THE REMOTE TRIAL, A VIRTUAL PARTICIPATORY PATIENT-CENTERED (PPC) CLINICAL TRIAL

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Challenges & Opportunities in Clinical Trials

Clinical Research Challenges

Clinical trial cost & complexity are a barrier to sustainable innovation

Patient recruitment delays

Limited geographic coverage (site-centric)

Decreasing pool of investigators

Disparities in access

Economics not scalable for small populations

Complexity burdensome to patients

Consistency and quality challenges for multiple sites

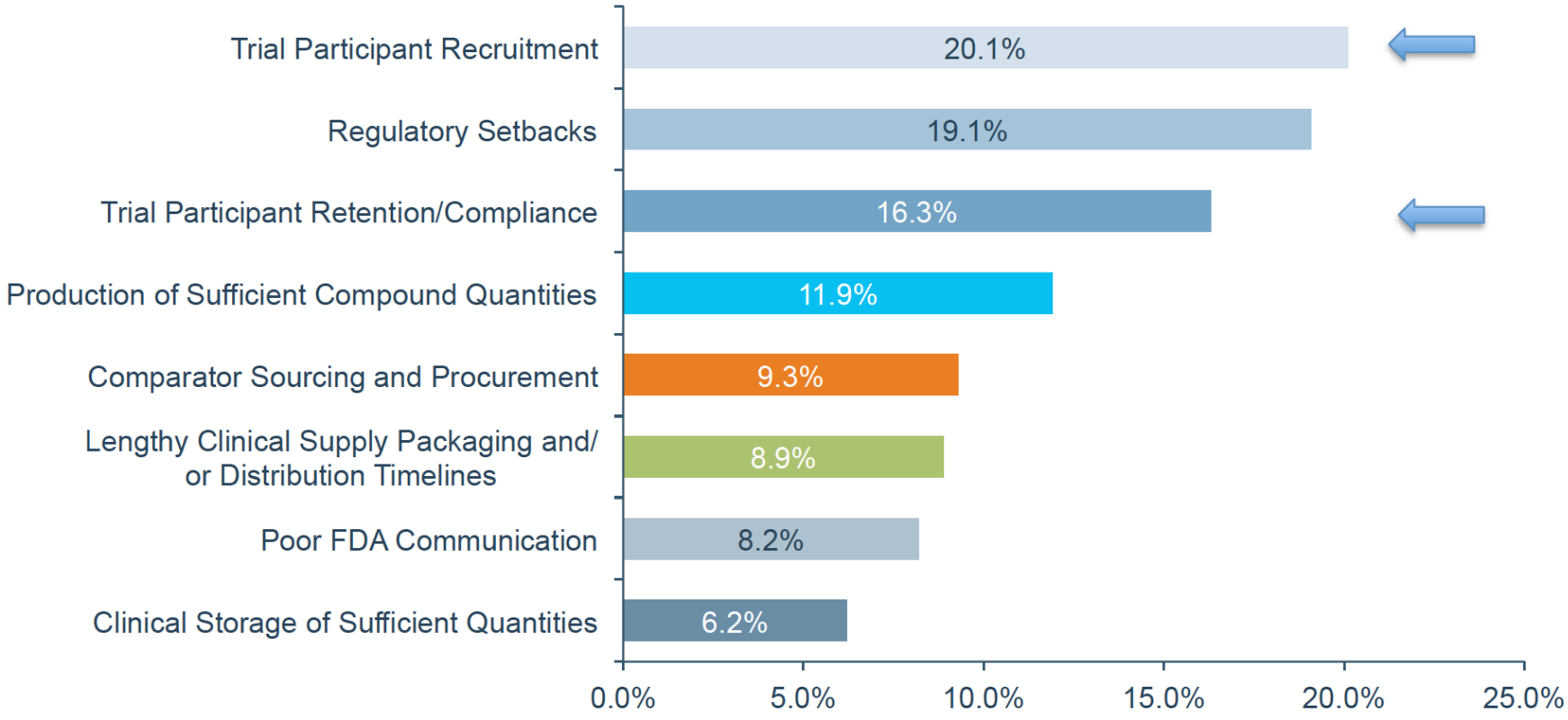
Increasing regulatory demand for large real-life studies

Drug Development Cost (Nov 2014)

Tufts Center for the Study of Drug Development (CSDD) pegs the cost of developing a prescription drug that gains market approval at $2.6 billion, a 145% increase, correcting for inflation, over the estimate the center made in 2003.

Biggest Challenges During Phase I-III Clinical Testing: 2016

Research into the biggest challenges faced during Phase I through Phase III clinical testing identify *Trial Participant Recruitment* (20.1%) as the most difficult. *Trial Participant Retention/Compliance* is the third most common selection with 16.3% of respondents indicating such.



Note:Values represent percent of responses from a survey of biopharma and life sciences researchers, executives and managers.

Sources: BioPharma DIVE, "2016 State of Drug Development: From Molecule to Market" – April 2016

Challenges & Opportunities

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Healthcare & Technology Trends

Participatory, connected, and pervasive healthcare

Rise of the ePatient & Participatory Medicine

Health Information Technology

Telemedicine and ambulatory monitors
(mHealth & quantified self)

Mobile phone proliferation

Health 2.0
→ Research 2.0

New clinical trial platforms

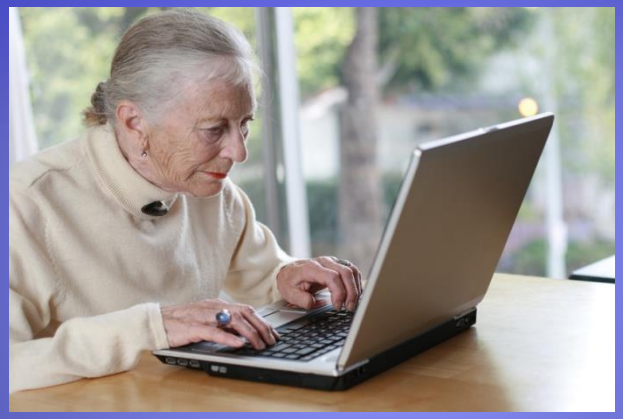
New roles

Global Smartphone Penetration

Rank	Country	Total Population	Smartphone Penetration	Smartphone Users
1	United Arab Emirates	9,398,000	80.6%	7,573,000
2	Sweden	9,921,000	72.2%	7,167,000
3	Switzerland	8,454,000	71.7%	6,061,000
4	South Korea	50,705,000	71.5%	36,262,000
5	Taiwan	23,564,000	70.4%	16,596,000
6	Canada	36,626,000	69.8%	25,556,000
7	United States	326,474,000	69.3%	226,289,000
8	Netherlands	17,033,000	68.8%	11,720,000
9	Germany	80,636,000	68.8%	55,492,000
10	United Kingdom	65,511,000	68.6%	44,953,000
11	Australia	24,642,000	67.7%	16,671,000
12	Belgium	11,444,000	67.3%	7,706,000
13	Spain	46,070,000	66.8%	30,771,000
14	Azerbaijan	9,974,000	66.4%	6,619,000
15	Italy	59,798,000	65.8%	39,323,000
16	France	64,939,000	65.3%	42,399,000
17	Saudi Arabia	32,743,000	65.2%	21,337,000
18	Portugal	10,265,000	65.0%	6,672,000
19	Czech Republic	10,555,000	64.8%	6,835,000
20	Malaysia	31,164,000	64.1%	19,967,000
26	China	1,388,233,000	51.7%	717,310,000
45	India	1,342,513,000	22.4%	300,124,000

Revisiting the Roles in Clinical Trials

Revisit the role of Principal Investigator

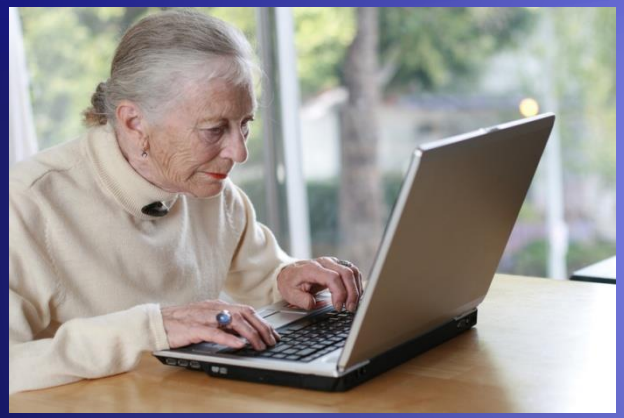


Revisit the role of Patient

Revisit the role of Treating Physician

The Engaged Patient

- ***Revisit the role of Patient***
- Quantified Self ~ Physiological Monitoring
- Tracking Apps ~ ePRO
- Aggregated Self-Reporting ~ Clinical Trials



Revisiting Roles – Treating Physicians

Today

Treating physicians have two potential roles:

Investigator
Infrastructure
Time commitment
Generally lose $

Referring physician
Lack incentives
Risk losing patient
General lack of contact with study

Tomorrow

New role enabled by patient-centered model:

"Heavy lifting" covered by PI in central coordinating center

Could IRB, paperwork, and monitoring all be covered centrally?

Enables treating MD to providing effective and engaged supporting role

Medical history to confirm diagnosis?

Support safety assessments?

Good for Patients - Good for Sponsors

For Patients

Improved Access

- Potentially no geographic constraints
- Improved socio-economic access

Engaged & Informed

- Actively engage in health management
- Self recruit into clinical trials
- Gain access to health information
- Obtain study results

For Pharma

Faster Recruitment

- Enroll patients anywhere

Improved efficiency

- Investigator site set-up
- Clinical monitoring

Better Patient Engagement

- Better retention
- Better quality data
- Real time safety data

Faster data lock

Participatory Patient-Centered Trial Key Elements

Subject

- Web-based recruitment
- Web-based consent process
- Web-based screening

Technology

- Mobile phone based efficacy assessment (e-diary)
- Study drug delivery by overnight courier
- Interactive data capture via secure website

Investigator site

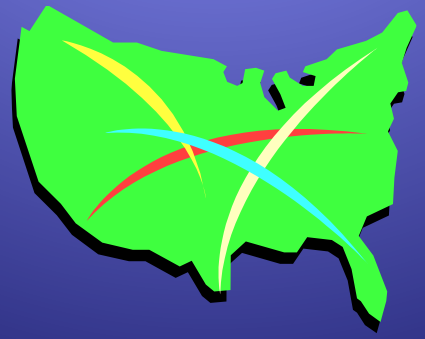
- Coordinating function for virtual site visits: patient will not attend investigator / site
- Study physician /call center available 24/7 by email & phone
- Return of study data back to subject

Testing the Paradigm

The REMOTE Study

(Research on Electronic Monitoring of OAB Treatment Experience)

New Phase 4 post-marketing study for the treatment of overactive bladder will mimic a previously completed trial in order to replicate the results and validate this novel approach	Single clinical coordinating centre Trial Investigators will enrol about 600 patients in a number of states across the U.S.	Pfizer has obtained FDA feedback as well as IRB approval for the study



Challenges

- Patient ID verification
- Informed consent process
- Telemedicine and privacy laws across US/Europe
- Availability of local labs and healthcare
- Drug shipment directly to patients
- Safety follow up in virtual setting
- Validation of tools
- Regulatory acceptability of data
- **Patient engagement**

Reasons for Subject Loss

- Account creation: >50% loss
  - too early in the process, patient did not know whether they qualify for the study, no established relationship
- Email confirmation: 25% loss
  - Confirmation went into spam filter, subjects expected to be contacted, disruption to flow
- Identity verification: up to 93% loss
  - Criteria too strict, no repeat after mistake, often lack of public information leading to automatic exclusion

What worked well

- Video based informed consent process sets new quality standard

- Electronic data capture tools allow for real time response
- Direct data entry from subjects/site with immediate logic checks

Informed Consent Process

- Standardised process across sites
- Information provided is documented
- Subject understanding is tested
- GCP compliant
- IRB acknowledged high standard
- Positive feedback from FDA and European regulators (MHRA and BfArM)
- Potentially sets new quality standard
- Allows time saving for the investigator

Data Quality

eData capture at source

- Upfront investment of time and resource
- Option for logic checks at time of data entry
- Remaining data queries can be addressed in real time
- Real time remote data monitoring
- Real time access to data/safety signals
- Number of data queries 4.5 per subject vs. 30-40 in previous studies
- Database lock achieved after 8 days post LSLV

ePRO

Diary

- Real time access to data
- Option to send reminders for non-compliance
- Option to limit data evaluation to compliant subjects
- Possibility to quantify compliance (>70% of micturitions have been reported within 1 hour)

REMOTE Clinical Trial Has Achieved a Number of Firsts

This is the first ever randomized clinical trial under an IND to:

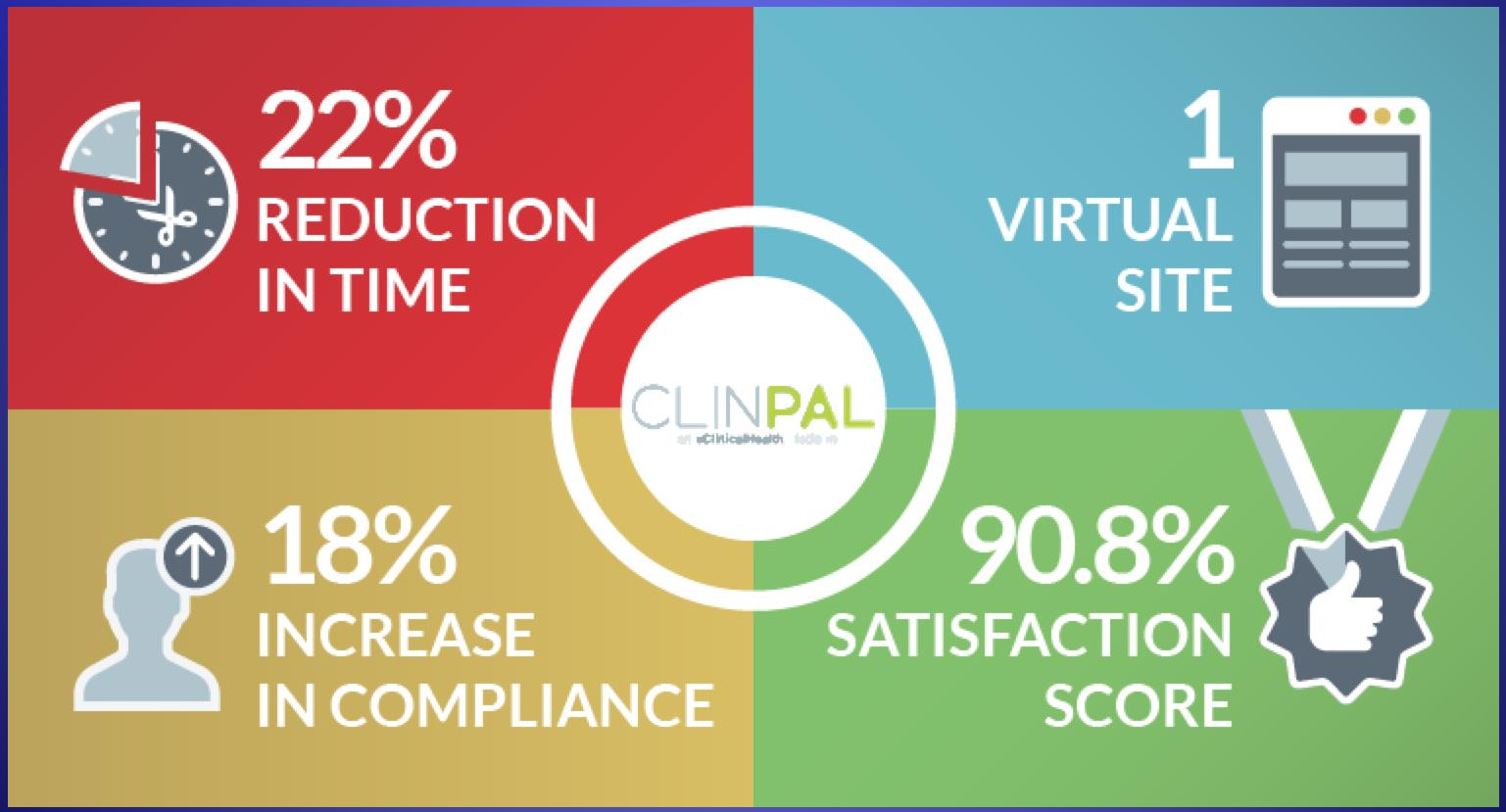
- **Secure patient consent online, using video/multimedia and online testing**
- **Ship all blinded study medication to patients at home**
- **Manage patients entirely in an remote manner**
- **Share clinical trial data and results back to the patient, to enable them to add it to their own personal health records**

… but what next?

REMOTE 2.0

- Enhance patient experience
- Engage patient early and "hand hold" through screening process
- Engage primary care physician as a familiar link to the patient
- Provide each patient with communication device
- Use local visiting nurse

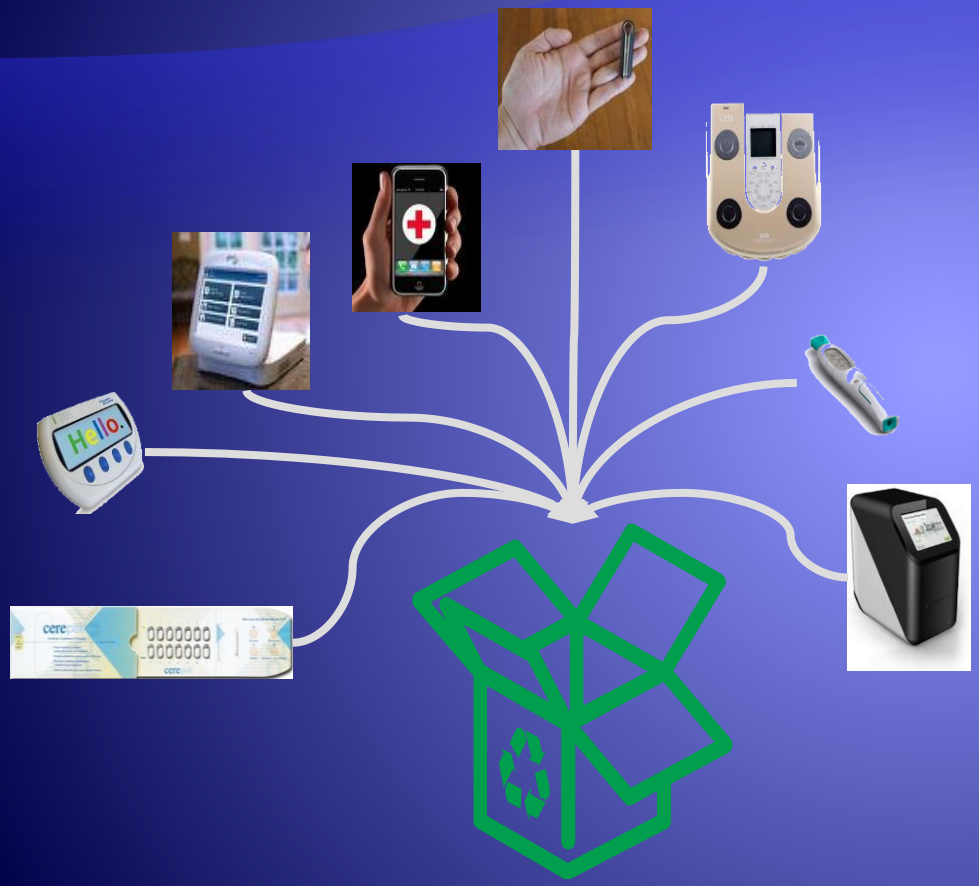
VERKKO Study Results



Virtual Studies in Pharmacovigilance

- Ideal for PASS (Post-Authorisation Safety Studies)
  - Prospective non-interventional studies
  - Large simple clinical trials
- Modular approach allows for flexibility and huge cost savings
- Availability of clinical trial platforms allow for quick setup and long-term follow up

Clinical Trial In-A-Box

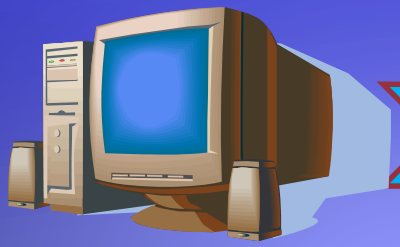


- Potential to further extend into new indications with use of other integrated technologies
  - Activity monitoring
  - Point-of-care diagnostics for blood, physiologic measurements (weight, BP, etc)
  - Other telemedicine appliances for "virtual patient visits"
  - Compliance monitoring / smart-packaging
  - Genetic testing & consumer genetics
  - Continuous diagnostic data

- Where are the boundaries and how can we move them while ensuring patient protection and data integrity?

Need for Integrated Health Information Technology

Electronic Health Records



Flag available clinical trials as treatment options

Payers Databases

Patient decides what data to share

Clinical Trials

Data imported

Entered by patient

Loaded from devices

PHR maintains "flag"/audit trail showing data source (EHR vs. self-report)

Where May the Future Take Us?

- Integrated data share between patients, primary care providers and clinical investigators
- More supporting legislation for virtual trials
- Country wide primary care trial networks
- Engagement of primary care physicians in clinical trials with regulatory support
- Patients take more responsibility in their health management
- Global access for patients to clinical trials

Conclusion

- "Virtual" trials are here to stay
- Post-Authorisation studies are ideal for virtual trials
- Patient engagement is paramount
- Data quality is a driving factor for industry
- EHR management systems and databases are the next revolution in clinical trials

DON'T TELL ME THE SKY IS THE LIMIT, THERE'S FOOTPRINTS ON THE MOON!

Paul Brandt

There's a world out there