” The development and characteristics of the new naloxone nasal spray in Norway ”

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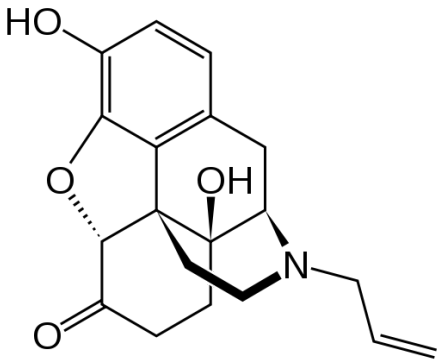
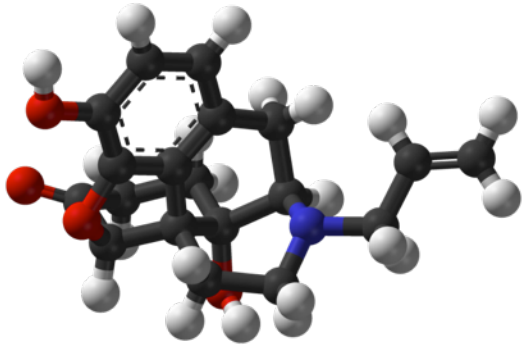




Early considerations regarding nasal naloxone

2008

- Formulations too dilute
- Complicated devices
- No pharmacokinetic data
- No evidence

Thus:

- Make a suitable formulation for a simple device
- Do pharmakokinetics (PK)
- Prepare a clinical trial (RCT)

2012

- PK under influence of an opioid
- Epidemiology of overdoses in the community

The Norwegian Board of Health Supervision

Report on a pilot project with naloxone nasal spray to combat overdose deaths 2010:

"Development of a new formulation, a nasal spray, would be time consuming and costly. Treatment of overdoses represent a small (commercial) market, which is probably why no manufacturers even in large countries like the US and UK have developed such a spray. It is also highly unlikely that there will be commercial interest in making such a development for the Norwegian market “.

Funding

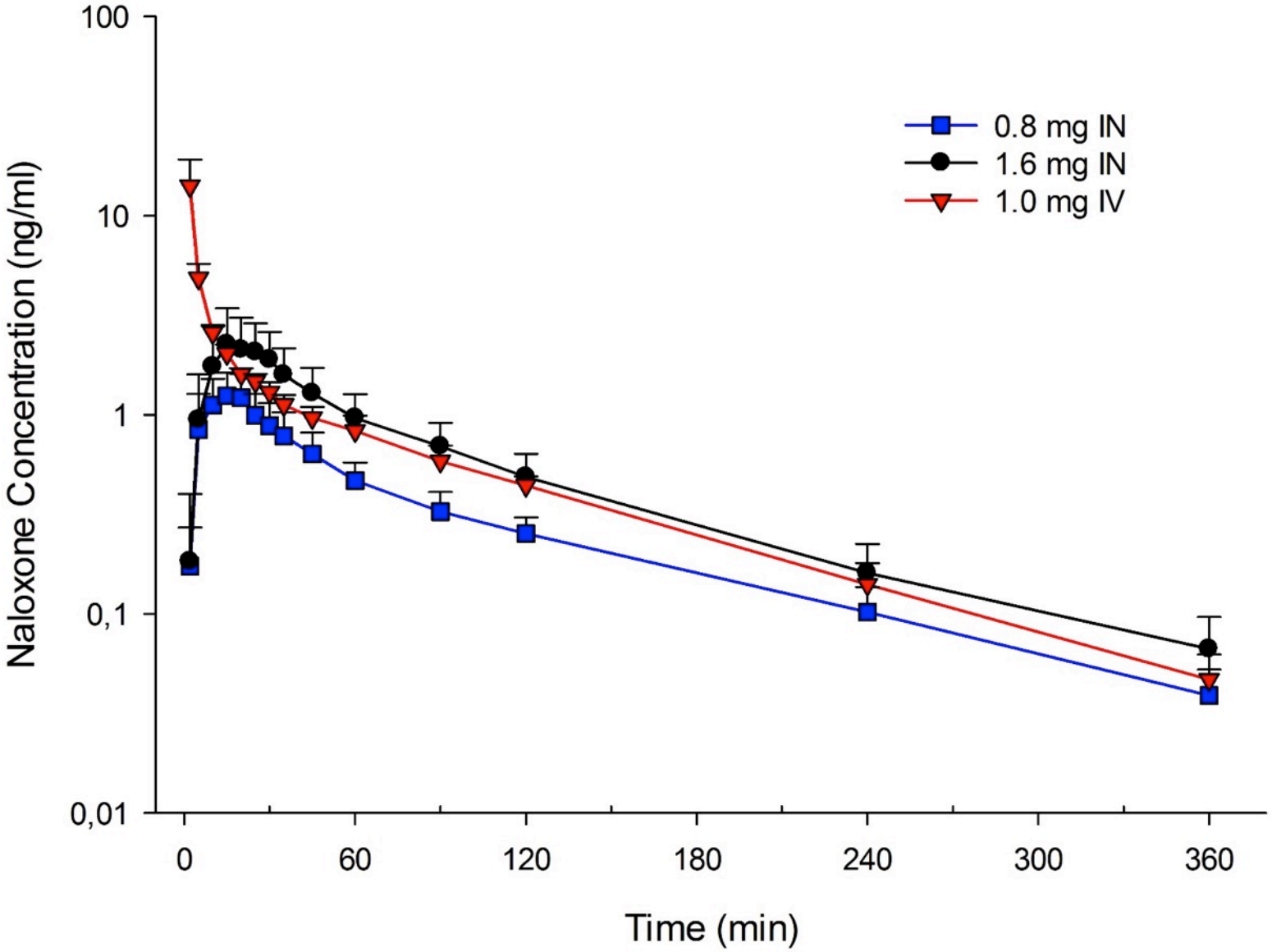
- No support from Central authorities!
- Starting grants (about £ 45000) in 2011
  - Lærdal foundation for Acute Medicine and our Hospital-Faculty
- Grant for PhD candidate
  - Regional Health Authorities
- Candidate for MD.PhD programme
  - Faculty
- A 2 years development grant (£ 100.000)
  - Regional Health Authorities
- Pivotal PK study
  - Funded by DNE-Pharma aiming at marketing approval

Drug development by «dummies»

The real (medical) world versus the regulatory universe:

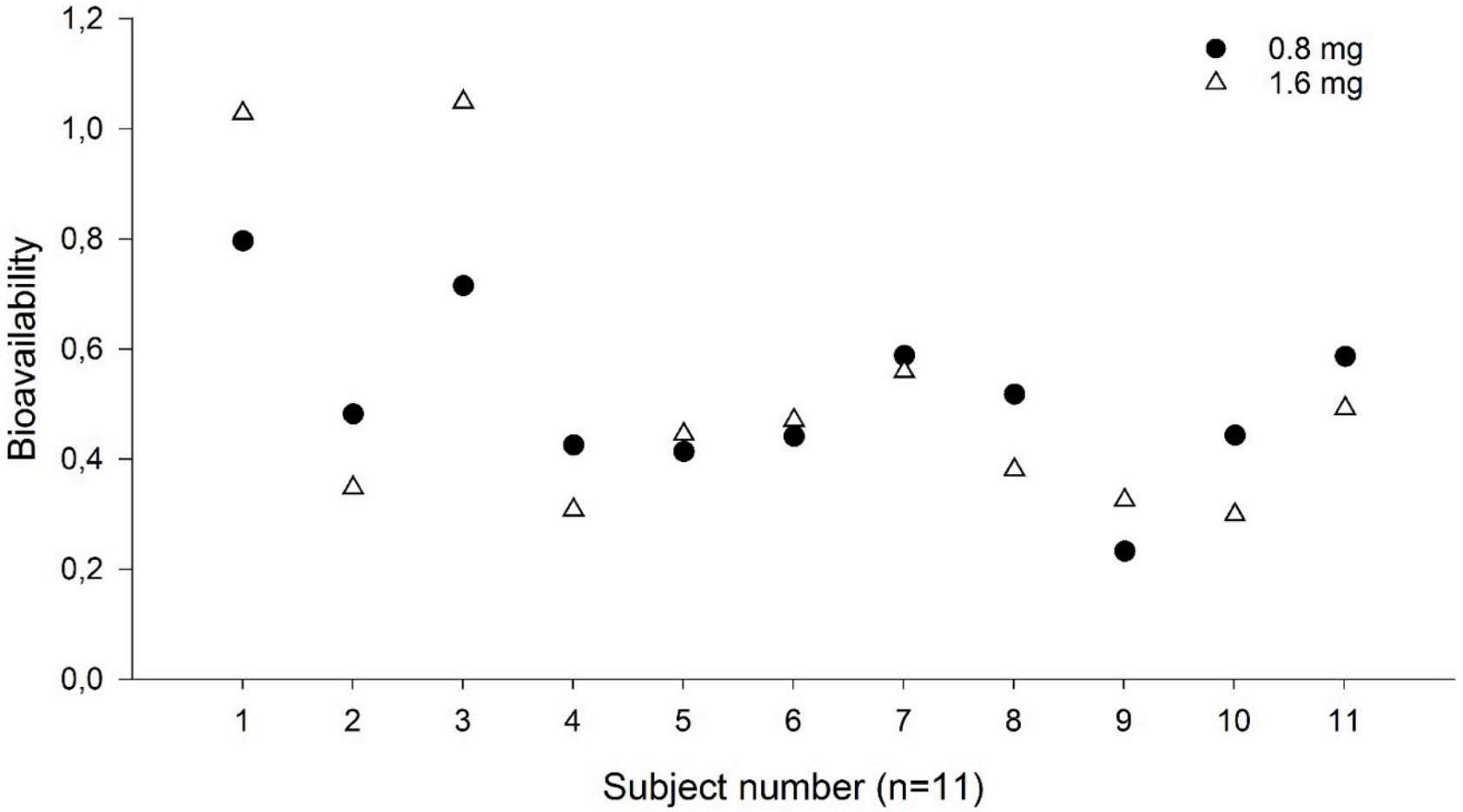
- Formulation developed as contractual work by academic formulation pharmacist (Phatsawee Jansook, PhD, supported by professor Thorsteinn Loftsson, Iceland)
- Manageable when it came to the clinical studies
- The hunt for a GCP approved production site
- But when it came to **Pharmaceutical and quality documentation** of the formulation…….you (may) need industry support:
  - Stability
  - Degradation products/ pathways- quantify
  - Spray characterization
  - Et cetera……

Time course for the serum concentrations of naloxone in healthy volunteers



Tylleskar I et al Pharmacokinetics of a new, nasal formulation of naloxone. Eur J Clin Pharmacol, 2017 DOI: 10.1007/s00228-016-2191-1

Between- and within- subject variability of bioavailability ~~and dose corrected Cmax~~ after two doses of nasal naloxone in healthy volunteers



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Intramuscular naloxone:
Dose corrected Cmax and Tmax

Dose corrected Cmax (ng(ml)	Tmax (min)
4.6	8
4.7	14
2.3	25
2.6	10
3.1	15
2,7	20

Proof of concept

***NTNU Intranasal Naloxone Trial*:**

Double Blinded, Double Dummy, Randomized Controlled Trial of Intranasal Naloxone for Pre Hospital Use

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