

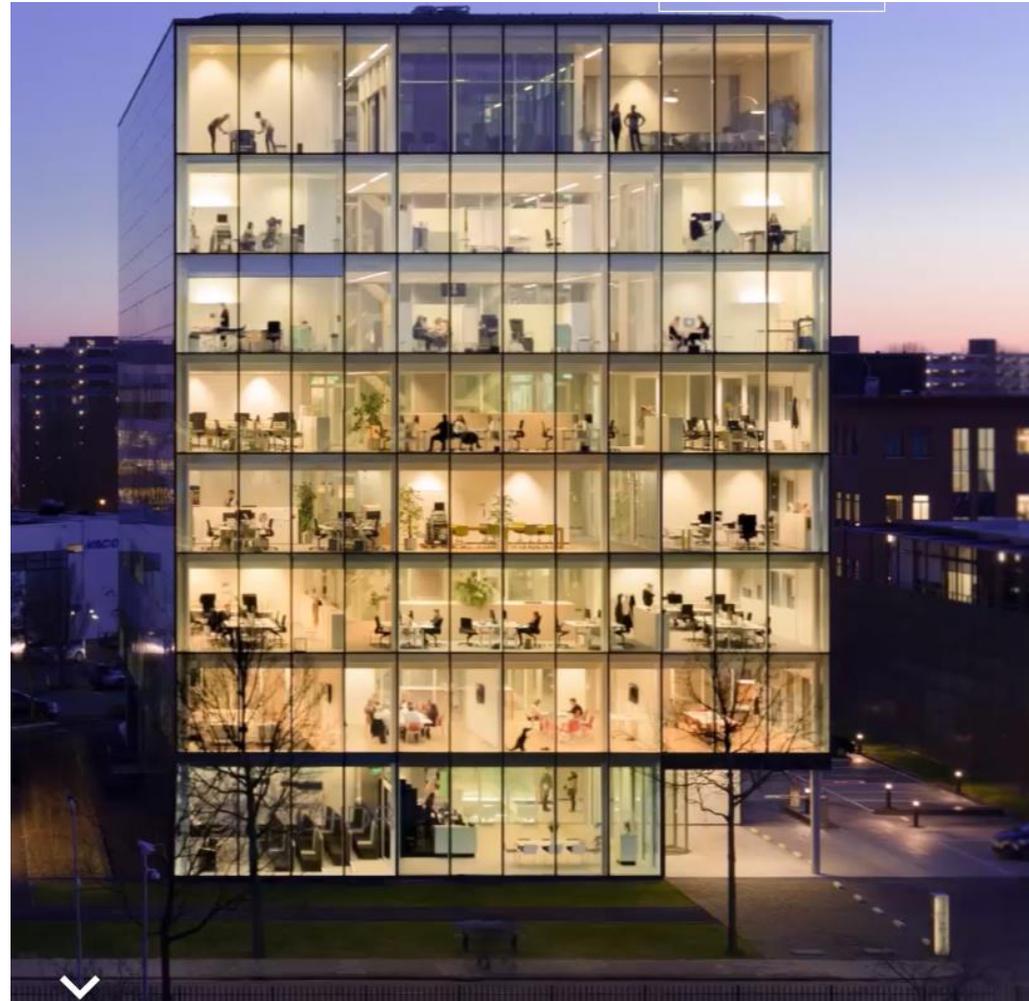
Digital support to study
performance in early phase
development
—
from recruitment to remote
data collection

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EUFEMED 16/17 May 2019

Disclosures

- **No personal shares, no personal financial disclosures**
- **CHDR as CRO collaborates with many pharmaceutical companies**
- **No shares or liaisons with any tech company**



the Apple Watch can help prevent strokes



Attrition in drug development

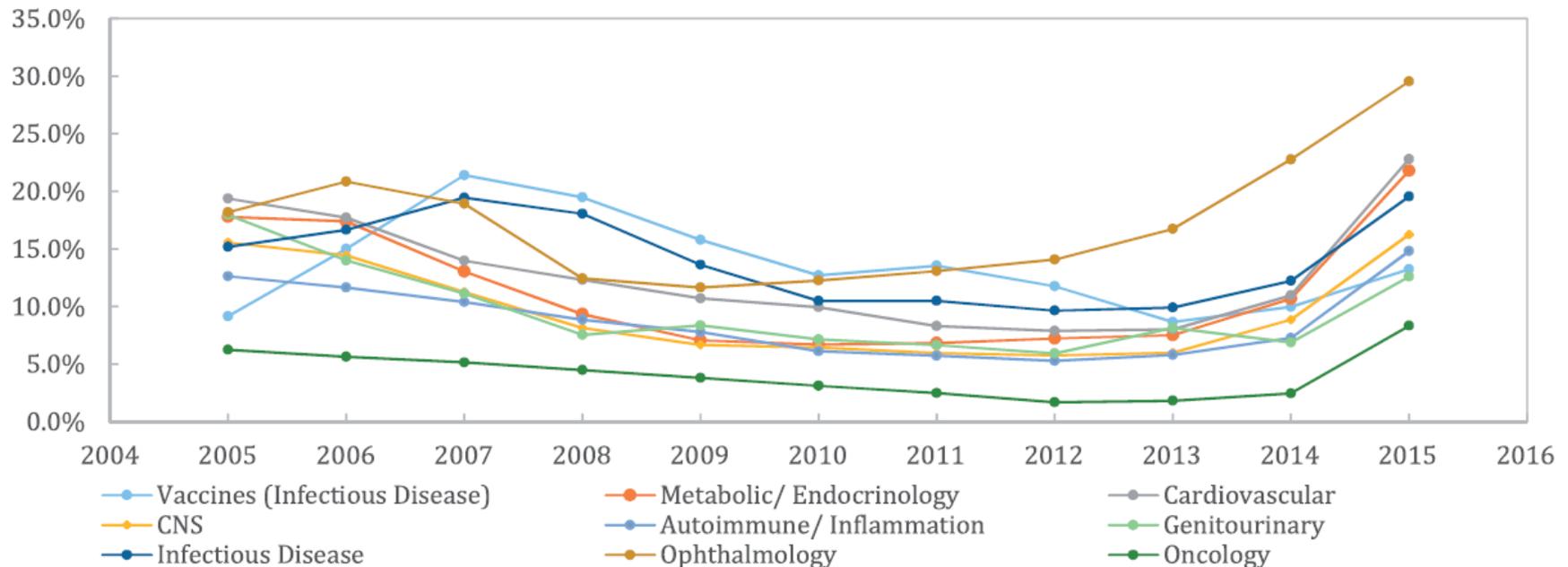
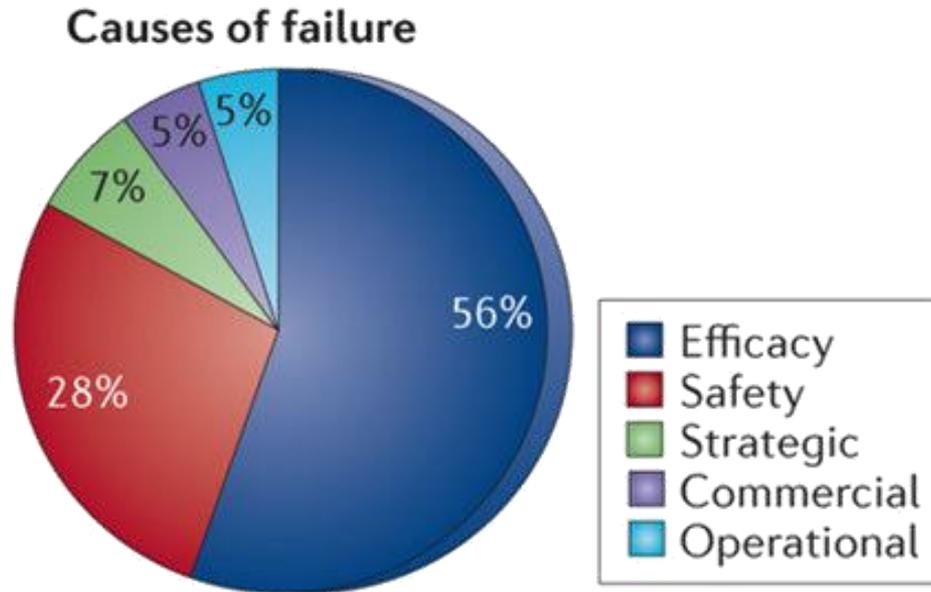


Fig. 1. The POS over the period of January 1, 2005, to October 31, 2015, computed using a 3-year rolling window

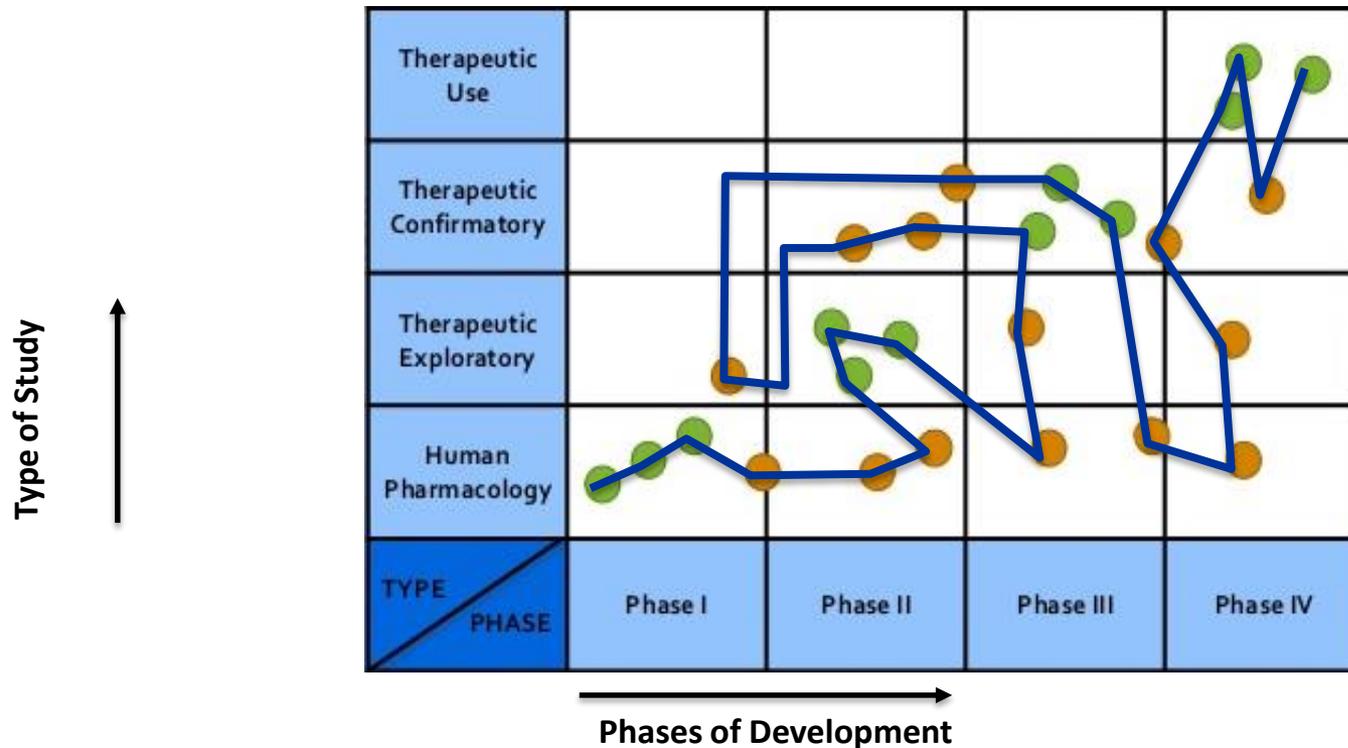
Main reasons for failure



Arrowsmith, J., Miller, P., Nature Reviews (12), 2013; 2) Ledford, H., Nature (477), 2011

Lessons for rational drug development

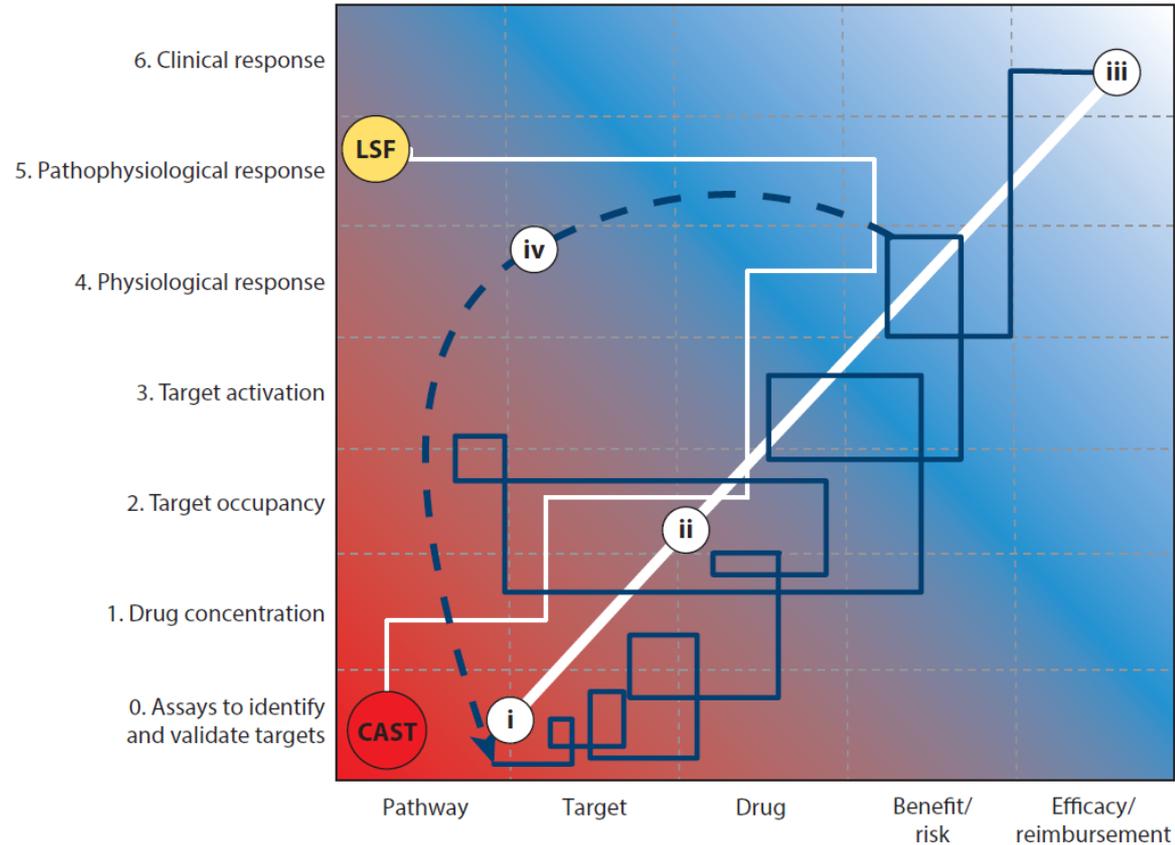
- PHASES ARE NOT ABSOLUTE



Federal Register / Vol. 62, No. 242 / Wednesday, December 17, 1997

- Frequently performed
- Sometimes performed

Learn and confirm cycles in drug development



Cohen *et al.* Annu. Rev. Pharmacol. Toxicol. 2015. 55:55–74

The challenge in drug development “ The method gap “



Technological revolution Opportunity for us drug developers!



New endpoints

Objective

Value-based

- Measure function patient (parent) cares about

Home-monitoring?

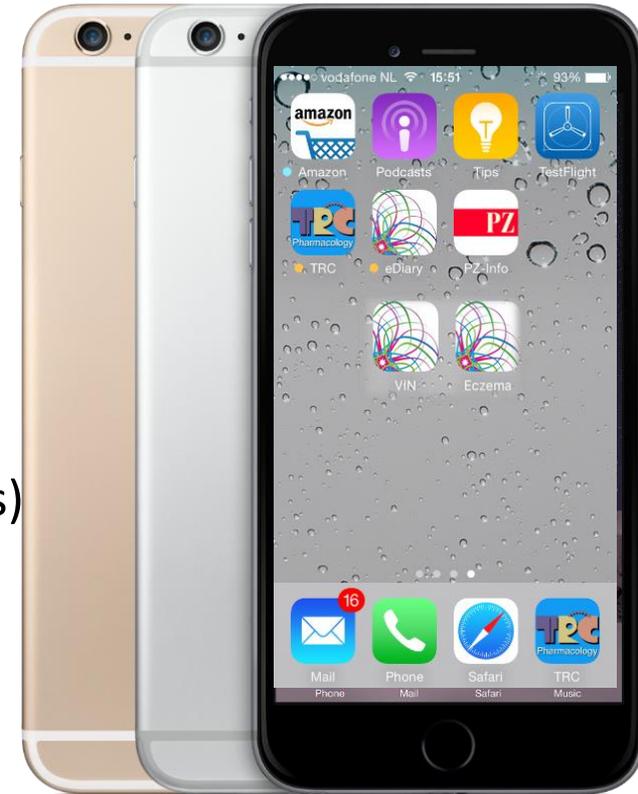
- Low burden
- 'Fun'
- Real-life data
- Continuous device monitoring
- High resolution
- Patient-centricity

Case 1: (e-) diary

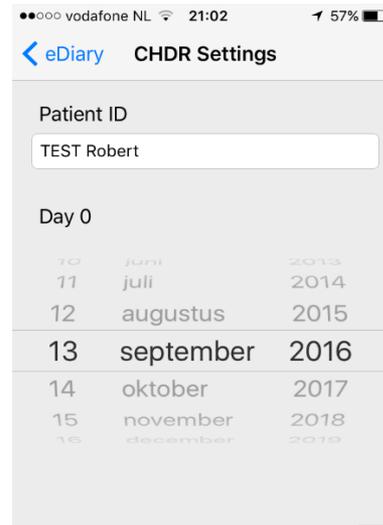


Mobile eDiary apps to perform clinical Trials@Home

- Fully validated (GAMP 5)
- For iPhone (subjects) / iPod touch
- Data capture with dense (customized) time intervals
- Patient reported outcomes (VAS, QoL, questionnaires)
- Accurate treatment compliance monitoring
- Reminder function
- Encrypted data transfer to CHDR server / into trial database



“Selfie app” for acne study



15

Treatment compliance with e-diary

Historic compliance dermatological trials

Verruca Vulgaris (warts)

Bruggink S et al. **71%**

Cockayne S et al. **77%**

Atopic Dermatitis (eczema)

Kütting B et al. **79%**

Wilson R et al. **70%**

Francis NA et al. **82%**

Conde JF et al. **70%**

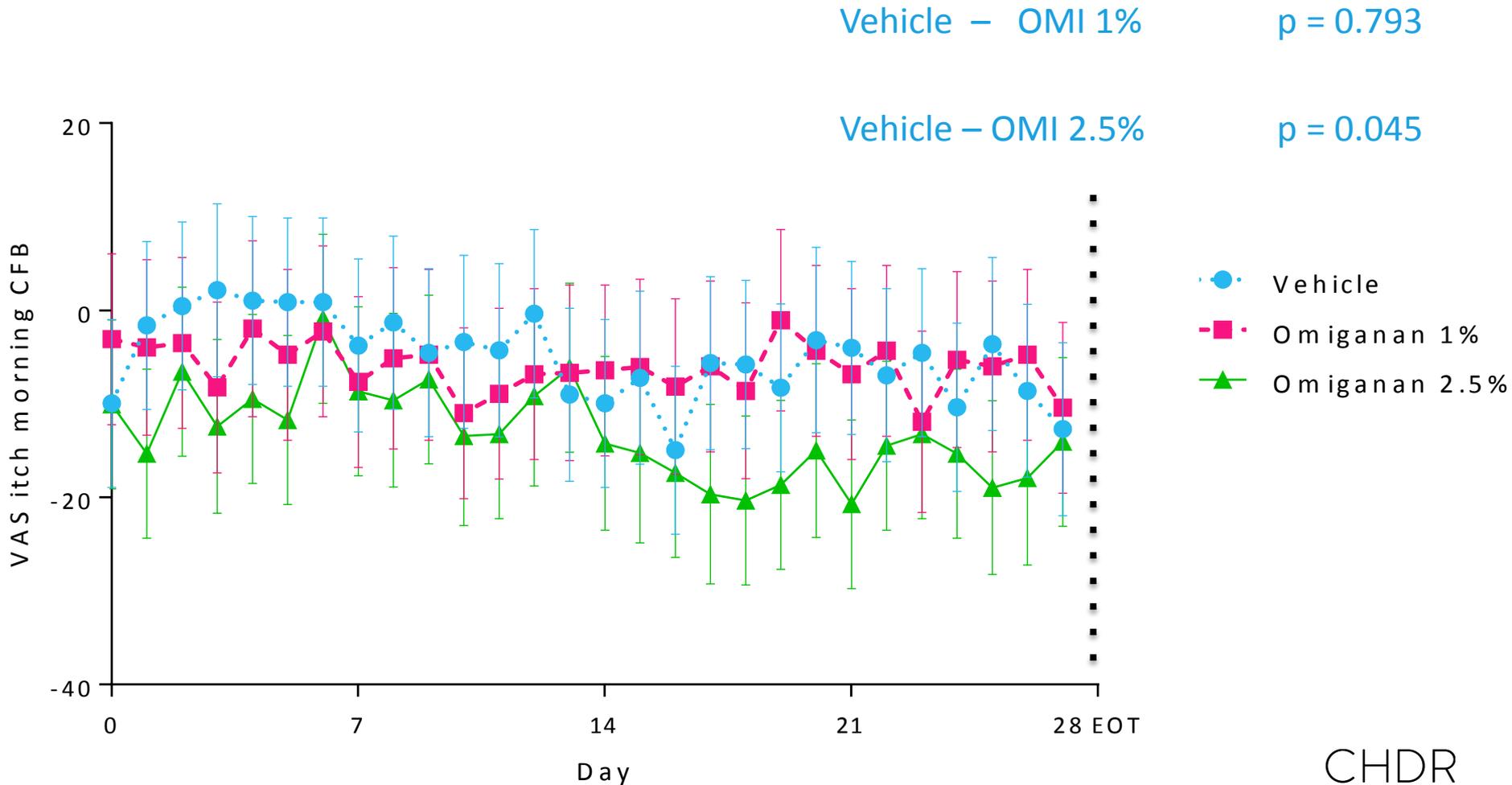
VIN (precancerous lesion vulva)

Tristram A et al. **87%**

6 trials with topical IMP and mobile app

	Expected admins	Actual admins	Treatment adherence
Cutaneous warts	3280	3187	97%
Atopic dermat QD	1013	991	98%
Atopic dermat BID	4318	4233	98%
Genital warts I	1960	1942	99%
Genital warts II	1008	998	99%
Vulvar hSIL	1020	1009	99%
Overall mean	12599	12360	98%

Patient-reported itch of atopic dermatitis patients via mobile app



Case 2: remote monitoring system

– Nokia Health platform

- Heart rate
- Blood pressure
- Sleep
- Weight
- Steps
- Temperature

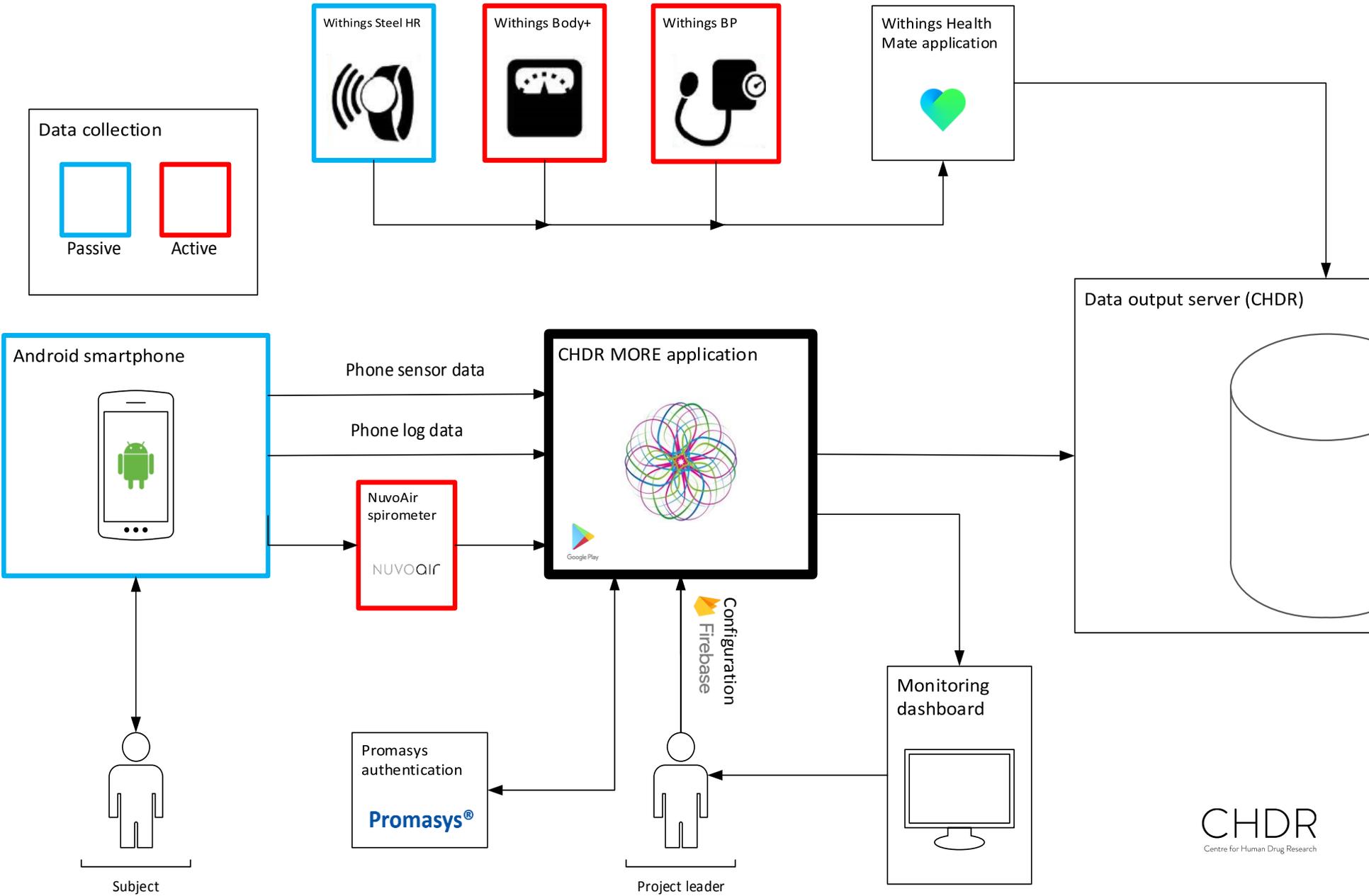


– NuvoAir Airnext spirometer

- FEV1
- FEV1%
- FVC
- FVC%
- FEV1/ FVC ratio
- PEF

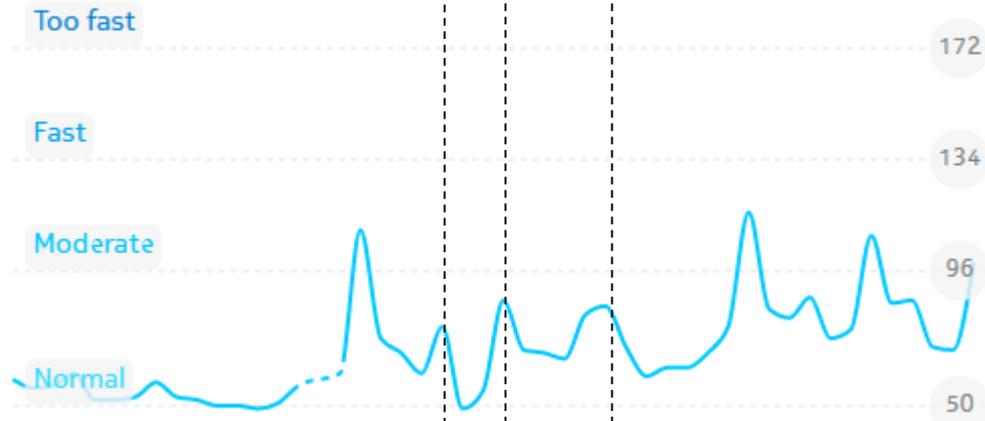


Data flow

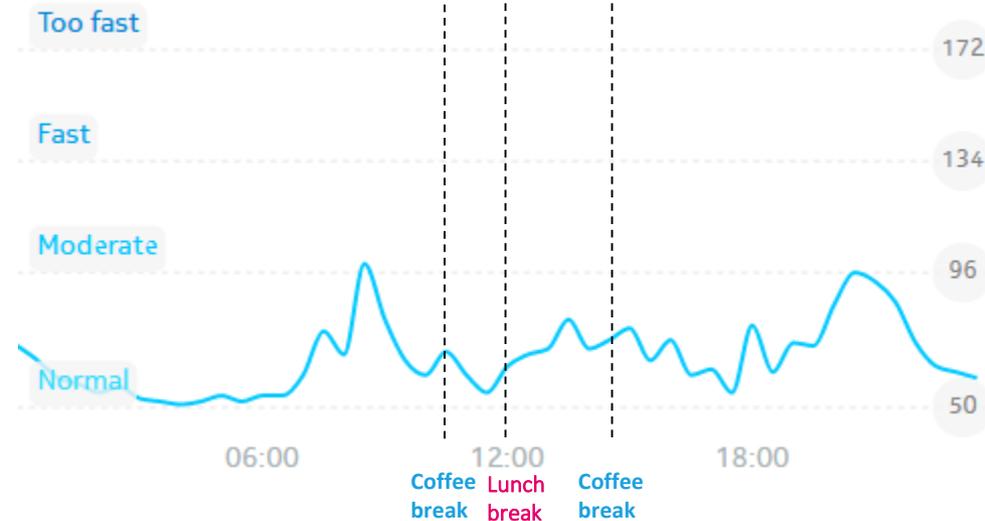


Results (pilot)

October 13, 2017



October 16, 2017



First steps taken

Validation of new endpoints

Confirm something we already knew

- Operations have a large impact on children
- Small pilot study
- One device
- Collaboration with Children's hospital Basel

Scale up and investigate multiple disease states

- Multiple large studies
- Measure disease-activity in chronically and acutely ill children
- Collaboration with Juliana Children's Hospital



CHDR
Centre for Human Drug Research

Case 3: Psoriasis

- CE marked device
- Real-time-monitoring of skin
- High quality data (standardized)
- Centralized data-storage with web-based access
- Machine learning tool for skin features



Automatic lesion quantification



Abb. 3: Klinische Bilder der Patientin zu unterschiedlichen Zeitpunkten der Therapie

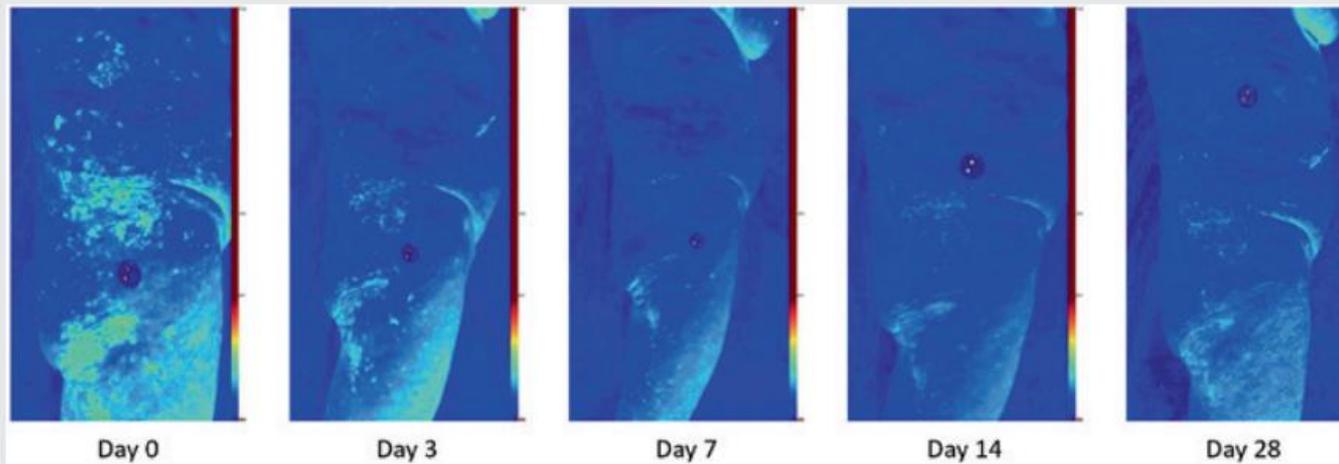


Abb. 4: SEV für ein repräsentatives Körperareal

Ethical and regulatory aspects

Approval process takes longer

- New methods
- More EC questions
- Study involving children or other vulnerable patient groups

Non-invasiveness helps with informed consent

All devices have CE-Mark

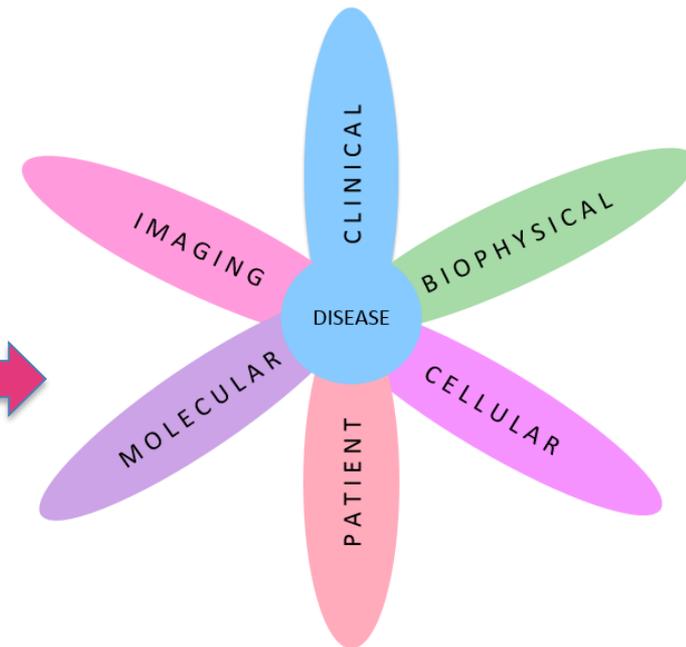
- Technical standards
- Safety

Not yet used in clinical decision making

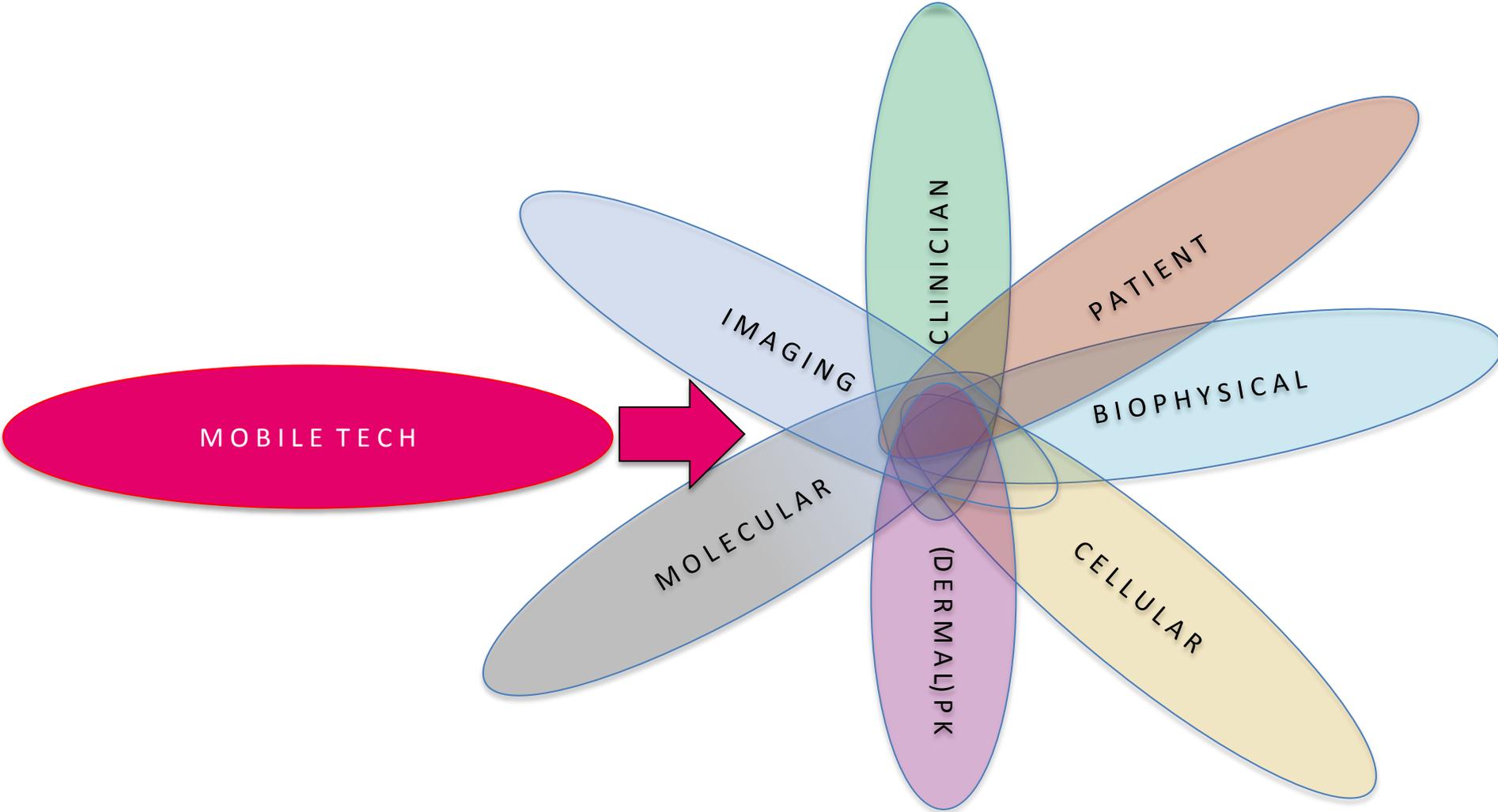
Systems approach

- Need for integration
- Multidimensional data analysis
- Artificial Intelligence

Biophysical  TEWL, Raman, Thermography, Laser Doppler	Clinical  Standard assessments	Patient reported  QoL, VAS, Cosmetic
Biochemistry  Biomarkers in biopsy, IHC, mRNA, FACS, Skin surface biomarkers, Microbiome	Imaging  2D, 3D, Fluorescence, Multispectral, OCT, PET, Total body imaging	Technology enhanced  Mobile apps



Future: multimodal drug development



Acknowledgements

Tessa Niemeyer - van der Kolk

Thomas Buters

Melanie Rijsbergen

Rianne Rijnveld

Mahdi Saghari

Hans Pinckaers

Martijn van Doorn

Ghobad Maleki

Matthijs Kruizinga

Max van Gent

Koos Burggraaf – Adam Cohen

