Measurement and optimization of injection force:

Two case studies on material selection and user perception

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Outline

1. Introduction to Ypsomed and devices for self injection
2. Case study 1: Modelling, measurement and material selection
3. Case study 2: Force measurement versus perception
4. Conclusions

1. Ypsomed – Key facts

- Turnover CHF ~466 M
- R&D-Investment CHF ~41 M
- Listed at SWX, majority shareholder and founder family owning ~75%
- > 1‘450 employees
  - ~990 in Switzerland
  - ~460 in Sales Affiliates
- Manufacturing & assembly
  - Reusable devices > 1 million units
  - Disposable devices > 80 million units
  - Pen needles > 600 million units

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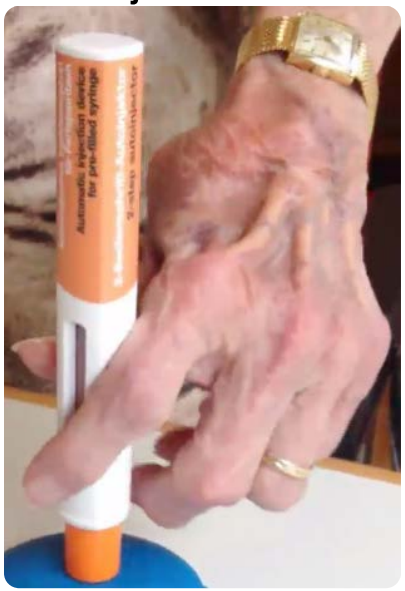
1. Devices for self-injection – Introduction

Autoinjector



Pre-filled syringe

Syringe and vial

Cartridge

Pen Injector

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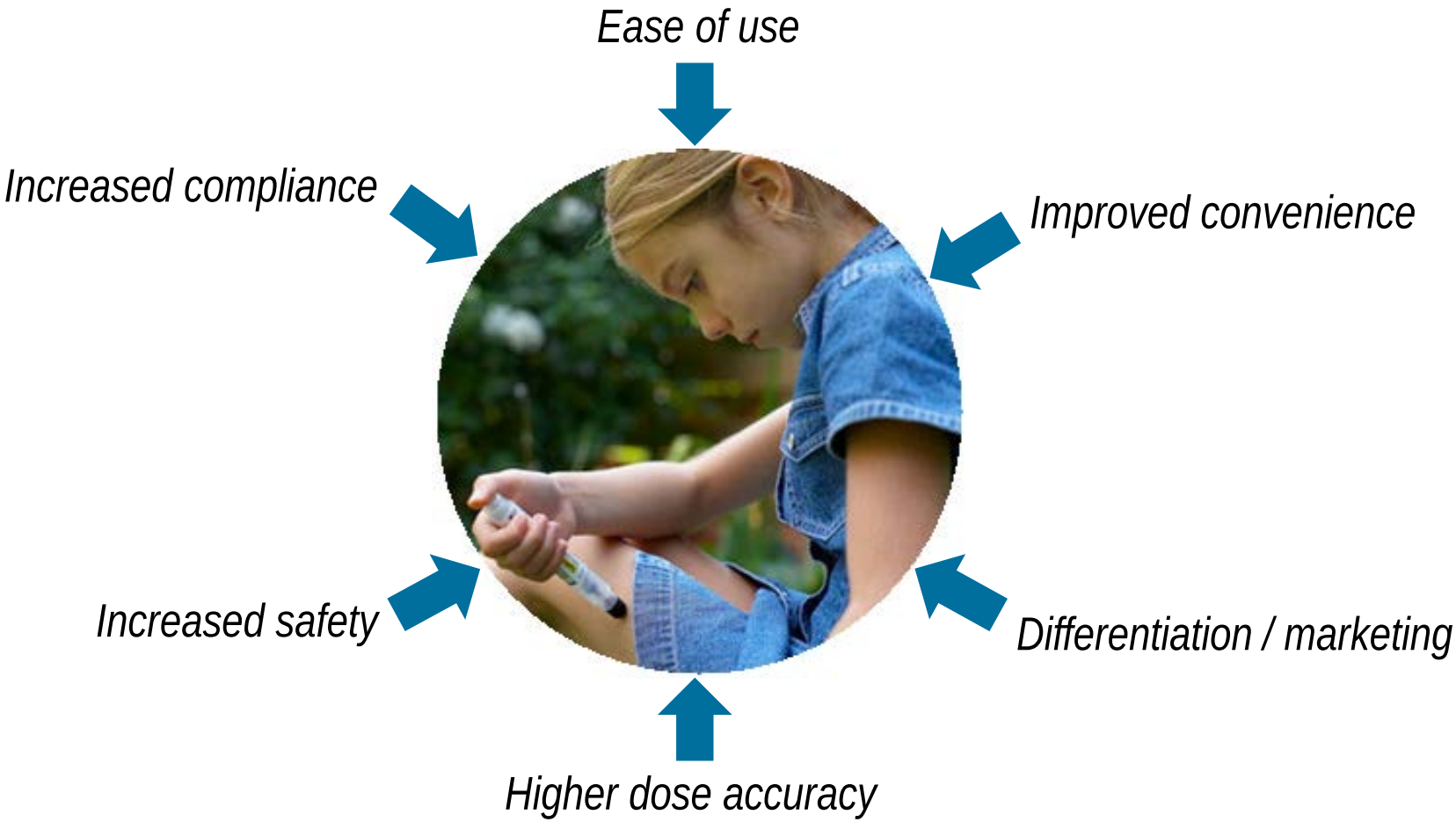
1. Devices for self-injection – Drivers



1. Devices for self-injection – Markets

8 million
reusable pens

1000 million
disposable pens

Diabetes hormones:
Insulins, GLP-1s
PCSK-9s

MABs: Autoimmune diseases, MS, RA, psoriasis, IBD, asthma Cancer, hep C

80+ million
disposable
autoinjectors

Other hormones:
hGH, infertility, osteoporosis

Emergency drugs:
Anaphylactic shock, migraine, military

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1. Devices for self-injection – Disposable pens

- Single use, come with the cartridge already inside
- Simple dial and dose or pull-push operation
- Range of devices for different applications
  - Variable dose
  - Fix-dose
- Insulin and diabetes largest market
- Efficient gearing mechanisms for optimized user handling forces

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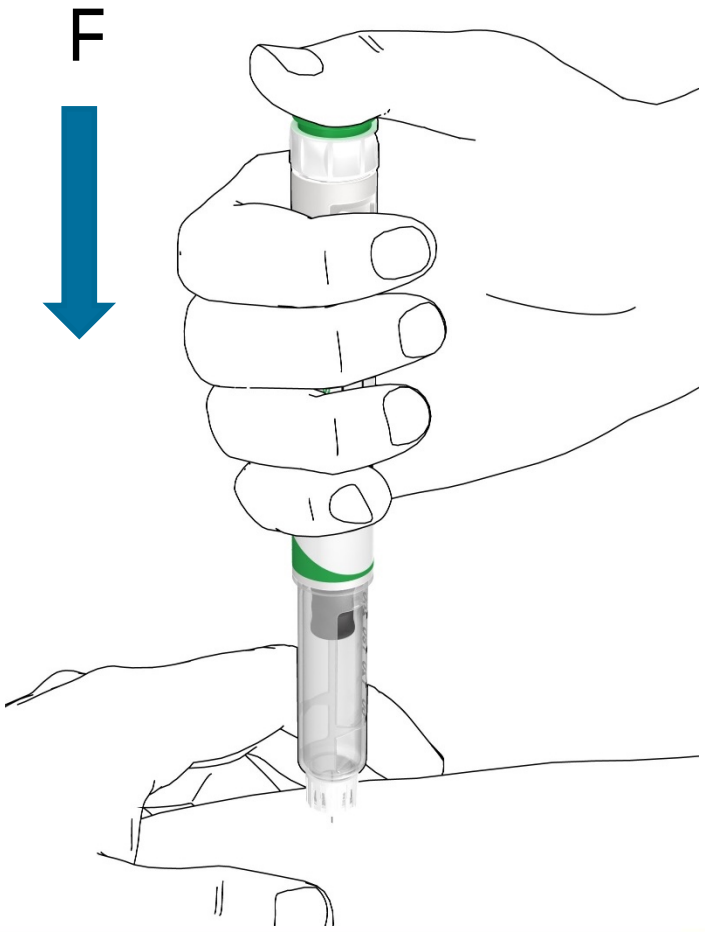
1. Injection force – Overview

- Everybody agrees injection force is important, is touted as the single most important performance parameter
- Lots of studies on mechanical injection force measurement have been conducted and published in the literature
- No systematic method comparison or agreement on how to best measure injection force – tensile tester is used but test setup / method not standardized
- Few people have studied how users actually inject or what they perceive



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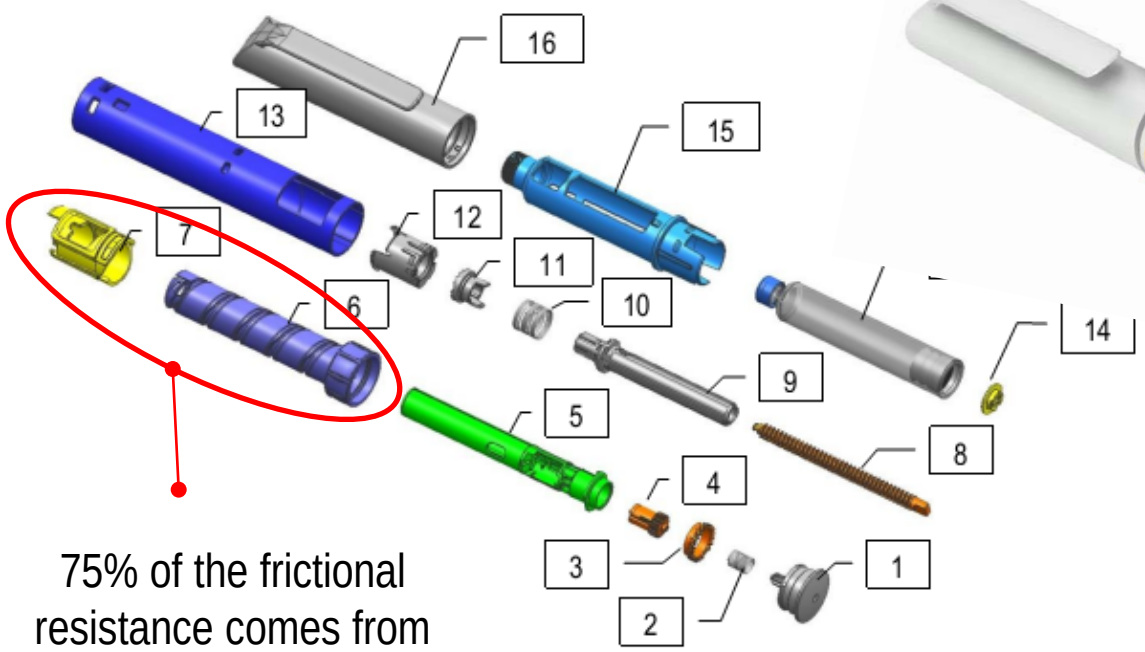
2. Case study 1 – The problem

- How can injection force be minimized?
- Optimize the efficiency of the pen mechanism through material selection!



75% of the frictional resistance comes from this interface

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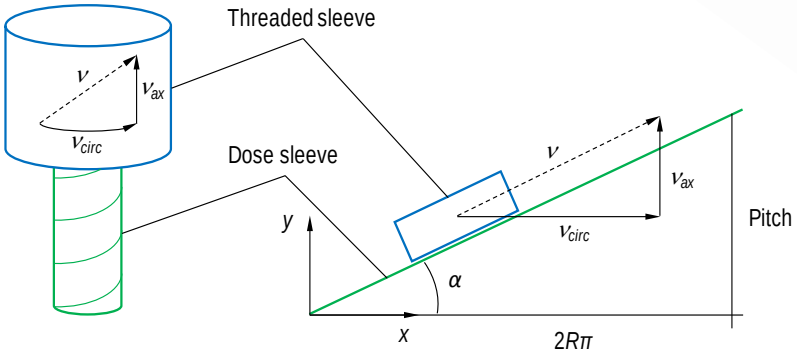
2. Case study 1 – The method

- Zwick Roell Z 2.5 universal test machine with custom fittings
- Measurement of force and torque over 450 degrees rotation 15 times back and forth at 90 degrees/s
- Force and torque converted to CoF through a simple analytical model



J Lange, L Urbanek, S Burren; Development of devices for self-injection: using tribological analysis to optimize injection force, *Medical Devices: Evidence and Research* 2016:9 93–103

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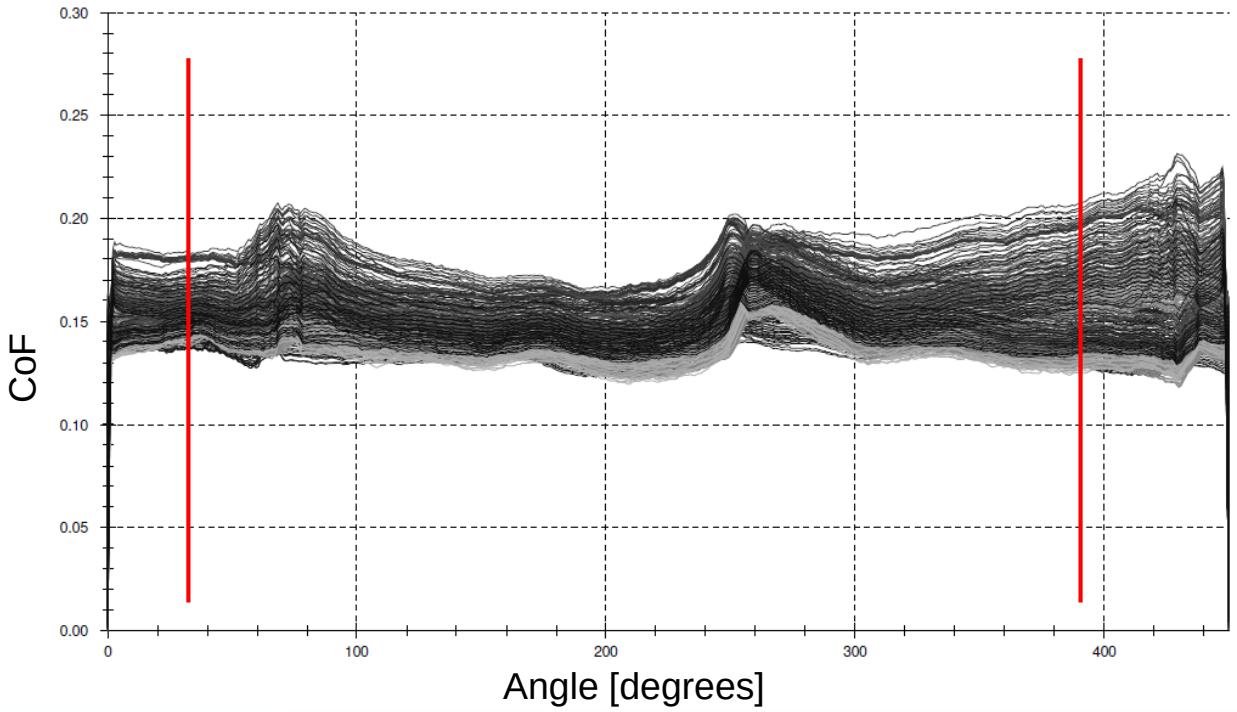
2. Case study 1 – Data evaluation

- Calculation of the average coefficient of friction for each individual pair of up and down runs, gives 15 data points per tested sample. 10 samples were tested for each material combination



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2. Case study 1 – The tests

- Testing was performed on a range of materials and combinations with different additives and lubricants:

Table 2 Combinations of materials tested

Number	Combination	Material dose sleeve	Material threaded sleeve	External lubricant
1	POM–PBT	Neat POM	PBT	–
2	POM–PC	Neat POM	PC	–
3	POM–PA12	Neat POM	PA12	–
4	Masterbatch internal lubricant	Neat POM with masterbatch POM	PBT	–
5	PTFE internal lubricant	POM PTFE	PBT	–
6	Glass beads internal lubricant	POM glass beads	PBT	–
7	Silicone internal lubricant	POM silicone	PBT	–
8	PTFE external lubricant	Neat POM	PBT	PTFE lubricant
9	Silicone external lubricant	Neat POM	PBT	Silicone lubricant
10	Combination external lubricant	Neat POM	PBT	Combination lubricant
11	Masterbatch internal + combination external lubricant	Neat POM with masterbatch POM	PBT with masterbatch PBT	Combination lubricant

Abbreviations: POM, polyoxymethylene; PBT, polybutylene terephthalate; PC, polycarbonate; PA, polyamide; PTFE, polytetrafluoroethylene.

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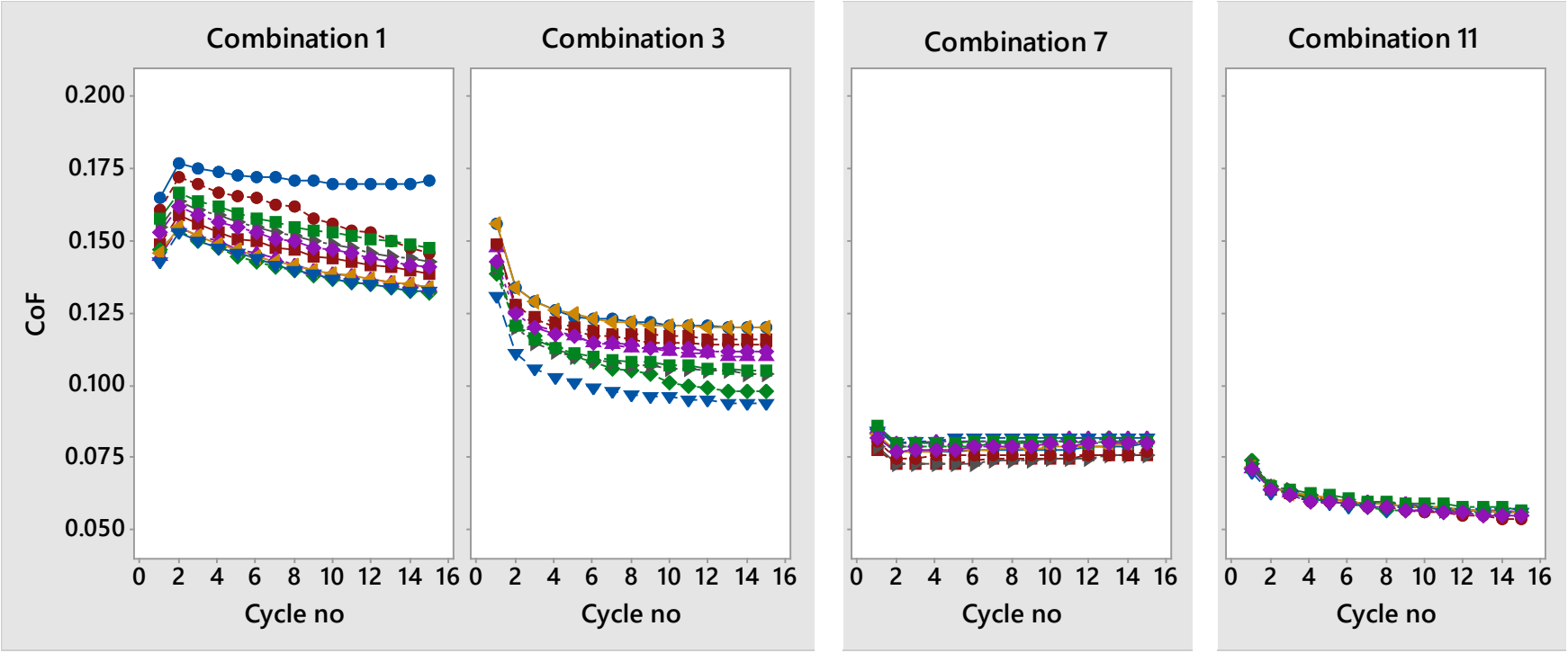
2. Case study 1 – The results 1



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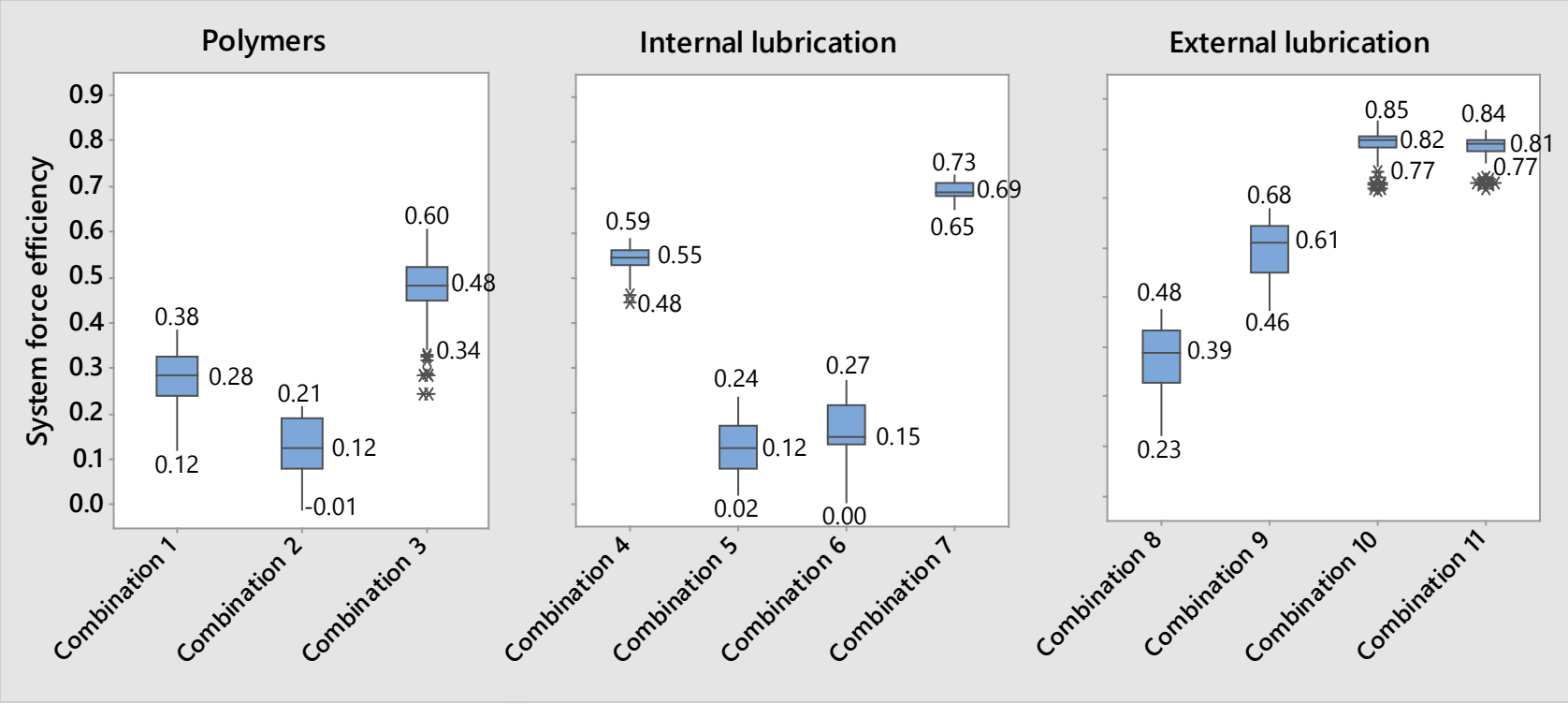
2. Case study 1 – The results 2



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3. Case study 2 – Force measurement versus perception

- Questions to be adressed:
  - Which is the best way to measure injection force?
  - Under what test conditions can / should pens be compared?
  - How do users actually perceive pens with different measured forces?

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3. Case study 2 – Force measurements

1. Three pens tested
   - Disposable pen (UnoPen™)
   - Reusable pen with the same gearing ratio (4:1)
   - Prototype disposable pen with different gearing ratio (3:1)
2. Injection force evaluated in different ways
   - Constant mechanical rate [mm/s]
   - Constant volumetric flow rate [U/s]
3. Tests with controlled rate
   - 2 different needle gauges (31G and 29G)
   - 25 measurements per pen type / condition (provides a resolution of at least ~1N)

Andreas E. Schneider & Jakob Lange (2018) Pen devices for self-injection: contrasting measured injection force with users' perceived ease of injection, *Expert Opinion on Drug Delivery*, 15:2, 115-125, DOI: 10.1080/17425247.2018.1415884

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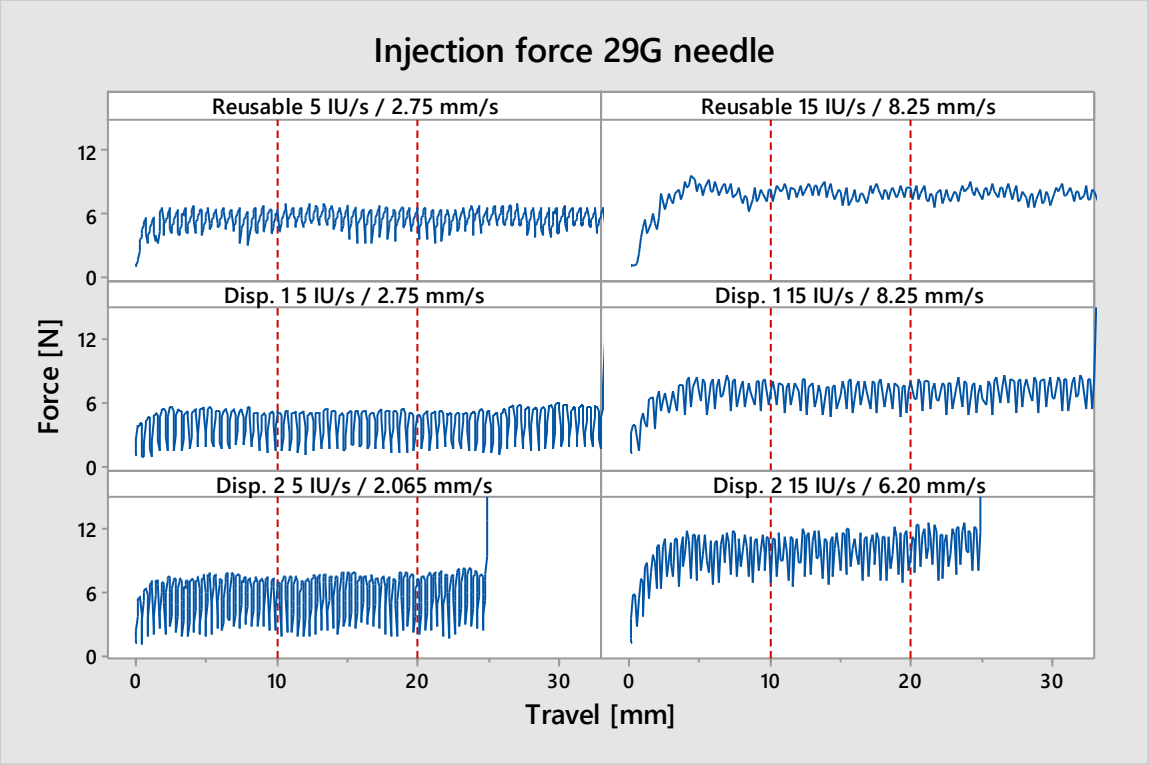
3. Case study 2 – Force raw data

- Force profiles are similar between pens
- Force level is different between pens
- Force increases with rate
- Plateau values can be used to compare between measurements
- *Force increases with needle gauge (thinner needle, data not shown)*



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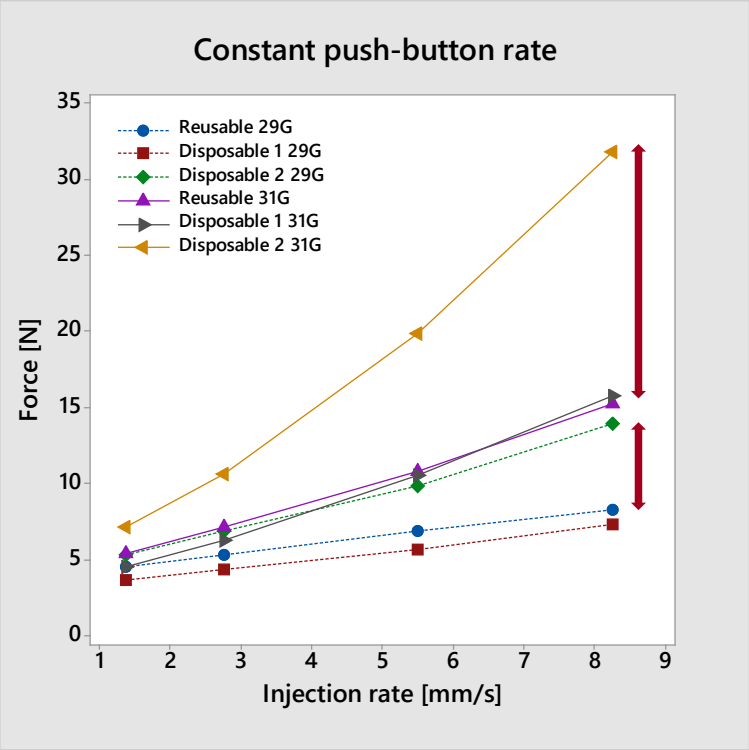
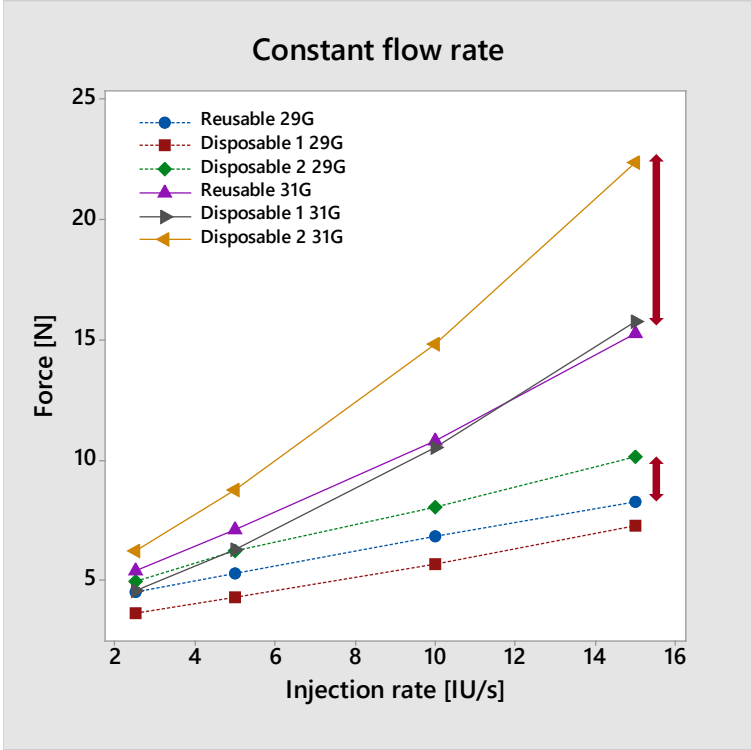
3. Case study 2 – Force results 1





- The two ways of comparing pens are not equivalent!
- Constant flow rate is considered the most appropriate (closest to user behaviour)

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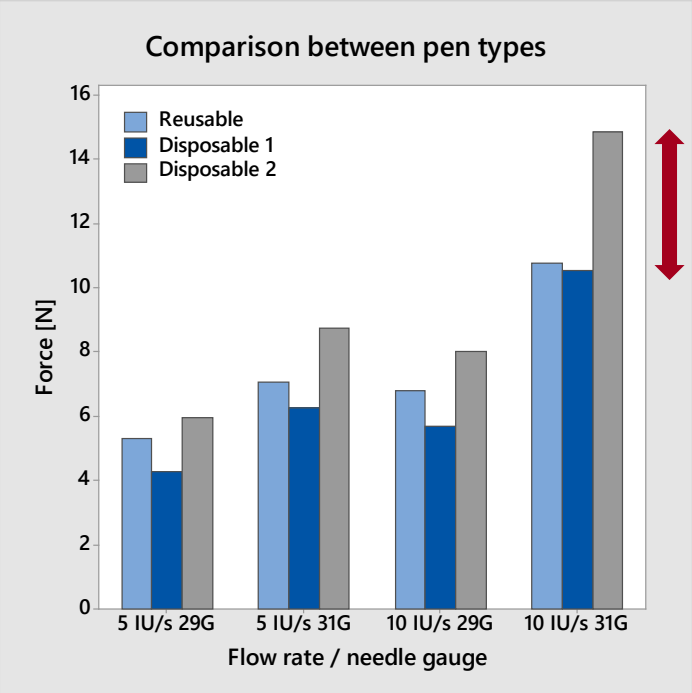
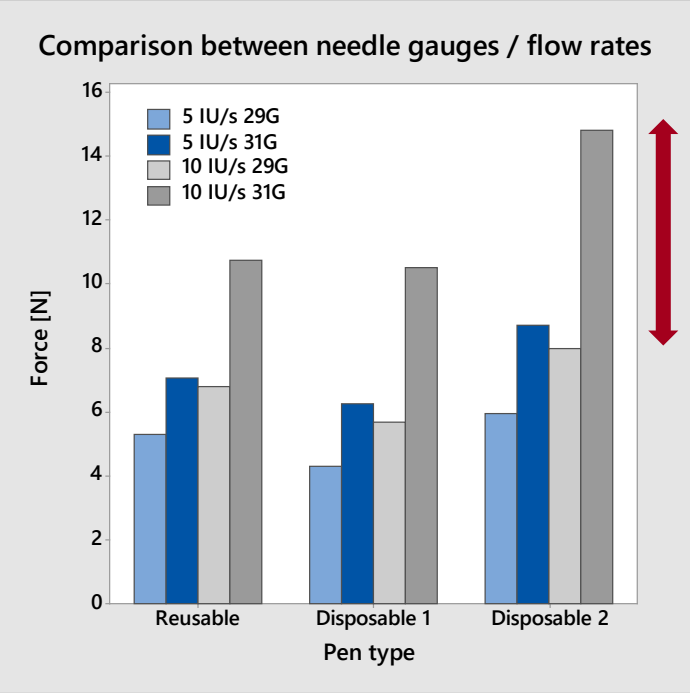
3. Case study 2 – Force results 2





- Larger differences between needle gauges (for a given pen and rate) than between pens (at a given rate and needle gauge) !

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3. Case study 2 – Patient perception study

- Simulated injections into an injection pad
  - All three pens tested, reusable pen included twice
  - Injection of 20 units (small dose) with 31G needle and 60 units (large / max dose) with 29G needle
  - Each participant performed every injection 2 times, in random order
- Participant rating of injection experience directly after each injection on a five-level Likert-Scale (1= strongly disagree; 5=strongly agree):
  - “How would you rate the handling comfort during the injection?”
  - “Please respond to the following statement: I had a pleasant feeling when performing an injection with this pen.”
- Participants
  - 39 participants, 19 female and 20 male
  - Age distribution 11-60 years
  - All injection naïve

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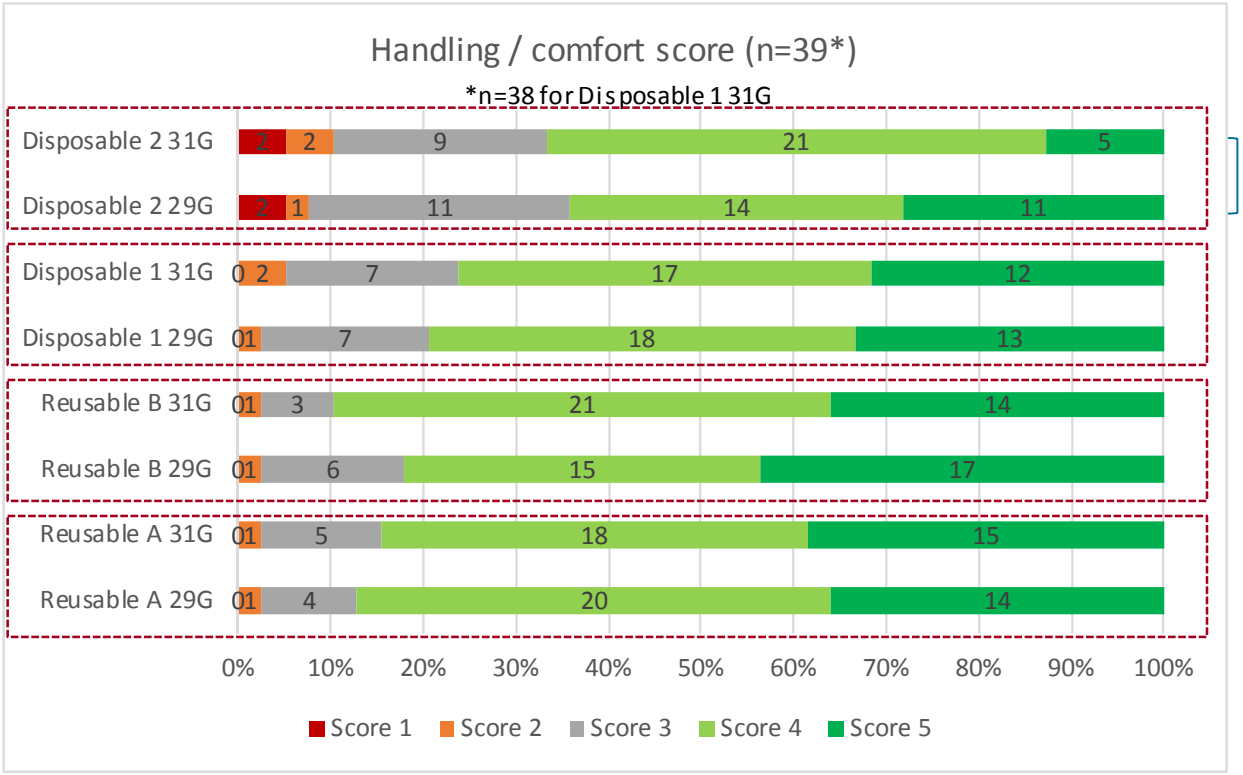
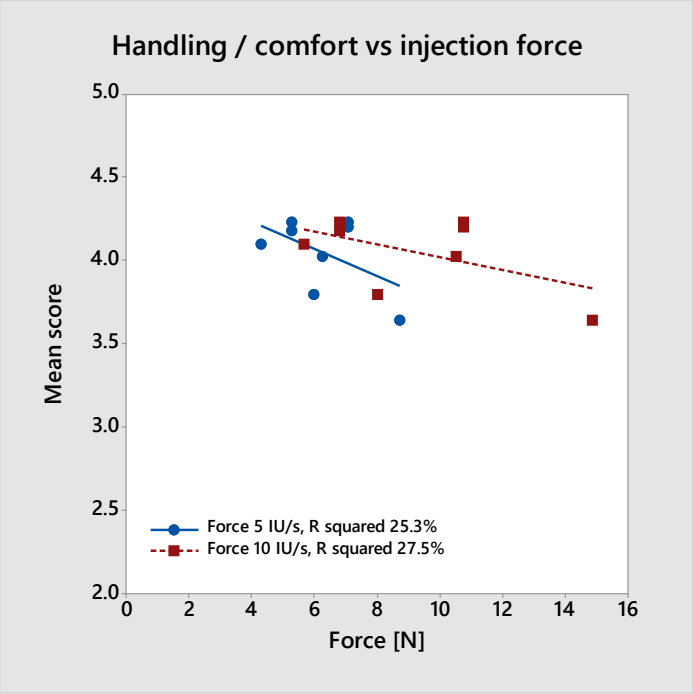
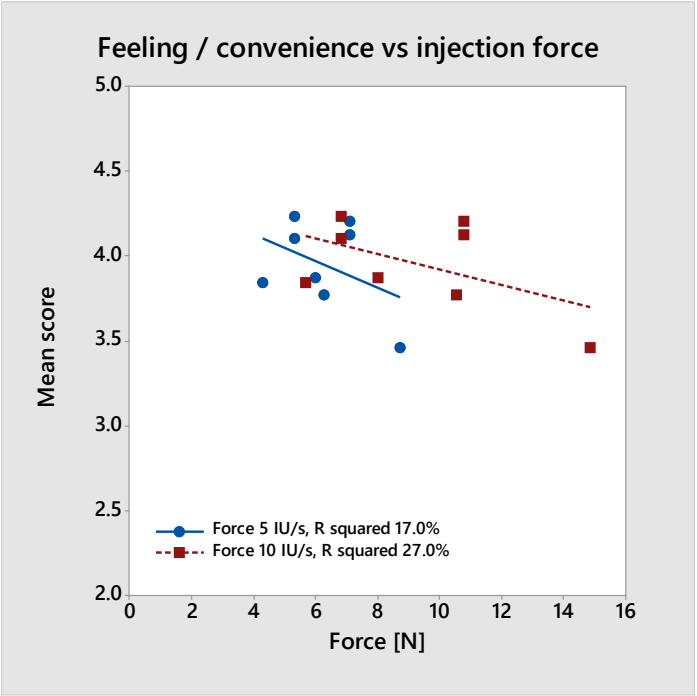
3. Case study injection force – Perception results



- Smaller differences between needle gauges (for a given pen) than between pens (at a given needle gauge) !

3. Case study 2 – Force versus perception





- Very little correlation is observed, other factors than measurable injection force must be at play!

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4. Conclusions

- Self-injection devices is an important and growing market
- Everybody agrees injection force is important but
  - There is no agreed standard for how to measure
  - Nobody has studied how users actually inject and what they prefer!
- Injection force is heavily influenced by the materials used in the pen
  - Frictional testing combined with modelling is a useful development tool
  - There are large differences between different materials
  - Additives / lubricants have as much influence on performance as the material itself
- Force measurement and perceptions
  - Measured forces / outcome depend strongly on the needle gauge, rate of injection and how pens are compared (constant push-button or flow rate)
  - Patients do perceive differences, but perception is only indirectly related to measured forces

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