

Improvised naloxone nasal sprays lack evidence of absorption and effect

Naloxone hydrochloride is a medication that can reverse the effects of an opioid overdose. First responders (peers, family, police, etc.) may prefer nasal sprays to injectable naloxone, which has led to widespread use of improvised naloxone kits with atomisers for nasal delivery of the drug. On 18 November 2015, the US Food and Drug Administration (FDA) approved a nasal naloxone product to replace those improvised kits.

In a debate paper published online today by the scientific journal *Addiction*, top researchers at the National Addiction Centre at King's College London criticise the extensive use of improvised nasal naloxone kits without testing and without regulatory approval. Improvised nasal naloxone kits were first introduced in the early 2000s in the absence of licensed non-injectable products, and today they continue to be used in the US (where improvised kits are still in circulation in the community) and also in an increasing number of countries where nasal Narcan has not yet been approved.

The authors point out that there isn't enough information available on improvised nasal naloxone kits to warrant this level of acceptance. Improvised nasal kits consist of standard naloxone syringes (developed and licensed for injection), to which a nasal atomizer is attached. The formulation is not concentrated, as naloxone syringes are only commercially available in concentrations of up to 1mg/ml. The single pharmacokinetic study published on non-concentrate naloxone showed that only 4% of naloxone is absorbed when administered nasally. Clinical trials on improvised nasal naloxone kits are underway, but no data on levels of naloxone absorbed have been published.

Lead author Professor John Strang says, "We are attracted to nasal naloxone as a concept, but we are concerned that improvised nasal sprays have been accepted by the treatment field without the sort of testing that would be demanded if a new drug delivery route were proposed for treatment of other populations. We wouldn't accept untested improvised nasal adrenaline/epinephrine for treating emergency allergic reactions. So why are makeshift nasal naloxone kits good enough for people with opioid dependence?"

Strang also points out that we also haven't considered how reliably nasal naloxone works in opioid users whose nasal mucosa may be damaged from drug snorting, or obstructed by vomit during overdose. Ambulance-based studies indicate that between 9 and 26% of opioid overdose victims fail to respond to nasal naloxone. Strang says, "It's one thing to use nasal naloxone in a hospital or from an ambulance, where a doctor or paramedic can administer naloxone by injection if the nasal dose doesn't work. But these nasal naloxone kits, whether FDA-approved or not, are designed to help caregivers save overdose victims on the spot, so they need to be reliable. More data are needed to understand how reliably nasal naloxone reverses opioid overdose in the community. With a naloxone spray now licensed (in the U.S. only) and licensed naloxone injections available internationally, clinicians should either prescribe the long-established injection naloxone or, in the US at least, the newly-approved naloxone nasal spray. They should not prescribe untested, improvised nasal sprays for which absorption remains unknown, probably poor and likely very variable."

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For editors:

Strang J, McDonald R, Tas B, and Day E. (2015) Clinical provision of nasal naloxone without

experimental testing and without regulatory approval: Imaginative shortcut or dangerous bypass of essential safety procedures? *Addiction* 111: [doi:10.1111/add.13209](https://doi.org/10.1111/add.13209)

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Addiction is a monthly international scientific journal publishing peer-reviewed research reports on alcohol, illicit drugs, tobacco, and gambling as well as editorials and other debate pieces. Owned by the Society for the Study of Addiction, it has been in continuous publication since 1884.

Addiction is the number one journal in the 2015 ISI Journal Citation Reports Ranking in the Substance Abuse Category (Social Science Edition).