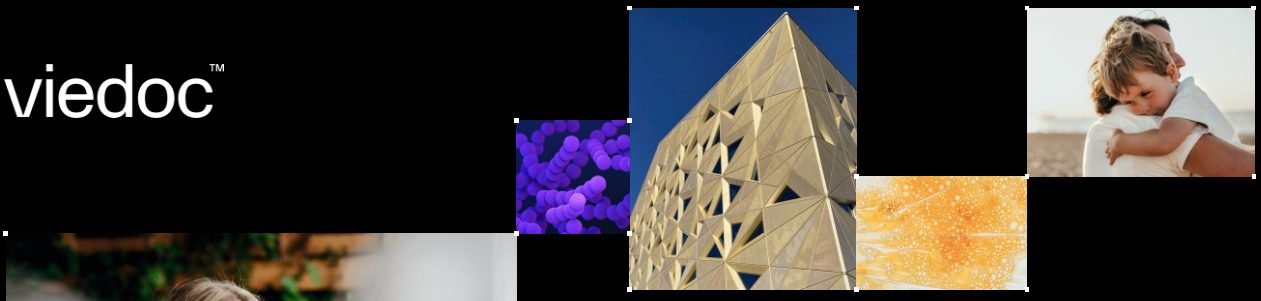
viedoc™



Digitalisation in early clinical trials: Theory and practical examples

1

Key facts

Studies
6 000+

Uptime
99.99%

Users
140 000+

Subjects
1 000 000+

Countries
75+

Sites
30 000+

2

Solutions overview

The essentials

viedoc clinic™	For the site staff and clinical professionals Manage all your trial data in one effortless solution
viedoc admin™	For the study manager Get your study started – and keep it running smoothly
viedoc designer™	For the study builder. Create your own professional study – no design or coding skills required

The addons

viedoc me™		For the subject Reliable data collection, directly from the source
viedoc connect™		For the decentralized trial Fully integrated support for Televisits and eConsent
viedoc logistics™		For the supply manager. Smooth, secure and seamless inventory tracking, dynamic and static randomization
viedoc tmf™ viedoc isf™		For the trial manager and the sites. Powerful documentation management from a single interface; site and project interface
viedoc pms™		For Japanese PMS studies Flexible data collection for the Japanese market
viedoc reports™	*Always included*	For the project manager. Tailorable reporting for quicker, deeper insights

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Traditional Clinical Trial Endpoints

Some of the limitations of traditional clinical trial endpoints:

- Subjective measures
- Limited data points
- Disruption to patients' daily lives
- Costly and time-consuming

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Digital Endpoints?

Objective, quantifiable, and electronically captured measures of health or disease that can be used to assess the effects of the medical intervention.

Some of the advantages of digital endpoints:
- Objective and continuous data collection
- Real-time monitoring
- Improved patient experience
- Cost-effectiveness

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Types of Digital Endpoints

Wearable devices
- Collect physiological data (heart rate, sleep patterns, activity levels)

Smartphone applications:
- Track patient-reported outcomes, medication adherence, and symptom monitoring

ePRO/eCOA:
- Patient-reported data in real-time, QoL questionnaires

Sensors:
- Monitor biomarkers (blood glucose, blood pressure) and external factors

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Possibilities: Smart-watches

Approx. 4 days battery life
Fast charge

Always ON display
Interactive touch ring

Calorie intake
(manual food/meal logging)

Alarm, timer, stopwatch

Sedentary behavior detection

Stainless steel housing
Gorrilla Glass display
Water resistant up to 1atm

Continuous Heart Rate monitoring
(incl. HR Zone, Resting HR, HR Recovery)

VO_2 max estimate, Respiration rate (EU)

Automatic activity tracking
for walking, running, biking: Calorie burn, Active minutes, steps

Automatic sleep tracking
incl. sleep patterns

- Medical device:
- Class 2a – EU
- Class 2 - US

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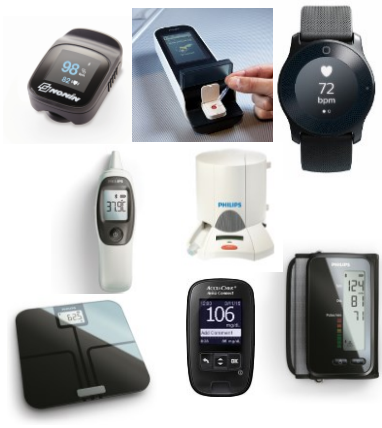
Home based data capture



Point of care diagnostics, (Glucose, cardiac and immunology markers)
Activity and sleep, scales, vitals, medicine dispensing, ePRO, diary, Respiratory support

Site based data capture

Vitals,
lab results,
Monitoring
Assessments

Additional data

Medical imaging
Digital Pathology
Genomics
Patient Monitoring in Critical Care
Ventilation

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Benefits of Digital Endpoints

- Enhanced data quality and quantity
- No parking lot syndrome
- Increased patient engagement and compliance
- Early identification of treatment effects
- Accelerated decision-making, all data now
- Actionable items/outcomes

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Table 9–3 Trial flowchart

Trial Periods	Information visit	Screening	Randomisation	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	Treatment	End of treatment
Clinic Visit (V) /Phone Contact(P)		V	V	P	V	P	V	P	V	P	V	P	V	P	V	P	V	P	P	V
Visit number		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Timing of visit (weeks)		-2	0	1	2	3	4	5	6	7	8	10	12	14	16	18	20	22	24	26
Visit window (days)				± 3	± 3	± 3	± 3	± 3	± 3	± 3	± 3	± 5	± 5	± 5	± 5	± 5	± 5	± 5	± 5	± 5
EFFICACY																				
Fasting plasma glucose			X								X				X					X
HbA_{1c}		X									X				X					X
Fasting C-peptide		X																		
2-point profile (twice daily)				X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]
7-point profile			X[4]								X[4]				X[4]					X[4]
SAFETY																				
Adverse events		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Allergic reactions		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Hypoglycaemic episodes		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Technical complaints				X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Body measurements		X	X								X				X					X
Physical examination		X																		X
Vital signs		X																		X
Pubertal status (Tanner staging)			X																	X[7]
Haematology		X																		X
Biochemistry		X																		X
Lipids			X																	X
Antibodies (anti-insulin)			X								X				X					X

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Digital versus centralized. What is the difference?

Decentralized clinical trials meet patients where they are.

Clinical-trial designs

Fully decentralized ← → **Hybrid** ← → **Fully centralized**

All trial procedures are conducted virtually, enabled by digital technologies and supply delivery	Less complex trial procedures that don't require in-person visits (eg, vital signs, electrocardiograms) are conducted via telehealthcare, remote data collection, or direct-to-patient supply	Less complex trial procedures that require in-person visits (eg, injections) are conducted via mobile clinicians or alternative sites (eg, mobile clinics, retail sites)	Complex trial procedures (eg, complex screening protocols, cell therapy, magnetic resonance imaging) are conducted via research sites (eg, academic medical centers) or local hospitals	All trial procedures are conducted at a research site (eg, academic medical center)

McKinsey & Company

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Digital trials more popular

- Patient experience is in focus; already at protocol stage
- Digital trials broaden access to a larger, more diverse range of patients while (hopefully) reducing the workload for investigators.
- Sites more comfortable with site- and patient-facing technologies
- Regulatory acceptance accelerated by the pandemic
  - Stay focused on patient-centricity
  - Televisits
  - eConsent
  - eCOA/ePRO

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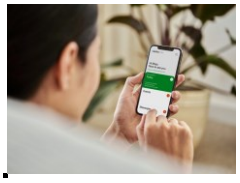
Retention

- Consider patient burden when preparing study protocols. Too much burden on patients cause drop-out and trial delays as well as inaccurate results.
- Have the patient responding as much as possible conveniently in ePRO/eCOA, connected devices etc with minimal person-to-person interaction.
- Utilize risk-based monitoring tools to track trends, allowing investigators to identify anomalies.
- Some patient groups may experience increased difficulty participating in a remote environment, e.g. teenagers or elderly. Always address special needs of different populations when preparing protocol.



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Points to consider for your digital trial (1)

- Data driven trial designs optimize around the needs of patient and trial needs, prove the hypothesis in the study protocol
- Ensure sites can function with same level of quality as if physical visit. The site will need to deliver care in multiple modes – how can we make it easy for the site while ensuring same level of quality.
- How to incorporate remote visits to lab, imaging etc
- Participant wellbeing and data privacy
  - Safety first! Study design and selection of sites, w/o placing undue burden on sites and patients
  - Can the population be supported remotely?
  - Where is data stored? Privacy issues, e.g. GDPR

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Points to consider for your digital trial (2)

- Proper training of staff and study participants
- Maintain data quality
  - Whatever solution you eventually choose, data must be accurate and of high quality
  - Data must be able to be monitored remotely
- Data integrity - thorough documentation of data and audit trails
  - Why/how/what/where and by whom data was captured and/or changed
- Support for both technology and processes

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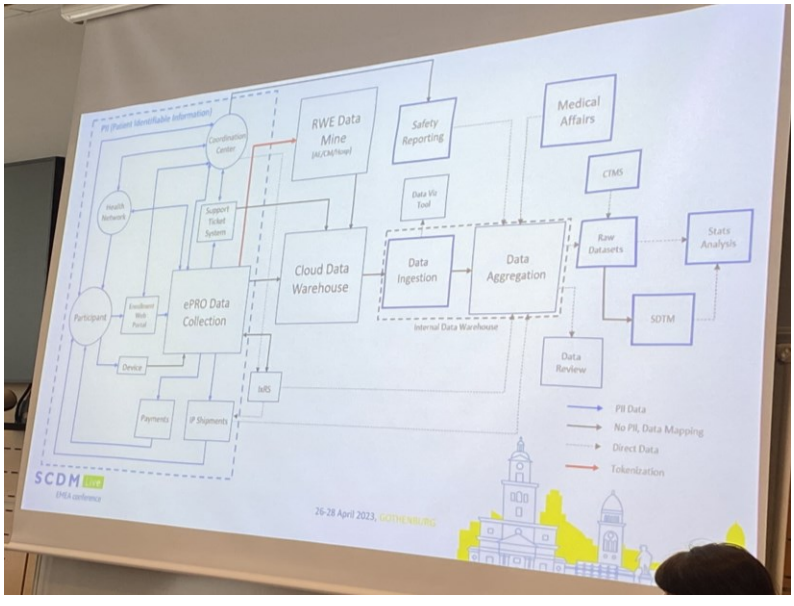
Digital trials rely on inte-grations



Presented by Manny Vasquez at SCDM April 27, 2023

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New roles and processes in digital trials

Set up	Vendor management	Data flows	Review and monitoring
- Vendor agreements - Setting up data flows - Setting up technology environments - Adding technology roles to your study	Vendor oversight - More vendors to manage - Combining many processes and technologies - Using eSource will reduce reconciliation	Oversight process - Dataflow review plan - Transmission oversight, checking for errors - Integrity checks	Data and monitoring review - Remote monitoring - Compliance checks - QTR checks - Data review

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New Clinical Data Management process

Traditional process	Digital process
• Data reconciliation	• Data integrity and compliance checks
• On-site monitoring	• Remote and central monitoring
• Data cleaning	• Data issue review and resolution
• EDC data entry	• eSource and EDC

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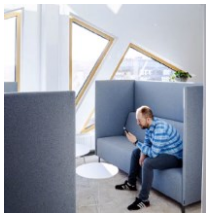
The volunteer / patient



- Patient engagement, it must fit into patient's regular lives, guide them
- Televisits, simplifies contact between patient and site, to support patients in all aspects
- Consumer-grade experience, devices/processes must be user-friendly and realistic to use for the patient.
- Direct data capture/eSource, collecting data from source is essential – lowers/eliminates the need for SDV
- Pre-enrollment, patient connectivity, eConsent and digital tools prepare patients for the upcoming trial

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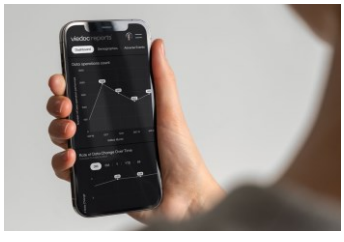
Consumer grade experience



- Companies such as Peloton®, Apple®, and Fitbit® leverage behavioral science principles to influence consumer decision-making and keep users engaged with their products.
- These companies have a deep understanding of what makes their customers tick, what their expectations are, and what their preferred experience is, and this insight drives innovation.
- In the consumer market, engagement through technology means allowing customers to set their own goals, overcome challenges, receive real-time feedback, and make transparent progress.
- Learn from them.

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The site

- The success (or failure) of digital trials will be heavily influenced by site adoption.
- If new technology integrations degrade the patient experience or interfere with the site/patient relationship, sites will continue to use their own processes – or don't participate.
- 3rd party vendors must be carefully added to the mix, if it creates uncertainty in terms of delegation, oversight and safety, sites simply won't offer it to their patients.

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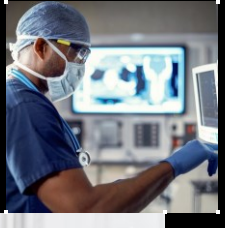
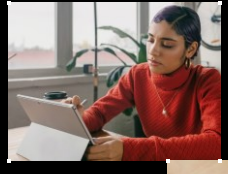
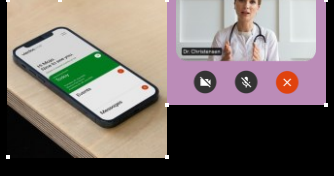
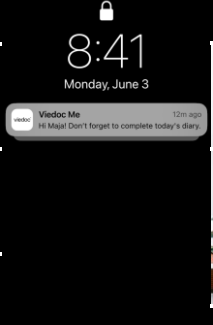
The building blocks of a digital solution

1. Candidate screening & consent
2. Direct Data Capture and Integrated RTSM
3. ePRO
4. Televisit
5. Visit Reminders
6. Integrated devices
7. Remote care by sites
8. Remote monitoring by clinical professionals









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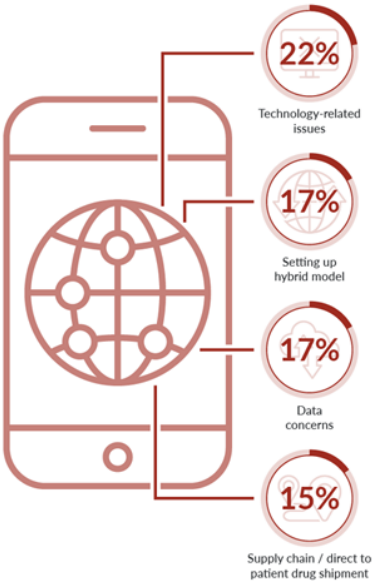
Top frustrating aspects



https://www.clinicalleader.com/doc/hybrid-trials-are-here-to-stay-0001

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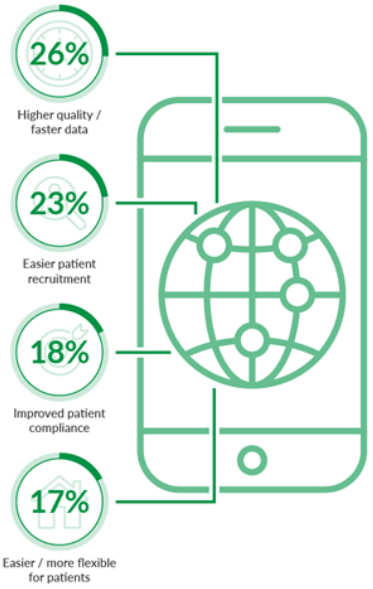
Top aspects that have gone well



https://www.clinicalleader.com/doc/hybrid-trials-are-here-to-stay-0001

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Trial oversight more important

Speed	Safety	Quality	Integrity
Time to data entry	Protocol Deviation Rate	Query Rate	Screen Failures
Key cycle times, e.g. query response time.	SAEs/AEs Rate by Site	Time to Query Resolution by Site	Missed Dose Rate
Site contractual doc signed to site initiation visit	SAEs/AEs Rate by Subject	Action items pending	Withdrawal/Enrollment
	SAEs/AEs Variance	Missing Pages	Out of Range Visit Rate
	Withdrawal/Enrollment	Missing Visit	Error Rate
		Protocol Compliance	Randomization Rate
		Overdue Visit Entries	Audit Trail Review
		Key Risk Indicators	Key Risk Indicators

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Hot Topic: Just out from the press

Decentralized Clinical Trials for Drugs, Biological Products, and Devices

Guidance for Industry, Investigators, and Other Stakeholders

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Ryan Robinson, 240-402-9756; (CBER) Office of Communication, Outreach, and Development, 800-835-4709 or 240-402-

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Conclusion

- Digital endpoints offer objective, real-time data in early clinical trials.
- They have several advantages over traditional endpoints.
- Challenges exist but can be overcome with proper planning and collaboration.
- Huge potential impact of digital endpoints on improving drug development and patient outcomes.

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Thank you

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