
CHDR
Centre for Human Drug Research
it's test day!
PLEASE FILL OUT YOUR TEST NOW
start
report health issue
Trial@home

What CHDR Trial@home offers

- Trial design and execution
- Data analytics
- Validated and novel digital endpoints
- Integration with digital technology
- Integration with our Electronic Data Capturing system

Trial@home

Trial@home, CHDR's dedicated strategy for off-site clinical trials, opens up the possibilities for data collection in the comfort of the subject's home. It enables investigators to collect valuable information as subjects go about their day-to-day lives, while reducing the number of visits to the unit. Trial@home leverages our secure and safe digital health platform, CHDR MORE®, featuring validated and exploratory digital endpoints. The technology can be implemented in studies within and outside CHDR. The Trial@home service can be customised to fit the needs of the sponsor and the investigator and can range from the provision of the platform to trial execution and data analysis.

Why CHDR Trial@home?

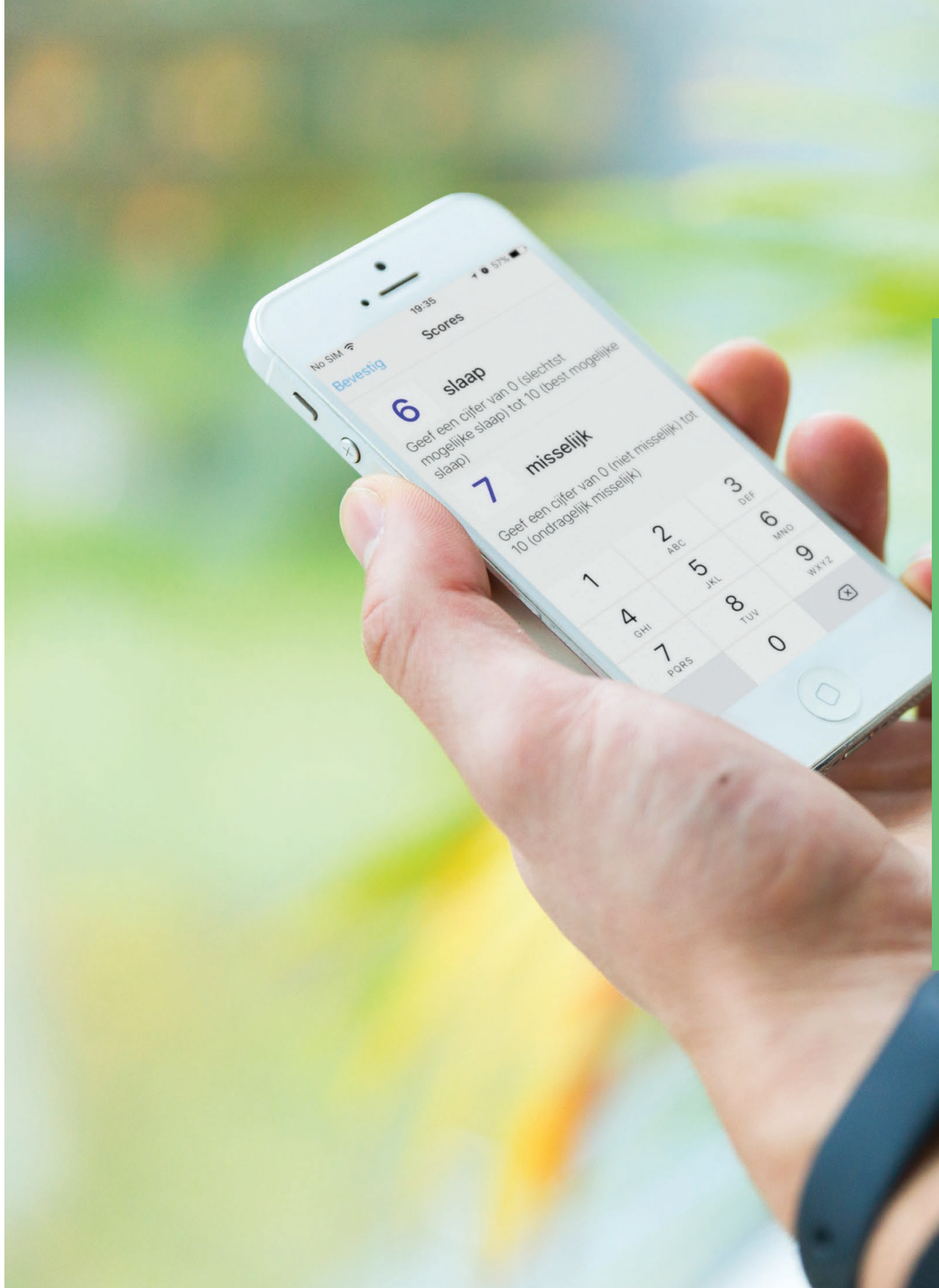
Establishing that medicines work, in the sense that they influence a certain pathophysiological mechanism, is a lot easier than demonstrating that they help. To show that they help, it is crucial to include value-based evaluation. This requires follow up of patients who do not necessarily have events of a condition (e.g. a stroke).

However, healthcare is increasingly delivered in an outpatient setting, which throws up challenges for conducting patient studies. The trend towards more outpatient care reduces the opportunity for patients to be recruited for studies, since these potential study subjects spend overall less time in the healthcare setting. Meanwhile, increased outpatient visits also place new demands on patients, who may not feel able to additionally participate in a clinical trial.

Overcoming these challenges calls for novel approaches that reduce both the threshold to recruitment and the burden of participation. This can be achieved with Trial@home, which offers unobtrusive monitoring of patients during their normal daily activities, combined with self-reported outcomes submitted electronically by study participants from the comfort of their own homes. This revolutionary approach to patient studies relies on the expert development and application of digital and wearable technology. Using these tools, we are able to gain more frequent and realistic measurements of the burden of disease, in a way that is both more objective and more individualised.

Digital health represents a trend that goes beyond the clinical setting, with wearable technology growing ever more popular. However, in order to leverage these novel technologies in the context of clinical trials, thorough validation is of paramount importance. CHDR's expert researchers have developed, validated and evaluated such technology in a broad range of patient populations and age groups, from paediatric to geriatric.

Our studies already demonstrate the benefits of this approach for recruitment – especially in populations that are traditionally difficult to recruit, such as paediatric and psychiatric patients. Coupled with CHDR's operational and scientific expertise, Trial@home provides the means to design and execute future-proof clinical trials.



Key benefits of Trial@home

- Data collected with Trial@home reflect the real-world situation of the subject better. This can reveal benefits or shortcomings of the intervention at an early stage in the trial. Early, data-rich insights into the effects of an intervention enable timely and well-informed strategic decisions.

- Subjects can be monitored for months or even years with relatively low effort and cost. This facilitates studies involving large research cohorts and monitoring of long-term health outcomes, upholding the principles of value-based healthcare.

- Data streams collected are transparent, fast and safe, ensuring data privacy, integrity and security (compliant with GDPR, EMA and FDA regulations).

Trial@home in overview

Trial design and execution services

CHDR has more than 30 years of experience in designing and executing clinical trials. And, thanks to our commitment to innovation and method development, our expertise is constantly being expanded. As part of the Trial@home service, CHDR's experts make sure that your trial is designed to the highest scientific standards. Validated SOPs are also used to ensure the successful execution of the trial.

Data analytics services

Apart from statistical evaluation of the endpoints, CHDR also offers the possibility of using the data collected to develop and validate novel digital biomarkers. This analysis aims to quantify the value that an intervention provides to the trial participants. Through this analysis, we can also gain an improved understanding of the disease and the macroscopic effects of an intervention.

The CHDR MORE® platform

The CHDR MORE® platform is a highly customisable environment that offers remote monitoring of study subjects, data ingestion, and data management. It consists of a smartphone app that enables unobtrusive data collection via multiple smartphone sensors as well as phone usage logs. The app also connects seamlessly to a range of digital platforms to retrieve and integrate additional relevant data (such as weather data, or environmental data concerning allergens). The CHDR MORE® platform has clear data management processes – a crucial requirement for comprehensive data analysis. Thanks to the monitoring dashboard, researchers are also able to monitor the streaming of data from devices to the server and prevent data loss.

Smartphone

- Sensors:
  Acceleration, Gyroscope, Magnetic field, Light, Steps
- Phone usage:
  App usage, User interaction, Phone calls, SMS
- Location:
  Places, Relative location
- Interaction
- Questionnaires
- Voice activation

ePRO

Withings

- Heartbeat *(Steel HR)*
- Steps *(Steel HR)*
- Sleep *(Steel HR/sleep)*
- Blood pressure *(BPM)*
- Body temperature *(Withings Thermo)*
- Weight *(Withings Body+)*
- Body composition *(Withings Body+)*

NuvoAir

- Spirometry *(AirNext)*

Enviroment

- Weather
- Environmental data
- Environmental allergens

Table 1. List of CHDR MORE App measurements.

Digital technology

The CHDR MORE® platform and app can connect to a variety of digital devices and wearables to collect continuous data in a non-clinic setting. This allows us to measure and quantify the intervention response as an outcome of the trial. The devices and the data collection process both undergo a thorough validation procedure to ensure the highest data quality. The platform is continuously being augmented with additional integrated measurement devices, based on the requirements of ongoing trials.

Promasys ePro app

The Promasys ePro app makes it possible to implement questionnaires outside the clinic. This app is an add-on to the integrated Anju Promasys Electronic Data Capture system and allows study participants to submit trial related data directly into the database using their own device or a device provided as part of the trial. In addition, the app can prompt study participants to perform an assessment. Compared with a paper diary, the Promasys ePro app improves compliance and reduces the risk of errors during data entry.

Trial@home in clinical trials: a showcase

Trial@home is the focus of continuous innovation and development. To date, it has been integrated and validated in a wide range of therapeutic areas at CHDR, including neurology (Parkinson's Disease and FSHD), psychiatry (unipolar depression), dermatology (psoriasis), and orthopaedics (knee surgery). Trial@home has proved most revolutionary, however, in paediatric studies, including paediatric surgery (tonsillectomy). Below, we showcase a number of paediatric studies involving Trial@home.

High compliance rates and user satisfaction in a paediatric trial

Using the Trial@home platform, we have been able to demonstrate not only increased rates of compliance but also a high level of user satisfaction. In a study involving 265 children (aged 2–16 years), a compliance rate of 94% was achieved, as illustrated in table 2.

Furthermore, only two children (<1%) dropped out of the study (aged 3 years) and 97% of the subjects reported they would participate in similar studies in the future. The median time required was eight minutes per day, and only 5% of the subjects reported that the time spent was too much.

Measurement	Median compliance (IQR)
Smartwatch	
Step count	100% (100% - 100%)
Heart rate	100% (100% - 100%)
Sleep	95% (85% - 100%)
Wear time per day	23.6h (22.8h - 23.9h)
Questionnaire	90% (81% - 100%)
Temperature	83% (67% - 100%)
Weight*	100% (67% - 100%)
Blood pressure*	85% (85% - 100%)
Spirometry*	83% (67% - 100%)
Overall compliance	**94% (87% - 97%)**

Table 2. Trial@home compliance rate in a paediatric trial involving 265 children aged 2-16 years. *Subjects ≥ 6 years old only.

A smartwatch for the registration of step count, heart rate and sleep parameters in patients with ARID1B

In this observational case-control study, twelve subjects with ARID1B-related intellectual disability (ID) and twelve age-matched controls wore a smartwatch (Withings Steel HR) for six days, which registered step count, heart rate and several accelerometer-derived sleep parameters. This approach successfully identified fit-for-purpose candidate endpoints for ARID1B-related ID and possibly for other neurodevelopmental disorders. All remotely collected data could be linked to the outcomes of a battery of non-invasive neurobehavioural and neurophysiological assessments, including cognition, executive functioning and eye tracking. The table 3 summarises the Trial@home measures and their link to CNS and ARID1B symptoms.

Trial@home measure	CNS domain	Corresponding ARID1B symptom
Physical activity	General daily activity	Hyperactivity, apathy, lethargy
Sleep parameters	Sleep	Insomnia
Heart rate	Sympathetic activation	Hyperactivity

Table 3. Fit-for-purpose candidate endpoints for ARID1B-related ID.

Novel digital endpoints for children with pulmonary diseases

In a series of studies, data were collected from healthy children and children with pulmonary diseases (controlled and uncontrolled asthma, and cystic fibrosis). Children were monitored for four weeks using a smartwatch (Withings Steel HR) which registered step count, heart rate and sleep. Daily pulmonary function tests were performed (using NuvoAir AirNext), and an electronic daily symptom diary was completed (Asthma Control Diary). Meanwhile, healthy subjects were monitored for three weeks with the smartwatch and performed biweekly pulmonary function tests.

With these data we have been able to demonstrate significant differences in physical activity between the groups of children studied. The data also revealed significant correlations between physical activity and traditional pulmonary function endpoints (such as FEV1). These results are illustrated in figure 1a and 1b.

Continuous monitoring of babies crying

Using Trial@home technology, CHDR researchers have developed an algorithm that is able to continuously monitor for infant crying sounds. This algorithm was developed and validated on independent datasets with exceptional results, as showcased in table 4.

Accuracy	98%
Sensitivity	90%
Specificity	99%
Matthews correlation coefficient	0.90

Table 4. Validation of our infant cry monitoring algorithm

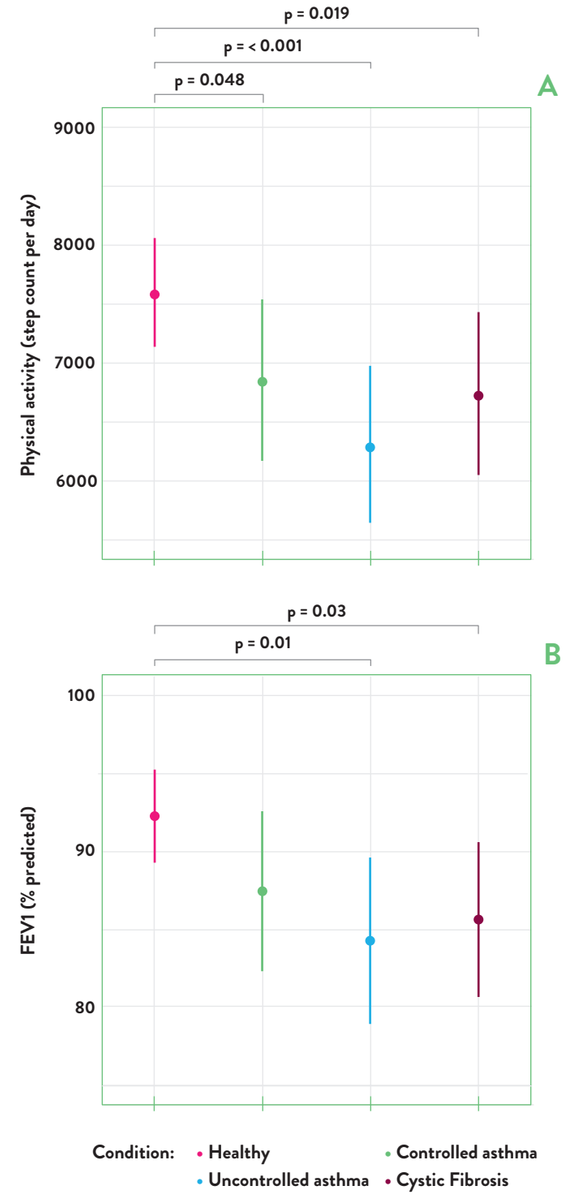


Figure 1. Differences in activity in healthy children and children with pulmonary diseases (controlled and uncontrolled asthma, and cystic fibrosis).
A: Physical activity (step count per day).
B: Forced expiratory volume in 1 second (FEV1).

A growing publication base

Trial@home and the CHDR MORE® platform are part of our vision for the future of clinical trials. Aside from published studies involving these approaches, we offer key contributions to the discussion around innovations and improvements in the field. Recent position papers include:

- Our perspective on how the standard trial paradigm needs to evolve in the face of both an ongoing decrease in the incidence of hard endpoints and spiralling trial costs

  Kruizinga MD, *et al*. The future of clinical trial design: The transition from hard endpoints to value-based endpoints. in *Handbook of Experimental Pharmacology*. Springer 2019; 260:371–397.[1]

- The vision of CHDR and our partner C-Path on the validation of digital biomarkers

  Kruizinga MD, *et al*. Development of novel, value-based, digital endpoints for clinical trials: A structured approach toward fit-for-purpose validation. *Pharmacol. Rev* 2020; 72:899–909.[2]

[1] https://chdr.nl/library/the-future-of-clinical-trial-design-the-transition-from-hard-endpoints-to-value-based-endpoints

[2] https://chdr.nl/library/development-of-novel-value-based-digital-endpoints-for-clinical-trials-a-structured-approach-toward-fit-for-purpose-validation

Can CHDR Trial@home be used in my trial?

Most trials can benefit from patient centric data collected outside the clinic. Trial@home can be integrated in a wide range of trials, offering a wealth of additional study data and validated digital endpoints without an increased burden for the subjects.

This platform is available not only for use in trials at CHDR, but also as a separate service for trials outside CHDR. We would be glad to offer an evaluation of the clinical utility of the platform for your trial (risk, benefits, relevance and usefulness) and the impact of imple-mentation in the project.

Why choose CHDR?

The Centre for Human Drug Research specialises in early-phase clinical drug research. CHDR's overall mission is to improve the drug development process by collecting as much information as possible regarding the candidate drug in the early phases of development. This information helps sponsors make informed decisions regarding the course of clinical development for their product.

Why choose CHDR?

Research at CHDR covers a wide range of fields, including the central nervous system (CNS) and pain, the cardiovascular system, haemostasis, immunology, and dermatology. In addition, CHDR is at the forefront in developing novel biomarkers and methods for measuring drug-related effects in all of these research areas.

Pharmacology matters

Whether studying a new cognitive-enhancing drug, a next-generation painkiller, or a new monoclonal antibody designed to treat rheumatoid arthritis, the goal is to determine how the compound's effects correlate with both the dose and blood concentration at any given moment. In addition, understanding which biological systems are activated is an essential first step towards quantifying this relationship. At CHDR, our focus on pharmacology is reflected clearly in what we call question-based drug development.

Question-based drug development

CHDR actively uses question-based drug development - or QBD - as a more rational approach to drug development compared to conventional approaches. QBD can be best described as a series of questions that are addressed throughout the process. These questions often seem simple enough, but failing to answer even one question - or even addressing the questions in the wrong order - can have dire consequences. Thus, using this approach can potentially save companies millions of dollars by helping predict a catastrophic issue early in the development process, before the more expensive latter stages (for example, large-scale clinical trials or the marketing phase).

From a general perspective, the most important questions are:

1. Does the biologically active compound and/or active metabolite(s) reach the intended site of action?
2. Does the compound cause its intended pharmacological and/or functional effect(s)?
3. Does the compound cause any unintended pharmacological and/or functional effect(s)?
4. Does the compound have a beneficial effect on the disease and/or clinical pathophysiology?
5. What is the compound's therapeutic window?
6. How does any variability with respect to the drug response in the target population affect the product's development?

Contact

To learn about CHDR's full range of services, contact us today.

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