





DCT/Hybrid trials: How to help patients and sites through technology and processes



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# Key facts

Studies	6 000+	Uptime	99.99%
Users	140 000+	Subjects	1 000 000+
Countries	75+	Sites	30 000+



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# Covid-19 brought problems to the surface

- Regular clinical trials too burdensome on the sites
- Increasingly complex protocols
- Neither patient nor site friendly
- Ever increasing volume of data captured, more procedures, visits etc
- Regulatory burdensome
- New tools available – but very little experience
- Ever increasing costs for clinical trials

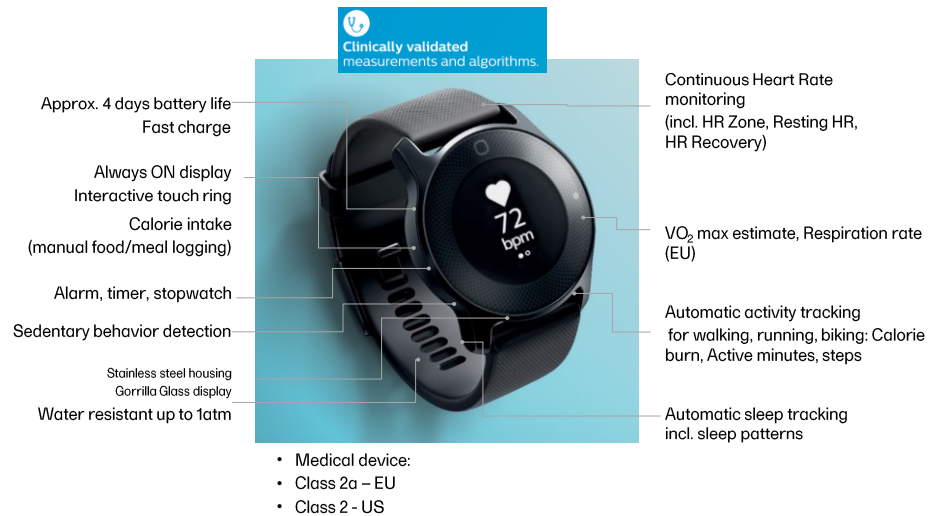
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Table 9–3 Trial flowchart

	Info ma tion visit	Scr een ing	Rando misati on	Treat ment	Treat ment	Treat ment	Treat ment	Treat ment	Treat ment	Treat ment	Treat ment	Treat ment	Treat ment	Treat ment	Treat ment	Treat ment	Treat ment	Treat ment	Treat ment	Treat ment	End of treat men t
Trial Periods																					
Clinic Visit (V) /Phone Contact(P)		V	V	P	V	P	V	P	V	P	V	P	V	P	V	P	V	P	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 <sub>1c</sub>		X									X				X					X	
Fasting C-peptide		X																			
2-point profile (twice daily)				X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	X <sup>3</sup>	
7-point profile			X <sup>4</sup>								X <sup>4</sup>				X <sup>4</sup>					X <sup>4</sup>	
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 <sup>7</sup>	
Haematology		X																		X	
Biochemistry		X																		X	
Lipids			X																	X	
Antibodies (anti- insulin)			X								X				X					X	

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## Possibilities: Smart watches



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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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# DCT/Hybrid

## 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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## Different from regular life?

	Visit #1	Visit #2	Visit #3	Visit #4	Visit #5	Visit #6	Visit #7
Grocery-defined Location	In-Store 	At-Home 	In-Store 	At-Home 	In-Store 	At-Home 	In-Store 
Protocol-defined Location	In-Clinic 	At-Home 	In-Clinic 	At-Home 	In-Clinic 	At-Home 	In-Clinic 

Source: Craig Lipset presentation

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# The rise of hybrid trials

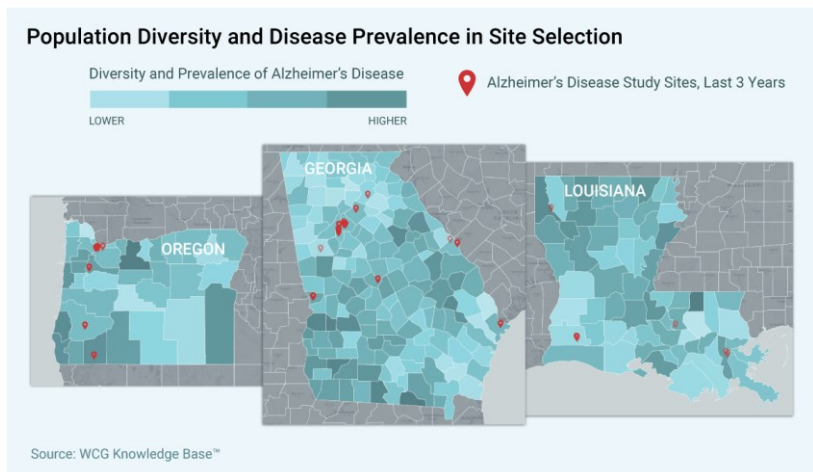
- The full decentralized trials are limited to cases where you have well-characterized drugs with minimal safety concerns and where endpoints are suited for remote monitoring.
- Hybrid trials uses decentralized technology such as eSource, wearables, in-home devices and eConsent, paired with regular in-clinic visits.
- Approximately 70 percent of potential patients live two+ hours from the nearest trial site – huge loss of potential patients
- Fewer than 5% of eligible patients are estimated to participate in clinical trials.
- *75 % of study participants live 30-60 minutes away from study sites*

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# Lost opportunities

Geographical distance will prevent many patients from the most diverse areas from participating in these studies.

Your ZIP code is a determining factor of health and possibility to participate in clinical trials.



<https://www.wcgclinical.com/covid-19/covid-19-trial-insights/>

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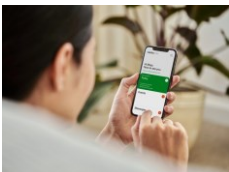
# Hybrid trials more popular

- Patient experience is in focus; already at protocol stage
- Hybrid 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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# Patient 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 DCT 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. Remember that 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
  - Where is data stored? Privacy issues, e.g. GDPR

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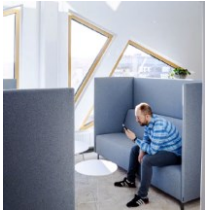
# Points to consider for your DCT trial (2)

- Proper training of staff and study participants
- Maintain data quality
  - Whatever solution you eventually choose, data must be accurate and of high quality
- Data 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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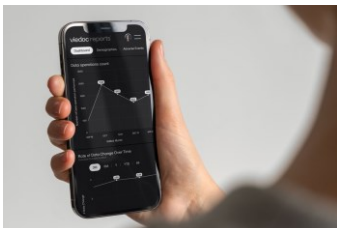
# The patient



- 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 DCT tools prepare patients for the upcoming trial
- Localization is very important, be culturally aware

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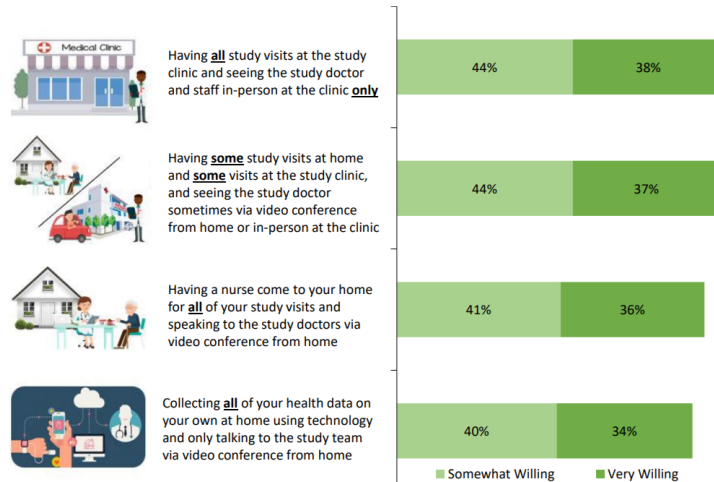
# Consumer grade experience



- 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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# Willingness to participate



Sample Size = 11,793; Base: All respondents

Center for Information and Study on Clinical Research Participation (CISCRP) : Perceptions and Insights Study 2021



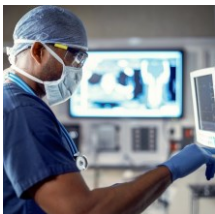
## Findings:

- Patient – Site relationship very important,
- Travel time significantly reduces participation
- Improve adherence by real-time or near real-time feedback from clinicians to patients
- Hybrid approach require sites to offer multiple models simultaneously
- DCT/Hybrid convenient, figure out personalized and customized patient experiences
- Privacy can be of concern for patients in DCT/Hybrid trials

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## The site (1)

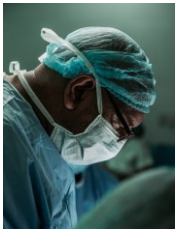
- An overwhelming majority of studies still (always?) need sites to run the studies and DCT methods are offered through the site.
- The success (or failure) of DCTs will be heavily influenced by site adoption.
- If new technology integrations degrade the patient experience or interfere with the site/patient relationship, sites will continue to use their own processes – or don't participate.



Adapted from Brad Hightower LinkedIn posts

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## The site (2)



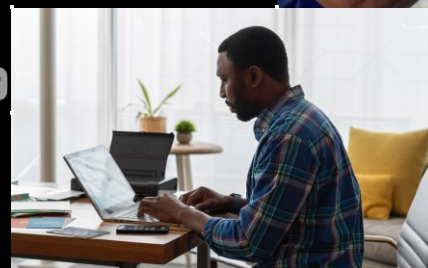
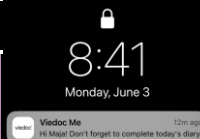
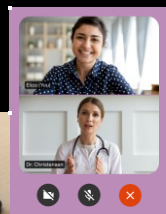
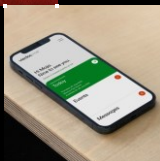
- 3rd party vendors must be carefully added to the mix, if it creates uncertainty in terms of delegation, oversight and safety, sites simply won't offer it to their patients.
- If eConsent doesn't provide any real value beyond the traditional consent process and is difficult to use, sites simply won't use it.
- Clearly demonstrate the value of your DCT to the sites.
- 80-90 % of investigators only participate in 1(!) clinical trial, 40 % will participate in a 2<sup>nd</sup> trial

Adapted from Brad Hightower LinkedIn posts

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## The building blocks of a DCT solution

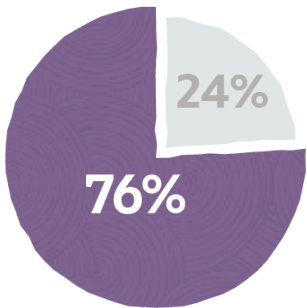
1. Candidate screening & consent
2. Direct Data Capture and Integrated RTSM
3. ePRO
4. Televisit
5. Visit Reminders
6. Integrated devices
7. Remote care by sites
8. Remote monitoring by clinical professionals



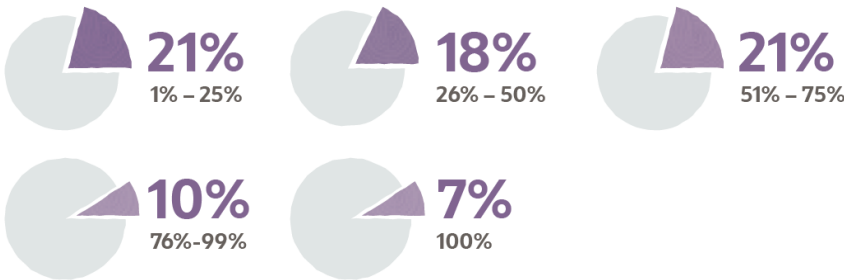
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# Decentralization – experience

% OF RESPONDENTS WITH AT LEAST SOME DECENTRALIZED TRIALS



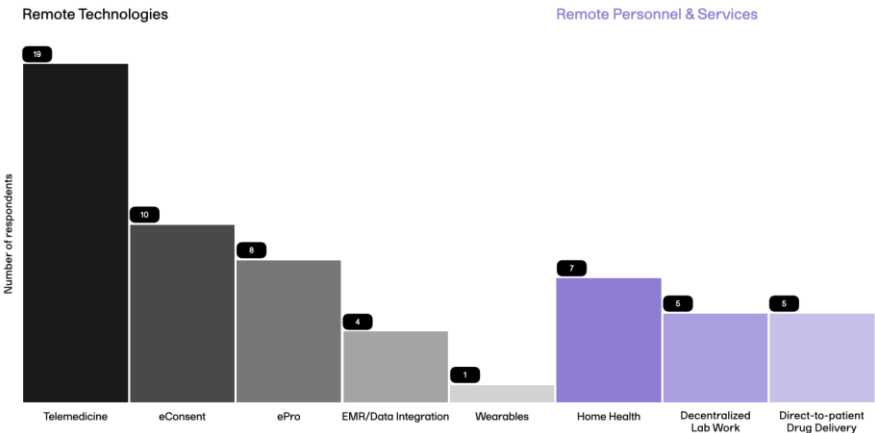
% OF TRIALS THAT ARE DECENTRALIZED



<https://www.outsourcing-pharma.com/Library/Is-clinical-development-prepared-for-the-paradigm-shift-caused-by-COVID-19>

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# Experience so far, what is being used?



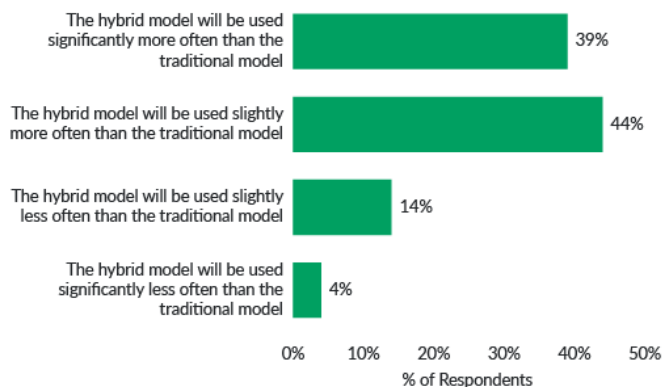
<https://www.appliedclinicaltrials.com/view/covid-19-and-its-impact-on-the-future-of-clinical-trial-execution>

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In recent research, 83 % say hybrid trials will be more used than the standard RCT

### Predictions for Hybrid Trial Use in 3 Years

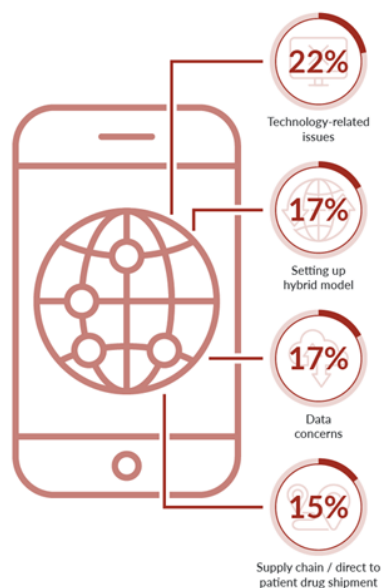
*"What is your outlook on hybrid trials' place in the biopharmaceutical industry over the next three years (in 2024)?"*



<https://www.clinicalleader.com/doc/hybridtrials-are-here-to-stay-0001>

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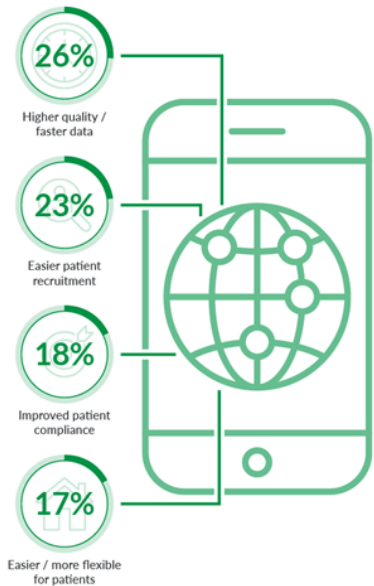
Top frustrating aspects



<https://www.clinicalleader.com/doc/hybridtrials-are-here-to-stay-0001>

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# Top aspects that have gone well



<https://www.clinicalleader.com/doc/hybridtrials-are-here-to-stay0001>

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# Trial oversight more important

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

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# Benefits of DCT

- **Patients**
  - Geographical and logistical benefits
  - Less burdensome and more flexible
  - Conducted in real world setting
- **Health Authorities**
  - Increased access to underserved populations
  - The D's, diversified and decentralized
  - Setting in clinical trials more like the real world
  - Compliance
- **Sites**
  - Eligible patients
  - Compliance, retention and adherence
- **Sponsors**
  - Recruitment, retention, compliance and less protocol deviations

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# 4 reasons Decentralized/ Hybrid trials are here to stay

- **Growing comfort with Health Technologies**
  - How to best interface with clinicians, sites, and patients
  - Experience and value is clearly shown
- **Technological and regulatory maturity**
  - More and more validated technologies
  - Regulatory acceptance prompted by the pandemic
- **Focus on Patient- and Site-Centricity**
  - eConsent
  - Televisits
  - eCOA/ePRO
  - Unified solutions
- **Emphasis on Real World Evidence**

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Thank you

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