

# Provision of Naloxone Nasal Spray: A Northern Territory Focus

Original Research

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## ABSTRACT

**Background:** Opioids play a key role in healthcare, however, the challenges of opioid overdoses, especially from pharmaceutical opioids, are rising significantly. Naloxone reverses an opioid overdose, and naloxone nasal spray is routinely used internationally as a harm-reduction tool to reduce opioid fatalities.

**Aim:** This study aimed to investigate the supply of naloxone nasal spray within Northern Territory (NT) pharmacies and the views of key professionals with experience in naloxone distribution and the related policies.

**Method:** A mixed-method observational study design was utilised. Relying on retrospective analysis of naloxone dispensing and over-the-counter supply data, the amount of naloxone supply distributed in NT community pharmacies from January 2018 to August 2021 was captured. Targeted qualitative analysis of barriers to naloxone supply in the community was based on interviews with key stakeholders in the NT.

**Results:** 23 out of 40 NT community pharmacies provided data, of which 35% had naloxone products available at some point from 2018 to 2021. The most commonly supplied form was the intramuscular injectable (35%) with pharmacies less likely to supply the nasal spray (17%). Interview responses showed several consistent themes affecting naloxone provision from services, including demand versus supply, prescriber control of access, financial considerations, legalities, and several factors that facilitated supply.

**Conclusion:** This study showed the supply of naloxone in the NT is limited. Barriers affecting the provision of naloxone nasal spray were the community pharmacy model of supply and thus increasing access points would assist to expand the supply.

## INTRODUCTION

As analgesics, opioids are vital in our healthcare system with 15.4 million prescriptions dispensed between 2016–2017.<sup>1</sup> The Australian Bureau of Statistics indicates that opioids are involved in two-thirds of all drug-induced deaths, with

pharmaceutical opioids involved in 70% of fatalities.<sup>2,3</sup> Overall, opioids have remained the most common drug class for drug-induced deaths over the past two decades.<sup>2</sup> However, the deaths caused by opioids can be prevented through the use of opioid antagonists.

Naloxone is an opioid receptor antagonist used as first-line treatment for opioid overdoses as it has a higher affinity for opioid receptors than other substrates including potent opioids.<sup>4</sup> Naloxone binds to opioid receptors and displaces the opioids currently binding through competitive inhibition to temporarily prevent the opioid related central nervous system depression.<sup>4</sup>

In Australia, intramuscular naloxone was originally a Prescription Only (Schedule 4) restricted substance only available from an authorised prescriber. However, in February 2016, the Therapeutic Goods Administration down-scheduled this to a Schedule 3 Pharmacist Only medication.<sup>5</sup> Thus, increasing the accessibility of the medication to the general public. In September 2018, an intranasal formulation of naloxone (Nyxoid®) was registered in Australia offering a viable alternative suitable for the general population.<sup>5,6</sup> Additionally, the intranasal route eliminates the risk of needle-stick injuries and blood-borne virus transmission, an attractive safety profile for the public.<sup>6</sup>

The pharmacokinetic profile of the nasal spray is equivalent to that of the intramuscular injection, restoring the respiratory rate to normal (RR = 12 breaths per minute) in 94% and 96% of cases respectively.<sup>7</sup>

An Australian study in 2020 by Tse et al. compared the prevalence of naloxone supply before and after the rescheduling to a Schedule 3 medicine to assess if this led to an increase in total supply.<sup>8</sup> However, only intramuscular naloxone was included in the study, hence it is unknown how much intranasal naloxone has been supplied since its release in 2018. Furthermore, it is unknown whether this alternative formulation has led to the increased supply by pharmacists and subsequent uptake by the community.<sup>8</sup>

The United States Centre for Disease Control and Prevention (CDC) recommends co-prescribing naloxone to patients taking 50 mg oral morphine equivalent/day or more.<sup>9</sup> The Australian Therapeutic Guidelines suggest naloxone should be given to “patients prescribed opioids for the management of chronic pain, especially in high doses”.<sup>10</sup> However, there are no explicit guidelines as to the morphine strength before naloxone should be prescribed.

Studies have shown that 78% of patients taking opioids for chronic non-cancer pain would likely meet a threshold where a supply of naloxone would be clinically appropriate

to prevent an unintended overdose.<sup>11</sup> Despite this, studies relevant to Australian patients have shown that post the rescheduling of naloxone, less than 3% of the supply is via the Pharmaceutical Benefits Scheme (PBS).<sup>11</sup> Due to the high rates of preventable overdoses involving prescribed opioids, prescribing naloxone in line with the recommendations by the CDC would result in fewer fatal overdoses.<sup>11</sup>

Several international studies have evaluated the number of opioid overdose deaths after the implementation of 'take-home naloxone' nasal spray programs. All studies showed a reduction in the number of fatalities.<sup>12-14</sup> Increasing the supply of naloxone through community pharmacies in Australia is supported by the sector's peak bodies. The Society of Hospital Pharmacists Australia raised the importance of naloxone as a harm reduction tool in their 2018 position paper on opioid harm.<sup>15</sup> Additionally, the Pharmaceutical Society of Australia has specially called for funding of 500 doses of intranasal naloxone in the Northern Territory (NT) to prevent harm to Territorians, especially those who need to travel long distances to access emergency care.<sup>16</sup>

The value of supplying naloxone to people at risk of overdose was the underpinning of the initiation of a \$19.6 million Australian Take Home Naloxone pilot project, which began in December 2019.<sup>17</sup> Under the pilot, naloxone (either intranasal or intramuscular) was made available free in community pharmacies in New South Wales, South Australia, and Western Australia, with a public campaign to promote offering the medication to anyone who is prescribed opioids, those who may be likely to witness an opioid overdose and those engaged in high-risk behaviours associated with opioids. The pilot was extended until 2023 and now includes all Australian States and Territories, including the NT. The report from the initial pilot presented the findings that take-home naloxone saved up to an estimated three lives per day, which includes improvements in prognosis and reductions in mortality.<sup>17</sup>

In light of both the revised scheduling arrangements for naloxone and the rise in prescription opioid overdoses, the need for take-home naloxone is growing. Community pharmacies have an important role in preventing opioid-related deaths through the provision of naloxone.<sup>18</sup> This study investigated the supply of naloxone nasal spray within NT pharmacies and the views of key professionals with experience in naloxone distribution and the related policies.

## METHODS

### Data collection

All 40 community pharmacies across the NT were invited to participate in the study by sharing the number of naloxone products they provided by prescription and over-the-counter between January 2018 and late August 2021, reflecting the period since the intranasal formulation was made available. To directly assess the supply of naloxone nasal spray, community pharmacies differentiated between the ampoules, prefilled syringes, and the nasal spray in their total volume of supply over the specified period. This information was recorded at monthly intervals and data was accessed by generating a report on the dispensing software of the overall supply. The brands of the products supplied by the pharmacies were not recorded. A pre-formed table was sent to the pharmacies to facilitate standardised data collection and ensure pharmacies provided comparable data for analysis.

### Data analysis

Descriptive statistics were used to analyse the prevalence of the different naloxone formulations supplied by the total number of participating community pharmacies, as well as trends over the 2018 to 2021 period to detect any patterns in supply.

### Interview development and collection

Semi-structured interviews were conducted to identify and investigate key barriers and enablers to naloxone supply in the NT. Participants were selected using purposive and

snowball sampling methods, given the small number of participating pharmacies and policymakers from government and non-government sectors. Two senior pharmacists, an NT government harms reduction specialist and a member of a non-government organisation for harm minimisation services were interviewed. All interviewees were asked the same five open-ended questions, related to the distribution and supply of naloxone.

### Interview analysis

All interviews were audio recorded and transcribed manually for qualitative content analysis. Transcripts were analysed using a grounded theory approach creating incremental codes, using the specific obstacles and enablers stated by the interviewees. Once coding was completed, the data was analysed to identify overlapping codes. The codes were subsequently sorted into categories based on codes that were frequently identified in the interviews. The categorisation was performed in several iterative steps, each with immediate reference to the literature.

### Ethics approval

Ethics was granted by Charles Darwin University Human Research Ethics Committee in May 2021.

## RESULTS

40 community pharmacies were invited to participate in this study, with 58% (n=23) agreeing to participate. From this,

**TABLE 1 - Semi-structured Interviews with Pharmacists and Key Stakeholders in the NT comprised of Themes, Categories and Codes**

THEMES				
Demand Versus Supply	Prescriber's Control of Access	Financial Considerations	Legalities of Provision	Factors that Facilitate the Supply
<ul style="list-style-type: none"> <li>• Stock movement</li> <li>- Frequency sold</li> <li>- Demand for naloxone</li> <li>• Inconsistency across pharmacies</li> <li>- Supply differences</li> <li>• Pharmacist's expectations</li> <li>- Impact</li> <li>- Presumptions</li> <li>• Wholesaler barriers</li> <li>- Cost</li> <li>- Minimum supply</li> </ul>	<ul style="list-style-type: none"> <li>• Pharmacist's recommendations</li> <li>- Responsibility</li> <li>- Supplying on prescription</li> <li>• Guidelines</li> <li>- At risk groups</li> <li>- Following recommendations</li> <li>• Best practice</li> <li>- Overdose prevention</li> <li>- Co-prescribing</li> <li>• Stigma</li> <li>- Opportunity to normalise</li> <li>- Regular supply</li> </ul>	<ul style="list-style-type: none"> <li>• For patient</li> <li>- Affordability</li> <li>- Cost vs Benefit</li> <li>• For pharmacy</li> <li>- Cost</li> <li>- Business Strategy</li> <li>• Operation Budget</li> <li>- NGO</li> <li>- Formulation costs</li> </ul>	<ul style="list-style-type: none"> <li>• Australian Commonwealth Government</li> <li>- THN pilot</li> <li>- State equality</li> <li>• NT Government</li> <li>- Waiting</li> <li>• Legalisations and Laws</li> <li>- Access locations</li> <li>- TGA</li> <li>- Non-pharmacy access points</li> </ul>	<ul style="list-style-type: none"> <li>• Engagement</li> <li>- Interest</li> <li>- Passionate</li> <li>• Importance</li> <li>- Understanding of overdose risk</li> <li>- Understanding of prevention</li> <li>• Overdose Prevention</li> <li>- Recognise at risk groups</li> <li>- Persons Who Inject Drugs</li> <li>- People who are prescribed opioids</li> </ul>

• indicate categories      - indicate codes

\*Codes, categories and themes are not listed in any order of importance, they are all equal.

only 17% (n=4) of pharmacies reported supplying intranasal naloxone with eight pharmacies (35%) supplying other formulations of naloxone; 35% (n=8) containing ampoules and 13% (n=3) the prefilled syringes. Those pharmacies that supplied intranasal naloxone also supplied other formulations of naloxone. Of the pharmacies that participated, 65% (n=15) never supplied any naloxone products.

Based on the pharmacies from this study, the NT community is unable to access intranasal naloxone from 83% (n=19) pharmacies. Which is almost half of all (n=40) NT pharmacies (48%; n=19/40).

The number of naloxone nasal spray products from 2018 until the middle of 2021 from all the pharmacies involved are presented in Figure 1. Unfortunately, due to time restraints, the study was unable to be continued until the end of 2021, thus it is unknown if the total number subsequently changed or remained the same.

The semi-structured interviews lasted between 8 to 19 minutes. Table 1 describes the five main categories identified through coding: demand versus supply, prescriber control of access, financial considerations, legalities, and several factors that facilitated supply.

**DISCUSSION**

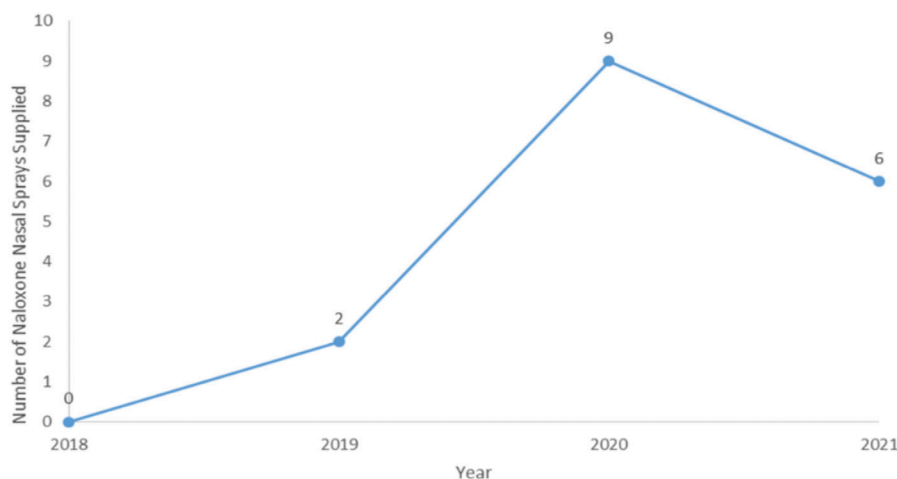
In the present study 17% (n=4) of NT community pharmacies were found to supply naloxone nasal spray. As a result, there is a need to increase naloxone access across

NT community pharmacies. European countries, such as Scotland, have achieved a high supply of naloxone in their pharmacies.<sup>12</sup> Additionally, Philadelphia (United States) has introduced a bill requiring all pharmacies to supply naloxone and have a readily accessible supply to the community.<sup>19</sup> This targets the obstacle of supply, allowing for demand from the community. Patients are less likely to use naloxone if there are difficulties accessing it such as a lack of supply in multiple pharmacies.<sup>19</sup> Furthermore, a study showed that increasing the supply improves patient inclusion of naloxone.<sup>20</sup>

The low availability of naloxone in the NT is concerning, as lower naloxone availability has been proportionally linked to opioid overdose deaths.<sup>18</sup> Although data was received from just over half, (58%; n=23), of all NT community pharmacies, it seems unlikely that there would be one pharmacy with a high supply of naloxone. During the interviews, the pharmacies that regularly supply naloxone were identified and they all provided data. The wholesaler model which has been utilised in previous studies may improve future studies as it would involve collecting data from more pharmacies.<sup>8</sup>

Furthermore, interviewees reported an obstacle to expanding naloxone access in the NT is the prescriber's role. However, this is not something that pharmacists can directly control. The data collected in this study also shows that currently, NT physicians do not prescribe naloxone concurrently with an opioid prescription. The low supply in pharmacies signifies the low uptake from consumers. Co-prescribing naloxone with an opioid prescription would

**FIGURE 1 - Naloxone Nasal Spray trend from Northern Territory Community Pharmacies over January 2018 - August 2021**



be particularly useful in some groups of patients where the benefits are well established and in line with naloxone recommendations outlined in the Therapeutic Guidelines.<sup>10</sup> To increase the provision of naloxone nasal spray, NT prescribers may require further education on co-prescribing naloxone with opioids for patients at high risk of having an overdose, such as those patients prescribed high doses of opioids for the management of chronic pain.<sup>10</sup>

The lack of consistency in supply-benefits between pharmacists and prescribers also hinders naloxone supply within the pharmacy. One interviewee discussed that patients with a valid Healthcare Card can access naloxone on a prescription at the subsidised cost for that year. Pharmacists can supply Schedule 3 medicines to patients such as naloxone but the cost would not be covered by the PBS. Providing this subsidised service within the pharmacy would likely increase the uptake of naloxone. Uptake may potentially improve if pharmacists are allowed to provide naloxone under the PBS to suitable patients.

Moreover, many countries identify the cost of naloxone as an obstacle to expanding supply, and several models implemented throughout Europe and the United States of America either subsidise the cost or provide the nasal spray for free to those who are at risk of an opioid overdose.<sup>12,19,20</sup> NT pharmacists considered the cost of naloxone as a barrier for the consumer and the pharmacy (Table 1). For the period the data was collected, the average cost of naloxone nasal spray was \$40.00. As a result, the Australian Take Home Naloxone trial supplies both pharmacies and community patients with naloxone free of charge.<sup>17</sup> However, further interventions are required when the pilot concludes in 2023. Interventions are required in the NT to elucidate the cost versus benefit of naloxone for both the pharmacy and patients. Furthermore, opioid overdoses place a significant cost burden on the healthcare system due to hospitalisations. Opioid overdoses are estimated to cost Australia around \$15.7 billion a year. Thus, the cost of an opioid overdose is higher than the cost of a naloxone nasal spray.<sup>21</sup>

Additionally, the participating pharmacists did not feel comfortable discussing the use and benefits of naloxone as they felt that the community pharmacy was not the appropriate place to do so. Training pharmacists on how to initiate discussions about naloxone with high-risk patients has shown to be successful.<sup>22</sup> Integrating naloxone education into other undergraduate university courses in healthcare, such as nursing, has allowed individuals to feel comfortable

initiating conversations and addressing the stigma associated with the drug.<sup>23</sup> A similar education model should be provided to pharmacy students in the NT as targeting their gaps in knowledge and stigma early in their careers may potentially assist in improving the overall supply of naloxone in the NT.

Naloxone is an unscheduled medicine in most countries around the world, making it accessible everywhere. However, as a Schedule 3 medicine in Australia, access is restricted.<sup>24</sup> Considering naloxone has a high safety profile, it would be beneficial for naloxone's poison standard to be reviewed in the Standard for the Uniform Scheduling of Medicines and Poisons, so it could be available in multiple locations such as supermarkets and harms minimisation services. It has been shown that states and jurisdictions with multiple naloxone access points have a high success in reducing opioid overdoses.<sup>25</sup>

A limitation of this study is that the prescriber's perspective was not captured and the sample size was small. Addressing this would have assisted in prioritising the barriers identified so as to develop better and more feasible solutions. Future studies should endeavour to capture the prescriber's view regarding naloxone and its use in the NT. This may provide a better guide for future directions on where the focus can be shifted. Future studies should also aim to use a larger sample size to continue to analyse the qualitative and quantitative trends in the NT regarding naloxone supply.

## CONCLUSION

The study achieved all intended aims. It was identified that the supply of naloxone nasal spray within NT pharmacies is low which in turn limits the community's access. The view of key professionals with experience in naloxone distribution was explored and responses suggested that there were barriers to supply and that overall supply was suboptimal. The NT, and possibly other jurisdictions with similar issues, would value policy changes to increase access points as well as directed educational campaigns focusing on health professionals and the target end consumer.

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