because in the USA, there are social conditions and a healthcare system that does not cover all citizens, along with a trend driven by a dramatic increase in opioid prescriptions from American doctors. Additionally, the possibility of substitution treatment is significantly less than in Denmark.

An article from 2018<sup>7</sup> describes 14 cases of drug users in treatment in Fredericia with mixed use of heroin and fentanyl, and in several cases, they were not registered as such but appeared with false negative tests for fentanyl. The article recommends being aware of the prescribing pattern for fentanyl patches from the healthcare system in general to prevent spread to drug environments, but also to try to determine if there is fentanyl in drug environments by conducting more drug analyses in the addiction treatment sector. In the end, it is an economic problem for the substance abuse centers if they have to conduct more analyses.

In 2018, the Danish Health Authority warned in the document "**Strong fentanyl analogs cost lives in the drug environment**"<sup>8</sup> about new fentanyl analogs reported in Denmark and at the European level, as well as the presence of the super-potent Carfentanyl in a seizure by customs and police. There is no simultaneous increase in the incidence of overdose cases and overdose deaths in the municipalities covered by Red Liv, and we have therefore perceived the situation as managed in terms of spreading.

In the EMCDDA's<sup>9</sup> "European Drug Report 2022: Trends and Developments"<sup>10</sup> p. 36, it is written in the Danish version: "... Although heroin continues to be Europe's most widespread illegal opioid and the substance responsible for most poisoning deaths, there has been growing concern about the role synthetic opioids play in Europe's drug problem. Fentanyl derivatives are particularly worrying due to the central role this group plays in the North American opioid problem. Deaths due to fentanyl have been reported in Europe, and traditionally, fentanyl derivatives have been the most common form of opioids used in Estonia and sometimes reported by other countries. The limited available data suggest that both fatal and non-fatal overdoses related to fentanyl decreased in 2020..."

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<sup>6</sup> <https://www.dr.dk/nyheder/indland/50-gange-staerkere-end-heroin-fentanyl-fik-misbrugslaege-til-erklaere-amerikanske>

<sup>7</sup> [https://kclpure.kcl.ac.uk/portal/files/93594118/Characteristics\\_of\\_opioid\\_maintained\\_KIMERGARD\\_Accepted12April2018\\_GREEN\\_AAM.pdf](https://kclpure.kcl.ac.uk/portal/files/93594118/Characteristics_of_opioid_maintained_KIMERGARD_Accepted12April2018_GREEN_AAM.pdf)

<sup>8</sup> <https://www.sst.dk/da/udgivelser/2018/staerke-fentanyl-analoger-koster-doedsfald-i-misbrugsmiljoeet>

<sup>9</sup> [https://www.emcdda.europa.eu/about\\_en](https://www.emcdda.europa.eu/about_en)

<sup>10</sup> [https://www.emcdda.europa.eu/publications/edr/trends-developments/2022\\_en](https://www.emcdda.europa.eu/publications/edr/trends-developments/2022_en)

## NPS – New Psychoactive Substances

New Psychoactive Substances are, according to EMCDDA, defined as new narcotic or psychotropic substances, in pure form or prepared, that are not controlled by the UN's drug conventions but may pose a threat to public health comparable to that posed by the narcotic substances listed in the drug



conventions<sup>11</sup>.

In Denmark, the occurrence of NPS is monitored through collaboration between the Danish Health Authority, the National Police, the Customs and the three forensic departments in Copenhagen, Odense, and Aarhus. An annual report is publicly available<sup>12,13</sup>

NPS can be seen as elements in an ongoing battle between authorities and illegal drug laboratories, where substances are constantly produced and released that are not covered by drug legislation but have psychoactive effects. Many of these substances are not necessarily "new" but were synthesized for the first time in medical laboratories years

ago. Examples include cannabinoids, cathinones, and phenethylamines, which are known chemical products, but their effects on humans may be unknown. These substances can be mixed into other products such as ecstasy pills or sprayed on plant material like cannabis, potentially leading to a powerful effect and, in some cases, lethality.

Various dynamics, such as COVID isolation and changing approaches to online drug trade, can alter the profile of substances used, especially by recreational users outside the treatment system, leading to overdose deaths in unexpected groups. Four overdose deaths on Bornholm in 2020<sup>14</sup> received significant attention and led, among other things, to Red Liv's training of outreach workers from across Bornholm as overdose trainers in April 2021. During this course, the workers reported changed drug use patterns during COVID, particularly substances from Sweden entering the island, including stronger opioids.

<sup>11</sup> [https://www.emcdda.europa.eu/topics/nps\\_en](https://www.emcdda.europa.eu/topics/nps_en)

<sup>12</sup> <https://www.sst.dk/da/udgivelser/2022/Nye-psykoaktive-stoffer-i-Danmark-AArsrapport-2021>

<sup>13</sup> <https://www.sst.dk/da/udgivelser/2022/Narkotika-paa-gadeplan-2021>

<sup>14</sup> <https://www.weekendavisen.dk/2020-48/samfund/rus-paa-recept>

Since this is a market that may not be well-informed about changes in supplies, and the trade routes for individual users are unknown, there is a significantly greater risk that the strength and composition of what is sold may not match what is advertised.

Ritalin is known to flow into the illegal market, and for many years, painkillers and benzodiazepines have been known.

Some types of medicines may appear as "NPS" in drug environments, and because they are also known, such as painkillers, they can penetrate a market for a long time without being noticed. OxyContin is known as one of the basic causes of the overdose problem in the USA, and in recent years, especially in rural areas, stories have emerged from Red Liv's trainer courses about a significant increase in the use of OxyContin tablets, especially among younger individuals<sup>15</sup>. At the same time, we have seen an increase in the number of poisoning cases but among those over 30.

How substances spread in environments is difficult to unravel, and EMCDDA also writes in the drug report for 2022: "*... Overall, however, there are also signs that other synthetic opioids may play a more important role in drug problems in some countries. An important caveat here is that current monitoring systems may not document trends in the use of synthetic opioids well, and this is an area where monitoring capacity needs to be improved.*"

An example of "NPS opioids" could be nitazenes. The first time we encounter nitazenes in Red Liv is in connection with a training course where there is talk of a death of a 23-year-old man in the municipality the night before the course. The suspected substance is referred to as "China" or "China morphine" and is likely a nitazene bought online.

Nitazenes belong to a group of opioids called benzimidazoles, synthesized in the 1950s in the pharmaceutical industry<sup>16</sup>. Only more than 60 years later, this group appears on the illegal market in the form of etonitazene, metonitazene, and isotonitazene, and in 2019, the EMCDDA became aware of the opioid<sup>17</sup>. The group of nitazenes is further characterized in 2021<sup>18</sup>, and it has become clear that some of the nitazenes are significantly more potent than fentanyl and therefore extremely risky substances, especially as they seem to spread among groups that are not already accustomed to them. Very potent opioids

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<sup>15</sup> [https://jyllands-posten.dk/indland/ECE15411728/farlig-pilletrend-spreder-sig-og-sender-unge-helt-ned-til-13-aar-ud-i-et-misbrug-lyder-advarsel/?utm\\_campaign=Nyhedsoverblik%2009.00&utm\\_content=2023-03-29&utm\\_medium=email&utm\\_source=jp](https://jyllands-posten.dk/indland/ECE15411728/farlig-pilletrend-spreder-sig-og-sender-unge-helt-ned-til-13-aar-ud-i-et-misbrug-lyder-advarsel/?utm_campaign=Nyhedsoverblik%2009.00&utm_content=2023-03-29&utm_medium=email&utm_source=jp)

<sup>16</sup> <https://www.caymanchem.com/literature/nitazenes-emerging-benzimidazole-opioids>

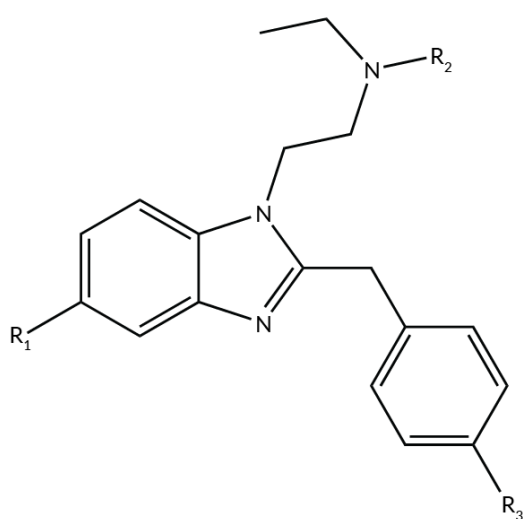
<sup>17</sup> [https://www.emcdda.europa.eu/publications/initial-reports/isotonitazene\\_en](https://www.emcdda.europa.eu/publications/initial-reports/isotonitazene_en)

<sup>18</sup> <https://pubs.acs.org/doi/abs/10.1021/acscemneuro.1c00064>



among young people who are already experimenting with opioid painkillers risk triggering unexpected deaths in that group, leading to considerations about the dissemination of knowledge and experience, including revival procedures with naloxone to a broader group than has happened so far.

The emergence of nitazenes is a clear example of how illegal production constantly finds new ways and introduces new opioids that can be at least as potent as the type of opioids everyone fears and is looking for. The mixing of opioids with cannabinoids and stimulants poses an additional risk of fatal overdoses. At the same time, it also underscores the importance of communication between frontline workers and authorities, both to implement local interventions and to provide data to central authorities



	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>
Isotonitazene	-NO <sub>2</sub>	-C <sub>2</sub> H <sub>5</sub>	-OCH(CH <sub>3</sub> ) <sub>2</sub>
N-desethyl Isotonitazene	-NO <sub>2</sub>	-H	-OCH(CH <sub>3</sub> ) <sub>2</sub>
4'-hydroxy Nitazene	-NO <sub>2</sub>	-C <sub>2</sub> H <sub>5</sub>	-OH
5-Aminoisotonitazene	-NH <sub>2</sub>	-C <sub>2</sub> H <sub>5</sub>	-OCH(CH <sub>3</sub> ) <sub>2</sub>
Metonitazene	-NO <sub>2</sub>	-C <sub>2</sub> H <sub>5</sub>	-OCH <sub>3</sub>
Etonitazene	-NO <sub>2</sub>	-C <sub>2</sub> H <sub>5</sub>	-OC <sub>2</sub> H <sub>5</sub>
N-desethyl Etonitazene	-NO <sub>2</sub>	-H	-OC <sub>2</sub> H <sub>5</sub>
Protonitazene	-NO <sub>2</sub>	-C <sub>2</sub> H <sub>5</sub>	-OC <sub>3</sub> H <sub>7</sub>
Butonitazene	-NO <sub>2</sub>	-C <sub>2</sub> H <sub>5</sub>	-OC <sub>4</sub> H <sub>9</sub>
Clonitazene	-NO <sub>2</sub>	-C <sub>2</sub> H <sub>5</sub>	-Cl
Flunitazene	-NO <sub>2</sub>	-C <sub>2</sub> H <sub>5</sub>	-F
Isotodesnitazene	-H	-C <sub>2</sub> H <sub>5</sub>	-OCH(CH <sub>3</sub> ) <sub>2</sub>
Metodesnitazene	-H	-C <sub>2</sub> H <sub>5</sub>	-OCH <sub>3</sub>
Etodesnitazene	-H	-C <sub>2</sub> H <sub>5</sub>	-OC <sub>2</sub> H <sub>5</sub>

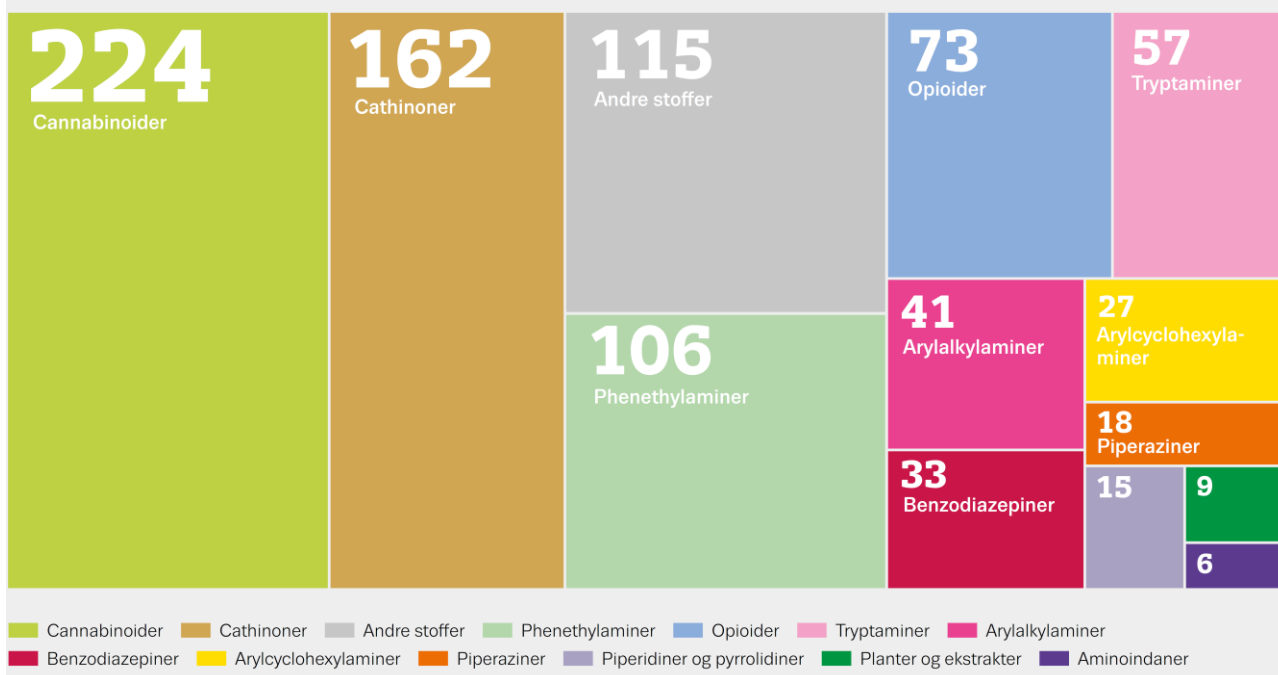
Types of synthetic nitazene opioids. Source Cayman Chemical<sup>19</sup>.

## The Naloxone Training Network as a Possible Sentinel System?

In the EU, there is a so-called early warning system abbreviated EWS (European Union Early Warning System on New Psychoactive Substances), which is operated by EMCDDA in close cooperation with Europol. This system plays a central role in supporting national and EU-level preparedness and the ability to respond to new psychoactive substances. The Danish monitoring is part of this system. As seen in the graph below, there are currently 73 NPS opioids under surveillance by EWS.

<sup>19</sup><https://www.caymanchem.com/news/characterization-of-nitazene-synthetic-opioids>

Antal stoffer, der overvåges af EU's system for tidlig varslig, efter kategori



EMCDDA (2022), *European Drug Report 2022: Trends and Developments*, European Union Publications Office, Luxembourg.

The significance of "sentinel" originally refers to an advanced soldier keeping watch. A locally well-rooted network could function as a sentinel surveillance system, quickly detecting changes in local drug user behavior, morbidity, mortality, and potentially combining it with the occurrence of new substances.

A sentinel network would promptly identify new problems and substances in a geographical area or a population subgroup, thus providing information to the national alert system for the general population. For a sentinel system to work, however, a coordinated network is needed. A loosely focused network would rely on individuals and disappear when these individuals are no longer present.

In addition to seizures of substances by the police and customs, toxicological studies, especially in drug consumption rooms, contribute to the discovery of new psychoactive substances (NPS). An opportunity to build an even closer warning network is through networks of drug consumption rooms, substance identification, and other harm reduction measures.

In drug consumption rooms, people consume their preferred substances in safe environments. In Copenhagen's drug consumption rooms, for example, there has been a contribution to a small preliminary study by EMCDDA on drug users and substance use.

A sentinel network attempted to be established under the auspices of the Correlation Harm Reduction Network<sup>20</sup> and with support from EMCDDA is INDCR (International Network of Drug Consumption Rooms)<sup>21</sup>. Various web meetings have been held, but due to the very broad international diversity in this area, there is currently no real sentinel function.

In contrast to drug consumption rooms, which are localized places often centrally located in large cities, the Danish naloxone training network is currently in contact with 70-80% of Danish local communities, and the individual trainers have local knowledge of street workers and others working with young people with recreational drug use. The evidence worked within such a network would primarily be anecdotal. Still, if this knowledge is collected and qualified, possibly in connection with drug testing, it would be relatively easy to react quickly to new findings of NPS or the reappearance of substances that have been on the market before. As it stands now, the Red Liv training network could relatively easily be expanded to such an effort.



European Monitoring Centre  
for Drugs and Drug Addiction



**INDCR**  
INTERNATIONAL NETWORK  
OF DRUG CONSUMPTION ROOMS

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<sup>20</sup> <https://www.correlation-net.org/>

<sup>21</sup> <https://www.drugconsumptionroom-international.org/>