Involving Service Users in the Development of a Novel Drug Formulation for Heroin Overdose Reversal

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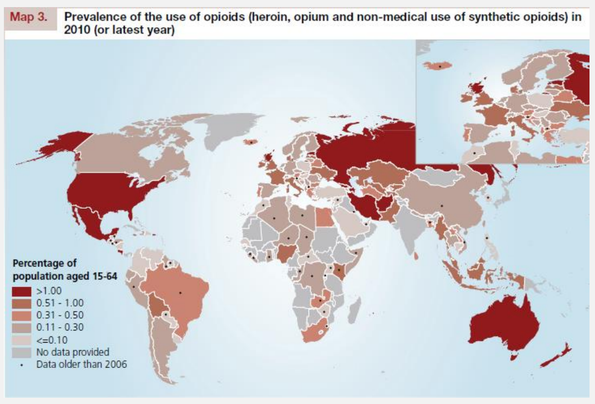
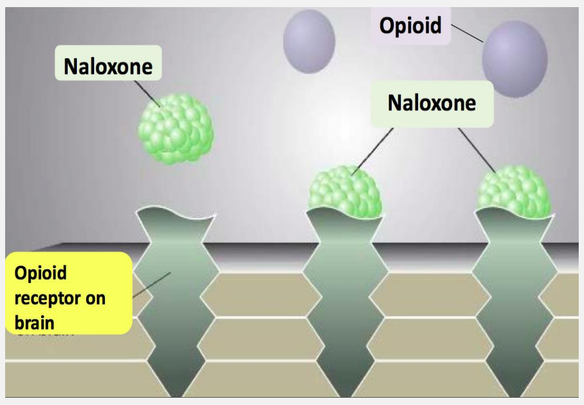
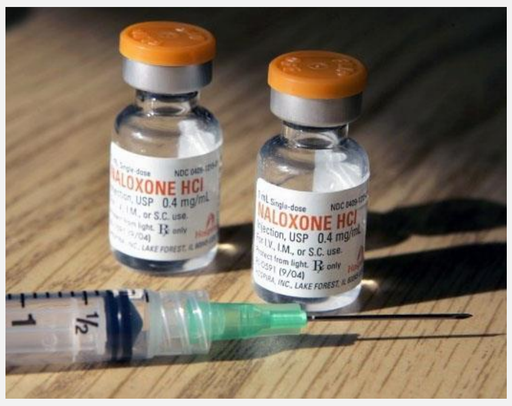
Introduction



Drug-related Deaths: England & Wales (ONS)	2009	2010	2011	2012	2013
All drugs (Δ past year)	**2,878**	**2,747** (-5%)	**2,652** (-4%)	**2,597** (-2%)	**2,955** (+14%)
Heroin/Morphine (Δ past year)	**880**	**791** (-10%)	**596** (-25%)	**579** (-3%)	**765** (+32%)
Methadone (Δ past year)	**408**	**355** (-13%)	**486** (+37%)	**414** (-15%)	**429** (+4%)
Other opiate (Δ past year)	**229**	**237** (+4%)	**221** (-7%)	**172** (-22%)	**237** (+38%)





Around the world, individuals who use heroin and other opioids experience sharply elevated excess mortality rates from overdose. Death by overdose can be prevented through timely administration of naloxone, an opioid-antidote. With heroin overdose deaths rising in the UK, the MHRA (2013) supports making naloxone directly accessible to opiate users and their families. By enabling family members to administer the life-saving antidote while awaiting an ambulance, take-home naloxone could significantly reduce overdose death rates. However, the necessary regulatory change to over-the-counter status remains unlikely for as long as naloxone is only available as injectable formulation.

Aims: 1) Develop a novel injection-free naloxone formulation; 2) Establish an ethically feasible research strategy to test the product for its potential to reverse opioid action.

Methods

We have partnered with the KCL Institute of Pharmaceutical Science to develop a buccal naloxone tablet by freeze-drying and have convened focus groups with current service users (n=7) and user representatives (n=2) to jointly design a research strategy that will allow us to test the new tablet for clinical effectiveness without exposing participants to severe withdrawal symptoms.

Results

Product Testing Strategy		
Stage	**Objective**	**Comparison**
Stage 1	Dose-ranging pilot in healthy volunteers	Licensed solution: buccal vs. IM vs. IV
Stage 2	PK in healthy volunteers	Licensed injection (IM, IV) vs. buccal tablet
Stage 3	PK/PD in dependent population : Dose escalation	Buccal tablet (ascending dose) + placebo

Views on Buccal Tablet (vs Injection)

A research strategy comprising a series of first-in-man clinical trials was jointly developed. For proof-of-concept in opioid users, an RCT was dismissed in favour of an open-label dose-escalation design. Users' views on the buccal tablet were recorded and demonstrate cautious acceptability.

Discussion

Through active involvement of service users with personal overdose experience, we have developed a research strategy that is sufficiently rigorous and reasonable from a user's perspective.
We are currently awaiting regulatory clearance to begin data collection on the first of three clinical trials.

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IoP/MRC studentship

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