

# Reversing opioid overdose: Concentrated naloxone nasal spray as good as injection

A new study published by the scientific journal *Addiction* has found that a concentrated 2mg intranasal naloxone spray delivers naloxone as effectively, over the critical first 15 minutes, as the standard 0.4mg intramuscular (IM) naloxone injection. The 2mg spray also maintains blood levels of naloxone more than twice as high as the 0.4mg IM levels for two hours after administration. It should therefore be highly effective in reversing opioid overdose.

These results support the recent announcement on 14 September 2017 that the European Medicines Agency (EMA) has issued a positive opinion for a 1.8mg naloxone nasal spray formulation (equivalent to 2mg naloxone hydrochloride), under the brand name Nyxoid.

Take-home naloxone (naloxone kits provided to drug users and other non-medical persons for use in emergency situations) helps to prevent death from heroin/opioid overdose. Naloxone is usually given by injection, but more user-friendly non-injectable alternatives are being developed, including nasal sprays. To be effective, the intranasal spray must be highly concentrated to achieve good absorption, the dose must be adequate but not excessive, and early absorption should be comparable to IM injection.

This study tested nasal naloxone at 1mg, 2mg, and 4mg doses on 38 healthy volunteers, compared with 0.4mg IM and 0.4mg intravenous doses. Each volunteer received all five study treatments, with one naloxone dose per session and each session separated by a washout period. Blood plasma concentrations of naloxone were measured nineteen times for each volunteer during each treatment session, with intense sampling in the first 15 minutes after dosing.

All three doses of naloxone nasal spray were well absorbed, with the 2mg spray most closely replicating the performance of the 0.4mg IM naloxone injection over the critical first 15 minutes. The volunteers experienced no severe adverse effects; the main mild adverse effect was headache, in six volunteers.

Professor Sir John Strang, who co-authored the report, is cautiously optimistic: "Our findings demonstrate good early absorption and overall bioavailability of naloxone in healthy subjects, but concentrated naloxone nasal spray has yet to be formally tested in the target population of opioid users. Nasal naloxone might be absorbed differently by opioid users due to damaged nasal mucosa, rhinitis, or nasal obstruction from mucus or vomit during overdose. Nevertheless we are very pleased that concentrated nasal naloxone formulations are now receiving regulatory approval and believe that they will help widen the provision of take-home naloxone and thereby save lives."

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For editors:

McDonald R, Lorch U, Woodward J, Bosse B, Dooner H, Mundin G, Smith K, and Strang J. (2017) Pharmacokinetics of concentrated naloxone nasal spray for opioid overdose reversal: Phase-I healthy volunteer study. *Addiction*, doi: [10.1111/add.14033](https://doi.org/10.1111/add.14033).

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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 2016 ISI Journal Citation Reports ranking in the substance abuse category for both science and social science editions.