

# Reconsidering PDE5 Inhibitors as a Harm Reduction Strategy in Receptive Anal Intercourse: Addressing the Regulatory and Clinical Gaps in Access to Amyl Nitrite

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## Background

Amyl nitrite is a potent relaxant of smooth muscle sometimes used by gay, bisexual, and other men having sex with men (GBMSM) as a measure to lessen risk for localised trauma during receptive anal intercourse.

Despite being classified as a prescription-only medicine in Australia, no regulated product is currently available. Access remains unregulated and inconsistent. Internationally actions, including raids and manufacturing closures in the USA, have disrupted availability and raised safety concerns.

## Problem Statement

The regulatory vacuum around amyl nitrite leaves sexually active populations at risk.

Without access to safe, standardised products, individuals rely on illicit supply chains or go without, potentially increasing the incidence of trauma, pain, and associated complications. This situation presents a pressing clinical and public health gap.

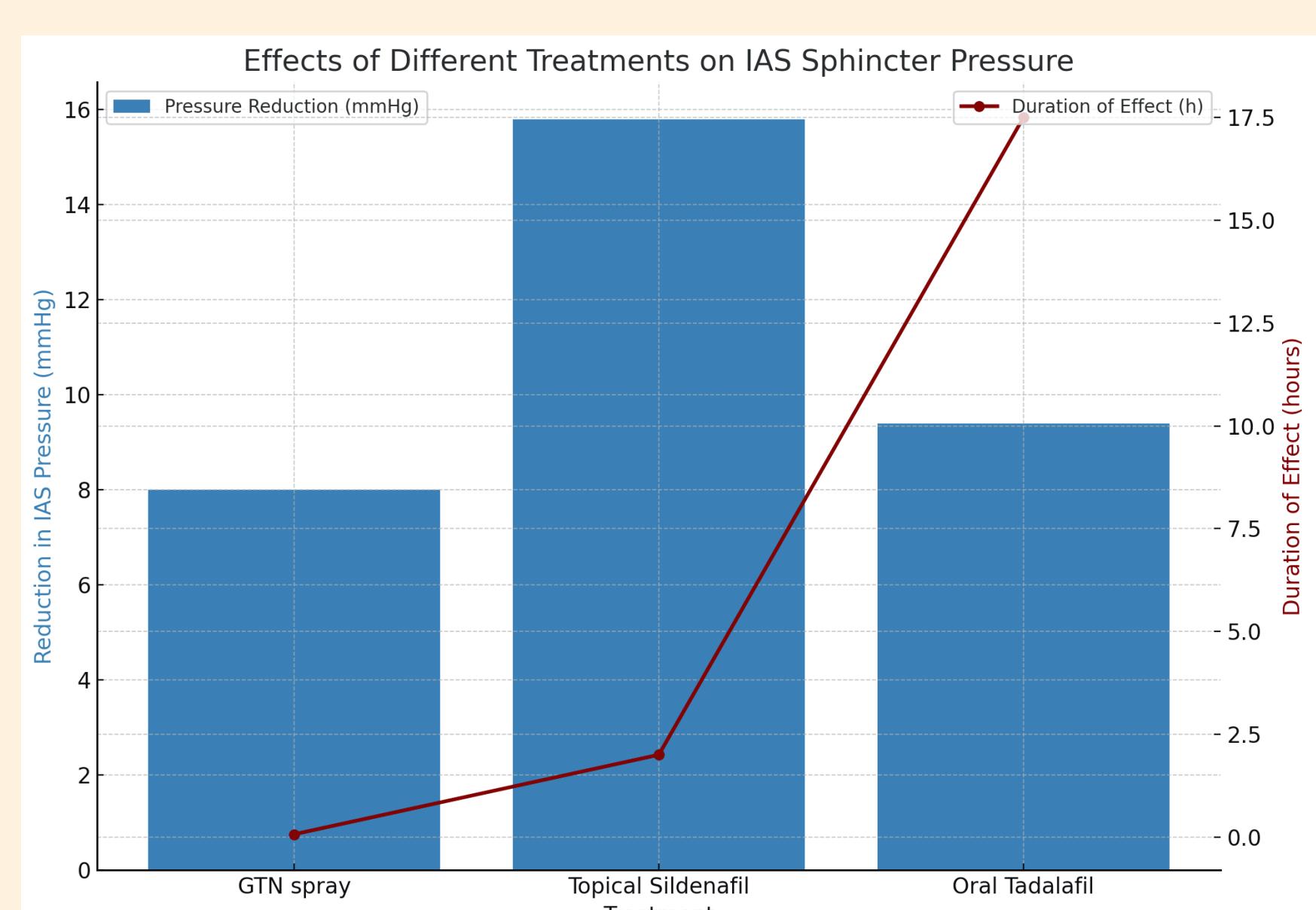
## Evidence and Opportunities

PDE5 inhibitors, such as sildenafil and tadalafil, act downstream in the same nitric oxide-cGMP pathway by inhibiting phosphodiesterase type 5 and sustaining smooth muscle relaxation including the internal anal sphincter (IAS). While Amyl Nitrites are not easily studied due to unregulated production, Glyceryl Trinitrate (GTN) is, offering a stable proxy for comparison.

Small studies suggest significant reductions in IAS tone:

- GTN reduced IAS pressure 8mmHg with rapid onset, and duration of effect 1-4 minutes. [1]
- 10% topical sildenafil reduced IAS pressure 15.8mmHg with peak effect at 3 minutes and duration of effect for 1-2 hours. [2]
- 40 mg oral tadalafil reduced IAS pressure 9.4mmHg with duration of effect 17.5+ hours. [3]

PDE5 inhibitors showed comparable efficacy to nitrates with fewer adverse events (headaches, drops in blood pressure, syncope. [2],[3]).



## Conclusion

There is now a credible pharmacological rationale, supported by early human data, to reframe PDE5 inhibitors as potential harm reduction tools in sexual health. With a known safety profile, legal availability, and demonstrated mechanism, these medications merit clinical trials and guideline consideration as regulated alternatives to amyl nitrite for anal relaxation and trauma prevention.

• \*References\*\*

[1] Connolly C, Tierney S, Grace P. Systemic glyceryl trinitrate reduces anal sphincter tone: is there a therapeutic indication? \*Ir J Med Sci.\* 2018 May;187(2):473-478. doi: 10.1007/s11845-017-1664-2. Epub 2017 Sep 13. PMID: 28905197.

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[3] Christoffersen T, Riis T, Kornholt J, Sonne D, Klarskov N. Single-dose tadalafil decreases anal pressure: a double-blind, randomized, placebo-controlled, crossover study in healthy women [abstract]. \*Continence\* 2022;2(S2):100370. doi:10.1016/j.cont.2022.100370