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The Paradigm Shift in Clinical Trials in the Pharmaceutical Industry:
The Economic and Management Implications of Digital Health
Technologies

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DOCTORAL THESIS DRAFT

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Budapest

2026

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List of abbreviations used in the thesis

ACT EU - Accelerating Clinical Trials in the European Union

ADME - Absorption, Distribution, Metabolism, Excretion

AI - Artificial Intelligence

API - Application Programming Interface

AR - Augmented Reality

CAPEX - Capital Expenditure

CHMP - Committee for Medicinal Products for Human Use

CISCRP - Center for Information and Study on Clinical Research Participation

COA - Clinical Outcome Assessment

CRA - Clinical Research Associate

CRO - Contract Research Organisation

CSAT - Clinical Sustainability Assessment Tool

CTD - Clinical Trials Directive (2001/20/EC)

CTIS - Clinical Trials Information System

CTR - Clinical Trials Regulation (536/2014/EU)

DC - Dynamic Capabilities

DCT - Digital Clinical Trial

DHT - Digital Health Technology

EC - European Commission

ECG - Electrocardiogram

eCOA - Electronic Clinical Outcome Assessment

eConsent - Electronic Informed Consent

eCRF - Electronic Case Report Form

EDC - Electronic Data Capture

EEA - European Economic Area

EESZT - National eHealth Infrastructure

EHDS - European Health Data Space

EHR / EMR - Electronic Health Record / Electronic Medical Record

EMA - European Medicines Agency

EMRN - European Medicines Regulatory Network

eNPV - Expected Net Present Value

ePRO - Electronic Patient-Reported Outcome

EU - European Union

FDA - Food and Drug Administration (US)

FHIR - Fast Healthcare Interoperability Resources

GCP - Good Clinical Practice

GDPR - General Data Protection Regulation

GTM - Go-to-market strategy

HEAT - Health Equity Assessment Tool

HIC / LMIC - High-Income Country / Low- and Middle-Income Country

HIPAA - Health Insurance Portability and Accountability Act (US)

HL7 - Health Level Seven

HMA - Heads of Medicines Agencies

HTA - Health Technology Assessment

ICH-GCP - International Council for Harmonisation - Good Clinical Practice

IMP - Investigational Medicinal Product

IVDR - In Vitro Diagnostic Regulation

KPI - Key Performance Indicator

ML - Machine Learning

MLP - Multi-Level Perspective

NNGYK - National Centre for Public Health and Pharmaceuticals
(formerly: OGYÉI - National Institute of Pharmacy and Nutrition)

OPEX - Operational Expenditure

PI - Principal Investigator

PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PRO - Patient-Reported Outcome

R&D&I - Research, Development and Innovation

ROI - Return on Investment

RWD - Real-World Data

RWE - Real-World Evidence

SAE - Serious Adverse Event

SDV - Source Data Verification

SIV - Site Initiation Visit

SLR - Systematic Literature Review

SME - Small and Medium-sized Enterprise

TOE - Technology-Organisation-Environment framework

USD - United States dollar

UX - User Experience

VR - Virtual Reality

WHO - World Health Organization

1. INTRODUCTION

1.1 Subject of the research

The subject of this doctoral thesis is the examination of digital health technologies and other digital solutions applicable in clinical trials involving human subjects within the pharmaceutical industry, with particular regard to their practical, economic and management implications. The research demonstrates how the emergence of digital innovations has transformed the conduct of clinical trials and explores the social, technological, economic and regulatory factors that influence the uptake and application of these solutions. Although the literature increasingly emphasises the benefits of digital clinical trials (DCTs), the issue of cost-effectiveness and its measurable and comparable indicators continue to feature only to a limited extent in the scientific discourse, which the author thus identifies as a research gap.

The thesis provides a detailed analysis of the potential applications, identified limitations and interrelationships of digital health technologies (DHTs) in clinical trials, and interprets the practical significance and economic impacts of DCTs. The research compares the traditional clinical trial environment with digital clinical trials using a multidimensional approach, highlighting the benefits arising from their application, the emerging challenges, and the dynamically changing regulatory conditions that shape today's pharmaceutical research and development strategies.

The aim of the thesis is also to present a practice-oriented approach that supports pharmaceutical professionals, researchers and health economists in the effective management and integration of digital innovations into clinical trials. The study not only addresses issues of process optimisation but also provides an outlook on expected future directions and trends, emphasising that the application of digital innovations holds significant, as yet partially untapped, potential for the pharmaceutical industry and healthcare. According to the research's approach, digitalisation offers not merely technological advantages, but also contributes to improving the quality of healthcare services, enhancing patients' quality of life, and enabling more efficient and sustainable implementation of pharmaceutical developments.

Reflecting on the terminological diversity of digital transformation, this thesis uses the term '*digital clinical trial*', which encompasses both decentralised trial solutions and other DHTs

used in clinical trials within a unified framework. The relevance of the research topic is further reinforced by the fact that clinical trials in the pharmaceutical industry represent the most costly and riskiest phase of the research, development and innovation (R&D&I) process, where rising development costs, lengthening cycle times and difficulties in patient recruitment pose ever-greater challenges. DHTs therefore offer new operational possibilities; however, their economic and managerial implications - particularly their impact on cost structures, timeframes and financial returns - require further, systematic analysis.

1.2 Reasons for choosing this topic

I graduated as a research biologist and then as a medical biotechnologist, and research and development has remained an integral part of my work ever since. After spending years in the laboratory, I turned to the pharmaceutical industry, where I currently work as a clinical trial project manager, contributing to the successful implementation of R&D&I processes, the development of new drug candidates¹, the coordination of clinical trials, and the management of regulatory approval processes. My work involves identifying and familiarising myself with the latest scientific and technological solutions, and integrating them into pharmaceutical development projects. As a result, it has become increasingly clear to me that the application of digital technology solutions has inevitably become part of daily practice in my field. I have come across numerous scientific publications, presentations at professional conferences and technology-driven clinical trial designs, all of which have demonstrated that digitalisation is leading to revolutionary changes in healthcare and medicine.

These technological developments had to be followed by regulatory changes within the industry, a process that was greatly accelerated by the COVID-19 pandemic that broke out in 2020. As a result, industry players faced significant challenges: the traditionally structured clinical trials used up to that point became unfeasible within a matter of weeks. The pandemic has radically transformed the usual conduct of clinical trials. When the coronavirus pandemic struck, the traditional clinical trial model - which required in-person attendance, institutional involvement, and dedicated trial sites - became virtually unsustainable. Professionals in the pharmaceutical industry and regulatory authorities had to adapt immediately: new, temporary provisions, methodological recommendations and amendments, valid until further notice, were

¹ Drug candidate: or lead compound. An active substance which, based on various laboratory tests, may be suitable for preclinical and clinical development (Keserű, 2015) .

published on a daily basis. In this unpredictable, rapidly changing regulatory environment, enormous pressure was placed not only on the authorities but also on pharmaceutical companies and researchers. Innovation has always been a driving force in the industry, but during the pandemic it set a pace never seen before. During the period of pandemic restrictions, pharmaceutical companies had only one choice: to develop and implement their previously planned or entirely new solutions as quickly as possible.

Keeping pace with the turbulent changes in the environment required a greater degree of adaptability than ever before, so medicines regulatory authorities responded to the situation by assessing applications to amend the plans of ongoing clinical trials within a short timeframe and under an accelerated procedure. However, this level of flexibility was essential for other stakeholders, as it ensured that trials did not come to a standstill and, indeed, gained new momentum thanks to digital solutions. The use of remote solutions enabled patients to continue accessing treatment and allowed a significant proportion of R&D&I processes to continue.

The tension within the industry was further exacerbated by the fact that, whereas the market had previously been slow to react and strictly regulated, users now expected a rapid response. This dual pressure continues to pose challenges for regulatory authorities even after the COVID crisis has subsided, as the development of the framework - intended to be transitional - still requires regular review and fine-tuning. Whilst weighing up best practices, the primary objective of regulatory authorities at all times is to ensure, with the utmost rigour, the safety of patients participating in clinical trials and the protection of their rights.

The biennial global survey conducted by the non-profit organisation the Center for Information and Study on Clinical Research Participation (CISCRP) helps to assess the practical significance of the changes affecting the industry brought about by the pandemic. In the latest study, published in 2025 (Center for Information and Study on Clinical Research Participation, 2025) 12,000 patients who had participated in clinical trials were asked about their experiences with DCT participation. The survey results highlighted that the integration of digital innovations into clinical trials contributes significantly to the creation of a patient-centred environment, which in turn has a positive impact on participants' willingness to participate, satisfaction, and sense of security. Overall, it can be said that the use of digital innovations in clinical trials is beneficial not only for pharmaceutical companies and regulatory authorities,

but also for users. Their use can lead to a faster, more efficient, more transparent and more cost-effective R&D&I process.

A comprehensive literature review was conducted to explore the topic and refine the doctoral research focus. The review indicated that, whilst numerous publications report on the benefits and challenges of DCTs, relatively few sources discuss the potential for process transformation and its impacts, particularly on financial outcomes. To date, only a handful of authors have examined specific examples and case studies.

1.3 The aim of the research

The identified research question reflects on issues of paramount importance today, as a complex understanding of the innovative solutions created by digitalisation and the new challenges associated with them is essential in a rapidly changing technological and regulatory environment. In the field of clinical development within the pharmaceutical industry, a transformation is taking place in both operational models and decision-making criteria, which justifies a systematic examination of the impacts of digital solutions.

The aim of this research is to explore and analyse the economic and management impacts of DCTs based on DHTs in pharmaceutical clinical development. The thesis focuses on examining how the application of DHTs transforms the cost structure, timeline and resource utilisation of clinical trials, as well as how it influences the return on investment (ROI).

The research objectives also include identifying the conditions and constraints under which DCTs can be conducted in an economically sustainable and management-viable manner. In this context, the thesis not only focuses on the benefits of DHTs but also interprets the challenges and decision-making dilemmas associated with their application, thereby contributing to a broader scientific and practical understanding of DCTs.

1.4 The relevance of the topic

The relevance of the research topic is justified by both industry demands and trends, as well as patients' growing expectations, which together drive the adoption of digital solutions in clinical research. Today, digitalisation and technological innovation are no longer merely optional

development paths, but are emerging as essential prerequisites for the sustainable and cost-effective conduct of future clinical trials in the pharmaceutical industry.

The timeliness of this topic is particularly underscored by the fact that the uptake of digital technologies in the field of clinical trials has accelerated significantly, fundamentally transforming the methodology of R&D&I in the pharmaceutical industry, as well as organisational operations and the regulatory environment. In this complex and dynamically changing technological and legal environment, the COVID-19 pandemic has led to a further, extraordinary acceleration. The extreme circumstances arising during the pandemic have highlighted the vulnerability of traditional clinical trial models, as well as the limited responsiveness of existing regulatory mechanisms.

As a result of the pandemic, cooperation between regulatory authorities and industry stakeholders intensified to an unprecedented degree, leading to the updating of relevant guidelines and recommendations in an unusually short timeframe. Through professional consultations and industry forums, regulations were developed in record time that enabled the application of innovative, digital, and decentralised solutions. However, these processes cannot be interpreted in isolation from one another, as technological, organisational and regulatory factors interact with one another, which justifies a holistic examination of the topic.

The relevance of this research is further reinforced by the fact that, although the benefits of DCTs are increasingly discussed in the literature, relatively few scientific studies have so far been produced that examine their economic, management and operational implications in a comprehensive and practical manner. In a rapidly changing technological and regulatory environment, it is therefore particularly justified to conduct research that interprets the opportunities offered by digitalisation and the associated new challenges in a complex manner. The identified research question thus reflects on the key issues of our time and is closely linked to the current and future directions of clinical development in the pharmaceutical industry.

1.5 Presentation of the research framework: research approach, study methods, limitations of the research

The development and successful market launch of a drug is a 10-15-year process (DiMasi et al., 2016; Hinkson et al., 2020). Drug candidates undergo a series of clinical trials and

regulatory approvals, as a result of which, out of approximately 10,000 molecules, ultimately only one receives marketing authorisation and reaches patients. The entire process is lengthy and time-consuming, with a total cost of USD 1.5-2.5 billion ² . As a drug candidate does not generate profit prior to market entry, alongside the early termination of unsuccessful developments, precise planning and timing are similarly decisive factors, as gaining a market advantage significantly increases the revenue generated by the original drug³ .

Clinical trials account for the largest share of the costs in the R&D&I process. In recent years, expenditure has risen further due to increasingly specialised therapies, greater difficulty in recruiting patients, and a shortage of trial sites and healthcare staff. In addition to being a regulatory requirement, clinical trials provide evidence of essential information regarding the therapy, such as dosing, pharmacokinetic characteristics⁴, safety and side effects, volunteers participating in trials gain free access to treatments for which they might otherwise have to wait years, yet which, alongside the risks they consciously accept, can save lives. Progress through the trial phases becomes increasingly expensive, as it requires the involvement of more and more patients, often in multinational, multicentre, comparative (multi-arm) trial designs. This is accompanied by additional costs related to logistics, the maintenance of trial sites, data management and processing, and patient follow-up.

The use of DHTs offers time- and cost-effective operational alternatives to these challenges. Digital solutions enable more targeted patient recruitment, automated data collection and processing, and real-time monitoring, which can result in shorter cycle times and, at the same time, a more inclusive, patient-centred trial environment. All of this can help ensure that innovative therapies reach patients more quickly and effectively.

The aim of my research is to map the economic processes involved in the digitalisation of clinical trials - the most costly element of the pharmaceutical R&D&I process - and to demonstrate the management-related impacts of digital innovations.

² USD exchange rate: 1 \$ = 360 HUF, calculated using the exchange rate as at 30 April 2026. The total cost of drug development referred to is 465,985,500,000 - 776,642,500,000 HUF.

³ Original drug: an original formulation which the first manufacturer may place on the market following a full authorisation process. The manufacturer is entitled to patent exclusivity (Directive 2001/83/EC, 2001) .

⁴ pharmacokinetic characteristics: pharmacokinetics is the branch of pharmacology that studies the fate of a drug within the body. Based on the ADME principle, it describes the absorption, distribution, metabolism and excretion of the drug. Knowledge of these properties is essential for determining the correct dosage, efficacy and safety (Keserű, 2015) .

The research questions identified during the literature review were tested in a Hungarian context. The research follows a mixed-methods approach, employing both qualitative and quantitative methods. Building on the literature review, expert interviews and a quantitative questionnaire survey examine the economic and management impacts of DCTs in the Hungarian context.

In order to explore the topic as thoroughly as possible, I interviewed experts working in various fields about their experiences and future outlooks, thereby ensuring a multidisciplinary approach to the research. As the experts interviewed have different backgrounds, I took into account the relevant contextual factors when interpreting the results, which further nuance the picture obtained. It became clear to me as early as the research objective stage that, due to the rapidly changing technological and regulatory environment, the long-term effects of individual solutions can only be estimated tentatively based on the information available today.

The research framework emphasises that the economic benefits of DCTs do not manifest in the same way in every case or in every environment. The realisation of these effects depends on the phase and complexity of the trial, the organisation's technological and operational readiness, and the stability of the regulatory environment. Accordingly, this paper interprets the effects of DCTs not as a general improvement in performance, but as the result of management decisions tied to specific circumstances.

The research framework developed is based on the fundamental assumption that the introduction of DHTs into clinical trials exerts its economic and management impacts not directly, but through the transformation of how trials operate. Accordingly, DCTs can be understood as an operational approach that influences patient recruitment, data collection, trial monitoring, and the spatial and temporal organisation of trials. These operational changes affect the cost structure of, the duration of trials and resource utilisation, and ultimately the financial returns and risks of clinical development. The framework emphasises that these impacts do not manifest in the same way in all cases and in all contexts, but depend on the phase and complexity of the trial, the organisation's preparedness and the regulatory environment.

1.6 Expected outcomes of the research, benefits of the research

The research findings provide a comprehensive picture of the industry, societal and technological changes that have influenced the emergence of DCTs, with particular regard to

the digitalisation processes accelerated by the COVID-19 pandemic. The study provides a nuanced analysis of the regulatory environment undergoing transformation as a result of these influences, and presents the currently applied regulatory frameworks in light of the identified challenges and opportunities. In parallel, it explores how digital health innovations are transforming the processes of organising, conducting and collecting data in clinical trials.

Through comparative analyses, the research highlights the cost-saving effects of applying DHTs in clinical trials and demonstrates how these solutions contribute to more efficient patient recruitment, reduced operational costs and simplified patient follow-up. The findings reveal the new opportunities that DCTs offer in the field of clinical development, the challenges the pharmaceutical industry must face in their implementation, and help identify the potential for cost savings and efficiency gains in clinical development.

The theoretical significance of the research lies in its evaluation of the R&D&I processes in the Hungarian pharmaceutical industry based on international examples, its mapping of the current state of digital transformation, and its identification of future directions and opportunities in the management of DCTs. The examination of the cost-reducing and efficiency-enhancing role of innovative technologies - particularly from an economic and management perspective - is an area that has received limited coverage in the international literature and represents a distinct gap in the Hungarian context. The results of this research thus contribute to broadening the economic perspective of clinical research, with particular regard to the interpretation of cost structure shifts and the ROI.

The practical significance of the research lies in the fact that it offers a structured, decision-support framework for stakeholders in the pharmaceutical and healthcare management sectors, at both domestic and international levels. The applied technology and innovation management approach supports the more efficient, faster and cost-effective implementation of clinical trials. The results of the analyses can be used to formulate models and recommendations that provide guidance on the practical application of current regulatory frameworks, the organisation of R&D&I activities, and the optimisation of innovation processes. The research's change management approach ensures that the results are interpretable in practice and provide support for strategic decision-making to promote the sustainable development of the pharmaceutical industry during a period of paradigm shift.

1.7 Structure of the doctoral thesis

The **first chapter** summarises the research topic and its relevance, framework, objectives, and theoretical and practical significance.

The **second chapter** reviews the practices in the domestic and international literature related to the research topic, as well as the research questions formulated on the basis of the literature review.

The **third chapter** outlines the research methodology, the characteristics of the research sample, and the research questions.

The **fourth chapter** presents the results of the expert interviews and the quantitative questionnaire conducted as part of the empirical research.

The **fifth chapter** contains a summary of the responses to the research questions, as well as the correlations identified as a result of the research.

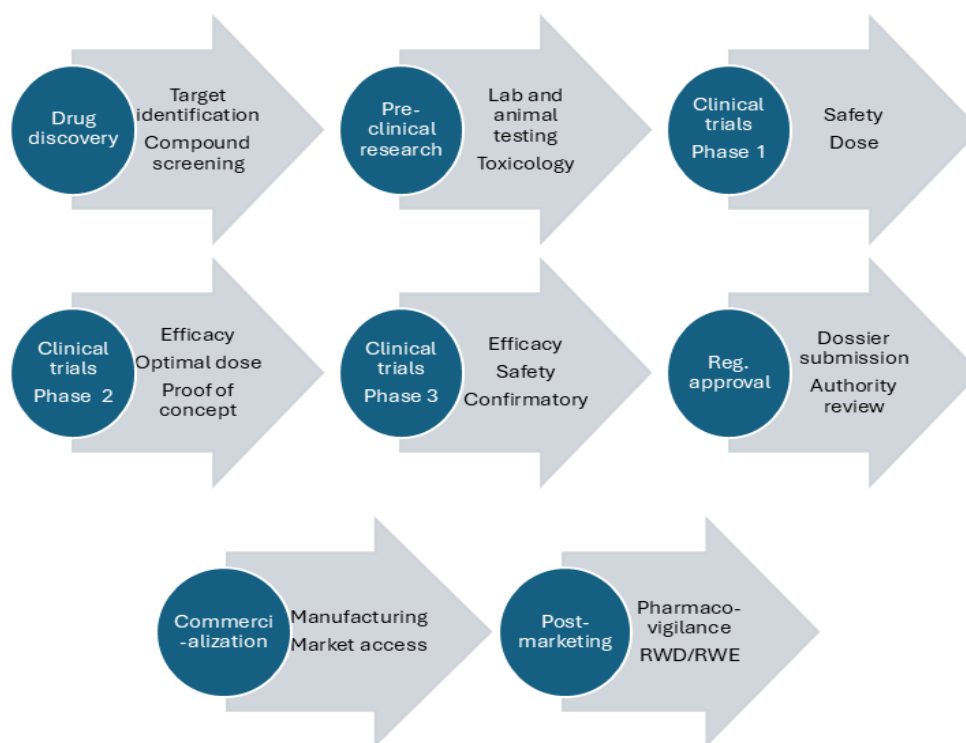
The **sixth chapter**, in addition to the discussion, outlines future research directions, the limitations of the research methodology, and recommendations for improvement.

2. LITERATURE REVIEW

2.1 The importance of clinical trials in drug development

According to the wording of Act XCV of 2005 on Medicines, a medicinal product is defined as ‘any substance or mixture of substances presented as a product intended for the prevention or treatment of human diseases, or those substances or mixtures which, through the induction of pharmacological, immunological or metabolic effects to restore, improve or modify a physiological function in humans, or for the purpose of establishing a medical diagnosis, and which may be used in or on the human body” (Act XCV of 2005, 2005). For a molecule to become a promising drug candidate and ultimately reach hundreds or thousands of patients as a medicine, it must undergo a long and costly process spanning decades.

The decades-long process of pharmaceutical research and development begins with research grounded in specific market needs and corporate strategy. A solution is sought for a particular clinical condition, which requires in-depth knowledge of the development and mechanisms of the disease, as well as the altered chemical pathways resulting from the human body’s response to it. It is, among other things, with this information that the relevant genes and their target gene products can be identified (Lo et al., 2009; Nag et al., 2022). If the target is relevant, laboratory design proceeds based on data from the literature and market needs. Researchers examine tens of thousands of molecules in available molecular libraries to identify a potential drug candidate, a so-called lead molecule, that could provide a solution for them. Today, classical analytical methods are supplemented by computer-aided design and prediction software. Following so-called in-silico studies, promising molecular candidates undergo in-vitro laboratory analysis - that is, in Petri dishes using cell cultures - during which researchers seek to identify the potential molecular candidate. If the previous steps are successful, the preclinical phase can begin. The promising drug candidate is evaluated for efficacy, safety and potential toxicity using further laboratory experiments and animal models. They examine whether the compound is carcinogenic, has no foetal-damaging effects (teratogenic), or causes genetic changes (mutagenic). In addition, it is evaluated in terms of stability and pharmacology. If the results continue to give cause for optimism, research proceeds to human clinical trials.



1 The process of R&D&I in the pharmaceutical industry

Source: own compilation

By definition, “any investigation in humans intended to: a) determine or confirm the clinical, pharmacological and/or other pharmacodynamic effects of one or more medicinal products; b) to identify the side effects of one or more medicinal products; or c) to study the absorption, distribution, metabolism and excretion of one or more medicinal products for the purpose of verifying the safety and/or efficacy of those medicinal products” (Regulation 536/2014/EU, 2014). The evaluation of medical devices⁵, interventions, other therapies and diagnostic procedures is also carried out through clinical trials. Depending on the countries involved in the

⁵ medical device: any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer, either alone or in combination, for use in humans for one or more of the specific medical purposes listed below:

- the diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,
- the diagnosis, monitoring, treatment, alleviation or compensation for an injury or disability,
- examination, replacement or modification of anatomy or of a physiological or pathological process or condition,
- providing information through the *in vitro* examination of samples derived from the human body, including organs, blood and tissues,

and which achieves its primary intended effect in the human body or on the human body not by pharmacological or immunological means, nor by metabolic means, but whose action may be assisted by the aforementioned mechanisms of action (Regulation (EU) 2017/745, 2017) .

trial, a national and/or international medicines regulatory authority approves the feasibility of the clinical trial based on a set of documents with legally defined content relating to the trial. Following thorough planning lasting several months, the compilation of comprehensive documentation covering every detail is also a time-consuming process. Once the authorisation fee has been paid and the authority has accepted the application, the trial can begin.

Clinical trials can be divided into four phases, each of which is essential and indispensable for understanding the properties of the drug.

The so-called Phase I trial is the first step in the use of the investigational product in humans. Generally, healthy volunteers take part, but in cases where this would be unethical, such as when testing anti-cancer drugs, patients are already included in the first phase. In such cases, the trial is classified as Phase I/II (Simmelweis University, n.d.). The number of patients involved varies; typically, the pharmacokinetic and pharmacodynamic⁶ (Ernstmeyer & Christman, 2023) properties and side effects of the drug substance are investigated in a group of a few dozen people, the tolerable dose is determined, and the mechanism of action of the drug on the body is studied.

Phase II trials are planned based on the results obtained. A group of several hundred patient volunteers is used to validate the effective and safe dose range and the method of administration determined in the previous phase, to ensure the expected effect is achieved. One group of patients receives the investigational drug in addition to the best currently available treatment, whilst the other group receives a placebo⁷ instead of the investigational drug. The drug candidate is assessed for the first time in terms of efficacy, and further information is gathered on short-term side effects, as well as the drug's efficacy and safety in the disease being treated. We distinguish between Phase II/A trials, in which the dose required to achieve the desired effect is determined, and Phase II/B trials, in which the efficacy of that dose is studied.

Phase III trials involve several thousand patients and are conducted to confirm the results obtained during Phase II, and to confirm clinical relevance and significance. The efficacy and safety of the specified dose level are investigated in a larger and more representative sample;

⁶ pharmacodynamics: describes the effect of medicines on the body. It helps to determine the potency of the administered dose, the mechanism of action of the drug, such as its binding to target receptors, interactions between enzymes and other targets, the identification of drug interactions, and the side effects produced (Keserű, 2015) .

⁷ placebo: an inactive substance or treatment - for example, sugar or a saline solution.

in addition, side effects are continuously recorded, and the drug is compared with another product or therapy already available on the market and used in everyday treatment. Typically, these are multinational trials conducted in parallel across multiple sites and countries based on an identical protocol, using the controlled trial design described for Phase II. Patients are divided into so-called treatment arms according to various trial protocols to evaluate the drug's mechanism of action. If the trial is conducted in an anonymised manner and neither the patient nor the treating physician knows which treatment the participant is receiving, this is referred to as a double-blind trial design. The aim of this is to ensure the reliability of the data (Magyarországi Klinikai Vizsgálatszervezők Társasága, n.d.).

The results obtained during phase trials provide regulatory authorities with the evidence required for marketing authorisation; following the evaluation of this evidence, the registration of the medicinal product, that is, the regulatory assessment process, can begin, and upon successful completion, the product is granted a marketing authorisation. During the marketing authorisation procedure, a regulatory authority assesses the quality, relative safety and efficacy of the new substance. If it meets the requirements, the product is designated as a medicinal product for the indicated use within the framework of an administrative procedure and subject to specific conditions” (NNGYK, 2023). However, this often requires documentation running to several thousand pages, containing a detailed description of manufacturing and quality control conditions, reports on preclinical (animal) studies, and results from human clinical trials. As part of the documentation, certain administrative data must be submitted, such as the so-called accompanying documents, information leaflets for healthcare professionals and patients, the packaging design, and samples of the active substance and finished product. It is also necessary to draw up a risk management and pharmacovigilance⁸ plan for the management of adverse events and the regular review of the safety of the medicinal product.

Under the national procedure, the assessment of the medicinal product is carried out by the National Centre for Public Health and Pharmacy (NNGYK) (formerly the National Institute of Pharmacy and Nutrition (OGYÉI)). The marketing authorisation issued through this procedure is valid only in Hungary. In addition to national authorities, the European Medicines Agency (EMA) and the Committee for Medicinal Products for Human Use (CHMP) are responsible for

⁸ pharmacovigilance: an activity aimed at monitoring the benefit-risk balance of a medicine to ensure its safety, with the aim of reducing risks and increasing benefits (Act XCV of 2005, 2005) .

issuing authorisations valid within the European Union, whilst in the United States this role is performed by the U.S. Food and Drug Administration (FDA). The successful registration process can take up to 210 days, so it is no exaggeration to say that every minute counts in the pharmaceutical industry.

Following marketing authorisation, clinical trials are concluded by so-called post-marketing or Phase IV trials. The aim of this is to assess long-term efficacy and safety, to understand how patients optimally use the medicine in real-life settings beyond laboratory conditions, and the large number of patients involved provides an opportunity to identify any rare side effects. It is also acceptable to generate real-world data/real-world evidence (RWD/RWE) based on real-world information obtained from databases through observational studies. The assessment of the product's risk-benefit analysis relies on Phase IV trial results. Evidence must be gathered during so-called post-marketing studies for further use, e.g. for the purpose of expanding indications, testing in new patient populations (e.g. children) or applying a new dosing regimen. The characteristics of the phases are summarised in the table below.

	Objective	Average number of patients involved (people)	Average total cost (\$)	Success rate (%)
Phase I	Safety, dosage, side effects	40-100 / 20-80	\$10 million	10
Phase II	efficacy, optimal dose	50-200 / 100-300	\$30-100 million	20
Phase III	Confirmation of efficacy and safety, comparison with standard therapy	1,000-10,000 / 1,000-3,000	\$200 million*	60
registration	regulatory approval	-	\$1.5-2.5 billion**	95
Phase IV	post-market optimisation of use, investigation of rare side effects			

*one trial is generally not sufficient to obtain authorisation

** including the costs of unsuccessful developments

1 Characteristics of clinical trial phases

Source: own compilation, based on the Hungarian Association of Pharmaceutical Manufacturers, 2022; National Institutes of Health, 2025.

There are also other types of clinical trials that are similarly subject to regulatory approval. “Non-interventional studies are clinical research activities that differ from clinical trials in that the procedures carried out do not deviate from standard healthcare practice” (235/2009. (X. 20.), 2025). The prescription of a medicinal product already holding a marketing authorisation is not for the purpose of the trial; it is used in the manner customary in clinical practice, and no additional diagnostic or monitoring procedures are applied to the patient (NNGYK, 2023). Data collection and database analysis are carried out in relation to patients’ medication or diagnostic methods applied in accordance with standard clinical practice, as in all types of clinical trials, whilst ensuring the protection of sensitive personal data. Medical devices may only obtain a marketing authorisation if they are backed by data from clinical trials demonstrating the device’s safety and performance (Regulation (EU) 2017/745, 2017).

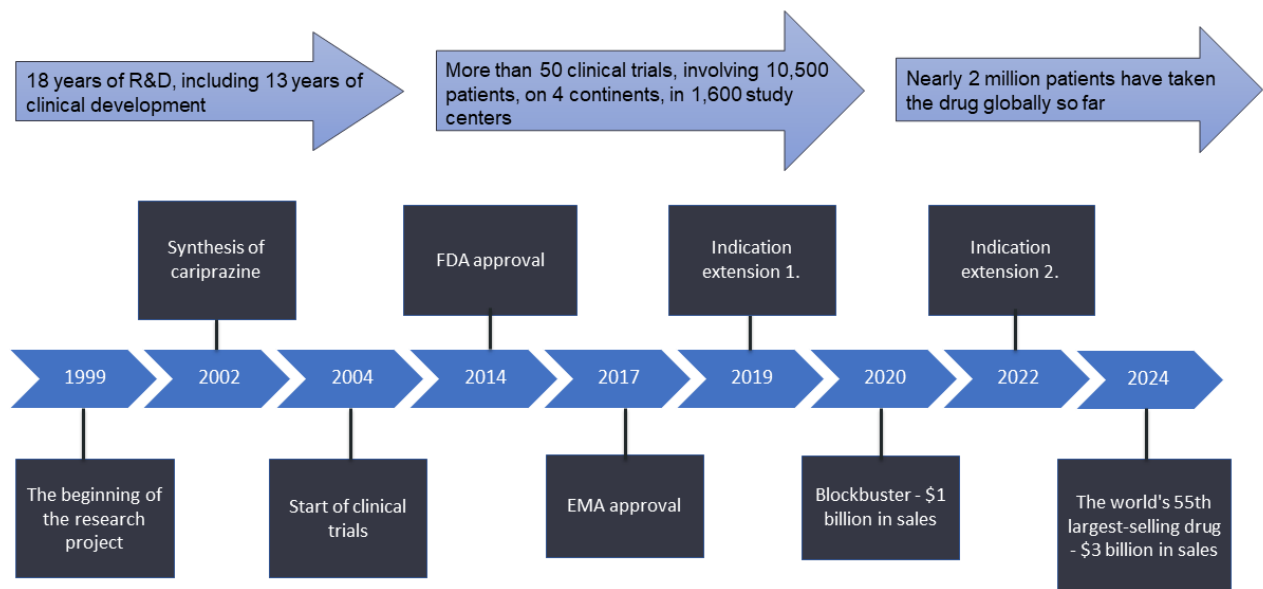
Once the product has entered the market, its life-cycle management is a phase that continues for many years. This includes marketing, the manufacturing process, distribution, and the operation and management of the pharmacovigilance system, but it may also involve further research and development if there is an extension of indications or if changes to the medicinal product are required, e.g. reformulation.

Long-term research and development, continuous and rigorous testing, and independent regulatory oversight ensure that only high-quality, safe and effective medicines reach patients.

The scale of these figures can be illustrated in practice by the following real-life example. Cariprazine, regarded as the most significant achievement of the Hungarian pharmaceutical industry, is the first original formulation invented in Hungary to receive FDA approval ⁹, with Hungarian researchers from Richter Gedeon participating throughout the R&D process. The research project dates back to 1999. The molecule was synthesised in 2002, and clinical trials began in 2004. It received FDA approval in the US 11 years later, and in the European Union in 2017. The first dossier submitted in the United States covered the indications of schizophrenia and bipolar mania, comprising a total of 4,500 files and approximately 1,200,000 pages. The first dossier submitted in the European Union for the treatment of schizophrenia, including dominant negative symptoms, consisted of 1,100 files and approximately 110,000 pages. In the field of scientific communication, more than 100 professional publications have

⁹ FDA approval: marketing authorisation granted by the US Food and Drug Administration for a given medicinal product.

been published worldwide, and approximately 500 posters and more than 25 oral presentations have been presented at international conferences. Thanks to the continuous expansion of indications, the now *blockbuster* antipsychotic¹⁰ is available in nearly 70 countries worldwide, providing relief to 2 million patients and their families. Figure 2 illustrates how Richter's unique development became a global success (Richter Gedeon Nyrt., 2025).



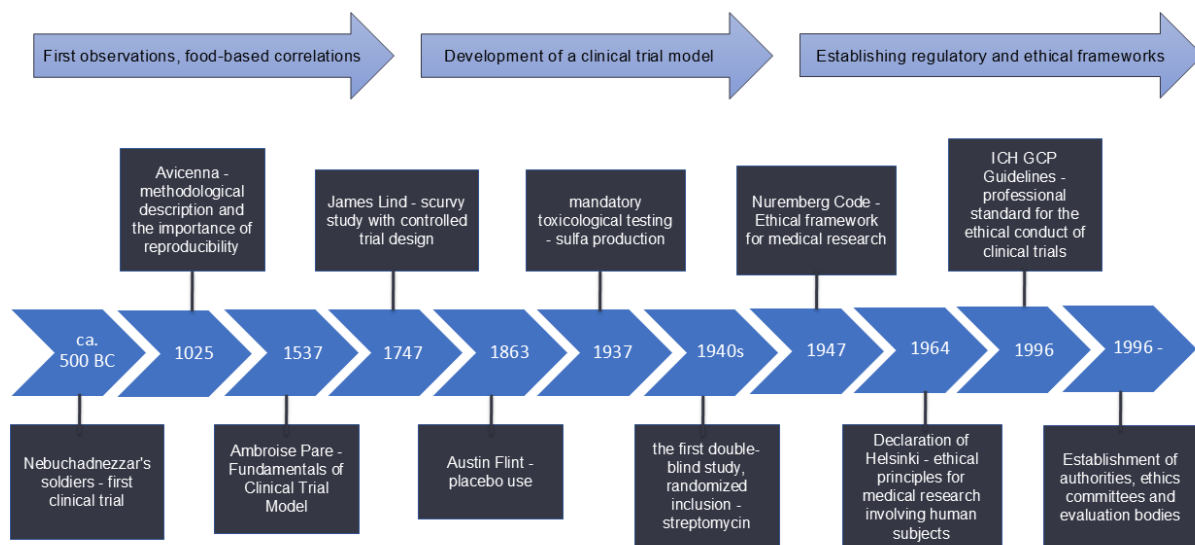
2 The cariprazine life-cycle management process

Compiled by the author based on information from gedeonrichter.com

2.2 The evolution of clinical trials

Clinical trials have undergone a development process spanning more than two thousand years, leading from the first documented observations in antiquity to the complex, strictly regulated trial environment of today's digital age. This evolution has taken place in three main areas: methodological development (control, randomisation, double-blind design), ethical regulation (protection of human rights, informed consent), and technological innovation (digitalisation, decentralisation).

¹⁰ blockbuster: a drug whose annual sales exceeded 1 billion.



3 A timeline of the evolution of clinical trials, highlighting key ethical and regulatory milestones from 500 BC to the present day

Source: own compilation

2.2.1 The Hippocratic Oath and the pre-modern regulatory era

In antiquity, the Hippocratic Oath (5th-3rd centuries BC) provided the fundamental ethical framework for medicine, which - albeit with additions - still forms the basis of the modern medical oath today. In addition to respect for human life and the patient, and beyond the principle of 'Do no harm', it emphasises the importance of medical confidentiality; however, whilst the protection of patients was considered more a moral duty of the doctor, research was subject to few legal regulations.

2.2.2 Early beginnings and the first principles

The roots of clinical research go back surprisingly far in history. The first known, documented clinical observation dates from around 500 BC, when the military commander Nebuchadnezzar investigated the relationship between a special diet and health status in two groups. His men were provided with meat and wine, but some at the royal court refused this, consuming legumes and water exclusively during this period. A reference to vegetarianism is also mentioned in the Bible, in the Book of Daniel (Szent Biblia, n.d.). This was the first recorded 'open-label, uncontrolled' experiment, in which both the investigator and the participants knew which of the interventions was being applied to the subject. In this case, two study groups were observed

without the involvement of a control group maintaining normal dietary habits (Collier, 2009; Nair, 2019).

In 1025, Avicenna made a significant contribution to laying the methodological foundations in his encyclopaedia, *The Canon*, regarded as a seminal work of European medicine. He formulated principles that reflect the contemporary approach to clinical trials today: comparative studies of two contrasting types of cases, analysis of duration of effect, and examination of the reproducibility of the effects of active substances and treatments (Bhatt, 2010; Bull, 1951).

2.2.3 The development of modern clinical trials

The first clinical trial in the classical sense was conducted by Ambroise Paré, a surgeon serving on the front line, in 1537. Later, Paré - referred to as the father of modern surgery - found himself running out of the oil he used for wound treatment, so, for lack of a better alternative, he developed his own mixture and applied it to some of the wounded (Bhatt, 2010; Twyman, 2004).

To his surprise, he found that the recovery rate of patients treated with his mixture was far superior to that of those receiving conventional treatment. Paré's innovation, a mixture of turpentine with antiseptic properties, offered a far more effective method than standard treatment (Collier, 2009; SciencePharma, n.d.). His observations gave rise to the idea of improving care through experimentation. Although by chance and unexpectedly, Paré thereby laid the foundations for the clinical trial model (ClinicalConnection, n.d.).

James Lind's 1747 study of scurvy was already a thoroughly planned and documented modern clinical trial. Under controlled conditions, he examined six groups receiving different treatments, comparing the effectiveness of citrus fruits with other remedies used (Dodgson, 2006).

He published the results of the treatment of the sick sailors, thereby laying the foundations of evidence-based medicine. Following his findings, the British Navy prescribed lime juice as a mandatory dietary supplement for seafarers, replacing lemons and oranges, which were very expensive at the time. Following the start date of Lind's study, 20 May was designated as International Clinical Trials Day (Chalmers et al., 2008; Collier, 2009).

2.2.4 The development of placebo use

Another century passed before the first known clinical use of the placebo. This occurred in 1863, when Austin Flint conducted a trial with patients suffering from rheumatic fever and compared the results of standard treatment with those of the placebo. Flint discovered that there was no difference in the natural course of the disease between active treatment and the placebo, suggesting that symptoms subsided naturally over time rather than as a result of conventional drug treatment (Collier, 2009). This marked a significant shift in medicine towards the objective evaluation of active treatments. The use of control groups and placebos enabled researchers to compare treatments. Their importance is underscored by their continued role as cornerstones of clinical trials.

2.2.5 Double-blind method and randomisation

History has played an extremely significant role in the development of ethical standards for clinical trials. The ethical framework was not established in a predetermined manner, but was often shaped by serious historical abuses, tragedies and social experiences, which highlighted the importance of human rights and trust in participation.

The sulphate tragedy of 1937 was a decisive turning point in the field of drug safety. Hundreds of manufacturers produced tens of thousands of tonnes of various sulphonamide drugs without supervision. When an improperly prepared sulphonamide preparation caused 107 deaths, mandatory toxicological testing was introduced. Subsequently, the Federal Food, Drug, and Cosmetic Act, passed in 1938, established the requirements for new medicines prior to their safe release onto the market (Wax, 1995).

Scientific methods developed following the Industrial Revolution. Following observations conducted under controlled conditions, trials involving control groups emerged in the 20th century. In these trials, the investigator compares the results with those of a control group receiving standard treatment, a placebo (without active ingredients), or no treatment at all (Nair, 2019). Later, double-blind trials (where neither the patient nor the doctor knows who is receiving which treatment) emerged, and finally randomised trials (where patients are randomly assigned to groups) (D'Arcy Hart, 1999; Hariton & Locascio, 2018). These methods allow the efficacy of treatments to be demonstrated objectively. The first double-blind trials began in the 1940s (e.g. the patulin test on patients with the common cold) (D'Arcy Hart, 1999), and in 1946, the randomised controlled trial of streptomycin for the treatment of tuberculosis became

the ‘gold standard’ (Bhatt, 2010). There was an acute shortage of this promising antibiotic, so to manage the limited supply of streptomycin, participants were randomly assigned to control and treatment groups. Furthermore, randomisation eliminated the frequently observed bias whereby clinicians placed healthier patients in the experimental group and sicker patients in the control group (British Medical Journal, 1948; D’Arcy Hart, 1999).

2.3 Changes in the regulatory environment surrounding clinical trials

2.3.1 The emergence of international ethical standards

2.3.1.1 The Nuremberg Code

The 1947 Nuremberg Code was the first international guideline on the ethics of medical research involving human subjects (Ananthakrishnan & Shanthi, 2012). During the Nuremberg trials, which were initiated due to the inhumane experiments carried out by Nazi doctors on concentration camp prisoners, the need for ethical regulation of medical research became clear. This led to the creation of the first official and internationally accepted document setting out the fundamental ethical principles of medical research involving human participants.

The document set out ten fundamental requirements aimed at protecting human subjects during clinical trials. Particular emphasis was placed on adequate information and voluntary consent, which have remained essential conditions for participation in any research ever since. Further principles include that the expected benefits of the research must be proportionate to the risks involved, that trials may only be conducted by suitably qualified doctors, and that participants must be guaranteed the option to withdraw from the research at any time (British Medical Journal, 1996).

2.3.1.2 The Tuskegee Study

The Nuremberg Code succeeded in establishing widespread acceptance of ethical research, but some researchers continued to violate it. The hallmark of unethical research practices is the ‘*Tuskegee Study of Untreated Syphilis in Black Men*’, which began in 1932 (Resnik, n.d.) and continued for forty years without regard for the standards established at Nuremberg. This blatant disregard for human life in the name of science consequently led to the death and infection of the participants’ partners and children. The Tuskegee study serves as a stark

example of the indispensability of protecting research subjects and serves as a reminder that humanity must always be placed above science (Sparks, 2002). This tragic event contributed significantly to the further strengthening of regulatory frameworks (World Medical Association, 2024).

2.3.1.3 The thalidomide disaster

The thalidomide tragedy of the late 1950s also had a major impact on the development of the regulatory framework. The drug, known as Contergan, which had a sedative effect and alleviated nausea, was prescribed by doctors to pregnant women; its use often led to miscarriage, but caused approximately 10,000 cases of severe organ malformations, limb shortening or absence worldwide. The disaster was caused by the fact that, in addition to inadequate testing, the product was brought to market without a clear understanding of the molecule's exact mechanism of action (it was not marketed in Hungary). It was withdrawn from the market worldwide in 1961, but today, following rigorous clinical trials, it is used as an anti-cancer drug precisely because of its anti-angiogenic effect. The Thalidomide disaster led to mandatory testing of the effects of medicines on foetal development (teratogenicity) and laid the foundations for pharmacovigilance. In the wake of the tragedy, the Kefauver-Harris Amendments were passed in 1962, mandating that the US Food and Drug Administration (FDA) assess the safety and efficacy of all new medicines prior to their marketing (Otte et al., 2005). This tragic incident highlighted the indispensability of drug safety protocols and the need for adverse reaction reporting, as well as for long-term, continuous drug surveillance.

2.3.1.4 Declaration of Helsinki

The Declaration of Helsinki was adopted in 1964 under the auspices of the World Health Organization (WHO) and has since been amended on several occasions, most recently in 2024. The document is considered a significant milestone in the development of medical research ethics, as it introduced a number of new principles for the regulation of research involving human participants. One of the Declaration's fundamental innovations is that it clearly places the responsibility for protecting the health and well-being of research participants on doctors. It also regulates in detail the process of informed consent, the application of research ethics principles, transparency requirements, and methods of risk management. The document also addresses the ethical implications of the use of anonymously collected data and biological samples, thereby ensuring the protection of participants' rights and personal data (Bhatt, 2010; World Medical Association, 2024).

In 1966, the International Covenant on Civil and Political Rights (ICCPR) explicitly stated: ‘No one shall be subjected to torture or to cruel, inhuman or degrading treatment or punishment. In particular, no one shall be subjected to medical or scientific experimentation without their consent (Council of Europe, 2023).

2.3.1.5 Belmont Report

To reinforce existing regulations and national laws on the ethics of human research, the Belmont Report was produced in the USA in 1979 following the conclusion of the Tuskegee experiment. It established three fundamental principles: respect for research participants (self-determination, protection), beneficence (maximum benefit, minimum harm) and justice (equal access, distributive principles) (U.S. Department of Health, Education, and Welfare, 1979).

2.3.2 Modern regulatory framework

2.3.2.1 Good Clinical Practice

In 1982, the WHO and the Council for International Organisations of Medical Sciences (CIOMS) published the document entitled ‘*International Guidelines for Biomedical Research Involving Human Subjects*’. This document was published to assist developing countries in applying the principles of the Declaration of Helsinki and the Nuremberg Code. Numerous organisations and committees worldwide have issued various documents and guidelines on the same subject. Therefore, in an effort to resolve international discrepancies, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) published the international professional guideline on Good Clinical Practice (Directive 2005/28/EC, 2005), which has become the universal standard for the ethical conduct of clinical trials in humans, establishing the foundations for global quality assurance. The GCP guidelines now standardise the rules governing the conduct of pharmaceutical research at an international level from EU to the US and Japan.

These guidelines were approved on 17 July 1996 and introduced into clinical trials from 17 January 1997. Representatives from the European Union, Japan and the United States, as well as Australia, Canada, the Nordic countries and the WHO, participated in the development of the guidelines. The ICH-GCP guidelines have become a harmonised standard that protects the rights, safety and well-being of human subjects, minimises exposure to investigational medicinal products, and improves data quality. Compliance with this standard provides public

assurance that the rights, safety and well-being of trial subjects are protected and in line with the principles of the Declaration of Helsinki, and that clinical trial data are reliable. The ICH-GCP guidelines are therefore regarded as the ‘Bible’ of clinical trials and have become globally accepted. It should be noted that the ICH-GCP guidelines are constantly evolving. Since 2016, the year the ICH GCP E6(R2) guideline was finalised, the clinical research sector has faced technological advancements, which have led to increasing complexity in trials and global challenges. Consequently, in May 2023, the ICH prepared a draft guidance document for the industry titled “ICH E6 (R3) Guidelines on Good Clinical Practice (GCP)” for the industry to address the growing gaps between existing regulations and real-world processes, such as the increasing diversity of trial types and data sources, and the resulting new types of quality concerns. Following a multi-stage consultation process, the new structure finally came into force on 23 July 2025 (European Medicines Agency, 2025).

2.3.2.2 The evolution of the European Union’s regulatory framework

The development of ethical standards for clinical trials has often been shaped by serious historical abuses, tragedies and social experiences, typically giving rise to increasingly robust and detailed regulations and new guiding principles.

These realisations have highlighted the importance of human rights and trust in participation. History has continually steered medical research towards a direction that is legally protected, transparent, participatory, fair and safe, shaping the regulatory environment that responds to current global issues to this day. Worldwide, Good Clinical Practice, the Declaration of Helsinki, and local legal provisions - e.g. FDA and EMA guidelines - form the basis of regulation. However, due to globalisation, the system that had operated until the 2000s became increasingly unsustainable. Phase III trials typically required a multinational trial design to ensure that their large and robust results would be considered sufficiently conclusive by the regulatory authorities. The key stages of clinical trials - from trial design through regulatory submission, the approval process, and on to trial implementation and subsequent regulatory assessment - are, however, processes requiring several months or years (or even decades, if we consider the entire timeline of drug development). From the pharmaceutical industry’s perspective, the date of market entry is crucial, as the drug generates no revenue until then, and if a single competitor beats the company to market by even a single day, the product can no longer be considered an originator product.

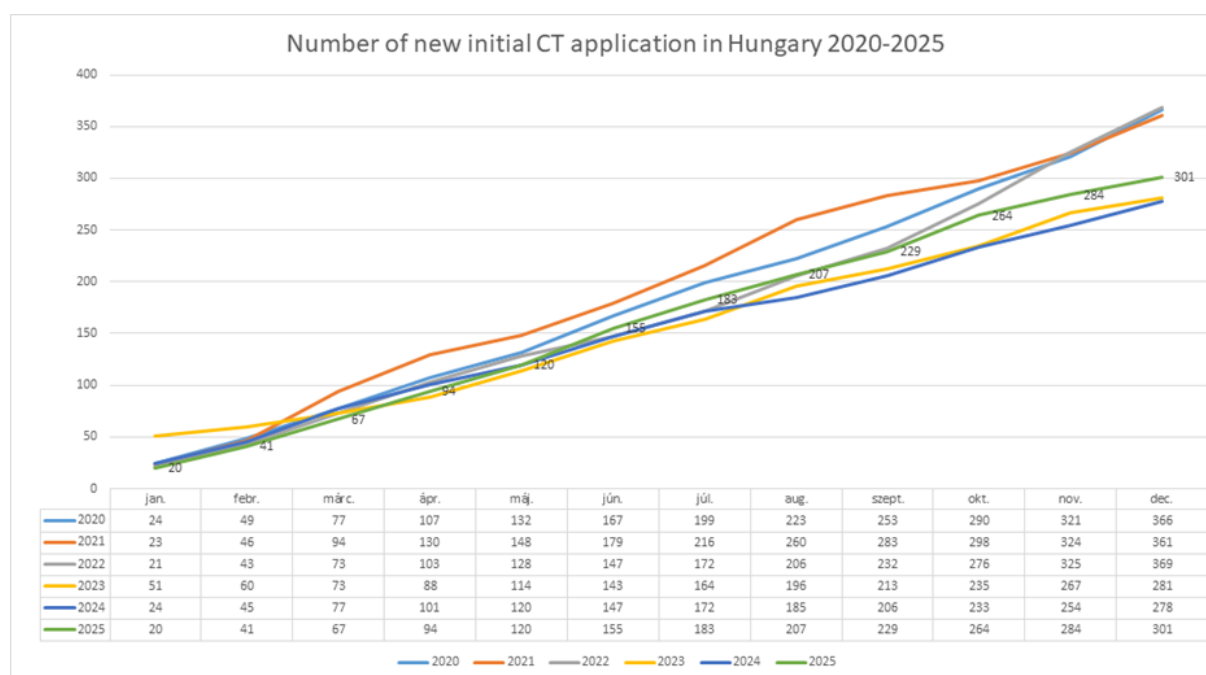
In addition to increasing efficiency in the pharmaceutical industry and improving the quality of research, the time factor is also crucial from the perspective of patients awaiting treatment, because the sooner the therapeutic product goes through the necessary steps to obtain regulatory approval, the sooner patients can access evidence-based, effective treatment. Advances in R&D&I processes are leading the industry into ever-new therapeutic areas and, thanks to the achievements of modern technology, are offering cures for problems that were previously unsolvable. Examples include rare diseases, which, due to their low incidence within a given region, often require clinical trials spanning continents. The development of the global pharmaceutical market has therefore led to the harmonisation of international clinical trial regulations.

The following section presents in greater detail the evolution of the regulatory environment surrounding clinical trials over the past 20 years. It illustrates the extent to which regulatory authorities must respond to changes affecting such dynamically evolving fields of science within the most knowledge-intensive and innovative sector of the manufacturing industry. It also provides insight into the system that exerts dual pressure on the pharmaceutical research and development process, which traditionally takes 10-15 years.

2.3.2.3 Clinical Trials Directive

Until the early 2000s, the regulation of clinical trials involving medicinal products for human use in the European Union was not uniform, as Member States applied different national regulatory frameworks. This lack of harmonisation caused numerous operational and administrative difficulties, particularly in the case of clinical trials involving several countries. The entry into force of EU Directive 2001/20/EC on 1 May 2004 marked a step forward. The Directive focused on the uniform introduction of GCP across the EU, which is a fundamental prerequisite for the scientific reliability of trials and the protection of participants (Clinical Trials Directive 2001/20/EC, 2001). However, implementation of the directive continued to vary, as Member States had to transpose it into their own legal systems, which differed in several respects, sometimes even from country to country. Divergent interpretations and bureaucratic obstacles continued to slow down the authorisation and conduct of trials. These shortcomings, combined with the industry's low success rate, rising costs and protracted regulatory procedures, led to a decline in the number of clinical trials. According to a 2013 report by the European Medicines Agency (EMA), there was a 25% decline in the number of new trial applications between 2007 and 2011 compared to the preceding period (Clinical Trials

Directive 2001/20/EC, 2001; European Commission, 2012; European Medicines Agency, 2013).



4 Clinical trials submitted for authorisation (2020-2025)

Source: https://ogyei.gov.hu/statisztikai_adatok

As a result of this trend, a broad-based professional initiative was launched in 2011 to urge a review of the Clinical Trials Directive. The proposals set out in a public petition in 2011 focused on simplifying authorisation and administrative processes, harmonising regulatory requirements, and issuing guidelines that could encourage the conduct of large-scale, multinational research at a systemic level (Mayor, 2011). The latter are of particular importance not only in facilitating the development of new therapies but also from a health economics perspective, as the simultaneous processing of databases collected from a wider population can lead to faster and scientifically more reliable results. Among the advantages of trials running simultaneously across multiple countries is that, thanks to this synchronisation, the research process can be shortened by as many as several years, thereby reducing overall costs. Furthermore, following the continuous evaluation of interim data, modifications to the trial design can be requested as necessary, which also saves time and money. According to the call for proposals, the situation at the time complicated the lengthy authorisation procedure for trials, as authorisation had to be sought separately from the relevant national authorities, based on slightly differing regulations. A harmonised, single-window submission system would

reduce research risk, which would act as an incentive for pharmaceutical companies and is likely to increase the number of clinical trials initiated; indeed, they might even undertake higher-risk research. In addition to supporting scientific progress, this would also improve savings rates.

2.3.2.4 Clinical trials regulation

Based on reports regularly produced by the European Commission and stakeholder feedback, Regulation (EU) No 536/2014 of the European Parliament and of the Council (Clinical Trials Regulation, CTR) was introduced on 31 January 2022, simultaneously repealing the previous directive. The eight-year period between the drafting and implementation of the Regulation was a lengthy process due to the development and launch of the EU portal and database for recording trials. As this is not a directive, the Regulation is directly applicable in all Member States in a uniform manner, thereby avoiding differences in interpretation arising from transposition into national law (European Commission, n.d.-a).

The Regulation has established a legal framework to fill a gap in the regulatory environment for clinical trials involving human subjects, with three strategic pillars: harmonisation, transparency, and the strengthening of the protection of trial subjects. The most significant institutional innovation of the new regulation is the Clinical Trial Information System (CTIS), which provides a single electronic portal for the notification, assessment and monitoring of trials, thereby placing cross-border cooperation on a new footing. From 2023, all newly submitted trial applications must be processed exclusively through this system, and from 2025, trials currently running under the previous system must also be transferred to the CTIS (European Commission, n.d.-a; European Medicines Agency, n.d.). This time, efforts to support full harmonisation and standardised processes covering all Member States have been established, ranging from the submission of clinical trials for approval right through to the evaluation process, which has emerged as the primary and indispensable criterion for conducting multinational trials. In addition, the launch of the aforementioned common EU portal and database facilitates transparent communication between Member States regarding clinical trials accepted by the authorities. To further promote multinational trials, the operation of the CTIS significantly reduces the administrative burden on both sponsors and authorities, enables the uniform and real-time processing of all Member State submissions, and makes relevant information transparent for researchers, healthcare organisations and decision-makers. In addition to knowledge sharing, scientific transparency serves to provide a higher level of

information not only to sponsors but also to patients and healthcare professionals, further increasing the willingness to participate voluntarily, and ultimately thereby supporting the advancement of science.

To elaborate, this means that all trial applications submitted to EU Member States, as well as access to trial data, are provided through a single channel. It also aims to enhance patients' willingness to participate and their commitment through transparency and widespread information, which is provided by the freely accessible open-access information platform on the euclinicaltrials.eu website. In addition to the approval process, the Regulation also covers the patient safety reporting pathway. Clinical trial sponsors are obliged to collect patient safety information and report adverse events during the trial; unlike previous practice, these no longer need to be reported separately to the authorities of the countries concerned, but must be submitted via the CTIS system. This step is also in line with the aim of increasing transparency and simplifying administration.

The CTIS harmonises the submission process within the EU/EEA, the evaluation of the trial dossier and the supervision required during the conduct of the trial, whilst also providing insight into the results of both ongoing and previous clinical trials. Transparency is further enhanced by the fact that it serves as a reliable source even at the trial planning stage, as the database can be used to find out when and where trials similar to the planned one have been conducted. The role of the CTIS is to further develop the requirements set out in the 2001 legislation, placing even greater emphasis on ensuring the ethical compliance of trials and the reliability of data derived from them. One of its tools is to make registered trials uniformly accessible to all Member States, thereby supporting collective regulatory decision-making and facilitating the launch of multinational trials. Trials run in parallel across several countries generate more data from more participants within a given timeframe, which may also come from a larger geographical area; consequently, their evaluation yields a more comprehensive result, particularly when investigating a rare condition, as opposed to the (partial) results of trials involving several smaller and/or fewer countries. It is clear that this approach plays a particularly important role in addressing unmet needs, rare diseases and public health crises.

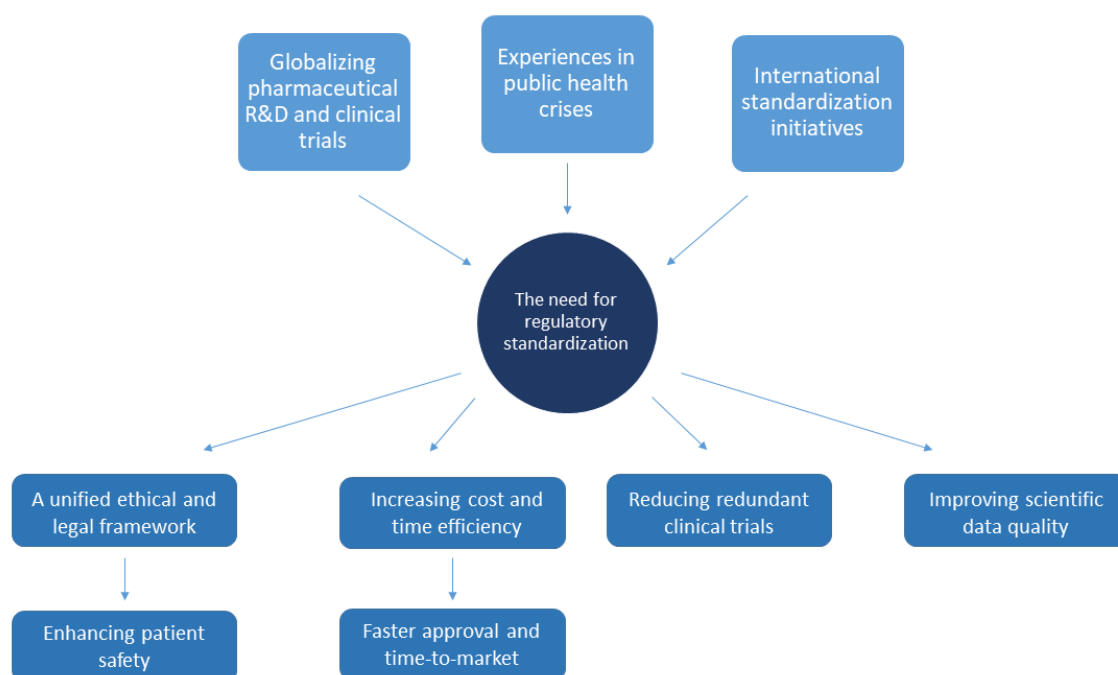
2.3.2.5 Areas for improvement in the CTR

In addition to the expected benefits of the CTR, the risks involved have also been assessed. The actual functioning of ethics committees was also weighed up in several articles. Criticism has

been voiced in the literature regarding the practice of freely choosing the reporting Member State, as this could lead to varying degrees of rigour in assessment and ethical oversight (Mayor, 2011). As an alternative solution, it has been proposed that the evaluation of the study be carried out by the ethics committee of the reporting Member State, thereby ensuring the consistency of the evaluation process and the protection of participants' rights. It is worth noting that research may be ethically objectionable despite a favourable risk-benefit balance for science and society if the research question could be answered using a method involving less risk to the participants. Such research designs must be assessed even more rigorously than usual, particularly where children or legally incapacitated persons are involved, who are deemed unable to give independent consent.

For the process to be conducted successfully and ethically, it is essential that the experts involved in the assessment have sufficient time to carry out detailed analyses and, where necessary, to consult additional specialist expertise (Gefenas et al., 2017; Westra et al., 2014). In summary, it can be concluded that the importance of the time factor and a detailed, thorough evaluation process has increased following the modernisation of regulations, which is intended to promote higher standards of quality and ethics in clinical trials.

The EMA publishes the results of authorisation processes and future development directions on a quarterly basis (European Medicines Agency, 2026), on the basis of which it defines its strategy and specific action plans. According to its key performance indicator (KPI)-based reports, the number of multinational trials has increased since the introduction of the CTR: by April 2023, it had risen by 33% to 230, and according to CTIS data, these trials involve an average of six Member States. Although EFPIA's figures at the end of 2022 mentioned a 38% increase, this figure is still low. According to the report, this means that 60,000 fewer patients are able to participate in clinical trials within the EEA, meaning that a large number of people living in Europe are missing out on the opportunity to access the latest therapies (EFPIA, 2022).



5 Drivers and benefits of regulatory standardisation

Source: own compilation

In addition to the CTR and CTIS systems, further supporting initiatives have been launched to further fine-tune regulatory reform.

2.4 COVID-19 and its impact on the digital revolution

The COVID-19 pandemic has definitively highlighted the importance of multinational clinical trials. The pandemic acted as a catalyst for the digital transformation of pharmaceutical processes and the spread of DHTs. This change has led to the integration of remote solutions into daily practice, but due to the extensive overhaul of the regulatory environment, there are still areas that need to be developed, such as the electronic signature process.

2.4.1 Decentralised clinical trial model

By definition, decentralised clinical trials utilise DHTs and remote procedures that enable some or all of the trial activities to take place outside traditional trial sites (telemedicine, electronic informed consent (eConsent)/electronic patient reported outcome (ePRO), wearable devices,

home logistics, local laboratories, etc.). The aim is to reduce the burden on patients, increase accessibility and participation, achieve potential cost savings, and improve representativeness.

One of the most important models of this paradigm shift is the decentralised clinical trial, which - depending on the therapeutic area and trial design - facilitates participation in the trial for enrolled participants through fully digitalised or hybrid organisational options. Instead of the traditional approach based solely on on-site visits, it is now possible to conduct online consultations using telemedicine tools; indeed, the preparations required for the trial can even be delivered directly to the volunteer's home. A further advantage is that certain examination procedures no longer require long-distance travel; instead, certain measurements can now be carried out at validated healthcare facilities closer to the volunteer's place of residence. Thanks to this complex digital-infrastructure integration, logistical burdens are significantly reduced, whilst the continuity and data security of the examination can be guaranteed at a higher level, and the flexibility of the research protocol is also significantly increased. Solutions such as these were not brought about solely by the pandemic, but it has undoubtedly accelerated their integration into daily practice.

2.4.2 The first measures of the COVID era

The COVID-19 pandemic has posed significant challenges to healthcare systems, which has also led to substantial changes in the feasibility of clinical trials. The restrictions introduced in response to the evolving epidemiological situation, quarantine measures, and the necessary public health protocols - such as continuous testing, and the additional tasks and workload placed on healthcare professionals - have resulted in significant capacity issues across Europe. All this has made it necessary to organise clinical research with greater flexibility than before. The development of guidelines tailored to the situation became a priority; however, it is an essential prerequisite that none of these measures - even if temporary - should jeopardise the rights, safety and well-being of trial participants or the staff conducting the trials.

The first guidance was published on 20 March 2020 (European Medicines Agency, 2020a), stating that the simplification measures justified by the COVID-19 pandemic remain in force until the guidance is withdrawn, i.e. for as long as the pandemic situation persists within the EU/EEA. Based on this position, both sponsors and investigators were asked to exercise particular caution when considering the need to initiate new clinical trials. For trials already underway, it was permitted to switch from in-person patient visits to consultations via telephone

or video conferencing, and to reduce the number of site visits to the minimum necessary. Furthermore, provision was made for the temporary suspension of trial activities, the temporary halt or slowing of patient recruitment, the extension of the planned trial duration, the cancellation of trial sites not yet opened, and the closure of sites already in operation. Where the infrastructure required to carry out the prescribed imaging, laboratory or diagnostic activities was not available at the site in question or at the designated institution, it became possible to carry out the activity in question at another authorised facility. Due to the prolonged nature of the pandemic, the document was updated on 4 February 2021, as a first step towards maintaining decentralised and digital solutions and best practices, whilst attempting to introduce them into everyday practice. This represented a significant step forward in the flexibility of the clinical trial framework, whilst strict regulatory conditions remained unchanged. Currently, version 5 of the document has been in force since February 2022 (European Medicines Agency, 2022a). A scientific methodological guide was also produced to support the application of adaptive modification options (European Medicines Agency, 2020). This guidance is no longer relevant in many contexts due to the subsiding of the COVID-19 pandemic, but unfortunately serves as a reference point in the context of the war in Ukraine.

2.4.3 ACT EU - a strategy for the renewal of clinical trials

At the same time as the pandemic broke out, the pharmaceutical industry underwent a paradigm shift. With daily news, innovative developments and the application of pioneering technologies in healthcare, a technological boom on a scale that was perhaps previously unimaginable has begun, driven by medical devices supporting AI/ML solutions.

Recognising the need for these developments, and in connection with the application of the Clinical Trials Regulation on 31 January 2022, the EMA, in collaboration with the European Commission (EC) and the Heads of National Medicines Agencies (HMA), launched the ACT EU (Accelerating Clinical Trials in the EU) programme in January 2022 (European Commission, 2022). This initiative has formulated strategic recommendations to support medical research and development and to advance innovation in clinical trials, at both societal and scientific levels.

The significance of this development is underlined by the fact that this is the first comprehensive collaboration of its kind between these three organisations, aimed at the joint development and modernisation of clinical trials. “The work plan is linked to the

recommendations of the European Medicines Regulatory Network (EMRN) strategy, as well as the European Commission's European medicines strategy (European Medicines Agency & Heads of Medicines Agencies, 2015). The plan is based on the Clinical Trials Regulation (CTR, Regulation (EU) No 536/2014) and activities aimed at supporting clinical trials.”

In August 2022, the EMA, the EC and the HMA published a multi-annual work plan setting out development priorities across ten strategic areas for the period 2022-2026. Among these, priority is given to strengthening dialogue among stakeholders, modernising Good Clinical Practice (GCP), developing and disseminating new EU guidance documents, and supporting innovative and decentralised trial methods through methodological guidelines (European Commission et al., 2022).

The ten priority actions of the ACT EU's multi-annual strategic programme aim to establish a unified regulatory approach at the European level, within the framework of which the coordinated provision of scientific advice has been renewed. Experience in previous years has shown that requirements between the European Medicines Agency and the national authorities of Member States could differ, leading to slowness and fragmentation in regulatory processes. The new strategy therefore aims to streamline the entire regulatory chain and harmonise procedures and requirements.

Harmonisation extends to various levels: from the planning and authorisation process for clinical trials, through the standardisation of patient safety monitoring mechanisms, to the broader analysis of scientific data from clinical trials - encompassing multiple countries and data sources. This complex data analysis approach can make a substantial contribution to underpinning evidence-based policy and funding decisions. At the same time, the diverse and increasingly multifaceted data sources give rise to significant biostatistical and data integration challenges, which are being addressed through the development of relevant methodological tools and guidelines (European Medicines Agency, 2025). The development of the GCP framework has also been necessitated by the increasingly complex, digital and hybrid types of clinical trials, as well as the rise of new technological solutions, which are transforming not only data collection but also the way participants are engaged. The digital collection of data also raises new, extended data security requirements.

Systematic monitoring of the process is essential for the comprehensive and effective implementation of the CTR, for which specific metrics and performance indicators have been

defined. The regulation encourages an increase in the proportion of academically sponsored trials - these currently account for around 40% of clinical trials in the EU, which typically cover fewer countries than larger-scale, industry-sponsored research. A key strategic element is the launch of a comprehensive communication and awareness-raising campaign targeting all stakeholder groups - regulatory and scientific experts, funders and healthcare providers.

A further priority is the development of practical and methodological guides, with particular regard to innovative AI/ML-based, complex or decentralised clinical trials, as well as the EU regulation on IVDR (In Vitro Diagnostic Regulation) (Regulation (EU) 2017/745, 2017) and the CTR interface. These development priorities aim to strengthen links between scientific advisory forums, support an innovative clinical trial environment, and facilitate the transfer of regulatory and methodological knowledge within the European Union. It also aims to ensure that the region once again becomes a competitive alternative for conducting clinical trials by providing more favorable conditions (PharmaOnline, 2024).

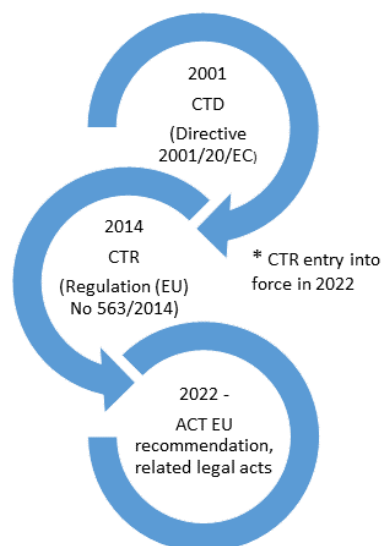
The work plan for the necessary changes, reinforced by the pandemic, was updated in November 2023, and the second version was published (European Commission et al., 2023). The current version, number three, published in December 2024, is the one currently in force (European Commission et al., 2024).

2.4.4 A new era and digital innovation - responding to the needs of the 21st century

One of the key outcomes of the ACT EU programme was the publication, at the end of 2022, of a methodological guide on decentralised clinical trial procedures, which supported the introduction of the new operating model (European Commission, 2022). The COVID-19 period significantly facilitated the everyday use of numerous digital solutions-some of which had been developed earlier but were less widespread-which, as a result of the emergency, became integrated into the set of best practices forming the standard for the organisation of clinical trials. The document was subsequently updated in October 2025 (European Commission, 2025b).

The aim of these measures is for decentralised elements to be applied during clinical trials according to specific needs (e.g. therapeutic area, patient population) and to form part of a toolkit that increases flexibility: the use of a hybrid model may be an obvious option on a scale

between fully decentralised and fully in-person trials. A fully decentralised approach may pose difficulties for patients who are less tech-savvy and who require a face-to-face meeting with a doctor - the latter consideration may be relevant not only to patients but also to healthcare providers (for further details, see Chapter 2.6). Incorporating participants' experiences and preferences into the development of protocols is essential, as patient adherence directly influences the effectiveness and evaluability of clinical trials. In October 2022, speaking on behalf of investigators at the ACT EU multi-stakeholder forum, Dr Filippo Pieralli emphasised that the views of patients and doctors must be taken into account when developing methodological elements, and that the success of implementation can only be ensured if these principles are upheld (European Medicines Agency, 2022c).



6 Timeline of the European Union's regulatory framework for clinical trials

Source: own compilation

2.4.4.1 The rise of innovative clinical trials

In addition to decentralised elements, the EMA, the European Council and the HMA published guidance on complex clinical trials (European Medicines Agency, 2022b) in May 2022 as part of the ACT EU initiative, thereby supporting the further development of innovative clinical research on yet another front (European Commission, n.d.-b).

In recent years, this type of trial approach has been adopted with increasing frequency. The COVID-19 pandemic that broke out in 2020 unquestionably highlighted the need to rethink the methodology for generating evidence, alongside flexible trial designs. These types of clinical

trials enable patients to access innovative therapies much more quickly, which was particularly urgent during the pandemic or for those suffering from rare diseases. Thanks to the novel structure of this innovative methodology - such as the master protocol and sub-protocols containing specific details - it enables the parallel testing of multiple treatments and investigational products, and in multiple patient groups simultaneously. In many cases, the flexible framework allows for trials with a larger number of enrolled patients, and it is possible to modify the sub-protocols even during the trial if interim data indicate a need to do so. In light of the large volume of data, regulatory decision-making can also be more efficient and faster, which is of crucial importance during the authorisation process for a new medicine or therapeutic option.

Point	Directive 2001/20/EC	CTR (536/2014/EU)	ACT EU Recommendation
Type of legislation	Directive (to be transposed into national law)	Regulation (directly applicable)	Strategic initiative, non-legislative
Objective	Harmonisation, ensuring GCP	Full harmonisation, transparency, rapid authorisation	Accelerating clinical research and increasing competitiveness
Authorisation	At Member State level, differing procedures	Uniform EU procedure via the CTIS portal	Support for CTR implementation, process optimisation
Transparency	Limited, EMA database	Full public access in CTIS	Strengthening data sharing and transparency
Role of the Ethics Committee	At national level, varying practices	Integrated assessment (Part II national, Part I common)	Modernisation of ethical processes
Shortcomings / focus	Slow, bureaucratic, differences between Member States	Efficiency, digitalisation, patient safety	Innovation, training, support for non-commercial sponsors
Timeframe	2004-2022 (transition to CTR)	Full implementation from 2022 (exclusive from 2025)	Continuous development from 2022, work plans until 2030

2 Comparative table of the European Union's regulatory framework for clinical trials

Source: own compilation

2.4.5 Continuous development - new challenges

Digital data recording, artificial intelligence, social media-based recruitment and real-time patient monitoring raise new ethical questions. Large data and human sample collections enable the development of new research strategies and models, as well as new types of predictive research and analysis. The use of big data and information technology is already transforming many aspects of research. The potential for inherent in such databases is enormous, but it may also harbour risks. Informing participants about data management is the cornerstone of their safe scientific applicability (Nurmsoo & Hayes, 2015). An analysis of existing scenarios regarding the use (and misuse) of health data and biobanks has shown that the main risk scenarios do not necessarily stem from science, but from the commercial, administrative or political use of such data (Gallese, 2024). Thus, since 2016, the Taipei Declaration (World Medical Association, 2016) on ethical considerations regarding health databases and biobanks has supplemented the Declaration of Helsinki. This policy applies to any use of health databases and biobanks, except for individual treatment, and is not limited to research.

Clinical trials involving human subjects have gradually become indispensable to scientific and social progress. However, the shameful episodes of our history, amongst other things, have made it clear that only a strict professional and legal framework can guarantee this progress. This entailed not only scientific requirements for trials, but also the development of an appreciation of the risks borne by trial participants and the establishment of humane limits. The ethical and regulatory framework for clinical trials draws on the traditions of medical ethics (See: *Figure 3: The evolution of clinical trials presented on a timeline, with major ethical and regulatory milestones from 500 BCE to the present day*), and has developed towards holistic legal, ethical and institutional protection systems. Modern international and national legislation is continually updated in light of new technological and societal challenges.

The regulatory environment is constantly evolving as new disciplines and technologies become part of drug development. This evolution, spanning more than two thousand years, shows that clinical trials have always stood at the intersection of scientific rigour, ethical responsibility and technological innovation - and this triad will continue to guide them in the future. The future of clinical trials points towards a patient-centred, digitally supported and globally harmonised approach. Whilst integrating new technologies - artificial intelligence, wearable devices, big data - they will preserve the ethical and scientific standards developed over the centuries.

The 1947 Nuremberg Code, the 1964 Declaration of Helsinki and subsequent international guidelines (e.g. GCP) have defined the protection of human subjects, informed consent, safety, as well as researchers' responsibilities and data protection. These are essential for respecting patients' rights. The development of clinical trials has led from primitive comparative experiments to modern trials governed by extremely strict, standardised and ethical standards. This development has involved scientific rigour, the protection of patients and respect for their rights, as well as ongoing methodological and regulatory renewal to this day.

The ethical and regulatory frameworks of clinical trials have undergone significant transformation over the centuries. This development has occurred in response to crises and abuses, as well as through the scientific community's self-reflection, leading to a system today that is strictly protected and regulated.

Authorities, ethics committees and review bodies have been established, which continue to this day to approve and monitor clinical trials and drug candidates. The regulatory and ethical environment is regularly updated and further developed as new scientific disciplines and technologies become part of drug development.

2.4.6 Data protection rules

One of the fundamental challenges in the approach to DCTs is the systematic consolidation and management of large volumes of data, as well as ensuring data security and strict compliance with relevant legislation, in particular the General Data Protection Regulation (GDPR). As health data is sensitive in nature, it requires particular attention in all aspects of electronic data management, including the use of electronic signatures, digitally stored documents, and the appropriate protection and handling of personal addresses provided in connection with the home delivery of investigational medicinal products. Data quality, comparability and the acceptability of results are all common expectations on the part of both researchers and regulatory authorities, whilst the primary consideration is to ensure the maximum protection of patients' rights, safety and well-being.

The dynamic evolution of the regulatory framework governing clinical trials is also influenced by the current state of technological maturity.

Since 2018, the GDPR has regulated the disclosure of personal data, including special categories of data, and thus the processing of health data, with effect across all EU Member

States (Regulation (EU) 2016/679, 2016). The processing of European health data is protected by a further specific framework. The European Health Data Space (EHDS) is a unified legal and technical framework “aimed at ensuring the harmonised and secure interoperability of health data, strengthening patients’ digital access rights, and regulating the secondary use of data - for research or innovation” (Regulation (EU) 2025/327, 2025). Thanks to the regulation, interoperable data flow between different health databases is ensured, whilst also providing broad access not only to patients but also to researchers for scientific and innovation purposes. The framework supports the secondary use of existing data in anonymised or pseudonymised form, which can even replace clinical trials thanks to the generation of RWD/RWE.

Following the entry into force of the regulation on 26 March 2025, a phased implementation period will begin, setting out obligations for EU Member States until 2035.

2.5 Reform of traditional clinical trials

In the previous chapters, I outlined the evolutionary process of clinical trials and, in parallel, the changes in the regulatory environment affecting trials. I touched upon the changes in social and consumer habits associated with the COVID-19 period, and we also gained an insight into the innovative processes driven by the technological boom of the 21st century. In this chapter, I would like to summarise the unmet needs that have arisen in relation to traditional clinical trials, this time also touching upon economic considerations. It is important to emphasise that these factors, closely intertwined, have led to a paradigm shift in clinical trials. According to the methodology of classically structured clinical trials, face-to-face meetings take place at a specific site between the sponsor, the healthcare staff involved in the trial, and the enrolled patient. The opening of the trial site, staff training, and the review and signing of documentation all take place in person. The same applies to patient information, the enrolment procedure, the trials themselves, and all monitoring activities. The sponsor makes regular in-person visits to the trial site, and further meetings may be required should any issues arise. The same applies to the patient. The investigational medicinal product is delivered to the trial site, where the patient has the opportunity to collect it. As described, you can receive a new dose of the medicine and return any unused portions. All the points mentioned above in a traditional clinical trial require scheduling appointments, which can involve the inconvenience we are all familiar with - however, travel to the site may be prevented due to illness or other ad hoc reasons. Furthermore, the scheduled completion date of the trial may be delayed due to the vagaries of everyday life.

2.5.1 Systemic health economics and institutional factors in digital clinical development

Reforming traditional clinical trial models must be considered within the broader context of national healthcare systems. (Orosz, 2006, 2022) highlights in her analyses that systemic transformations and technological advancements in healthcare are closely linked to the institutional capacity, resource limitations, and operational workloads of the delivery system. In Central and Eastern Europe, particularly in Hungary, the clinical research ecosystem heavily depends on public university medical centres and tertiary hospitals. Consequently, any operational challenges or administrative burdens within the public health infrastructure directly affect site feasibility, investigator availability, and patient enrolment rates. Additionally, from a health economics perspective, the evolution of clinical trials goes beyond traditional regulatory marketing approval. As (Brixner et al. 2018) and Németh et al. (2020) point out in the context of Health Technology Assessment (HTA) and evidence transferability, the value assessment of modern pharmaceuticals increasingly incorporates broader evidence beyond traditional regulatory approval. This includes cost-effectiveness considerations and, in relevant contexts, RWE (Kaló et al., 2021).

The emergence of digitally transformed clinical trials offers a new way to capture continuous RWD during the early stages of the development life-cycle. This approach aligns the generation of trial data with the requirements of health technology assessment bodies and reimbursement authorities, thereby facilitating a connection between clinical efficacy and market access (Kaló et al., 2021). From a management perspective, it becomes clear that traditional trial reforms often fail when viewed merely as protocol modifications. Without addressing the macro-institutional constraints highlighted by Orosz and aligning with the downstream HTA considerations emphasised by Kaló, any operational reforms will remain superficial and will not resolve the underlying systemic bottlenecks affecting site capacity and long-term market access.

2.5.2 Changing social needs

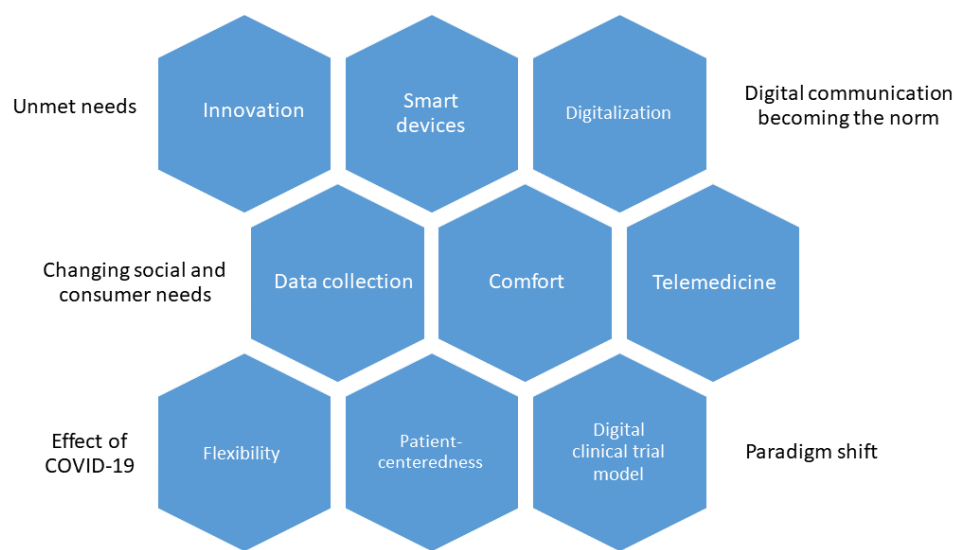
Paper-based document management can cause inconvenience for everyone involved. Patients have to bring their medical records with them, which often amount to a very thick stack of papers. As it passes through the hands of doctors practising at different locations, members of the healthcare team involved in the trial, laboratory staff performing diagnostics and nurses, it

gradually becomes an unmanageable and untraceable volume. By the end of a trial lasting up to several years and running across multiple sites, thousands of pages of documentation are generated. The handling of paper-based trial material requires particular care during both processing and archiving - GCP stipulates that all documentation relating to the clinical trial must be retained at the trial site for 15 years, and, in accordance with the CTR, the sponsor must retain it for 25 years.

Let us not forget that, in this case, they have become carriers of personal and sensitive information. The processing of the data and the assessment prepared for the regulatory authority (dossier) may already run to tens of thousands of pages - see Figure 2: *The life-cycle management process for cariprazine*. Given the structure of multicentre and multinational trials, the paperless approach has undoubtedly simplified data management. Thanks to shared, and where applicable, interoperable databases and platforms, there is no need to print multiple copies of the full trial documentation. Cloud-based storage ensures continuous data collection, which can be accessed at any time by authorised experts. Participants' trial results, detailed descriptions of adverse events experienced, and, if a measurement device is used during the clinical trial, the regular measurement results from that device are also available. Continuous access enables, for example, prompt intervention should technical difficulties arise. An alert configured on the data collection interface notifies the Principal Investigator (PI) if the system fails to detect data. This allows the investigator to contact the participant to report the problem encountered. Even such an automatic message can ensure the quantity and quality of evaluable data. In contrast, in a traditional clinical trial setting, any problem experienced by a participant may only come to light during a scheduled in-person monitoring visit, but this can take weeks or even months. During this time, no evaluable data is generated, which can easily lead to the trial cycle being prolonged or rendered invalid.

As the spread of various DHTs began to take hold in everyday practice, the use of mobile applications and wearable devices for healthcare or to support it became increasingly widespread. Alongside digital transformation, the restrictions imposed by COVID-19 had a major impact on this process. Taking into account changing social needs and the opportunities created by the restrictions, a paradigm shift has taken place at breakneck speed in the field of clinical trials. The fast-paced nature of the modern world has made the widespread use of innovative technologies inevitable. Their use is convenient and improves efficiency, as they enable us to book appointments with our doctor from home, download the consent form from

the cloud, request home delivery of smart devices, and conduct monitoring visits via video call. We can save time and energy, as we no longer need to spend hours travelling and waiting, or, in the case of minors or patients in need of care, ask family members or nursing staff for help with these tasks. It places less of a burden on time off work, as there is no need to take a full day or several days' leave, and the cost of travel and other expenses is not a barrier. In response to unmet needs, digitalisation, the pandemic and the changing social and consumer habits that accompany them have led to a paradigm shift in the field of clinical trials.



7 Contributing factors to the formation of DCTs

Source: own compilation

2.6 The emergence of DCTs

DCTs offer methodological innovations that hold significant potential for enhancing equity, particularly in terms of the inclusion of historically underrepresented populations (Rodriguez-Chavez, 2021). The use of online recruitment can, on the one hand, result in significant cost savings compared to traditional recruitment methods, and on the other hand, eliminate the need for a medical referral, thereby lowering the entry threshold. The option to participate from home reduces the burden of travel, which is particularly beneficial for patients who are immobile, elderly or living in rural areas. Approaches based on local, community-based locations further

increase accessibility, as participants can make use of resources close to their own living environment. Solutions providing digital and remote access enable information to be conveyed in multiple languages and different formats, which facilitates the involvement of culturally and linguistically diverse populations. Furthermore, ensuring anonymity, particularly in the case of stigmatised conditions such as HIV infection, can create a safer and more private environment for participation. Finally, community engagement based on digital platforms facilitates connections between participants, fosters peer support and strengthens the community experience, which can contribute to the sustainability and quality of participation in trials (Stern & Trusheim, 2024).

2.6.1 DCT trends and DHTs currently in use

The range of technological solutions used in digital and decentralised clinical trials is extremely broad and includes, amongst other things, decentralised trial designs, remote monitoring, wearable devices, Big Data-based analyses, and the role of blockchain, artificial intelligence and machine learning solutions in data processing. These technologies enable the identification of digital biomarkers, the performance of predictive analyses, and the structured integration of real-world data and evidence into clinical research. In practice, this is achieved through tools and solutions such as wearable sensors, mobile health applications, electronic diaries, telemedicine services, home sampling methods, and support systems based on augmented or artificial intelligence, which together create new opportunities, but also present specific challenges during the planning and implementation of clinical trials.

DCTs typically involve the use of cloud-based, integrated platforms which, when combined with mobile applications, wearable devices and telemedicine solutions, are capable of supporting remote data collection, patient monitoring and the automation of trial processes. These technologies help to reduce the number of physical site visits, increase patient convenience and willingness to participate, and potentially improve data quality and the continuity of data collection. At the same time, their use requires rigorous validation and regulatory compliance, particularly to ensure adherence to FDA and EMA guidelines.

The primary aim of introducing digital solutions is to make clinical trials more patient-centred and to achieve a comprehensive digital transformation of operations, not merely to exploit the possibilities of remote delivery. As part of this, paperless processes and digitised data management solutions, such as ePRO or Electronic Case Report Form (eCRF), are becoming

increasingly prominent. At the same time, decentralised clinical trials are prioritising the ‘siteless’ approach, whereby elements of the trial process are brought into participants’ homes, and the use of remote solutions becomes the central organising principle. Accordingly, it can be concluded that all decentralised clinical trials necessarily employ digital solutions; however, not all DCTs can be considered decentralised, as in the latter case, the primary focus is not necessarily on the separation from a physical site.

In decentralised clinical trials, the emphasis is primarily on increasing flexibility arising from the decentralised structure and on the adaptability provided by technological developments. The widespread adoption of mobile health applications and wearable devices has significantly contributed to these solutions becoming commonplace in clinical research, as they enable continuous data collection in the home environment, as well as the active involvement and support of patients, for example, through gamified reminders and feedback that promote adherence to treatment.

Perspective	Technology	Application in DCT
Remote consent and engagement	eConsent platforms with multimedia content, electronic signatures	Online patient involvement, interactive information, version tracking
Patient-reported outcomes	ePRO/eCOA mobile and web apps with push notifications and validated questionnaires	Frequent patient diary entries, PRO collection from home, electronic data capture (EDC) integration
Remote consultations	Telemedicine platforms (video consultations, chat, document sharing)	Video consultations, SAE follow-up, appointment booking
Wearable and home devices (DHTs)	Smartwatches (activity, heart rate), ECG patches, continuous glucose monitors, blood pressure monitors	Real-time/continuous data collection (e.g. step count, ECG, vital signs)
Central data management systems	Cloud-based EDC/DCT platforms, API integrations with EHR/RWD	Data integration from all sources, centralised monitoring, automated quality checks
Recruitment and retention	Digital recruitment tools (online advertisements, matching apps), AI-	Targeted patient selection, retention via push notifications, virtual communities

	powered database analysis, gamification apps	
Logistics and home sampling	Home sampling kits, temperature- controlled delivery systems, mobile laboratories	Remote blood sampling/laboratory, medicine delivery, home care nursing

3 The main categories of digital technologies currently used in DCTs

Source: own compilation

According to the biennial global survey conducted by the CISCRP (Center for Information and Study on Clinical Research Participation), an international non-profit organisation, more than half of the over 12,000 volunteers surveyed between April and June 2023 identified the distance of the trial site from their home as a key criterion for, whilst 34% of respondents also rated the option of home delivery of the test kit as a decisive factor. Similarly, 44% of respondents cited a reduction in the number of visits, whilst 28% cited the option of home-based visits as factors influencing their willingness to participate (Center for Information and Study on Clinical Research Participation, 2023). Based on the results of a study published in 2025, 49% of respondents rated the possibility of conducting visits from home as an influencing factor (Center for Information and Study on Clinical Research Participation, 2025). The flexibility of the trial has become an important requirement for participants to remain in the study. In the event of a high drop-out rate, fewer evaluable data are generated from the trial, which may even lead to the entire trial having to be repeated. This, in turn, consumes further costs and time.

One of the main advantages of decentralised trials is that they overcome the recruitment limitations of the previous approach: this is particularly beneficial in the case of rare diseases, paediatric patients, or populations with special care needs and limited access; at the same time, the right to withdraw from the trial at any time remains a legal entitlement, with no obligation for the volunteer to provide any justification and without any personal disadvantage. With this year's data published by the CISCRP, respondents confirm that they find the use of decentralised elements in clinical trials very convenient. Whilst in the traditional model all participants had to adapt to the trial site, the patient-centred approach of the DCT to participation study management and data collection - thereby reducing administrative and logistical burdens, improving the quality of research data and increasing the flexibility of the system. Reflecting on the needs that have emerged in recent years, the 2025 study has been

expanded to include a chapter on artificial intelligence and related data management, which provides detailed insight into respondents' digital maturity, whilst also evaluating their perceptions regarding the protection of their health data processed by AI.

The technological solutions provided by telemedicine today go far beyond the now classic remote consultation with a GP. In clinical trials, the range of digital tools is extremely wide: for example, trial participants can receive patient information via an online platform and even fulfil the requirements of the informed consent form with a digital signature. The investigational medicinal product (IMP) can even be delivered directly to the patient's home, and the use of smart devices (such as smartwatches) or mobile applications for data collection and monitoring is becoming increasingly common. Data from these devices is collected in cloud-based digital storage, which enables continuous analysis of interim data, but technical issues can also be detected if the system flags missing data.

When applying decentralised models, fundamental human rights, patient safety and the protection of participants' well-being - alongside full compliance with the European and national regulatory environment - must be ensured, and the risk-benefit ratio is carefully weighed during the introduction of each decentralised element, in line with the study's professional objectives and the characteristics of the participant population. Digital and remote data collection, monitoring and intervention processes also require new safeguards: particular emphasis should be placed on the technological training of research staff and participants, ensuring reliable data management, and developing emergency protocols, for example in the event of device failure or internet access problems. At the same time, we must be prepared to manage novel sources of error arising from the application of this new method, as remote data collection relies heavily on equipment and infrastructure that also require technological expertise.

2.6.2 Challenges arising from DCTs

A study (Jong et al., 2022) examined the views of regulators, as 20 European regulatory bodies were asked for their recommendations regarding the spread of DCTs. According to the authorities surveyed, the greatest concern is maintaining the standard of patient safety monitoring, particularly in relation to the reduction in the number of face-to-face meetings. They also agreed that, to ensure high-quality safety monitoring, a hybrid model - that is, the

combined use of on-site and remote (or even home-based) solutions-could represent the optimal approach during the conduct of the trial.

The concept of DCTs combines the benefits of technological advancement and scientific innovation to make the research process more transparent, efficient and user-friendly for both patients and professionals. Whilst the traditional, site-based model strictly requires in-person attendance, DCT integrates a range of hybrid and digital solutions: these include, for example, home healthcare services based on teleconsultations or telephone consultations, or the direct home delivery of trial materials via a logistics chain. In addition to all this, compliance with the applicable GCP and GDPR regulations is essential, particularly to ensure the integrity of the pharmaceutical supply chain and the protection of personal data.

Under the traditional procedure, the participant (or the legal representative of a minor or incapacitated person) attends their doctor's surgery in person, where, following a detailed verbal briefing, they make a decision regarding participation, submit a hand-signed consent form, and then attend the visits and undergo the necessary examinations as specified in the trial protocol. Today, all of this can also be carried out digitally, supporting home-based care: through electronic patient information, digital signatures, and a smart device or tablet provided for the duration of participation in the trial, with which the participant can monitor and document the entire trial process, and even contact the doctor via video call. In addition to quality assurance, these solutions also raise new expectations regarding privacy rights and cybersecurity. In all cases, the protection of sensitive data must be guaranteed, and participants must be provided with detailed information regarding access to their data, its storage, and the protocol for handling any incidents that may occur during data processing (such as unauthorised access or data loss). Compliance with standards and regulations is an essential prerequisite for the successful implementation of modern, digitally supported clinical trial processes, not only from a legal perspective but also from an ethical and quality assurance standpoint.

However, there were high hopes that it would help engage under-represented and marginalised patients by potentially providing wider geographical coverage, thereby facilitating the inclusion of patient groups that had previously been difficult to reach. DCTs enable more extensive data collection through real-time data gathering in real-world settings, which, thanks to these settings, provides valuable information for clinical and decision-making processes. However, the setup itself - particularly the reduction in face-to-face contact - presents new challenges.

Whilst the logistical and travel burdens on participants are reduced, regulators have highlighted that this may also have implications for patient safety risks. During remote consultations, whether conducted by telephone or via video link, the scope for medical observation is often more limited, meaning that certain risks, side effects, or critical events leading to exclusion may remain undetected.

From the perspective of ensuring data integrity and data quality, a further challenge may be that DCTs rely to a greater extent on events reported by participants - including adverse events, device usage anomalies, and the handling of incomplete or missing data. These factors require particular attention both during the planning phase and when developing data management and quality assurance protocols, so that DCTs can truly serve the goals of innovative drug development in a safe and scientifically sound manner.

However, unexpected situations may arise: a malfunction of the digital device (for example, it does not report in the validated manner, or not in the way or at the time specified), intermittent internet access, or simple hardware problems (such as a flat battery) may disrupt the process; therefore, a contingency plan must be submitted to the regulatory authority to address all types of risk. However, this requires a clear understanding of the limitations of the applicable tool or method, as well as knowledge of the specific characteristics of the therapeutic area and the competencies of the users. When applying DCT components, particular attention must be paid to the characteristics of the specific therapeutic area, the digital competencies of participants, and ensuring that the validity of the data is not compromised from a statistical perspective - that is, that the results do not merely reflect technically proficient or well-resourced populations. It is worth considering whether, from the perspective of statistical validity, decentralised elements may cause distortion for various reasons; conversely, can we draw general conclusions from the study's results, for example, due to the exclusion of areas with limited internet access or the marginalisation of a less digitally advanced population?

Type	Advantages	Disadvantages / challenges
Traditional clinical trial	Controlled, standardised environment (site) with well-established GCP processes. 7	Limited geographical reach, more difficult recruitment and lower diversity. ⁹
	Direct, face-to-face doctor-patient interaction, easier physical examination and sampling. 7	High infrastructure and staffing costs, expensive site network.

	A standard model well known to regulators and ethics committees. 8	Slower data collection and processing: visit-based, non-continuous data flow. 7
	On-site data and process control, simpler IT security architecture.	High patient burden (travel, loss of working hours), higher risk of dropout. 6
Digital clinical trial	Wider geographical reach, better representativeness and diversity, easier recruitment from under-represented populations. 4	Inequalities in access to technology and digital literacy, potential selection bias. 5
	Less travel, flexible participation, better patient experience and retention.	Ensuring data quality and adherence in a home setting; handling large volumes of sensor data. 3
	Potential cost reductions (site, travel and monitoring costs), faster recruitment and time savings.	More complex data protection, multiple jurisdictions, and the legal/ethical complexities of remote consent and oversight. 2
	Richer, real-world and continuous digital data, better long-term monitoring. 1	More vendors, integrated platform ecosystems, and a greater need for governance and quality management.

1 (Wang et al., 2025)

2 (Tenti et al., 2025)

3 (Clemons et al., 2025)

4 (de Jong et al., 2022)

5 (Jean-Louis & Seixas, 2024)

4 Comparison table of the most significant benefits and risks associated with traditional and digital clinical trials

Source: own compilation

From a technological perspective, data consolidation, the collection and management of large volumes of data, data security and ensuring compliance with GDPR requirements may present further challenges during the implementation of DCTs. Given that health data is classified as sensitive data, every step of electronic data management - such as digital signatures, electronically stored documents, and the handling of addresses recorded during the home delivery of IMPs - is also addressed in the methodological recommendations. In line with this, ensuring data quality, the comparability of results and metrics, and their acceptability are shared expectations of all parties.

It is important to emphasise that global economic developments - such as the occasional vulnerability of supply chains - may also influence DCT practice, for example in terms of IMP delivery or technical support for digital tools. Taking into account the principles of necessity and proportionality, patients must be guaranteed access to the staff organising the trial in all

situations, whilst at the same time avoiding excessive bureaucratisation of trials and an unnecessary increase in administrative burdens. Overall, this supports the view that the decentralised trial model can serve patient-centred care, scientific quality assurance and cost-effective research.

2.7 Comparative innovation frameworks in digital clinical development

Digital transformation in clinical development should not be understood simply as the replacement of site-based activities with digital tools. It also changes where innovation is generated, how activities and knowledge are coordinated, and which capabilities are required from sponsors, CROs and clinical trial sites. For this reason, the strategic implications of DCT adoption can be examined through complementary innovation and technology-management perspectives. In particular, the distinction between closed and open innovation provides a useful starting point for understanding changing organisational boundaries and external dependencies (Chesbrough, 2003; Gassmann et al., 2010).

The closed innovation model emphasises internal control over knowledge, intellectual property and the innovation process, whereas open innovation relies more strongly on external knowledge flows, collaboration and complementary capabilities (Chesbrough, 2003; Gassmann et al., 2010). In digital clinical development, the growing use of specialised vendors, CROs, data platforms, wearable technologies and remote services increases the importance of such external linkages. However, this does not imply a simple transition from closed to open innovation. Rather, DCTs create a hybrid governance problem in which openness must be combined with internal oversight, regulatory accountability, data governance and control over critical trial activities.

2.7.1 Tension and strategic trade-offs between closed and open models

- The allocation of resources and the development of capabilities. A predominantly closed model concentrates knowledge, infrastructure and operational capabilities internally, while open innovation gives greater weight to external expertise and inter-organisational coordination. For DCTs, the strategic issue is therefore not whether capabilities should be internal or external, but which capabilities should remain under

direct organisational control and which can be accessed through partners. This makes coordination, knowledge integration and resource orchestration important managerial capabilities (Gassmann et al., 2010; Teece, 2007).

- Intellectual property and data governance. Greater external connectivity can improve access to specialised technologies and knowledge, but it also increases the number of organisational interfaces through which sensitive trial data, software dependencies and operational responsibilities are managed. In DCTs, therefore, open innovation must be accompanied by clear governance of data access, interoperability, cybersecurity, vendor responsibilities and regulatory compliance. Openness and control should consequently be treated as complementary rather than mutually exclusive principles.
- Financial risk versus flexibility. External digital platforms may reduce the need for some fixed investments and can provide access to specialised capabilities without building all resources internally. At the same time, the financial consequences of digital adoption cannot be reduced to licence costs or headline efficiency gains. Integration work, vendor management, training, data governance, cybersecurity and dependence on specialised suppliers may create additional direct or indirect costs. The strategic value of a DCT therefore depends on the configuration of the entire operating model rather than on the adoption of individual technologies.

Consequently, the strategic management of digital clinical development is best conceptualised as the design and governance of a hybrid innovation model. Such a model combines internal control of critical clinical, scientific and regulatory responsibilities with selective openness to external technologies, knowledge and service capabilities. This framing also creates a direct link to the subsequent discussion of organisational readiness and dynamic capabilities (DC) (Teece, 2007): successful adoption depends on the ability to integrate external innovation into existing routines while simultaneously redesigning those routines where necessary.

2.7.2 Strategic management and innovation perspectives in digital health adoption

Technology adoption at organisational level requires more than a favourable assessment of a technology itself. The Technology-organisation-Environment (TOE) framework provides a useful starting point because it distinguishes among technological characteristics, organisational conditions and the external environment as determinants of organisational

innovation adoption (Tornatzky & Fleischer, 1990). This is particularly relevant to DCTs, where adoption decisions are simultaneously shaped by the characteristics of the DHTs, organisational resources and capabilities, inter-organisational dependencies, and the regulatory and institutional environment.

A second complementary perspective is organisational readiness for change. Weiner (2009) conceptualises readiness as a shared organisational state involving both commitment to change and collective confidence in the organisation's capacity to implement it. In healthcare, readiness is particularly relevant where implementation requires coordinated changes in staffing, workflows, communication and decision-making. Applied to DCTs, this perspective directs attention to whether sponsors and sites possess sufficient time, skills, resources and shared commitment to integrate digital processes into routine trial operations. It therefore complements, rather than substitutes for, technology-centred adoption models.

DC theory adds a strategic explanation for how organisations respond to technological and market change. Teece (2007) describes DC through the interrelated activities of sensing opportunities and threats, seizing opportunities through investment and strategic choice, and transforming or reconfiguring organisational resources and routines. In DCT implementation, sensing includes recognising relevant technological and regulatory developments; seizing involves selecting viable digital architectures, partners and investment priorities; and transforming involves redesigning trial workflows, responsibilities and capabilities. The framework is therefore well suited to analysing why the same digital technology may generate different organisational outcomes across sponsors or sites.

The relationship between DC and business model innovation further strengthens this interpretation. Teece (2018) argues that business models, organisational design and DC are interdependent, and that DC support the design and implementation of changing business models. In clinical development, DCT adoption can therefore be interpreted as a potential change in the operating and coordination logic of the trial rather than as a discrete software procurement decision. This interpretation is consistent with Hungarian evidence from technology and digital transformation research. Deutsch and Berényi (2023) emphasise adaptive competencies and the strategic management of technology, while Móricz et al. (2022) show in the Hungarian business services sector that digital transformation can be driven both

by existing capabilities and by organisational renewal. These studies are not clinical-trial studies and are therefore used here as contextual rather than DCT-specific evidence.

The Hungarian and Central and Eastern European context also highlights that organisational adoption cannot be separated from the wider health-system environment. Research involving Zoltán Kaló and co-authors has shown that the generation, use and transferability of RWE in CEE depend on governance arrangements, data access and integration, methodological expectations, financial resources and available expertise (Kamusheva et al., 2022; Németh et al., 2023). More recent work led by Kaló further highlights the importance of local RWD and transferability when advanced evidence methods are applied in lower-income European settings (Kaló et al., 2026). These considerations are relevant to DCTs because digitally enabled trials increasingly interact with real-world data infrastructures and downstream evidence requirements. At the macro level, Geels' (2002, 2011) Multi-Level Perspective (MLP) complements these organisational theories by explaining technological transitions as interactions among landscape pressures, socio-technical regimes and emerging niches. Taken together, the frameworks used in this thesis imply that DCT adoption is conditional rather than linear: the effects of digital technologies depend on organisational capabilities and readiness as well as on trial-specific, regulatory, data-governance and evidence-generation conditions. This provides the theoretical rationale for the moderating factors incorporated later into the conceptual model.

2.8 The sustainability of DCTs

In the previous sections, I have outlined the advantages of DCTs, as well as the challenges associated with this type of trial. Moving forward, and interpreting the practical implications of these factors, in this chapter I examine their impact on the sustainability of DCTs from a multidimensional perspective.

DCTs represent one of the most significant areas of innovation in global drug development; however, their long-term sustainability continues to face significant environmental, economic, social, institutional and technological challenges. Current practice is characterised by attempts to transfer digital solutions developed predominantly in high-income economies to lower-resource settings without modification, which, due to the heterogeneity of digital access, infrastructure and regulatory frameworks, often results not in equity but in the reinforcement of

structural inequalities. It follows that examining the sustainability of DCTs is not merely a technological issue but requires a complex, multidimensional analysis.

According to research summarising international regulation and practice, sustainability should be understood as the persistence of the long-term benefits of digital solutions, which takes shape across six well-defined dimensions: environmental, economic, social, technological, regulatory and institutional (Ebenso et al., 2025).

The Clinical Sustainability Assessment Tool (CSAT) can be used to complement this framework. The CSAT is a validated measurement tool that determines the maturity of a clinical programme's sustainability; through a structured assessment of seven domains, it highlights aspects requiring further development (Malone et al., 2021).

2.8.1 Regulatory sustainability

Regulatory sustainability is significantly hampered by the complexity of international and cross-jurisdictional regulatory frameworks, which makes the uniform operation of decentralised clinical trials particularly challenging. The differing approaches of regulatory authorities - primarily the FDA and the EMA - further increase the difficulty of harmonisation; furthermore, globally divergent data protection legislation - such as the GDPR in the European Union, Health Insurance Portability and Accountability Act (HIPAA) in the United States, and various standards in force in other countries - further fragments the regulatory environment. Consequently, the cross-border operation of decentralised trials can only be sustainable if sponsors adopt flexible, multi-jurisdictional compliance strategies capable of harmonising the various data protection and quality assurance requirements (Yang, 2025).

2.8.2 Global-level objectives

The global landscape of DCTs shows significant regional differences across the United States, the European Union, and Central and Eastern European (CEE) markets such as Hungary. Hungary has an established clinical research ecosystem supported by academic institutions, hospitals, research centres, CROs and pharmaceutical companies (Fehérváry et al., 2024). At the same time, the country's centralised healthcare structure shapes institutional decision-making and managerial autonomy, which can affect the organisational conditions under which clinical research is conducted (Krenyácz & Révész, 2025). The transfer of digital trial models into national practice is further influenced by the maturity of digital infrastructure,

interoperability and institutional arrangements. In Hungary, the EESZT provides an important national digital-health infrastructure, but recent European Commission work identifies remaining semantic-interoperability and regulatory gaps that can constrain the effective reuse and integration of health data. These factors are relevant to the long-term sustainability of DCTs because the feasibility of integration depends on the surrounding health-system architecture rather than on trial technology alone (European Commission, 2025).

Digital technologies are fundamentally transforming healthcare at a global level, creating new opportunities to improve the quality of patient care, increase the efficiency of systems and strengthen public health awareness. Amidst this transformation, it is essential to develop a comprehensive national strategy that provides direction for developments, coordinates the activities of stakeholders, and ensures that technological innovations serve the interests of society as a whole, in line with the WHO's global objectives. The WHO's global digital health strategy sets out four key principles to ensure that the introduction of digital technologies supports national health systems in a sustainable manner. The strategy emphasises that the institutionalisation of digital health can only be successful if it is integrated into the national system in line with a country's own health policy priorities and resources. In addition, an integrated, comprehensive strategic approach is needed to align leadership, financial, organisational and technological capacities, and to avoid the fragmentation resulting from disjointed, parallel digital developments. The WHO guidelines also emphasise the responsible and appropriate use of digital technologies, ensuring the consistent application of ethical standards, patient safety, data protection and interoperability. Finally, the strategy emphasises addressing the specific barriers faced by the least developed countries, particularly overcoming constraints arising from a lack of infrastructure, human resources and financing capacities, so that digital health innovations can truly create global access and equity (World Health Organization, 2020).

The UN 2030 Agenda for Sustainable Development also highlights that global connectivity holds enormous potential for accelerating development and bridging the digital divide. Technology has become key to improving access to healthcare, enabling more and more people to access services that were previously out of reach. The strategic and innovative use of digital tools is essential to achieving the goal of universal health coverage and the health-related Sustainable Development Goals (United Nations, 2015).

Overall, an examination of the sustainability of DCTs shows that the future of DCTs depends on whether digital innovation can be seamlessly integrated into social, economic and

institutional structures. Only a DCT model that is context-sensitive, equitable, interoperable and financially viable in the long term, whilst supporting the efficiency and inclusivity of health research at a systemic level, can be considered sustainable.

2.8.3 Environmental sustainability

Traditional clinical trials have a significant environmental footprint: it is estimated that a single trial emits approximately 100 tonnes of CO₂ equivalents, 60-75% of which stems from travel by patients and research staff, as well as associated logistical operations (DayOne, 2025).

decentralised clinical trials offer a promising opportunity to reduce these emissions, as enabling remote patient participation significantly reduces the number of visits requiring in-person attendance. The reduction in monitoring activities - particularly in multicentre trials (Mackillop et al., 2023) - along with paperless operations and other digital solutions, leads to further carbon savings.

However, decentralisation also results in an environmental impact for certain processes. The delivery of investigational medicinal products to individual patients - as opposed to the traditional bulk logistics to centralised trial sites - may increase transport-related emissions (docs24, n.d.). At the same time, the energy requirements of the digital infrastructure, including data centres, servers, video-based consultations and electronic data recording systems, generates significant additional CO₂ emissions, which must be taken into account in sustainability assessments (Kohl & Schmidt-Lucke, 2023).

Standardised methodologies are now available for estimating environmental impacts. The Sustainable Healthcare Coalition, the Pistoia Alliance and the Sustainable Markets Initiative have jointly developed a procedure for measuring the carbon footprint of clinical trials and created the *Clinical Trial Carbon Calculator* tool (Sustainable Carbon Coalition, 2026), which enables the identification of emission sources and the comparison of trials' environmental performance. These methodological developments are critical to understanding where and to what extent DCTs contribute to emissions reductions, and where potential offsetting effects may arise (Adshead et al., 2025).

2.8.4 Infrastructural and technological sustainability

The fragmentation of digital health systems results in significant additional costs and data quality risks. The introduction of interoperability standards is therefore an important prerequisite for sustainability.

The central challenge to the technological sustainability of DCTs is the lack of interoperability. Electronic data recording systems from different manufacturers, operating on different principles, are in many cases incompatible platforms. The use of such systems makes data integration costly; furthermore, they pose data management risks and, in practice, hinder the efficiency of monitoring, analytical and regulatory processes. The application of uniform data standards is therefore a critical prerequisite for the functionality of the digital regulatory ecosystem (Integra IT, 2022; Malik et al., 2025).

In the case of low- and middle-income countries (LMICs), infrastructure constraints - limited internet access, low digital literacy, a lack of devices, poor server capacity and outdated IT systems - significantly reduce the scalability of digital solutions. In this environment, sustainable technological adaptation can only be achieved if systems are adapted to the local context, rather than simply transposing resource-intensive industry standards (Ebenso et al., 2025; Tambe, 2025).

The third fundamental condition for technological sustainability is long-term capacity building. Training programmes provided by international research institutes and organisations - particularly approaches based on the '*train-the-trainer*' model¹¹, which are continuous and tailored to local needs - are essential to ensure that research staff are able to manage the technological and operational requirements of decentralised trials. A sustainable digital infrastructure is therefore not merely a technological investment, but the result of a long-term process of knowledge and capacity building.

Furthermore, interoperability is an important prerequisite for technological sustainability: fragmented, incompatible systems pose significant costs and data management risks. The application of global standards ensures that the data architecture of trials remains viable in the long term.

¹¹ train-the-trainer model: a structured approach aimed at preparing individuals to effectively train others within an organisation (Cserti, 2024) .

2.8.5 Economic sustainability

The economic sustainability of DCTs is characterised by the duality of high initial investment requirements and long-term return potential. Digital infrastructure - including software platforms, training and support systems - imposes significant upfront costs on sponsors, which are particularly burdensome when implementation requires integration across multiple systems. At the same time, larger and more mature DCT deployments may generate financial value through operational efficiencies and time-related benefits, although the magnitude of such benefits depends on study scale and implementation conditions (DiMasi et al., 2023).

DiMasi and colleagues (2023) illustrate the economic significance of the initial investment and the potential for value creation when decentralised approaches are implemented at sufficient scale. However, long-term economic viability is also constrained by the sustainability of funding, maintenance and capability-building arrangements. Sustainability therefore depends not only on projected returns but also on institutional commitment and the systemic embedding of digital transformation (Ebenso et al., 2025; Exemplars In Global Health, n.d.).

Factors determining cost-effectiveness include implementation costs, user-friendly design, accessibility for participants, ongoing technical support and the scalability of solutions. In addition to the fact that digital solutions are easier to scale globally, which can have a cost-effective and positive impact on LMIC catch-up in the long term, I would refer back to the importance of the local context mentioned in section 5.3.4. Together, these factors determine whether the digital screening ecosystem can ensure long-term and economically sustainable operation.

2.8.6 Social sustainability and health equity

DCTs have a dual impact in terms of social sustainability: whilst they can improve access, they may further exacerbate health and digital inequalities through the digital divide. The linguistic, technological and access requirements of digital platforms can easily exclude groups that are already disadvantaged in terms of access to health research. For marginalised groups, limited

infrastructure, a lack of digital literacy, adverse social determinants¹² and historical mistrust represent the greatest barriers (Adedinsewo et al., 2023). .

Lack of infrastructure	Digital illiteracy	Stigma and lack of trust	Social factors
• internet access • mobile phones & other devices are not available to everyone	• elderly • low-educated • low-income populations may be less confident with digital devices	• distrust regarding historical abuse of health research • type of disease • data protection	• economic stability • housing security • education level • healthcare access • language barriers

8 Factors influencing health and digital inequalities

Source: own compilation

decentralised research models and DHT solutions, however, offer new opportunities to enhance equity. Online recruitment, home-based participation, the provision of information in multiple languages and formats, and digital channels offering anonymity all facilitate the engagement of hard-to-reach populations (King et al., 2024; Stern & Trusheim, 2024). To mitigate structural exclusion, it is essential to systematically assess equity considerations, ensure access to digital tools, provide training and technological support, and develop hybrid participation options. DCTs are more equitable due to careful planning that takes these considerations into account: if the conditions for participation in research implicitly exclude certain populations, DCTs will reproduce or further exacerbate existing structural inequalities. In addition to the social implications of fairness and equal access, such systematic asymmetry may also distort the statistical results of clinical trials. Furthermore, it would be misleading to draw conclusions for a wider population and formulate therapeutic goals in this manner. To avoid this, the WHO Health Equity Assessment Tool (HEAT) software can be utilised, which can help identify regional and national health characteristics, as well as the differences between them through

¹² social determinant: a key concept in health sciences and sociology, referring to the social, economic and environmental conditions that influence people’s health status, well-being and quality of life, including housing, education, employment, income, community and social relationships.

comparative analysis. Furthermore, the use of an evaluation framework that identifies potential exclusion mechanisms in a given trial protocol would greatly support planning, thereby helping to make the trial design socially sustainable.

However, these potential benefits will only materialise if equity is consciously supported at every level of the system. The regulatory environment must allow for the application of diverse approaches; organisations must provide human resources alongside regular training; trials must employ flexibly structured online and offline strategies and targeted training; and at the participant level, not only digital access but also the actual provision of devices where necessary must be guaranteed. All this highlights that technological access alone is not sufficient: maintaining social equity requires active, structural interventions (Adedinsewo et al., 2023; Rodriguez-Chavez, 2021).

2.8.7 Ecosystem sustainability and organizational change management

A critical analysis of DCT sustainability reveals that long-term viability is contingent on more than financial solvency or environmental performance. It is also dependent on institutional embeddedness, organisational learning, and the capacity to manage change when digital technologies alter established routines and responsibilities (Csedő et al., 2018, 2019, 2022).

Hungarian management research provides relevant contextual evidence for this mechanism, although it does not concern clinical trials specifically. Csedő et al. (2018), studying large Hungarian energy companies, found that the implementation of innovation was constrained by established structures, organisational culture and knowledge-management conditions, and that organisational change could be required to support renewal. In a financial-services case, Csedő et al. (2019) similarly showed that digitalisation becomes strategically meaningful when organisations adapt to external change and combine technological development with organisational and business-model renewal. These findings support treating DCT implementation as an organisational transformation challenge rather than as a stand-alone technology procurement exercise.

At the ecosystem level, Csedő et al. (2021) demonstrated how innovation knowledge networks can connect higher-education institutions, corporate innovation and regulatory institutions through knowledge flows and collaborative relationships. Although their case concerns a power-to-gas innovation ecosystem rather than healthcare, the governance principle is relevant to DCTs: sustainable digital clinical research also requires coordination among sponsors, sites,

technology providers, research institutions, regulators and patient organisations. The value of this reference is therefore contextual and ecosystem-oriented, not healthcare-specific.

From a strategic technology-management perspective, Deutsch et al. (2019) emphasise the strategic role of technology, while Deutsch and Berényi (2023) argue that accelerating technological and environmental change increases the importance of adaptive competencies and the systematic management of technology at strategic level. Applied to DCT sustainability, this perspective implies that technology choices should be connected to long-term capability development, organisational processes and strategic priorities rather than assessed solely through short-term implementation indicators.

At the level of individual technology adoption, Hungarian evidence also indicates that technology availability alone is insufficient. Berenyi et al. (2021) identified both positive adoption propensity and concerns related to vulnerability among Hungarian business students, while Deutsch and Berényi (2023) found variation in technology acceptance and adoption-related factors among Hungarian higher-education students. These studies do not constitute evidence from clinical trial sites, but they provide useful Hungarian contextual support for treating competence, perceptions and perceived vulnerability as relevant components of technology adoption.

Change management is therefore a central mechanism of sustainable digital transformation. (Csedo et al., 2017) found that successful digitalisation projects combined ICT, project-management and change-management competencies, while leadership, communication and stakeholder management were important change drivers. Their findings also indicate that institutionalisation of digitalisation can affect strategy, organisational structure and employee behaviour. This is consistent with the present study's interpretation that remote monitoring, electronic consent and continuous digital data collection require not only technical deployment but also deliberate redesign of roles, workflows, communication and capability development.

2.8.8 Sustainability at the level of the healthcare system

The long-term sustainability of DCTs fundamentally depends on whether they can be organically integrated into existing healthcare systems, or conversely, become isolated and fall victim to the '*pilot project syndrome*', in which initial initiatives fail to become enduring, system-embedded solutions.

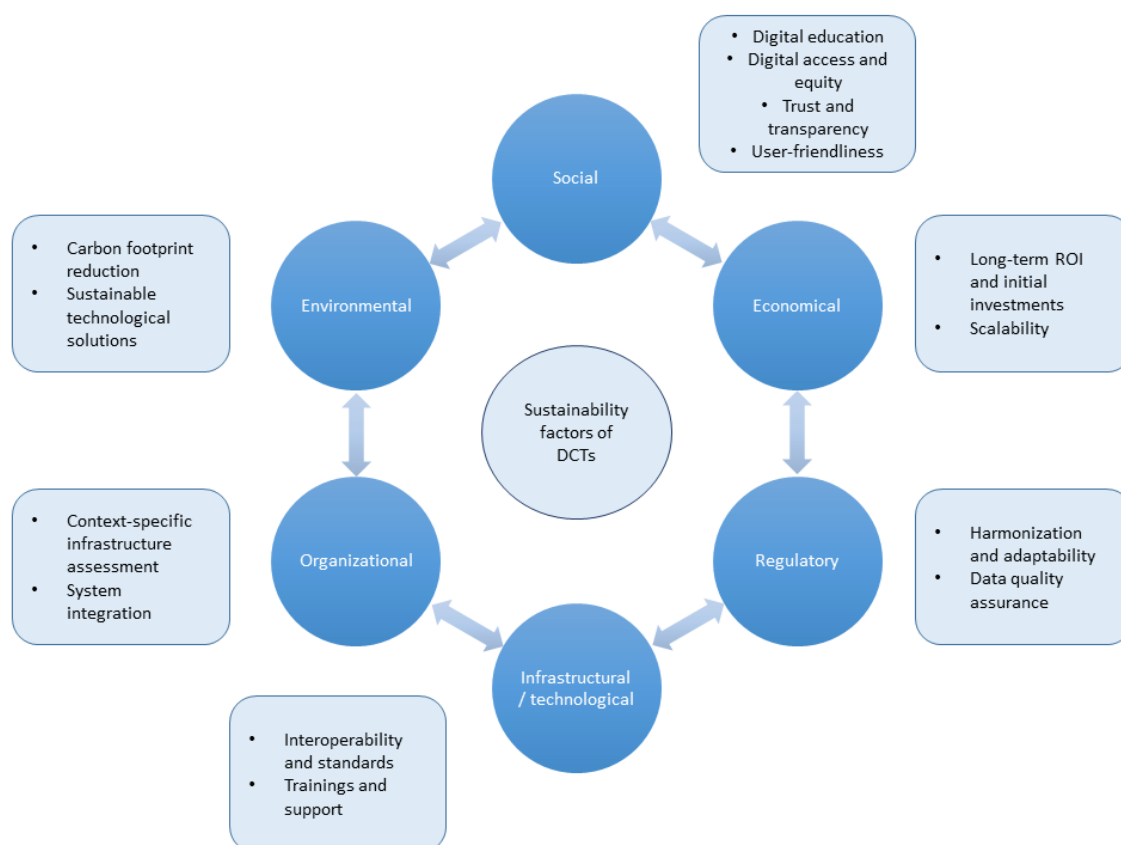
A key factor in sustainability is the accurate assessment of local infrastructure, as the fundamental elements of the digital health ecosystem - such as internet access, digital literacy, device availability and the regulatory environment - can vary significantly between countries and even within countries. The design of DCTs requires a systematic assessment of local digital and institutional capacities. The heterogeneity of HIC/LMIC¹³ differences (broadband coverage, device access, digital skills, data costs, regulatory framework) justifies the use of local adaptations rather than global templates. DCTs can only generate real added value if the platforms and protocols are aligned with the actual capacities of the given healthcare system. Trial protocols developed in this way are better suited to the actual capabilities of the target populations.

Long-term financial stability is a further fundamental prerequisite for the sustainable operation of DCTs. Short-term, pilot-style projects often fail to survive because, once initial funding ceases, there are insufficient resources available to maintain the platform, provide user support, ensure data security and retain the necessary specialist staff. Therefore, only those models can be considered sustainable that are based on funding cycles planned several years in advance, ensure continuous coverage of operating costs, and are based on transparent resource allocation linked to milestones. The sustainability of DCTs can only be achieved if they operate as part of a broader digital health infrastructure, rather than as isolated projects (Ebenso et al., 2025).

The uncoordinated, parallel roll-out of DHTs can easily lead to system fragmentation and the emergence of siloed infrastructures that do not communicate with one another. Platforms and technologies operating in isolation from one another are unsustainable in the long term, as they require either complete replacement or costly integration, which entails a significant waste of resources. Sustainable digital transformation can therefore only be achieved within an integrated strategic framework at the level of the healthcare system, supported by stable funding, long-term political commitment, a unified regulatory framework, and data and interoperability standards followed by all stakeholders (Exemplars In Global Health, n.d.).

The sustainability of DCTs can only be measured using a complex approach. Figure 9 illustrates an integrated conceptual framework of these influencing factors.

¹³ Classification based on GNI (Gross National Income) per capita. HIC: high-income countries. \$13,935 or more; LMIC: lower-middle-income countries. \$1,136 - \$4,495 (World Bank Group, n.d.) .



9 Factors influencing the sustainability of DCTs

Source: own compilation

The external factors associated with the six interrelated dimensions of sustainability shown in the figure - social, economic, infrastructural/technological, regulatory, environmental and organisational dimensions - represent the key factors that determine the long-term feasibility and system integration of DCTs. The model approaches the issue of sustainability from a systems perspective, emphasising that the individual dimensions do not influence the effectiveness, social acceptance and scalability of trials in isolation, but rather through their interaction with one another.

A detailed breakdown of the dimensions and factors shown in the figure is provided in Annex 3.

2.9 The cost structure of clinical trials

In the pharmaceutical industry, clinical trials represent one of the most critical and cost-intensive stages of the R&D&I process. The outcome of trials remains uncertain at this stage,

so the significant investment of resources does not guarantee subsequent market success. Consequently, clinical trials are among the activities associated with the highest financial and operational risks in drug development (Lo et al., 2009). Clinical trials require significant financial investment, which, combined with development risks, necessitates rigorous planning and financial control. According to industry analyses, the costs of clinical trials can range from a few million USD in Phase I to over 100 million USD in Phase III, whilst costs per patient can typically reach six figures. The total budget is typically divided between site-related expenses, patient recruitment, data management, regulatory compliance and general overheads (Beauroyre, 2025).

The budget for clinical trials is complex, comprising several interrelated cost categories. These items cover the entire life cycle of the trial, from protocol development to data lock, and are typically planned on a project basis. The cost structure is influenced by numerous factors, including the phase of the trial, sample size, geographical scope, the complexity of endpoints, and the operational model employed.

In a narrative overview, the main cost categories of clinical trials can be classified into the following groups:

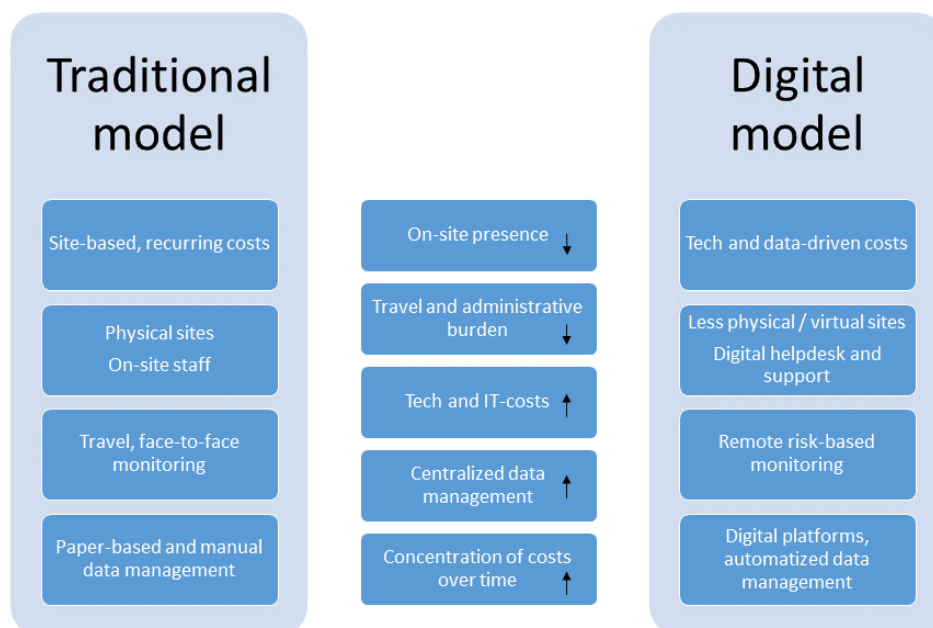
- Protocol development and regulatory preparation, which includes the development of the trial plan, statistical planning, regulatory documentation, and ethical approvals.
- Site-related costs, including site initiation, contract signing, training, and operational and administrative fees incurred during the trial.
- Patient-related costs, such as recruitment, screening, conducting visits, compensation and logistical support related to participation.
- Monitoring and quality assurance, which ensures the verification of trial compliance, data quality and adherence to the protocol.
- Data collection and data management, including electronic data collection systems, data validation, statistical analysis and data closure.
- Technology and IT infrastructure, which provides the technical foundation for trial data management, system integration and information security.
- Project management and general overhead costs, covering sponsor and CRO coordination, vendor management and administrative operations.

These cost elements cannot be interpreted in a static manner on their own, as their relative weight and temporal distribution depend significantly on the trial model employed. The

transformation of the operational logic of clinical research - particularly the emergence of digital and decentralised approaches - does not result in the complete emergence or disappearance of new cost categories, but primarily in a structural reorganisation of existing cost items.

2.9.1 Differences in cost structure between traditional and digital clinical trials

The cost structures of traditional and digital clinical trials differ structurally in several respects. The cost burden of the traditional model is primarily linked to physical trial sites, on-site staff and on-site monitoring, whereas the digital approach emphasises technological, data management and organisational expenses, partly replacing them with new technological costs (Weber, 2021). These differences do not signify the elimination of cost elements, but rather their reallocation, which determines the design and operational logic of clinical trials.



10 Differences in cost structures between traditional and digital clinical trial designs

Source: own compilation

2.9.2 Planning and regulatory costs

In traditional clinical trials, planning is typically based on site-specific protocols, where regulatory and ethical approvals are geographically fragmented. In DCTs, by contrast, protocol design is supplemented by elements of data protection, digital process documentation and technological compliance (e.g. eConsent, remote data collection, audit trail).

Consequently, the focus of planning costs shifts from physical infrastructure towards digital compliance and documentation, whilst the number and complexity of approval processes exhibit varying patterns.

2.9.3 Costs associated with trial sites

In the cost structure of traditional clinical trials, site initiation, training, contract signing and the ongoing operation of sites constitute the dominant items. The involvement of multiple sites increases administrative burdens and coordination costs.

In DCTs, the number of physical sites typically decreases, or is supplemented by partially virtual or hybrid operations. As a result, fixed costs associated with physical infrastructure are reduced, whilst new types of platform implementation and service costs emerge.

Site activation and staffing costs play a key role in the cost structure of traditional clinical trials. Typical items include site-specific start-up fees, which cover administrative processes, training and documentation, as well as the remuneration of the PI and clinical research coordinators. In the case of multi-site trials, the ongoing maintenance of each site further increases the budget.

Based on institutional and industry reviews, site start-up costs - including feasibility studies, contract negotiation, ethical approval, training and the conduct of the site initiation visit (SIV) - can vary widely, ranging from a few thousand dollars to as much as USD 25,000 per site (IntuitionLabs, n.d.). Due to the recurring nature of these costs, together with staffing costs, they account for a significant proportion of the total budget.

In the case of digital and decentralised trials, site activation fees and the need for on-site staff can be partially replaced by the use of telemedicine, remote monitoring and remote SDV (source data verification). At the same time, new cost elements emerge, such as helpdesk services related to digital operations, patient support systems and device logistics, which replace part of the traditional staffing costs.

2.9.4 Monitoring and quality control

In traditional clinical trials, monitoring is typically based on on-site visits, including significant travel costs, flights, accommodation and daily subsistence allowances. Several empirical studies confirm that the use of hybrid monitoring models (combining on-site and remote elements) can result in cost reductions of up to 46.2% compared to exclusively on-site monitoring (Fu et al., 2023). These models also increase the number of patients that can be monitored during a single visit by one-third and reduce the time required for monitoring by 13.8%, whilst maintaining the quality of monitoring. Access to real-time data allows safety and data quality signals to be detected earlier (Daly et al., 2024; Fu et al., 2023).

Digital and hybrid monitoring models, by contrast, are based on remote data verification and risk-based approaches. This shift results in a structural transformation of monitoring costs: the need for on-site presence decreases, whilst the role of data-driven, centralised verification processes increases. This results in a structural shift in quality control costs: expenditure on on-site presence decreases, whilst the role of data-driven control processes and centralised monitoring increases (Hummel et al., 2019) .

2.9.5 Costs associated with patient recruitment and retention

Patient recruitment is one of the most critical and cost-intensive processes in clinical trials, the success of which has a direct impact on the timeline of the trial. Based on empirical data, the average cost of online recruitment is approximately USD 72 per patient, whilst for traditional offline methods this figure is around USD 199, representing a difference of nearly threefold. Traditional approaches using print advertisements are even more expensive, with some estimates putting the cost at USD 1,100-1,500 per active patient (IntuitionLabs, n.d.). In contrast, in 80% of trials, it is not possible to meet the patient recruitment target and maintain the planned schedule, which has led to the opening of new sites and, in any case, to the extension of the trial. These necessary interventions can result in a daily revenue loss of up to \$8 million for pharmaceutical companies (Brøgger-Mikkelsen et al., 2020). According to a global survey by Sinha and colleagues (2024), the average enrolment rate for phase III and phase IV trials was below 40%.

Digital channels typically enable higher daily recruitment activity, but with a lower screen-to-enrol conversion rate. In contrast, traditional methods use fewer channels but often achieve a higher final enrolment rate. One key advantage of decentralised clinical trials, however, is

improved patient retention: participation from home, a flexible visit structure and telemedicine solutions reduce the burden on patients, resulting in lower dropout rates and thus cost-saving effects in the long term (Moseson et al., 2020).

In DCTs, online channels provide wider geographical reach, yet operate with different conversion dynamics to traditional, on-site recruitment. The difference in cost structure in this case is not reflected solely in unit costs, but also in the fact that a larger proportion of recruitment expenditure is concentrated on digital campaigns, data-driven selection and solutions that support the patient experience.

In this case, the difference in cost structure does not signify the elimination of the element, but rather a shift in the direction of cost allocation: alongside traditional site-based screening, digital campaigns and solutions supporting the patient experience are coming to the fore.

2.9.6 Data collection, data management and technological infrastructure

Data management in traditional clinical trials is often based on a combination of electronic and manual processes, which requires significant expenditure on data verification and data cleansing. In contrast, DCTs utilise integrated data collection solutions, including EDC, electronic clinical outcome assessments (eCOA), eDiary and sensor-based systems.

Electronic data capture systems represent a significant cost factor in both trial models, the extent of which depends on the system's functionality and complexity: according to industry estimates, the monthly fee for EDC licences typically ranges from USD 1,000 to USD 5,000, supplemented by initial implementation costs of around USD 5,000 to USD 12,000, as well as additional data management expenses such as specification, form design, data cleaning and analytical services (Ledesma, 2024). The complex design of eCRFs, the large number of trial sites, the integration of ePRO systems and validation requirements collectively drive up costs further.

In digital trials, real-time data collection and automated data validation reduce data cleaning time (IQVIA, 2022b), whilst reduced manual query handling enables relative cost savings and faster decision support (Laurent, 2026).

Although the structural transformation of costs requires higher expenditure on technology and IT security, it simultaneously reduces the human resource requirements associated with manual data processing, improves the efficiency of decision support and shortens the development

cycle (Shah et al., 2010), resulting in a shift in the cost structure towards technological investments.

2.9.7 Costs of sensors, wearable devices and digital solutions

However, DCTs do not introduce cost-reducing elements exclusively. The development, validation and regulatory approval of sensors, wearable devices, mobile applications and other digital solutions generate significant new entry costs. In the short term, these costs may increase the overall cost of trials, particularly in the case of DCTs involving innovative medical devices. According to industry analyses, development and regulatory costs can reach millions or even tens of millions of USD, depending on the risk class (Millstone Medical, 2025). Although these entry costs are high, the devices can be economically viable through long-term, reusable and scalable use (De Sario Velasquez et al., 2024). At the same time, one must account for depreciation, the repair or replacement of devices, and the logistical challenges of delivering and collecting them from patients' homes, all of which influence the sustainability of the digital model.

Overall, it can be concluded that DCTs are not merely a 'cheaper' alternative to the traditional model, but represent a different cost logic: some of the recurring costs associated with physical infrastructure and human resources are replaced by technological investments, which are initially higher but scalable in the long term. This shift in cost structure fundamentally influences the planning of clinical development, particularly in the case of trials involving large sample sizes, geographically dispersed sites, or those requiring long-term follow-up.

2.9.8 Project management and overhead

In traditional trials, the focus of project management is on the coordination of a large number of sites and the associated administrative processes. In DCTs, the involvement of more technology and service providers becomes necessary alongside fewer physical sites, creating a different overhead structure.

This difference does not necessarily mean lower overall costs, but reflects a shift in project management tasks and resource requirements.

2.9.9 Structural summary

Overall, the difference in cost structure between traditional and DCTs is primarily not captured in the number of cost elements, but in their distribution and weighting. In the traditional model, costs related to physical infrastructure, on-site presence and travel dominate, whereas the digital approach emphasises expenditure on technology, data management and governance.

Cost category	Traditional analysis (base = 100%)	Estimated DCT level compared to the baseline	Comment
Site start-up (initiation, SIV, training)	100%	50-70%	Fewer physical sites, more ‘virtual’ operations. ¹
Site operating fees / investigator fee	100%	60-80%	Fewer on-site visits, partly shifted to remote services. ¹
On-site monitoring (CRA travel)	100%	30-50%	Remote/risk-based monitoring, fewer trips.
Patient travel and travel expense reimbursement	100%	20-40%	Significantly fewer face-to-face visits. ¹
On-site administration, paper-based processes	100%	40-60%	More digital processes, less manual data entry on-site.
Sampling on-site	100%	50-80%	Partially home-based / local laboratory sampling.
Digital platform, DHTs, IT security	0-30%	120-200%	New / higher cost bracket (platform, wearables, cybersecurity). ²

¹ (Weber, 2021)

² (Laurent, 2026)

5 The shift in cost allocation for DCTs

Source: own compilation

This table conceptually illustrates which items in the cost structure of a traditional trial decrease significantly in a DCT (Weber, 2021). The relative decrease and increase in individual cost

items provide the basis for interpreting the financial return on DCTs as a separate analytical dimension.

2.10 ROI of DCTs

The financial return on DCTs is not derived directly from the elimination of individual cost items, but - as illustrated in Figure 10 in Chapter 2.9 - from the restructuring of costs and their temporal effects. ROI analysis should therefore be interpreted not as an isolated cost-reduction exercise, but as the result of complex financial and operational effects.

2.10.1 Comparison of cost and time dimensions

Table 5 summarises the key financial and temporal differences between traditional and digital clinical trials. The table highlights that whilst in the traditional model a significant proportion of operational costs is linked to physical trial sites, travel and on-site staff, in the digital approach the weight of these items is reduced, whilst the proportion of technology and platform-related investments increases.

In the case of DCTs, the literature typically identifies a potential reduction in total operating costs of between 10-25%, primarily resulting from fewer physical trial sites, lower travel expenses and more efficient monitoring models (DiMasi et al., 2023; Nair, 2019). However, it is important to emphasise that these savings do not occur evenly throughout the trial's entire life-cycle, as DCTs typically involve higher initial technological investment.

2.10.2 The financial significance of the time factor

The time dimension is a key element of ROI-based analyses. The operational model of DCTs - particularly through online recruitment, faster study start-up and real-time data collection - can shorten certain phases of the clinical development cycle. According to the findings of Fu et al. (2023), a development time saving of 1-3 months can be achieved in Phase II trials, whilst a similar order of magnitude of acceleration is observed in Phase III. The reduction in clinical development time represents significant economic value indirectly, particularly through bringing forward the time to market (IQVIA, 2022a).

The reduction in clinical development time is of particular significance in late-phase trials, where time savings can result in significant revenue benefits through earlier market entry. In

ROI analyses, this effect is often given greater weight than the direct reduction in individual cost items.

2.10.3 Empirical ROI results and model-based estimates

Most studies examining the financial ROI of DCTs trials are based on model-based analyses that estimate ROI using industry data (particularly from the Tufts CSDD and Medable databases). These analyses suggest that the use of DCT components can result in an average five-fold ROI in Phase II and up to a fourteen-fold ROI in Phase III, primarily through time savings, lower screen failure rates and fewer protocol amendments (DiMasi et al., 2023).

It is important to note, however, that in terms of total trial costs, direct savings are typically more modest. According to phase-specific analyses, DCT solutions on their own result in a direct cost reduction of between 2.58% and 3.61%, whilst certain operational components - such as hybrid monitoring models - can reduce monitoring costs by up to 46.2% compared to models based solely on on-site presence (Fu et al., 2023).

2.10.4 Methodological limitations and interpretative considerations

When interpreting ROI results, it is particularly important to take methodological limitations into account. The costs of clinical trials are highly dependent on the institution, country, phase and indication, and industry reports typically rely on heterogeneous data sources and estimates. The number of empirical studies examining the financial return on DCTs is currently limited, and most of them employ a retrospective or model-based approach.

Although an exemplary small-scale empirical programme (Zhang et al., 2025) and an analysis focusing on specific trial designs - such as platform trials (Park et al., 2022) - also support the potential for a favourable ROI, further large-scale, prospective, independent trials are needed to confirm the generalisability of the results.

2.10.5 Strategic significance

Based on the available evidence, the use of DCTs is primarily justified in settings where cost-effectiveness and operational flexibility are realised in the long term. This applies in particular to multi-centre trials with large sample sizes, where the accumulation of traditional infrastructure and site activation costs offers significant potential for savings. Similarly, the DCT approach is particularly advantageous in Phase II and III trials, where the ROI is highest,

as well as in longer-term programmes where technological investments and equipment developments can be amortised.

In contrast, the traditional clinical trial model continues to play a dominant role in early-phase trials and for populations where intensive in-person monitoring or low technological readiness limits the extent of digitalisation (Rosa et al., 2021). The financial return on DCTs is therefore not universal, but depends on the indication, phase and context, which requires a conscious strategic decision during the planning of clinical developments.

2.10.6 Further - often underestimated - considerations and cost implications

When comparing the cost structures of traditional and digital clinical trials, a number of factors can be identified that are often underestimated during initial cost planning, yet have a significant impact on total life-cycle costs and operational feasibility. These considerations typically do not fall into a single cost category, but rather cut across regulatory compliance, technological infrastructure, human resources and patient experience.

Ensuring regulatory and data protection compliance is of paramount importance in digital assessments. Due to the increased digital flow of personal and sensitive health data, solutions such as electronic consent, audit trails and logging mechanisms, role- and permission-based access management, and cyber security measures based on encryption and access control are becoming indispensable. The implementation and ongoing maintenance of these measures - including regular penetration testing and security audits - place a more significant and sustained cost burden on sponsors and service providers in the case of DCTs than in traditional, site-centric models.

Another frequently underestimated cost factor is the issue of interoperability and standardisation. A prerequisite for the effective operation of decentralised data collection is integration with EHR/EMR systems, the establishment of Health Level Seven/Fast Healthcare Interoperability Resources (HL7/FHIR) compatibility (Gomez, 2023), and the development and maintenance of data standards at the device and protocol levels. While these solutions initially incur significant implementation costs, in the longer term they reduce the complexity of data management, minimise the need for manual data conversion and cleansing, and facilitate scalability, particularly in the case of digital portfolios spanning multiple examinations.

Testing logistics and home-based services represent a further specific cost dimension of decentralised models. Direct home delivery of test kits, temperature and supply chain

monitoring, home or mobile sampling, patient training, and the collection of devices all appear as separate cost items. Although these expenses increase operating costs, they also help to reduce the burden on patients and improve retention, which may indirectly offset the initial expenditure.

The successful roll-out of decentralised testing is closely linked to the effectiveness of training and change management. The digital training of site staff and patients, the adoption of new workflows, and the maintenance of continuously available helpdesk and support channels are not merely operational issues, but are also critical in terms of protocol compliance, data quality and trial scheduling. Neglecting these elements may suggest cost savings in the short term, but in the longer term it can lead to significant losses in efficiency and hidden additional costs.

Device validation and maintenance require ongoing expenditure. Regular calibration of wearable devices, software updates and version management, as well as testing for compatibility with various operating systems and device types, are essential to ensure measurement accuracy and data consistency. These activities generate recurring costs throughout the entire duration of the study, which often only become apparent during the implementation phase.

Addressing equal access and the digital divide is not only an ethical and social issue, but also entails direct costs. The provision of equipment, data packages or internet support, ensuring adequate network coverage, and making the language and user interface accessible are all factors without which decentralised trials may skew the composition of the enrolled population. At the same time, incorporating these solutions increases cost sensitivity, particularly in the case of large and heterogeneous patient populations.

decentralised operations also alter insurance and liability structures. Liability issues related to remote interventions, home sampling and device use may necessitate different insurance terms and premium structures, which do not always align with the frameworks used in traditional clinical trials.

Last but not least, the choice of endpoints and methodology also has a significant cost impact. The design, validation and regulatory approval of digital endpoints - particularly measurements based on passive and active sensor data - influence development timelines and the costs of the authorisation process. The advantage of these endpoints is objective, high-resolution data collection; however, from a methodological and regulatory perspective, they may require a higher initial investment.

2.11 Conclusion of the literature review

In parallel with post-COVID-19 industry adaptation, several corporate and academic analyses suggest that the use of DCT elements accelerates recruitment and shortens cycle times, improving financial value and patient-centredness (Daly et al., 2024; Sinha et al., 2024).

The use of digital elements in clinical trials is reshaping the cost structure: it reduces on-site and travel expenses, enhances investments in technology, data protection and interoperability, and accelerates recruitment, monitoring and data flow. The net economic benefit - particularly in Phase II-III, multi-site and long-term trials - is increasingly supported by evidence; however, costs related to equipment and cybersecurity, as well as ensuring equitable access, require conscious planning and change management (Sinha et al., 2024) .

The cost structure of clinical trials is undergoing a significant transformation with the proliferation of digital elements. Our findings indicate that DCTs directly reduce on-site and travel costs, improve the efficiency of recruitment and retention, and achieve substantial cost savings through remote and hybrid monitoring models, whilst new cost items (related to technology, cybersecurity and interoperability) emerge. Several analyses demonstrate significant financial added value in Phase II-III trials when DCT elements are systematically applied.

Overall, it can be concluded that the cost structure of DCTs does not merely represent a reallocation of traditional cost items, but reflects a fundamentally different, system-level operational logic. The apparent cost savings - particularly in the areas of on-site infrastructure, travel and on-site monitoring - can only be interpreted as sustainable benefits if we take into account the often underestimated but structurally decisive costs associated with regulatory compliance, interoperable data management, in-house logistics, and the ongoing operation of the digital ecosystem.

One of the most important lessons of the digital approach is that the timing of costs changes: initial investment and implementation costs - particularly on the technological, data protection and methodological fronts - may be higher, whilst in the longer term the burdens arising from manual processes, data inconsistencies and patient attrition are reduced. Consequently, the economic evaluation of DCTs cannot be based solely on short-term cost comparisons, but necessarily requires a life-cycle approach that also takes into account repeatability, scalability and the effects of organisational learning.

It should also be emphasised that DCTs are not universal alternatives to traditional models, but strategic tools capable of creating genuine added value when applied to the appropriate indication, patient population and trial phase. The key to the successful application of DCTs lies not in the isolated introduction of technological elements, but in their integrated, regulated and patient-centred application. In the absence of this, DCTs can easily become new cost centres rather than drivers of efficiency and evidence generation.

Consequently, the future competitiveness of DCTs depends crucially on the extent to which sponsors and research organisers are able to consciously assess and manage the often hidden cost implications, and to implement cost optimisation in a manner consistent with the scientific quality, ethical soundness and social inclusivity.

On the other hand, a review of the existing literature indicates a lack of consistent estimates regarding the economic and operational value of DCTs. The observed discrepancies in these estimates can be categorised into three interrelated areas.

Firstly, there is considerable variation among studies in their assessment of economic benefits. Model-based analyses and industry benchmarks often report significant ROI and notable time-related value. However, empirical evidence and phase-specific data suggest that actual cost reductions may be much more modest and are heavily influenced by the underlying trial design.

Secondly, the operational advantages of DCTs are not uniformly observed across all studies, particularly in terms of recruitment, retention, monitoring efficiency, and cycle time reduction. These variations can be attributed to several factors, including the phase of the clinical trial, the therapeutic indication, the sample size, the extent of geographic dispersion, the technology configuration, and the percentage of trial activities that can realistically be decentralised.

Thirdly, the robustness and transferability of the evidence vary according to the institutional and implementation context. Evidence generated by vendors, financial simulations, and retrospective benchmark analyses may illustrate potential value under favorable implementation assumptions. However, they do not necessarily account for the costs associated with technology onboarding, validation, organisational change, legacy-system integration, training, cybersecurity, and site-level adaptation that arise under typical conditions.

In contrast, empirical studies provide greater contextual realism; however, they are limited in number and often confined to specific trial configurations or organisational environments. Consequently, the most substantiated conclusion drawn from the existing literature is not that

DCTs universally reduce costs or guarantee a specific level of ROI. Instead, it emphasises that the economic and operational impacts of DCTs are contingent upon changes in recruitment, monitoring, communication, and data collection.

3. RESEARCH METHODOLOGY

3.1 Research questions, areas of investigation

Bringing a new drug to market is among the most capital-intensive and strategically risky activities in the modern economy. Estimates of the capitalised costs of pharmaceutical development range from USD 879 million to USD 4.46 billion per approved molecule (DiMasi et al., 2016; Sertkaya et al., 2024). Against a backdrop of rising research and development expenditure and increasing pressure on innovation productivity, DCTs have emerged as a potentially transformative model for clinical research. By integrating digital technologies into trial operations, DCTs may improve efficiency, shorten development timelines, and support more effective resource allocation (de Jong et al., 2024; Harmon et al., 2023). Nevertheless, considerable uncertainty remains regarding the economic value, implementation costs, and long-term ROI associated with DCT adoption.

Despite growing interest in DCTs, their economic implications remain insufficiently understood. The available evidence base is characterised by a limited number of peer-reviewed empirical studies reporting real-world cost data. Much of the literature relies on simulation models, financial projections, and industry-generated benchmarks rather than prospective economic evaluations. As a result, there remains considerable uncertainty regarding the extent to which reported efficiencies translate into realised economic benefits in routine clinical trial settings.

This challenge is compounded by the absence of standardised terminology. Related concepts, including decentralised, virtual, siteless, hybrid, and digitally enabled clinical trials, are frequently used interchangeably despite important operational differences (Santa-Ana-Tellez et al., 2023). The resulting conceptual fragmentation complicates evidence synthesis and limits comparability across studies.

The fragmented nature of the literature presents additional methodological challenges for evidence synthesis. Conventional database searches may fail to identify relevant studies scattered across multiple disciplines and publication types. To address this limitation, the present study combines a systematic literature review with citation-network mapping using Litmaps. This approach facilitates the identification of influential publications, thematic

connections, and potentially overlooked sources, thereby providing a broader perspective on the economic evidence surrounding DCTs.

Accordingly, this study seeks to address three central research questions. Firstly, the study examines how implementing DCT components transforms the traditional cost structure of clinical trials, particularly with regard to CAPEX and OPEX allocation. Secondly, the study will investigate the extent and quality of the empirical and model-based quantitative evidence concerning DCT operational efficiencies, including patient recruitment costs, monitoring expenditure and trial cycle time reductions. It will also critically assess the methodological limitations associated with these findings. Thirdly, it explores how the fragmented body of economic evidence can be integrated into a coherent conceptual framework capable of supporting strategic decision-making in biopharmaceutical portfolio management.

The aim of the study is to explore the ecosystem of domestic DCTs from the perspective of the stakeholder groups (medicines regulatory authority, sponsors, CROs, service providers, PIs, patient organisations and participants). The questions in the questionnaire were compiled based on the results of CISCRP studies, relevant literature on health technologies used in DCTs and cost-reduction mechanisms, as well as topics identified through my experience as a clinical trial project manager. The main dimensions also cover aspects influencing the management of clinical trials and, in addition to examining the regulatory framework and the burdens on patients and institutions, place emphasis on exploring data protection and economic dimensions. The exploratory approach and pragmatic perspective adopted in the research aim to maximise evidence for decision-making alongside high-quality practical relevance (Creswell & Poth, 2018; Patton, 2015).

By combining qualitative and quantitative data collection, the research focused on the following questions:

- 1.) Which DHT solutions are typically used in domestic practice?
- 2.) What are the benefits and challenges perceived by stakeholders during the implementation and operation of DHT?
- 3.) What organisational, regulatory and data protection factors influence the adoption and scalability of DHT in clinical trials?

- 4.) What cost-saving mechanisms can be identified in DCTs according to the perceptions of stakeholders, and how do these mechanisms affect the cost structure of DCTs?

The methodological framework of this doctoral research integrates several empirical approaches. I supplemented qualitative expert interviews with quantitative data collection in accordance with mixed-methods methodology. Due to these methodological characteristics, the application of statistical hypothesis testing in the classical sense is not applicable; therefore, from a methodological perspective, it must be distinguished from research hypotheses in the scientific sense.

In examining the methodological requirements for exploratory research in emerging technological domains (Pörzse et al., 2021), it is important to distinguish clearly between formal statistical hypothesis testing and exploratory research questions. Given the structural characteristics of the domestic pharmaceutical research sample - where the quantitative component (N = 11) is intended to standardise and triangulate the qualitative expert findings (N = 13) - the analytical framework does not seek to generalise statistically across the entire industry. As a result, the foundational principles of this study are framed as Exploratory Research Questions (RQ1-RQ6) rather than as formal deductive hypotheses. The quantitative metrics (means, medians, and standard deviations based on Likert scales) are utilised solely for descriptive statistics and pattern recognition to support qualitative findings, thereby avoiding over-generalisation while ensuring methodological rigour (Creswell & Plano Clark, 2018; Pörzse et al., 2021).

3.2 Research methodological framework and sample characteristics

The research is based on qualitative-interpretivist principles, supplemented by a quantitative component. Semi-structured expert interviews allow the discussion to proceed along predefined themes, whilst also providing flexible scope for the emergence of new perspectives (Brinkmann & Kvale, 2018; Kvale, 1996). The content validity of the entire questionnaire was reviewed by an independent expert - a doctor who had previously worked as a clinical trial project manager, was employed by a sponsor, and later took up a position with a service provider. Based on the suggestions, I refined the wording of the items and the scaling, after which the questionnaire was tested. During this process, with the involvement of a relevant expert - who was therefore

excluded from the interviews - I examined the clarity of the questions, the response time and any potential redundancies. An iterative approach characterised the development of the questionnaire throughout, as I sought feedback from each subsequent interviewee regarding improvements to the questionnaire's structure, the topics covered, and the overall interview process.

3.2.1 Systematic literature review

To ensure transparency and reproducibility, explicit eligibility criteria were established prior to the screening process. In order to be considered for inclusion, studies had to comprise peer-reviewed empirical research, financial simulation models, or industry benchmark reports examining DCTs or related DHTs, and, if applicable, report quantitative, empirical, or model-based economic metrics. Publications written in English or Hungarian were deemed to be eligible for consideration. The exclusion criteria applied to the studies included the following: the absence of quantitative or model-based economic evidence; an exclusive focus on clinical efficacy, pharmacological outcomes, or technical performance without assessing economic implications; or the presence of duplicate records. Secondary publications, narrative commentaries, and opinion papers that reproduced previously published findings without contributing original data or novel analytical approaches were also excluded from the study.

To mitigate the risk of relevant evidence being overlooked, the initial search strategy was intentionally broad, with no restrictions applied to therapeutic area, clinical trial phase, sponsor type, or geographical setting. This approach reflected the exploratory nature of the review and acknowledged the multidisciplinary nature of DCT research. After the identification stage, a structured, multi-stage screening process was conducted. This comprised a review of titles and abstracts, followed by a full-text assessment, and was facilitated by Rayyan software. The predefined eligibility criteria were applied systematically throughout the process to ensure consistency in study selection. The identification of publications providing original empirical evidence, model-based estimates, or quantitative assessments of the economic impact of DCT implementation was of particular importance. In the final synthesis, studies that described clinical, technological, or operational aspects without evaluating economic outcomes were excluded. Similarly, publications that merely reiterated previously reported benchmark figures without presenting new empirical evidence, analytical insights, or modelling frameworks were not retained.

3.2.2 Expert interviews

In the primary research, semi-structured expert interviews were employed to explore and deepen understanding of the experiences, perceptions, and contextual factors of stakeholders involved in domestic clinical trials (Creswell & Poth, 2018; Kvale, 1996). The semi-structured format enabled the discussion to proceed along predefined topics while allowing novel perspectives to emerge during the interviews (Patton, 2015). In light of the heterogeneity in participants' professional backgrounds, a set of core questions was devised to ensure uniformity of the interview framework while allowing for the introduction of supplementary questions based on participants' individual experiences (see Appendix 5 for details).

The qualitative component's sampling frame comprised identifiable stakeholder groups within the Hungarian clinical trial ecosystem that were directly relevant to the implementation, management, or regulation of digital clinical trial solutions. These included pharmaceutical sponsors, CROs, clinical investigators, and other healthcare professionals involved in clinical trials, patient organisations and patients, and regulatory stakeholders. In the absence of a comprehensive public register of individuals with direct experience of DCTs, the sampling frame was developed through professional networks, relevant Hungarian organisations, stakeholder associations, and targeted outreach. In instances where participant groups were particularly difficult to access, such as patients and specialised experts, snowball sampling was employed to broaden the reach of eligible participants (Noy, 2008).

The selection of participants was purposive rather than probability-based. The primary criterion for determining eligibility was professional relevance and direct or experience-based exposure to clinical research and/or DCT practices within the Hungarian context. The sampling strategy was designed to achieve stakeholder diversity and information richness, rather than statistical representativeness (Palinkas et al., 2015).

The determination of the sample size was informed by the extant methodological literature concerning qualitative research and thematic saturation. The point at which saturation was reached was identified by recurring patterns across the main thematic categories. Subsequent interviews primarily served to confirm existing codes and thematic dimensions, rather than introducing new ones (Guest et al., 2006; Saunders et al., 2018). Thematic saturation was achieved after conducting 13 interview sessions.

A total of 13 invitations to participate in interviews were accepted. In one instance, two representatives from the same patient organisation participated jointly in a single interview. Consequently, the qualitative component comprised 13 interview sessions involving 14 individual participants. In this instance, the two representatives collectively presented the organisation's viewpoint.

During the sampling process, particular attention was paid to the representation of clinical trial sponsors, as these stakeholders were expected to provide insights into trial design and the payer perspective. The pharmaceutical company representatives included in the sample had significant experience in both traditional and DCT environments. A representative of a smaller, Hungarian-owned CRO specialising in DCTs was also included in the study. In addition, endeavors were undertaken to recruit CRAs and service providers engaged by prominent international corporations. Nevertheless, these interviews failed to materialise, primarily due to capacity constraints on the part of the parties approached.

To incorporate the patient perspective, the author contacted the Hungarian Federation of Patient organisations (BEMOSZ) and the National Association of People Living with Rare and Congenital Disorders (RIROSZ) and asked them to forward the request to individuals registered in their systems. Following the questionnaire administration, one patient was willing to participate in an interview. Furthermore, the president of RIROSZ and a volunteer participated in their capacity as representatives of the patient organisation. Furthermore, an additional strand of research involved in-depth interviews with physicians who had previously participated in DCTs. The sample was further complemented by a data-driven healthcare expert and a futurist doctor, one of whom contributed through an interview, while the other contributed by sharing professional publications.

In addition, regulatory stakeholders were approached. However, the relevant staff member at the National Centre for Public Health and Pharmacy (NNGYK) was unable to participate in an interview or provide written information. This is indicative of a limitation in the composition of the stakeholder group, which is considered when interpreting the findings.

The interviews were conducted in a semi-structured format and lasted between 60 and 90 minutes. The interviews were conducted via the Microsoft Teams platform. Prior to each interview, all participants were apprised of the purpose and procedure of the interviews. Verbal consent was obtained from all participants at the start of each interview, authorising the

recording of the conversation and the use of the recordings for research purposes. The interviews were transcribed using Alrite speech recognition software (version 2.35.1), and subsequent processing was conducted with MAXQDA Analytics Pro (version 26.2.1). A comprehensive overview of the interview participants is provided in Appendix 4.

3.2.3 Quantitative questionnaire

The quantitative element of the research was based on a self-developed questionnaire designed to capture stakeholder attitudes and perceptions throughout the clinical trial life cycle. The rationale for developing the questionnaire was that, during the literature review, no existing instrument was found that fully addressed the research objectives and the specific domestic context. International sources, including the CISCRP studies, provided relevant background evidence and informed the development of the questionnaire; however, they were not used as direct measurement instruments in the primary research.

The questionnaire comprised structured statements covering the main stages and dimensions of the clinical trial process and used a four-point Likert scale (Joshi et al., 2015; Likert, 1932). The objective of the study was not to provide a statistically representative measurement of the Hungarian pharmaceutical ecosystem, but rather to provide a standardised descriptive assessment of stakeholder perceptions. This was intended to complement the qualitative findings within the mixed-methods framework. The qualitative and quantitative components were collected concurrently and integrated during the interpretation of the findings (Creswell & Plano Clark, 2018; Johnson et al., 2007).

The administration of the questionnaire occurred concomitantly with the conduction of the qualitative interviews. A total of 13 interview invitations were accepted. In one case, two representatives of the same patient organisation participated jointly in a single interview and submitted a single questionnaire response on behalf of the organisation. Consequently, 13 questionnaire response units were approached, and 11 completed questionnaires were returned, yielding a response rate of 84.6% (11/13). The response rate is reported at the level of the questionnaire response unit rather than at the individual participant level because the questionnaire was designed to capture the stakeholder or organisational perspective represented in the interviews.

In light of the purposive, non-probability sampling strategy and the modest quantitative sample size ($N = 11$), the response rate should not be construed as evidence of population-level representativeness. The quantitative component was explicitly intended to serve as an exploratory and descriptive element of the mixed-methods design. The utilisation of the questionnaire findings was thus primarily to provide structured numerical data to bolster the interpretation and triangulation of the qualitative findings, rather than to conduct inferential statistical testing or establish population-level relationships. The 19 impact areas were treated as separate indicators of stakeholder perceptions rather than as items forming composite psychometric scales. Consequently, no aggregate scale scores were constructed and no internal consistency coefficient was calculated for the questionnaire.

The development of the questionnaire was a self-initiated process, and, as such, particular attention was paid to the instrument's quality throughout its development. The items constituting the questionnaire were derived from the research questions and the thematic domains identified in the literature review. The questionnaire was reviewed by an independent expert with professional experience in clinical trial management, with particular regard to the items' relevance, clarity, and wording. Following the expert review, several items and the response scale were refined. A subsequent pilot test was conducted with an expert who was not included in the interview sample. The pilot assessment concentrated on the clarity and comprehensibility of the questions, the interpretation of the response options, completion time, and the identification of redundant or ambiguous items.

The questionnaire was designed as an exploratory instrument for the structured description of stakeholder perceptions, rather than as a psychometrically validated measurement scale. Consequently, formal statistical construct validation and internal consistency analysis were not conducted. With a sample size of only 11 respondents, the quantitative component was not designed to support population-level inference or formal statistical hypothesis testing. The questionnaire findings were analysed descriptively, using means, medians, and standard deviations. These findings were then interpreted in conjunction with the qualitative evidence. The study's methodological limitations are recognised to be the limited sample size and the exploratory nature of the questionnaire.

The questionnaire encompassed five primary thematic domains:

- 1) the characteristics of the technology portfolio and data management, as well as factors promoting and hindering implementation
- 2) health economics dimensions, with particular regard to efficiency gains and cost factors
- 3) aspects of risk and quality management, including data protection, regulatory factors and the burden on participants
- 4) social implications, challenges arising from digitalisation, patient experience, patient-centredness and accessibility
- 5) overarching perceptions, such as scalability, future trends and market outlook.

4. EMPIRICAL RESEARCH FINDINGS

4.1 Research questions identified based on a literature review

During the literature review, I formulated the following research questions. I substantiated the validity of the questions at the heart of the study not only through relevant literature references but also through the primary research framework. To confirm these research questions, I found only a small number of widely cited references in the international context prior to the start of my research, and no evidence at all relating to Hungary. The formulated questions - through the interviewees - are primarily applicable to stakeholders in the Hungarian pharmaceutical industry.

My main research questions (RQ1-RQ3) examine the most frequently described phenomena.

RQ1: *Do DCTs involve a shorter trial duration compared to traditional clinical trials?*

RQ2: *Is the cost structure of DCTs generally more favourable than that of the traditional clinical trial model?*

RQ3: *Do the quality, reliability and data integration characteristics of data collected during DCTs differ from those of traditional clinical trials?*

Further research questions (RQ4-RQ6) analysed factors acting as mediators.

RQ4: *Does recruitment efficiency influence the relationship between the trial design and the duration of the trial?*

RQ5: *Does the digitalisation of patient communication influence the relationship between the trial design and the cost structure?*

RQ6: *Does the frequency and method of data collection influence the relationship between the study design and data quality?*

4.2 Systematic literature review

To ensure transparency and reproducibility, explicit eligibility criteria were established prior to the screening process. To be considered for inclusion, studies had to comprise peer-reviewed empirical research, financial simulation models, or industry benchmark reports that examined DCTs or related DHTs. If applicable, the studies also had to report quantitative, empirical, or model-based economic metrics. The relevant outcomes encompassed a range of financial and operational metrics, including ROI, OPEX, CAPEX, cost per patient, recruitment costs, monitoring costs, cycle-time reductions, and other indicators of economic performance. It was determined that publications authored in either English or Hungarian would be considered for review. The exclusion criteria applied to the studies were as follows: the absence of quantitative or model-based economic evidence; an exclusive focus on clinical efficacy, pharmacological outcomes, or technical performance without assessing economic implications; or the presence of duplicate records. Secondary publications, narrative commentaries, and opinion papers that reproduced previously published findings without contributing original data or novel analytical approaches were also excluded from the study.

To mitigate the risk of relevant evidence being overlooked, the initial search strategy was intentionally broad, with no restrictions on therapeutic area, clinical trial phase, sponsor type, or geographical setting. This approach reflected the exploratory nature of the review and acknowledged the multidisciplinary nature of DCT research. After the identification stage, a structured, multi-stage screening process was conducted. The process entailed a preliminary evaluation of titles and abstracts, followed by a comprehensive assessment of the full texts. The Rayyan software facilitated this. The predefined eligibility criteria were applied systematically throughout the process to ensure consistency in study selection. The identification of publications providing original empirical evidence, model-based estimates, or quantitative assessments of the economic impact of DCT implementation was of particular importance. In the final synthesis, studies that described clinical, technological, or operational aspects without evaluating economic outcomes were excluded. Similarly, publications that merely reiterated previously reported benchmark figures without presenting new empirical evidence, analytical insights, or modelling frameworks were not retained.

Database	Hits (n)
Embase	167
Scopus	154
EBSCO	142
PubMed	95
Web of Science	82
Litmaps	71

6 Systematic literature review databases and the following hits

Source: own compilation

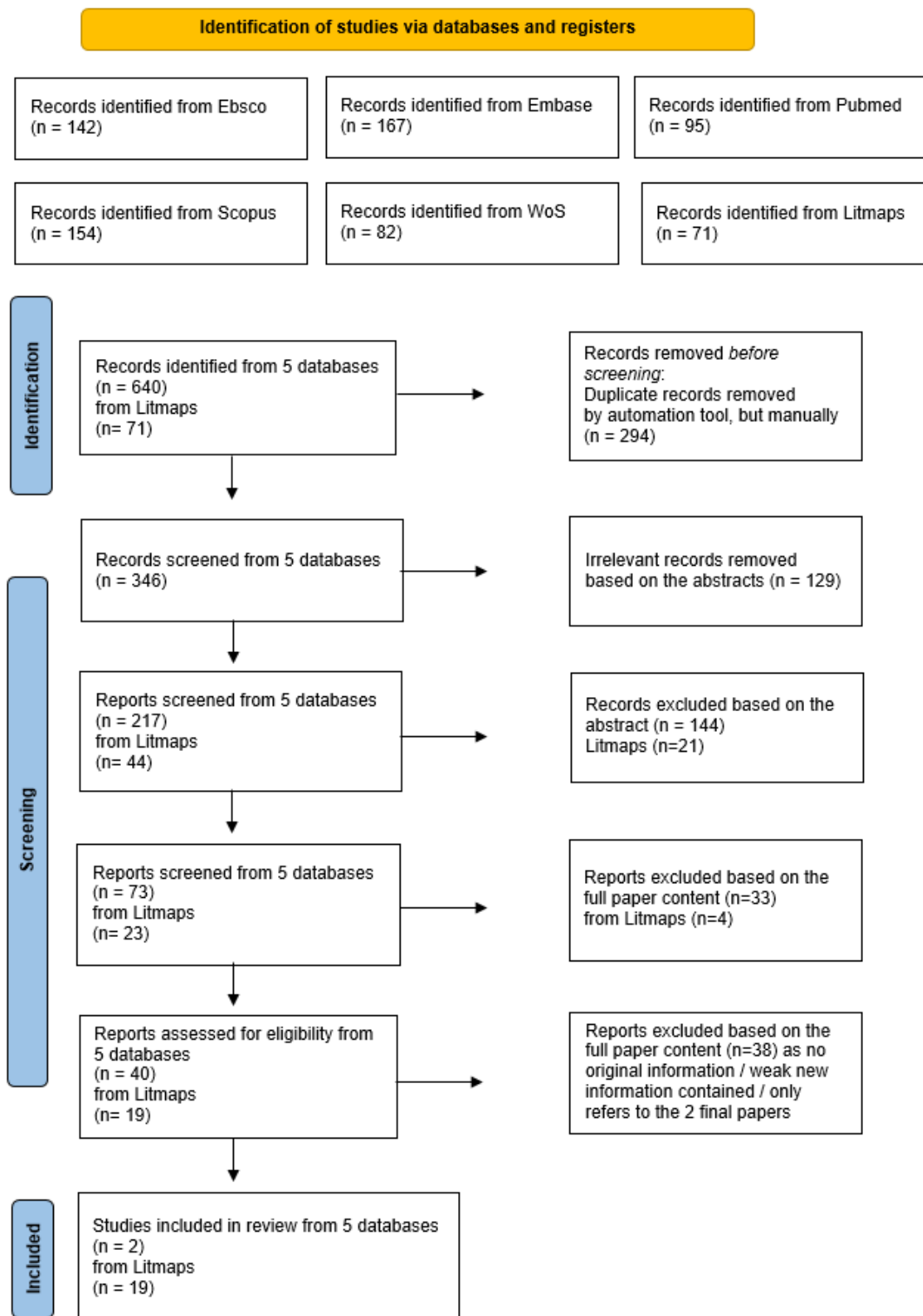
The resulting unique records were then subjected to a staged screening process, with this stage based on titles, abstracts, and author keywords. In this phase, studies that were evidently unrelated to clinical trials, DHTs, or economic evaluation were excluded. A particular focus was placed on identifying publications that addressed the economic performance of DCTs and related DHTs. Records that focused exclusively on technological development, software engineering, clinical efficacy, or pharmacological outcomes and did not assess economic implications were excluded from further consideration.

Publications that met the preliminary screening criteria were then retrieved for full-text assessment. At this stage, the studies were evaluated against predefined eligibility criteria relating to methodological relevance and the presence of economic evidence. It is important to note that particular emphasis was placed on incorporating original empirical evidence, model-based estimates, and quantitative assessments of economic outcomes. Publications were only retained if they reported explicit economic metrics, such as cost savings, ROI, OPEX, CAPEX, monitoring costs, recruitment costs, cycle-time reductions, and other measures relevant to economic evaluation. The exclusion criteria applied to the studies included those that relied exclusively on qualitative efficiency claims without quantitative evidence, those that were narrative reviews or opinion papers that reproduced previously published findings without introducing original data or novel analytical frameworks, and those that fell outside the context of regulated clinical trials. It should be noted that the present study excluded studies that examined general telehealth services without incorporating a clinical research component.

The full-text evaluation also revealed a significant feature of the evidence base. Whilst traditional database searches yielded most studies that met the predefined quantitative eligibility criteria, citation-network mapping identified several highly relevant publications that offered

valuable contextual and methodological insights. After the conclusion of the final eligibility assessment, publications containing redundant secondary information or inadequate economic evidence were excluded from the synthesis. The resulting corpus comprised studies providing empirical and model-based evidence, as well as industry-generated benchmarks, all of which were relevant to the economic evaluation of DCTs. This systematic selection process ensured that the final evidence base remained focused on publications that could inform assessments of economic value, while maintaining methodological transparency and consistency throughout the review.

The PRISMA flowchart below (Page et al., 2021) illustrates the SLR process and the results obtained. Furthermore, the figure provides a comprehensive overview of the findings from Litmaps.



11 Overview of PRISMA flowchart

Source: own compilation

The extensive list of 640 results suggests that the topic is indeed timely. According to the Scimago Journal Ranking, all articles are classified as Q1, with the exception of three (Q2). The earliest result is an article published in 2003 that also emphasises the topic's relevance. Following the analysis, only two studies were identified across the five scientific databases. These two papers contain original, added information, both of which were also researched by DiMasi and colleagues. In many cases, the filtered articles refer to DiMasi's research or mention the cost-effectiveness of DHTs, but do not contain specific data.

However, using Litmaps scientific tool by searching for keywords and mapping the citation network of the most influential literature, an additional 19 relevant publications were identified.

4.3 Expert interviews

The qualitative analysis of the research was justified by the richness of content in the semi-structured expert interviews, as the organisational and technological processes of DCTs are highly context-dependent and can only be understood through a deeper exploration of experiential perspectives. To process the 13 interviews, I applied the methodological framework of thematic analysis, following the steps defined by Braun and Clarke (2006): producing verbatim transcripts, anonymisation, familiarisation with the data, creating primary codes, developing themes, reviewing the coding system, and finalising the structure.

For the analysis, I employed thematic analysis using inductive-deductive hybrid coding (Braun & Clarke, 2006; Miles et al., 2014; Saldana, 2016). The deductive codes formed the backbone of the thematic structure, ensuring that the analysis was comparable and coherent with the international industry discourse. Any phenomenon that went beyond the standardised technological, regulatory or economic categories found in the literature (e.g. EDC/eCRF, ePRO, eConsent, home-visit, AI, ROI) was coded inductively, capturing the specific operational experiences, challenges and insights associated with them. In this way, the deductive framework provided a stable foundation, whilst the inductive layer enabled the integration of new, empirical content.

In addition to the deductive framework, I applied open coding to the interview data in order to uncover those experiences and meanings that stem from practice and do not appear among the standard concepts in the literature. The inductive codes highlighted phenomena such as the

usability limitations of digital solutions (e.g. reminder fatigue or the spam effect), data quality issues (e.g. limitations of telemedicine), cultural and organisational resistance (e.g. refusal of home visits), or risks associated with vendor competence. These were organised into thematically arranged categories through axial coding, which supplemented the deductive framework with contextual depth. In the next step of the process, conceptually related groups of codes coalesced into coherent ‘narratives’, which provided the themes for the qualitative research.

Following the consolidation of the codes, the final three-level coding system (main themes, categories, inductive codes) was established. On this basis, I compiled the codebook, which contained definitions, inclusion and exclusion criteria, and example sentences. The codebook is included in Appendix 6.

Thematic saturation was achieved on the basis of the 13 interviews: subsequent interviews primarily served to confirm and refine existing themes, rather than introducing new main themes. This supported the conclusion that the interview process could be closed, whilst also confirming that the research was working with empirical material of sufficient breadth and depth. As a result of the entire coding process, a stable and complex thematic framework was established, built simultaneously on the literature and international theoretical frameworks of DCTs, as well as on the practical experiences of the interviewees. This dual approach enabled the research to interpret the functioning and economic impacts of digital trials in a nuanced, empirically grounded and theoretically relevant manner.

The coding process thus resulted not merely in a descriptive analysis, but in an interpretative and contextualised analysis suitable for an integrated understanding of the operational, economic, technological and organisational aspects of DCTs.

The methodological quality of the qualitative and quantitative components was addressed through procedures appropriate to their respective research designs. Credibility was supported by triangulation involving multiple stakeholder groups, as well as professional consultations (peer debriefing). Generalisability was supported by a detailed description of the research context, sampling and data collection. Reliability was reinforced by the documentation of a version-controlled code book and analysis memos, whilst confirmability was aided by reflective journaling and the support of interpretations with interview quotations.

I supported the interpretation of the results obtained using visual methods. One such method is the code frequency matrix (Table 7), which shows in which interviews each code occurred and also allowed for a quantitative overview of code density and the thematic coverage of the interviews. The creation of the code relation matrix (Table 8) and the heatmap (Table 9) provided further insight into the relative intensity of the codes, which supported the relationships between themes and the thematic saturation. The matrix displaying the subcategories of the codes is included in Appendix 6.

Code System	1. inte...	2. inte...	3. inte...	4. inte...	5. inte...	6. inte...	7. inte...	8. inte...	9. inte...	10. int...	11. int...	12. int...	13. int...
> Economic & Business Impacts	14	15	10		14	29	7	15	31	30	16	26	28
> Clinical Operations & Trial Management	19	3	9		8	15	9	9	13	1	11	8	7
> Strategy, Innovation & Vision	10	6	10	1	2	2	11	4	5	3	11	15	4
> Stakeholder Impacts & Burden	16	13	6		16	20	11	6	20	15	11	15	12
> Regulatory Environment		5	9	2	7	7	9	3	3	7	24	3	8
> Data Management & Quality	1	2	3		5	6	3	3	7	9	3	13	12
> Patient-Centeredness & Access	2	8	7	2	3	2	4	4	3	4	6	6	11
> Disruptive Digital Technologies	18	19	25	7	31	44	34	31	20	24	49	30	27
> Social & Demographic Challenges		3	6		3	2	12	3	4	6	2	6	4

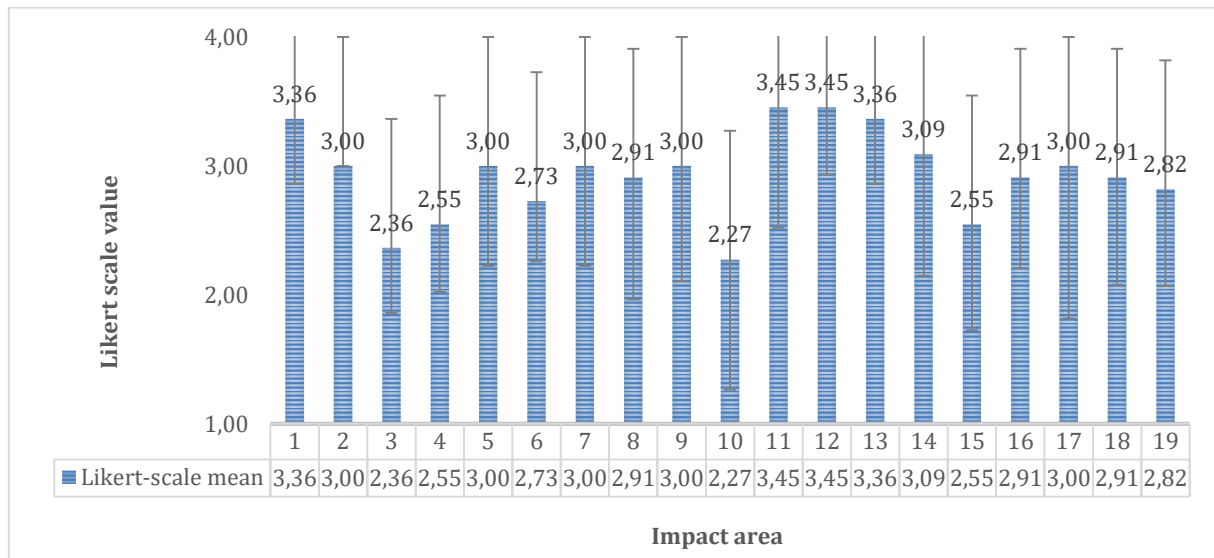
7 The MAXQDA code frequency matrix of the main themes

4.4 Quantitative questionnaire for various stakeholders in the domestic pharmaceutical industry

The quantitative component of the research consisted of a questionnaire in tabular format completed by the interviewees (Appendix 5; Expert interview, Question 22). Of the 13 interviewees, 11 returned the completed questionnaire. Data processing was carried out using the Excel spreadsheet programme. Respondents rated the 19 identified impact areas in the questionnaire on a four-point Likert scale (1-4):

1. the applicability/acceptability of the DHT in clinical trials
2. the design of the trial
3. the selection of the principal investigator
4. the regulatory approval process
5. compliance with regulations
6. reducing the number of protocol amendments
7. improving the screening error rate / the recruitment process
8. patient recruitability / trust
9. the patient retention rate
10. ensuring data security
11. the volume of data collected
12. the quality / reliability / information content of the data collected
13. the usability / processability of the collected data
14. patient-centred care
15. doctor-patient communication / relationship
16. the process for reporting adverse events
17. the duration of the study
18. reduction of trial costs / cost-effectiveness
19. return on examination costs

Descriptive statistics - mean, standard deviation and median - were calculated for each impact area, and I have also presented these in graphical form (Figure 12) to ensure clarity and comparability.



12 Answers to the quantitative questionnaire, presented as the mean on a Likert scale, with the standard deviation indicated

Source: own compilation

The development of the questionnaire followed a theory-informed and expert-reviewed process, with particular attention to content relevance, clarity and comprehensibility. The initial item pool was derived from the research questions and themes identified in the literature review. An independent clinical trial expert, who possesses extensive experience both on the sponsor side and as a service provider, was engaged to assess the questionnaire for content relevance, clarity, and coverage of the intended topic domains. After a comprehensive review, several items were refined in terms of wording and scaling. The pilot assessment focused on the clarity of the questions, the interpretation of response options, the completion time, and the identification of redundant or ambiguous items. Further refinements to the questionnaire were made prior to its deployment in the primary data collection.

5. CONCLUSIONS

5.1 Evaluation of research findings and conclusions

5.1.1 Systematic literature review

The study employed a systematic literature review methodology, supplemented by the Litmaps scientific tool. The variability of industry terminology complicated the creation of the search query; therefore, it cannot be guaranteed that all relevant publications were identified. This discrepancy is particularly pronounced given that the number of results from the conventional methodology ($N = 2$) differs considerably from the number reported by Litmaps ($N = 19$). A review of the extant literature revealed a clear research gap, namely the paucity of academic papers that precisely quantify DCT cost-effectiveness.

As a consequence of the SLR, there is a paucity of empirical, phase-specific cost and cost-effectiveness analyses in both the Hungarian and international literature that examine the economic impacts of DCTs.

The substantial number of preliminary database queries underscores the growing relevance and impetus for research on DCTs. However, a significant gap in the current evidence base is highlighted by the substantial reduction in studies during the final eligibility screening. A dearth of peer-reviewed publications reports original empirical data on the economic performance of DCTs. This scarcity of academic evidence appears to stem from several interconnected factors. Firstly, DCT models have only recently been widely adopted, meaning that only a limited number of completed trials have generated sufficient financial and operational data to allow for a rigorous economic evaluation. Secondly, detailed cost structures, budget allocations, and site-level financial metrics are generally considered commercially sensitive information, and as such, are rarely disclosed by pharmaceutical sponsors in peer-reviewed scientific publications.

This structural reliance on model-based evidence introduces an inherent risk of commercial optimism bias, which was explicitly considered during the synthesis of findings. A significant proportion of the economic data currently available originates from commercial reports, vendor white papers, and industry benchmarks. Whilst these sources provide valuable and timely insights into the potential economic impact of DCT implementation, it is important to note that

they may also reflect the commercial interests of technology providers and solution vendors. Consequently, reported projections of cost savings and ROI may represent favorable implementation scenarios rather than typical real-world outcomes. It has been demonstrated that biopharmaceutical sponsors frequently incur implementation costs for platform onboarding, organisational change management, and legacy system integration. These costs could temporarily offset the theoretical operational efficiencies and cost savings associated with decentralised trial models.

A substantial proportion of the extant data is contingent on model-based estimates, industry reports, and benchmarks of variable quality, which demonstrate considerable variation by country, sponsor, and technology portfolio. This uncertainty is particularly relevant to the domestic clinical trial ecosystem, where the adoption of digital components remains fragmented, and decision-makers often lack context-sensitive, cost-based decision-support tools.

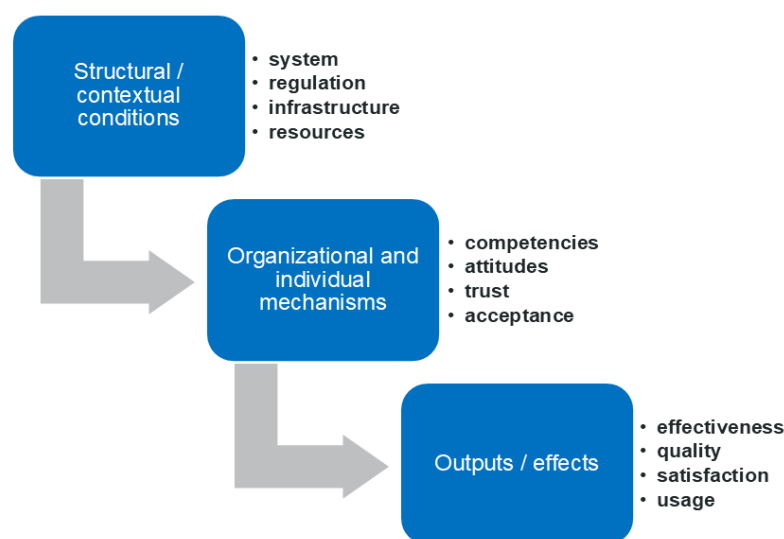
5.1.2 Evaluation of qualitative research findings

As a result of the entire coding process, a robust, multidimensional thematic framework was established that captures the actual functioning of DCTs in an accurate, nuanced and theoretically grounded manner. The coding process thus yielded not merely a descriptive analysis, but an interpretative and contextualised one, which, in terms of its scientific value, is suitable for an integrated interpretation of the operational, economic, technological and organisational aspects of DCTs.

I categorised the groups of sub-codes developed during the coding process into 9 main themes:

- Economic and business impacts
- Clinical operations and trial organisation
- Strategy, innovation and vision
- Stakeholder impacts and burden
- Regulatory environment
- Data management and quality
- Patient-centred care and access
- Disruptive digital technologies
- Social and demographic challenges

I have grouped the main themes listed above into 7 report groups. I have paired the sub-themes relating to Data management and quality with those on Disruptive digital technologies, and the sub-themes on Social and demographic challenges with those on Patient-centred care and access. The keywords appearing in the interviews are generally organised across three levels, and the meta-pattern emerging from this formed the basis for the groupings. The operational mechanisms linked to the perceived structural and contextual conditions determine the cross-section of measurable outputs and impacts. The seven groups of reports are therefore typically not independent of one another, but are linked as elements of a process model.



13 A process model illustrating the elements of the meta-pattern derived from the data groups

Source: own compilation

One of the most prominent patterns observed during the analysis of economic and business impacts was the interpretation of ROI as being time-delayed. The majority of interviewees described the introduction of digital solutions as a cost-increasing factor in the short term, particularly in relation to infrastructure development, system integration and training requirements. However, alongside these initial outlays, a longer-term narrative emerged, which saw the value of DCTs primarily in increased operational efficiency, time savings and organisational flexibility. In this form, the ROI was typically expressed not in direct financial metrics but in indirect benefits, which in itself reflects uncertainty regarding the method of economic evaluation.

This uncertainty was further reinforced by the lack of KPI-based performance measurement, which emerged as a recurring theme in the interviews. Although the majority of stakeholders reported positive experiences regarding the operation of DCTs, these assessments rarely relied on formally recorded and regularly measured indicators. Economic impacts were often articulated in the form of anecdotal impressions, intuitions and ad hoc observations, which makes it difficult to evaluate digital solutions in a way that is both comparable and relevant at an organisational level. Consequently, business decision-making was in many cases based more on strategic expectations and narratives regarding the future than on empirically supported economic data.

During the analysis of the operational and organisational dimensions, it became clear that the impact of digitalisation is not evident in a clear reduction in workload, but rather in its redistribution. Whilst certain traditional tasks, such as paper-based documentation or on-site presence, have decreased, new types of tasks have emerged relating to the use, monitoring and troubleshooting of digital systems. This shift was particularly pronounced in the case of doctors and examination centres, where the technological and administrative workload has increased alongside clinical work. For patients, the burden was primarily linked to continuous data collection and the use of digital devices. According to the interviews, the assessment of the impact of digitalisation often depended on whether a reduction or an increase in the burden was the dominant factor for the individual concerned.

In this complex operational environment, patient experience emerged as a factor of paramount importance. Based on the interviews, patient experience was not merely a matter of patients' subjective satisfaction, but an operational factor directly influencing the continuity of study participation and data quality. Well-designed, understandable and intuitive digital solutions facilitated patient engagement and retention, whilst systems that were overly complex or required participation across multiple platforms caused frustration and increased the risk of dropout. The patient experience can thus be interpreted as an intermediary dimension that links human and operational aspects.

When examining the technological dimension, the interviews clearly highlighted the varying levels of maturity of digital solutions. Whilst certain systems, such as EDC or ePRO solutions, have already been routinely integrated into clinical research practice, other technologies, including AI-based analyses or virtual reality applications, appeared to be more future-oriented and in an experimental stage. This difference in maturity has influenced not only technological acceptance but also economic and operational assessments, as more mature systems have been

associated with more stable experiences, whilst newer solutions have been dominated by higher expectations and greater uncertainties.

Based on a summary interpretation of the results, it can be concluded that the successful implementation of DCTs is not solely a technological issue. The creation of economic value, operational stability and human acceptance are inseparable factors, the coordinated functioning of which is only partially ensured by current practice. The time-sensitive nature of ROI, the lack of KPIs, the redistribution of workloads and the prominent role of patient experience all suggest that the interpretation of DCTs is currently in a transitional phase. In this phase, the technological potential is widely recognised, yet the organisational, economic and human conditions do not yet always support the full realisation of this potential.

This complexity has necessitated an integrated interpretative framework that treats DCTs not as isolated technological innovations, but as multidimensional organisational and social phenomena. The empirical findings of this thesis contribute to this framework by exploring the tensions and points of connection that define the current and future role of DCTs in clinical research.

5.1.3 Evaluation of quantitative research findings

The descriptive statistics of the Likert-scale evaluations provide a nuanced picture of how DHTs are perceived across different domains of clinical trials. The results of the study suggest a moderately positive assessment of DHTs implementation, with mean values predominantly clustering around the upper range of the scale (approximately 3), indicating a generally favourable but not unequivocal perception.

The most consistent positive evaluations are associated with data-related domains. Specifically, the perceived impact of DHTs on the quantity, quality, and usability of collected data exhibits the highest mean scores, all exceeding 3.3. This pattern indicates a strong consensus among respondents that digital solutions enhance the data-generating capacity of clinical trials, both in terms of volume and informational value. These findings are consistent with the prevailing expectation that digitalisation primarily contributes to enhanced data capture and processing capabilities, which are pivotal to contemporary clinical research.

Conversely, lower mean values are observed in domains associated with regulatory processes, operational implementation, and trust-sensitive issues. The lowest-rated area is data security, with a mean of approximately 2.27, suggesting considerable concern or uncertainty among

respondents regarding the ability of digital systems to ensure secure data handling. In a similar vein, the selection of PIs and regulatory approval processes have received comparatively low ratings, with mean scores of below 2.6. The findings suggest that while DHTs may offer technical advantages, its integration into established institutional and regulatory frameworks remains problematic or insufficiently substantiated in practice.

A critical dimension of the analysis concerns the variability of responses, as captured by standard deviations. The highest dispersion is observed in the domain of trial cycle time, where the standard deviation exceeds 1.18. This substantial variability is indicative of a pronounced lack of consensus among respondents, suggesting that the effect of DHTs on trial duration is highly context-dependent. While certain participants have reported significant efficiency gains, others have reported neutral or even negative experiences.

A comparable level of variability is observed in data security (standard deviation 1.01) and patient-related dimensions, including recruitment feasibility, patient trust, and patient-centricity (standard deviations around 0.94). These findings indicate that there are significant variations in perception, which are likely attributable to differences in technological maturity, institutional readiness, or prior experience with digital tools. The combination of low mean and high variance in data security underscores its role as a critical and contested domain.

Conversely, certain areas demonstrate near-universal consensus. For instance, the evaluation of study design demonstrates a standard deviation of zero, thus indicating identical responses among participants. The results indicate that other domains, including the reduction of protocol amendments and general applicability, demonstrate low variability. These results suggest that certain aspects of DHTs integration are relatively well understood and consistently evaluated across stakeholders.

An analysis of discrepancies across response patterns further corroborates these conclusions. The results also indicate that a number of domains exhibit significant variability in their individual scores, with ranges extending from 0 to 4, including trial cycle time, data quantity, and patient recruitment. Such disparities indicate that respondents' experiences with DHTs are far from uniform and may depend on specific organisational, technological, or methodological contexts. The variability in patient-related dimensions is of particular interest, as it suggests that the purported benefits of digitalisation for patient engagement are not universally realised.

In summary, the findings reveal a dual pattern. On the one hand, there is a clear and robust perception that DHTs enhances data-related aspects of clinical trials. Conversely, substantial

uncertainty and disagreement persist in areas related to implementation, regulation, and patient interaction. The most significant discrepancies have been observed in domains where digital transformation intersects with complex organisational and human factors, such as data security, patient engagement, and operational efficiency. The results of this study underscore the significance of contextual factors in influencing the perceived impact of DHTs, thereby signifying the necessity for further standardisation and the generation of evidence with the aim of mitigating variability in stakeholder experience.

5.1.4 Mixed-methods integrated matrix

Based on the findings, it became clear that the perception of DCTs is not uniform, but rather takes shape along multiple interpretative frameworks that exist in parallel and are often in tension with one another.

The research was conducted within a mixed-methods framework, the central element of which was data integration. This integration was supported by the use of convergence tables, also known as joint displays, which linked qualitative themes with the corresponding quantitative indicators within a single matrix. This approach did not merely place the different data types side by side, but made their convergence, complementarity or, indeed, divergence visible. The advantage of this approach was the nuanced exploration of complex phenomena; at the same time, the interpretation of qualitative data necessarily carries the risk of researcher subjectivity. To present the results in a credible manner, the so-called ‘weaving’ technique was also employed, whereby qualitative and quantitative findings appeared in the same sections of text, reinforcing one another.

The aim of the integrated qualitative-quantitative analysis was to explore the conditions under which DHTs contribute to the efficiency, quality and acceptance of clinical trials. Using a mixed-methods approach, I examined the phenomenon from a multidimensional perspective. Qualitative expert interviews, focusing on the underlying mechanisms, enable the exploration of causal relationships and modes of operation, whilst quantitative indicators quantify the frequency, intensity and extent of the phenomena. This combined approach provides a more comprehensive and in-depth understanding to answer the research questions.

Quantitative topic	Interpretation	Areas of impact	Qualitative indicators		
			Mean / SD / Median		
Clinical performance	generally good	Clinical applicability/acceptance of DHTs	3.36	0.50	3
Clinical performance	Positive effect	development of a study protocol	3.00	0.00	3
Stakeholder impacts	Changing attitudes	selection of the PIs	2.36	0.50	2
Tech and data	CTIS, acceptance	regulatory approval process	2.55	0.52	3
Regulation	Over-regulated, changing	compliance with regulations	3.00	0.77	3
Economic factors	better	reduction in the number of protocol amendments	2.73	0.47	3
Clinical operations	Targeted, faster	improvement in screening error rate / inclusion process	3.00	0.77	3
Clinical operations	variable	patient engagement / trust	2.91	0.94	3
Clinical operations	Positive impact	Patient retention rate	3.00	0.89	3
Tech and data	better	ensuring data security	2.27	1.01	3
Tech and data	more data	Amount of data collected	3.45	0.93	4
Tech and data	better	quality / reliability / information content of collected data	3.45	0.52	3
Tech and data	faster	usability/processability of collected data	3.36	0.50	3
Stakeholder	More flexible	patient-centred	3.09	0.94	3
Stakeholder	trust	doctor-patient communication / relationship	2.55	0.82	3
Clinical practice	weak point	Adverse event reporting process	2.91	0.70	3
Economic	is shortened	cycle time	3.00	1.18	3
Economic	Yes, in the long term	reduction in testing costs / cost-effectiveness	2.91	0.83	3
Economic	Yes, in the long term	return on research costs	2.82	0.75	3

10 A matrix illustrating the integrated interpretation of qualitative themes and quantitative metrics

Source: own compilation

The quantitative metrics typically showed moderate to good values on their own; however, based on the interviews, it became clear that these results were not the outcome of linear technological effects, but rather of complex, conditional mechanisms.

5.1.5 Clinical operations and examination processes

Based on the quantitative data, the clinical applicability and acceptability of DHTs can be described as favourable overall (average: 3.36). This is unanimously confirmed by the interviews, which also emphasise that the positive effect is not automatic, but depends heavily on the quality of the trial design and the correct integration of the technological elements. According to the qualitative results, DHTs supports clinical operations most effectively when it is not introduced as a ‘stopgap solution’, but is adapted at an early stage of protocol design, taking into account the therapeutic area and the patient population concerned, and aligned with the trial’s objectives.

This explains why the quantitative score for trial design is stable but not outstanding (average: 3.00): the potential of the technology is widely accepted, but its implementation requires significant preparation, resources and organisational learning.

The process of improving screening error rates and patient engagement also showed moderately good results (average: 3.00). The interviews highlight that digital tools - particularly retrospective database analysis and AI-based pre-screening - can significantly reduce the screening failure rate through targeted selection, provided the target population is realistically defined. Otherwise, the technology may even exacerbate structural problems.

5.1.6 Stakeholder influences and human dimensions

The most critical points of tension in the study arose in relation to the human dimensions. The quantitative score for the selection of the PI was notably low (average: 2.36 on a scale of 4), which is clearly explained by the qualitative results. Based on the interviews, the attitude of PIs plays a key role: digital solutions often represent an additional workload, a need for training and administrative responsibility for them, which leads to selective acceptance.

Patient engagement and trust (average: 2.91) present an ambivalent picture. According to the qualitative data, convenience, reduced travel burdens and home-based data collection increase willingness to participate, whilst digital illiteracy, data security fears and cultural differences can pose significant barriers. This ambivalence explains the relatively high standard deviation in this dimension.

The quantitative value for doctor-patient communication is lower (average: 2.55), a finding consistently supported by the interviews. Fully remote solutions often undermine the quality of the personal relationship, particularly in the case of longer or sensitive examinations; consequently, the majority of respondents identified the hybrid model as the optimal solution.

5.1.7 Technology and data dimensions

The strongest convergent results emerged in the areas of technology and data. The quantity (mean: 3.45; median: 4) and quality (mean: 3.45) of the data collected proved to be particularly high. According to the interviews, real-time data collection, audit trails, time-stamping and integrated databases (e.g. EESZT, RWE) clearly enhance data integrity and analytical capabilities. Several respondents highlighted the significance of the untapped potential inherent in EESZT.

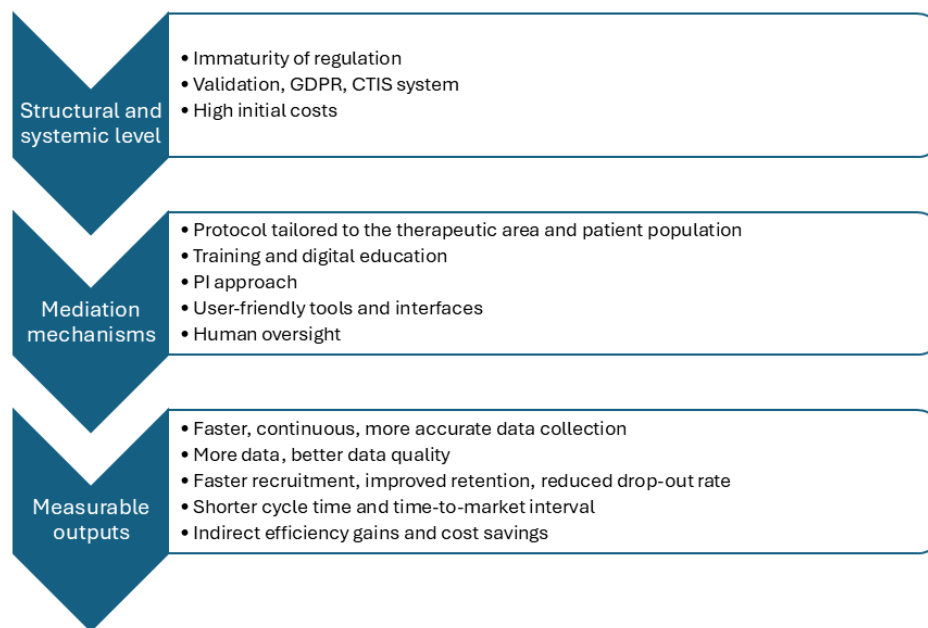
In contrast, the assessment of data security showed the lowest average and the highest standard deviation (average: 2.27; standard deviation: 1.01). According to the qualitative data, issues of data protection, validation, GDPR compliance and data sovereignty generate significant uncertainty and mistrust, which directly impacts technological adoption.

5.1.8 Economic factors

The quantitative values for the economic dimensions fall within a moderate range. The assessment of development cycle time (mean: 3.00) and cost-effectiveness (mean: 2.91) is nuanced by the qualitative results: DHT solutions are typically costly initially and create a new cost structure; however, they can provide ROI indirectly - through shorter cycle times, faster time-to-market and better data quality - particularly in cases involving large sample sizes and hard-to-reach, remote regions or populations, such as rare diseases.

5.2 Conditional impact model of DCTs

Based on the integrated matrix, it can be concluded that the application of DHTs in clinical trials is not merely a technological issue, but a conditional operational model. The strongest impact of digital solutions is evident in the data and time dimensions, whilst human and regulatory factors play a mediating role in the development of measurable outcomes.



14 A conditional impact model for DCTs

Source: own compilation

Figure 14 illustrates the impact of DHTs on clinical trials using a conditional, three-level model. The structural and regulatory environment influences measurable outcomes not directly, but through mediating mechanisms. The results suggest that the realisation of technological potential depends primarily on the degree of acceptance and effectiveness. The human and regulatory aspects, meanwhile, are most strongly influenced by the quality of implementation.

Based on the research findings, it can be concluded that DCTs are currently in a transitional phase of development. Although the potential of technological solutions is widely recognised, business, organisational and human conditions do not always support the full realisation of this potential.

The interpretation of DCTs is often fragmented: economic expectations, operational experiences and human experiences do not always align. This fragmentation may explain why tensions arise between expectations and practical reality.

5.3 Conceptual modelling

The present study employs a mixed-methods explanatory research design to examine how the digitalisation of clinical trials affects operational performance. The conceptual model framework posits that the benefits of DCTs are not directly attributable to technology itself, but rather emerge through an operational causal chain: structural inputs drive changes in mediating operational processes (specifically patient recruitment, continuous communication, and remote data collection), which ultimately transform trial outcomes (duration, cost structure, and data quality).

The integrated conceptual model (Figure 14) synthesises this macro-meso-micro transition logic based on the MLP (Geels, 2011). At the macro level, the digitalisation of the clinical research socio-technical regime is driven by technological evolution, regulatory reforms, and cost pressures. At the organisational micro level, the transition is interpreted through DC (Teece, 2007) particularly sensing, seizing and transforming, while Hungarian empirical research on digitalisation and innovation management provides contextual evidence on adaptive capabilities and organisational renewal (Csedő et al., 2019). The model also incorporates strategic technology management considerations, because the value of digital solutions depends on the alignment of technology choices with organisational capabilities and strategic priorities (Deutsch et al., 2019; Deutsch & Berényi, 2023). Site digital readiness is treated as a contextual condition linked to organisational readiness for change (Weiner, 2009) and to the change-management requirements identified in digitalisation research (Csedo et al., 2017). Therapeutic complexity and HTA/RWE alignment are retained as further moderators, with the latter grounded in CEE evidence on the use and transferability of real-world evidence (Kaló et al., 2026; Kamusheva et al., 2022; Németh et al., 2023).

From an economic perspective, the model formalises a fundamental shift in the financial architecture of clinical trials:

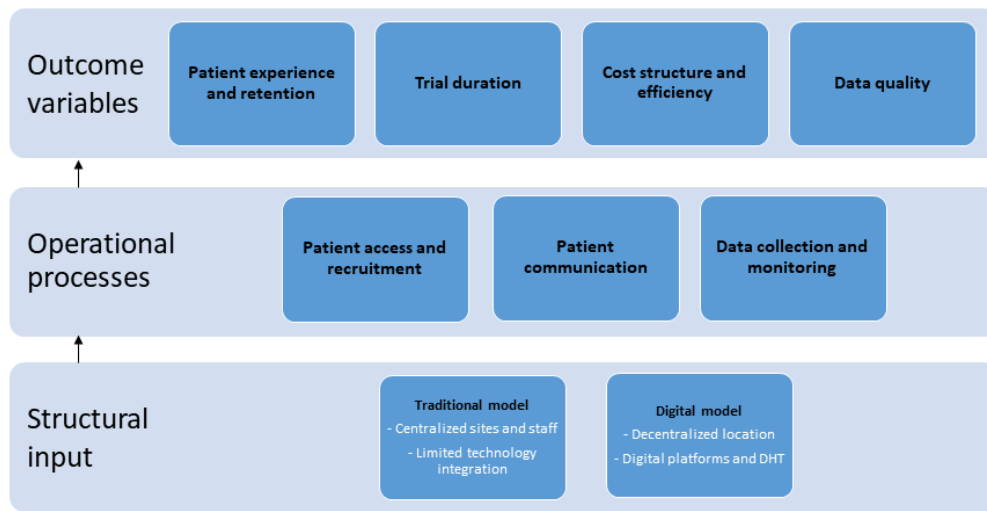
- CAPEX vs. OPEX realignment: The implementation of DCTs requires a substantial initial CAPEX for software licensing, cyber-infrastructure, and training, creating immediate financial commitments.

- Long-term value creation: These upfront investments are offset over time by OPEX reductions achieved through accelerated recruitment, lower screen failure rates, reduced patient dropouts, and streamlined remote monitoring workflows (DiMasi et al., 2023; Fu et al., 2023).
- Portfolio expected net present value (eNPV) optimisation: Beyond the direct site-level cost savings (estimated at 2.58-3.61% for Phase II-III trials), the monetary value generated by DCTs relies heavily on "soft money" operational returns. Such returns may take the form of reduced overall cycle times, earlier market entry, and improved portfolio-level eNPV.

The model goes beyond immediate financial metrics by conceptualising DCT adoption as a transition at the ecosystem level rather than a series of isolated software implementations. This operational evolution entails a shift from a site-centric, episodic data-generation model to a continuous, patient-centric research-network paradigm.

Nevertheless, the economic value realised through DCT approaches is context-dependent and non-uniform. The magnitude of return may be influenced by trial design (virtual versus hybrid), therapeutic indication, organisational readiness, and regional governance, including data-protection and evidence requirements. This contextual interpretation is consistent with CEE research showing that the generation, use and transferability of real-world evidence depend on local data availability, governance arrangements, methodological expectations, expertise and system conditions (Kaló et al., 2026; Kamusheva et al., 2022; Németh et al., 2023). It is also consistent with strategic technology-management research emphasising the need to align technology investments with organisational capabilities and strategic priorities (Deutsch & Berényi, 2023).

Consequently, the successful capitalisation of DCT investments requires institutional adaptation, including advanced data platforms, dynamic analytics, strategic cross-sector partnerships and the organisational capacity to redesign established routines. Research on innovation-induced organisational change in Hungary highlights the importance of organisational structures, culture, knowledge management and deliberate change processes in enabling innovation (Csedo et al., 2017; Csedő et al., 2019, 2022).



15 Structural, operational, and outcome relationships between digital and traditional clinical trial models

Source: own compilation

5.4 Integration of contextual moderating variables into the conceptual framework

To enhance the structural model illustrated in Figure 14, and drawing on DC and contingency perspectives within strategic management (Csedő et al., 2019; Teece, 2007), the relationship between digital structural inputs and operational/economic outcomes is framed as conditional. Hungarian research on digital transformation further supports this interpretation by showing that technology-related change interacts with organisational structures, capabilities, culture and renewal processes (Csedő et al., 2019). Strategic technology-management research likewise emphasises adaptive competencies and the strategic integration of technology into organisational decision-making (Deutsch & Berényi, 2023). The operational efficiencies of DCTs are therefore not expected to be uniform; rather, they are influenced by several key contextual variables:

1. Clinical trial phase: trial phase is treated as a moderator because the scale and operational configuration of decentralised components may differ across development stages. Later-phase trials often involve larger and more geographically distributed participant populations, whereas early-phase studies may require more intensive in-person supervision; consequently, the value

and feasibility of remote components should not be assumed to be uniform across phases (DiMasi et al., 2023).

2. Therapeutic indication and procedural complexity: the feasibility and value of decentralisation depend on the extent to which a protocol relies on activities that can be performed remotely versus procedures requiring physical examination, imaging, invasive sampling or other site-based interventions. Therapeutic area is therefore treated as a contextual moderator rather than as a fixed predictor of DCT success.

3. Organisational and site digital readiness: the digital maturity of the sponsor, the CRO, and the trial site serves as a crucial moderator. This construct is grounded primarily in organisational readiness for change (Weiner, 2009) and in change-management evidence showing that digital transformation requires appropriate competencies, leadership, communication and stakeholder management (Csedo et al., 2017). Hungarian technology-adoption research further indicates that user competence and perceived vulnerability can shape technology acceptance, although these findings come from higher-education samples and should therefore be treated as contextual rather than site-specific evidence (Berenyi et al., 2021; Deutsch & Berényi, 2023).

4. Regulatory and data governance landscape: factors such as the speed of protocol approvals, eSignature validity, responsibilities across jurisdictions, and capabilities for cross-border data transfer are influenced by regional regulatory constraints. Regulatory adaptation and governance are therefore treated as contextual conditions of DCT implementation (European Medicines Agency, 2025; Yang, 2025).

6. SUMMARY AND FUTURE RESEARCH DIRECTIONS

6.1 Research findings

The research employed a systematic literature review methodology, supplemented by the Litmaps scientific tool. The variability of industry terminology posed a significant challenge to formulating the search query, thereby precluding assurance of comprehensive identification of all pertinent publications. This discrepancy is particularly pronounced given that the number of results from the conventional methodology ($N = 2$) differs considerably from the number reported by Litmaps ($N = 19$). A comprehensive review of extant literature revealed a discernible research gap concerning the precise quantification of DCT cost-effectiveness.

The study's findings indicate that the increased use of digital technologies for precise data collection has a significant impact on R&D&I. The use of remote modes has been shown to facilitate widespread patient access, thereby promoting equity, inclusivity, and generalisability by reaching marginalised populations often missed by conventional methods. The potential of DCTs to achieve direct and indirect cost reductions is primarily attributable to their ability to optimise patient recruitment and reduce time-to-market. Nevertheless, to ensure the long-term economic sustainability of DCTs, patient-centredness and equity must remain firmly embedded in trial design. Measures such as the provision of equipment, training, community engagement, and hybrid participation models have been demonstrated to be effective in addressing the digital divide (Aiyegbusi et al., 2024; de Bruin et al., 2025; Jean-Louis & Seixas, 2024; Polhemus et al., 2018; Simmons et al., 2022). It is important to note that these actions represent investments that reduce recruitment and retention risks and enhance statistical validity.

However, achieving competitive advantages and operational flexibility is contingent upon meticulous, trial-specific planning. The process of recouping investments in technological development and licensing necessitates prolonged trials and multi-use applications. In early-phase (Phase I) trials, where the patient cohort is small and rigorous in-person monitoring is paramount, traditional and hybrid approaches remain the preferred option. Conversely, the unwarranted deployment of digital technologies can induce digital fatigue among personnel and participants. To avoid counterproductivity and the concomitant increase in patient burden, technology selection must be tailored to the specific therapeutic area and study design.

It is imperative to establish a clear distinction between the sponsor's commercial requirements and the professional/medical KPIs essential to maintaining study quality. Achieving financial

and business objectives, including reduced cycle time, lower infusion costs, and accelerated market presence (ROI), is contingent upon the strict adherence to professional and operational KPIs (e.g., data integrity, patient safety, ePRO protocol compliance, doctor-patient satisfaction, and screening accuracy).

In future research, exploration should be made of emerging technological and business domains, such as 'beyond-the-pill' service ecosystems, AI-driven protocol optimisation, digital twins, and Pharma 4.0 platforms. Empirical studies are recommended to examine how the adoption of these novel tools and global partner networks directly influences DCT trial budgets, economic viability, and overall ROI, thereby bridging current theoretical expectations with empirical evidence.

The theoretical analysis indicates that DCTs are not merely technology-enabled variants of traditional models but paradigms that fundamentally transform the operational logic of trials. The selection of the trial model influences daily organisational processes, specifically patient recruitment patterns, staff-participant interactions, and high-frequency data collection. Consequently, shorter trial cycles, distinct cost structures, and high-temporal-resolution data are not isolated outcome metrics, but rather direct structural results of this reorganised operational framework.

6.2 Scientific contribution

The present study makes three principal contributions to the fields of science and business. Firstly, it provides a structured overview of the principal cost drivers associated with DCT implementation, explaining how digitalisation alters traditional trial cost structures. Secondly, it synthesises and critically evaluates the available evidence regarding recruitment efficiency, monitoring costs, retention outcomes, and development-cycle acceleration. Thirdly, it proposes an integrated conceptual framework that bridges economic and operational perspectives with patient experience, linking cost drivers and operational mechanisms to economic outcomes for pharmaceutical R&D portfolio management.

Moreover, the findings offer practical implications across multiple stakeholder levels.

- Sponsors and decision-makers: Performance evaluation must shift towards indicators that are time- and efficiency-sensitive and can capture indirect benefits, such as time savings and enhanced data quality. Furthermore, the implementation of technology

should be a gradual process, aligned with the organisational maturity model, in order to mitigate the risks associated with hasty or inadequately prepared implementation.

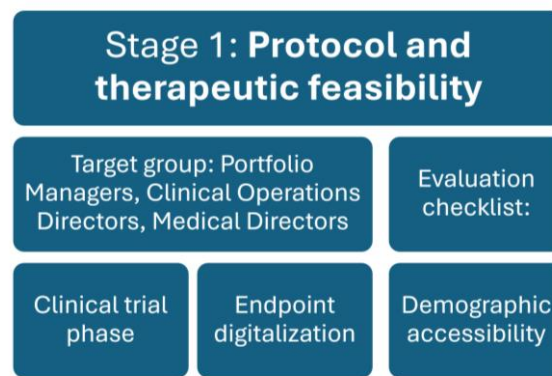
- **Clinical trial sites and investigators:** The implementation of DHTs necessitates a deliberate restructuring of daily workloads. Achieving key operational successes is contingent on redesigning task allocations and integrating structured training into routine workflows. This approach has been demonstrated to reduce staff resistance and increase technology adoption.
- **Patient-centred design:** User Experience (UX) testing should be an integral component of the design process. It is also important to address prevailing disparities in digital access and literacy, given their direct impact on patient engagement, overall experience, and trial inclusivity.
- **Regulators and senior leadership:** The research emphasises the necessity of flexible, technology-neutral regulatory frameworks that can keep pace with rapid innovation. The establishment of controlled pilot environments is recommended to facilitate the safe testing of novel digital solutions whilst safeguarding patient safety and data integrity.

6.3 Practical and managerial contributions

6.3.1 Decision-making framework

In order to transform the empirical and conceptual insights from this research into a practical tool for industry application, this section introduces a structured managerial decision-making framework and checklist (Figure 16-18). To operationalise the findings, this framework offers a fresh perspective on the adoption of DHTs challenging the traditional view of it as merely a binary technological upgrade. Instead, it is reframed as a strategic, multi-stage governance process that encourages a deeper understanding of digital transformation in modern contexts. The primary goal of this framework is to provide biopharmaceutical sponsors, CROs, technology vendors, and PIs with a practical roadmap for evaluating, organising, and executing DCTs. This approach aims to optimise ROI while minimising operational friction.

The framework begins with protocol and therapeutic area feasibility, during which portfolio managers and clinical operations directors carry out a preliminary structural evaluation of the protocol's compatibility prior to committing resources to the onboarding of digital platforms.



16 Stage 1: Protocol and therapeutic area feasibility check

Source: own compilation

In this phase, leaders assess whether the study is a Phase II or Phase III trial that involves a large, geographically dispersed sample size, where the acceleration of recruitment directly affects the project timeline. This stands in contrast to early Phase I studies, which necessitate intensive, in-person clinical oversight. The evaluation focuses on the potential for capturing primary and secondary clinical endpoints through passive digital biomarkers, validated ePRO or eCOA, and wearable continuous monitoring sensors. This is particularly pertinent when targeting populations with rare diseases, those with mobility impairments, or geographically remote cohorts. If at least two feasibility criteria are satisfied, the trial will advance to the second stage. Conversely, if these criteria are not met, managers will opt to maintain a traditional, site-centric operational model to avoid inducing "digital fatigue" among investigators and participants.



17 Stage 2: Financial strategy - hard money vs. soft money alignment

Source: own compilation

A key insight from this study revolves around the temporal disconnect between immediate "hard money" expenditures - such as upfront software licensing, hardware validation, and

platform onboarding - and the delayed "soft money" returns, which encompass benefits like accelerated cycle times, enhanced temporal resolution of data, and reduced patient dropouts. This stage is crucial for ensuring the financial viability of the project before its execution.

Stage 2 specifically highlights this critical issue: the timing gap between immediate costs and future benefits. Financial officers and programme directors must confirm the availability of upfront capital to manage initial expenses related to platform customisation and cybersecurity validation. This should be integrated with the monetisation strategies for market launch acceleration, taking into account daily opportunity losses estimated between \$40,000 and \$8 million for each day of delay in their valuation models. Additionally, the operational plan must proactively implement hybrid or risk-based monitoring approaches to achieve an estimated 30-40% reduction in CRA travel and site-monitoring overhead costs.

To move forward to the final stage, it is essential that the eNPV and savings in cycle times sufficiently compensate for the initial costs associated with technology implementation.



18 Stage 3: Site readiness, human factors, and change management protocol

Source: own compilation

Empirical evidence highlights that advanced DCT designs often face operational challenges stemming from investigator burden and friction in user interfaces. The final phase of the process focuses on fostering human-centric adoption and ensuring regional compliance.

To alleviate administrative overload for site personnel, clinical research associates, site coordinators, and change management teams must spearhead the implementation of workflow-integrated digital training, user-friendly single-sign-on interfaces, and round-the-clock technical helpdesk support. To promote digital equity and mitigate selection bias, the protocol mandates the distribution of pre-configured, cellular-enabled devices to participants, thereby accommodating varying levels of digital literacy. Additionally, regulatory affairs managers are

tasked with ensuring that the digital infrastructure fully complies with local regulations and infrastructural requirements, including GDPR compliance, EU CTR 536/2014 standards, and readiness for integration with national systems such as Hungary's EESZT. The full rollout of the hybrid or decentralised trial model will commence only after validating site readiness and change management protocols.

The following table summarises the practical benefits of this decision framework for key industry actors:

Stakeholder Group	Primary Operational Dilemma	Framework Value Add & Practical Output
Biopharmaceutical Sponsors	Unpredictable ROI and high initial CAPEX commitments.	Provides a structured gate-system to monetise time-to-market savings and balance hard vs. soft money dynamics.
CROs & Tech Vendors	Overpromising technology capabilities leading to site resistance.	Establishes realistic feasibility criteria, preventing commercial optimism bias and platform overload.
PIs	Administrative overload and digital fatigue from fragmented systems.	Enforces a dedicated change management protocol and helpdesk support to reduce site-level operational burden.
Patients & Patient Advocacy Groups	High travel burden, digital exclusion, and privacy concerns.	Guarantees provisioned device support, hybrid flexibility, and user-centric trial design.

11 Key stakeholder value proposition

Source: own compilation

6.3.2 Integrated KPI matrix for DCT performance evaluation

To systematically evaluate the economic and operational returns of DHTs biopharmaceutical sponsors and other stakeholders in clinical research require a well-balanced performance measurement tool. Traditional metrics often fall short in capturing the true value of digital transformation, as they tend to focus solely on immediate, direct costs, while overlooking essential factors such as time-to-market acceleration, risk mitigation, and improvements in data quality.

This study addresses the decision-making challenge between immediate "hard money" expenditures (direct capital and operational costs) and the long-term benefits of "soft money" returns (indirect gains related to operations, timing, and quality). To this end, an Integrated Management KPI Matrix has been established.

The proposed framework categorises KPIs across two distinct operational dimensions:

1. Portfolio & Financial Indicators (Hard Money / Sponsor-level): Quantifiable monetary and portfolio-valuation metrics directly tied to capital allocation, cycle-time acceleration, and time-to-market monetisation.
2. Process & Operational Quality Indicators (Soft Money / Site- & Patient-level): Intermediate operational, behavioural, and data-integrity metrics that capture process efficiency, protocol adherence, and workload distribution.

To successfully operationalise the Integrated KPI Matrix during the planning and execution of clinical trials, project leaders and biopharmaceutical executives must engage in a continuous, three-phase monitoring routine. Unlike the traditional method of assessing key metrics post-trial, this structured approach integrates performance tracking throughout the entire life-cycle of the trial. During the preliminary pre-trial feasibility stage, known as baseline setting, operational management establishes benchmark targets for critical efficiency indicators, specifically the screen failure rate and the cost per enrolled patient. These targets are determined by analysing historical data from traditional trials conducted within the same therapeutic indication. As the trial moves into the active patient enrolment phase, the focus shifts to operational execution and mid-stream monitoring. In this stage, management is responsible for continuously overseeing real-time data flow metrics, including, but not limited to, data latency.

Additionally, human-centric factors are monitored through the Investigator Burden Index. If monitoring reveals a sudden increase in missing data or an unacceptable rise in investigator fatigue, clinical operations teams can proactively implement targeted site-helpdesk interventions and streamline workflows to sustain data integrity and site-level engagement. In conclusion, once the trial process is complete, a thorough review of the existing portfolio (Post-Trial Valuation) is conducted. At this juncture, management calculates the realised time-to-market acceleration and reassesses the overall eNPV impact. This analysis translates operational outcomes into refined financial models that directly inform capital allocation strategies for future DCTs.

Dimension	KPI Type	KPI	Measurement Source & Formula	Strategic & Practical Business Impact
Portfolio & Financial (Hard Money)	Sponsor / Portfolio-Level	eNPV	Financial portfolio models discounted for clinical success probability.	Preserves and maximises overall portfolio capital value across multi-year development life-cycles.
		Cost per Enrolled Patient	Sponsor/CRO trial budget accounting: $\frac{\text{Total Recruitment Expenditure}}{\text{Enrolled Patients}}$	Evaluates the cost-efficiency of digital recruitment vs. traditional site screening.
		Time-to-Market Acceleration	Clinical trial milestone tracking (SIV to Data Lock duration vs. baseline).	Monetises cycle-time savings by avoiding daily opportunity losses estimated between \$40,000 and \$8M per day of delay.
		OPEX Reallocation Ratio	Financial balance sheet: $\frac{\text{Digital Platform \& Remote Services Cost}}{\text{Saved On-Site Travel \& Administrative Fees}}$	Measures the structural shift from fixed physical site overheads to flexible technology platform licenses.
Process & Operational Quality (Soft Money)	Process Efficiency	Screen Failure Rate	EDC / AI pre-screening database: $\frac{\text{Screened Patients} - \text{Enrolled Patients}}{\text{Total Screened Patients}} \times 100$	Reduces unnecessary laboratory, diagnostic, and site visit expenses by targeting eligible participants early.

		Patient Retention & Dropout Rate	ePRO / eCOA compliance logs: $\frac{\text{Withdrawn Participants}}{\text{Total Randomized Participants}} \times 100$	Minimises protocol non-completion risks, preventing costly sample size recalculations or trial repetitions.
	Data & Technology	Data Latency & Missingness	Cloud audit trail logs: Time elapsed between remote data entry and centralised EDC verification.	Enables real-time safety signal detection and cuts data cleaning/lock timelines significantly.
	Human Factors	Investigator Burden Index	Standardised site survey measuring system usability and admin time spent per participant.	Monitors and mitigates investigator digital fatigue, reducing site-level resistance and system misuse.

12 Integrated KPI matrix for evaluating DCT

Source: own compilation

6.4 Limitations of the research and areas for improvement

To ensure a balanced and critical interpretation of the findings, it is necessary to acknowledge the methodological, empirical, and contextual limitations of this study.

A fundamental methodological limitation of the research stems from the nature of the sampling strategy. Participants were selected through targeted sampling, focusing on experts who play a relevant role in conducting domestic clinical trials, have direct experience with digital components, and have at least 5 years of professional experience. Whilst this approach guaranteed the accumulation of data-rich, in-depth qualitative information, it concomitantly restricts the generalisability of the findings to broader international settings. Furthermore, potential participants who were developers or owners of digital solutions were excluded to prevent conflicts of interest, thereby strengthening internal validity but concomitantly narrowing the scope of the included technological perspectives. To avoid sampling bias from the over-representation of sponsors, I intended to interview a variety of stakeholders. However, as outlined below, this was not possible for the reasons subsequently described. By their own admission, the respondents did not possess such information; however, the questionnaire's focus on personal data and sensitive corporate information may also have led to the negative attitude they exhibited.

The procurement of multi-stakeholder representation also proved challenging. Despite repeated attempts, formal regulatory perspectives (e.g., from the NNGYK) could not be integrated into the primary research due to institutional data availability constraints. Similarly, direct access to clinical trial participants was subject to stringent restrictions imposed by rigorous health data protection regulations (GDPR). In consideration of the sensitivity inherent to health data, legal provisions have been established to govern the process of contacting study participants. However, to represent the limited patient perspective, an approach was made to patient organisations, who in turn forwarded the interview invitation to patients they were able to contact. In this manner, I received three responses, one of which resulted in an interview. Given the specialised nature of the research topic, open social media platforms were not considered a suitable means of recruitment.

Furthermore, there was an absence of groups that might have been relevant to the subject. Notwithstanding, even if such knowledge had been available, it would have been possible to

anticipate only incomplete information, given that study participants generally possess no understanding of the financial aspects. Despite the valuable insights provided by patient organisation representatives, direct input from active trial participants remained limited.

Beyond the constraints of empirical data collection, significant limitations arise from the existing evidence base and the methodological literature analysed in the SLR. The number of peer-reviewed empirical studies explicitly evaluating the cost-effectiveness of DCTs remains limited. The field is characterised by inconsistent terminology, with studies referring to decentralised, virtual, digital, site-less, or hybrid trials interchangeably. This absence of terminological standardisation engenders inherent search constraints and increases the likelihood that relevant studies employing alternative keywords may have been overlooked (Santa-Ana-Tellez et al., 2023; Vayena et al., 2023). Despite the utilisation of Litmaps citation mapping to facilitate source identification, inadvertent omissions remain possible.

Moreover, the extant evidence is susceptible to commercial vendor and publication bias. A substantial proportion of the quantitative economic evidence is derived from vendor white papers, consultancy reports, and sponsor-supported financial simulations (IQVIA, 2022a). These sources place significant emphasis on the highly favorable outcomes achieved, including reductions in monitoring costs of up to 46.2% and cycle time improvements of almost 49%. However, there is a paucity of data on implementation expenditures for platform onboarding, organisational change management, integration with legacy systems, and cybersecurity (Daly et al., 2024; Jiang et al., 2025; Tenti et al., 2025). Consequently, the economic benefits presented in such sources may reflect best-case implementation scenarios rather than routine operational reality.

Methodological heterogeneity across available studies further restricts external validity. The included literature varies considerably in terms of research design, underlying assumptions, therapeutic focus, and operational context. Model-based studies reporting substantial operational efficiencies typically assume optimised multicentre Phase II or Phase III trial designs (DiMasi et al., 2023; IQVIA, 2022b), whereas retrospective observational studies evaluate hybrid implementations within specific therapeutic areas (Fu et al., 2023). Consequently, cost savings and ROI estimates must be interpreted as context-dependent outcomes shaped by protocol complexity and sponsor capabilities, rather than as universally achievable benchmarks.

A further challenge is the limited availability of transparent financial data. Sponsors generally regard detailed trial budgets, site-level expenditure, and unit-cost structures as commercially sensitive. Consequently, peer-reviewed research relies heavily on industry benchmarks and indirect simulation models rather than observed cost data (DiMasi et al., 2023; Sertkaya et al., 2024), which restricts precision and independent validation.

The economic impact of DCTs varies significantly by trial phase and therapeutic area. Large Phase II and III studies, involving geographically dispersed populations, benefit most from remote recruitment and centralised monitoring. Conversely, Phase I trials and protocols that require intensive in-person assessments or complex interventions (e.g., oncology) are not readily amenable to replacement with site-based activities. In such cases, sponsors face cost duplication, as they must maintain traditional site infrastructure while simultaneously funding digital platforms and remote logistics (Kijewski et al., 2026; Getz et al., 2023; Sertkaya et al., 2024). Furthermore, initiatives aimed at addressing the digital divide (i.e., the provision of devices, internet access, and technical support) often result in operational expenses that are frequently omitted from financial models (Aiyegbusi et al., 2024; de Bruin et al., 2025; Jean-Louis & Seixas, 2024; Moore et al., 2022).

The generalisability of these findings may be limited by geographical and regulatory constraints. A significant portion of published economic evaluations originates from healthcare settings in North America and Western Europe. As a result, differences in infrastructure, funding mechanisms, labour costs, and data governance - such as the distinctions between the EHDS and U.S. regulatory standards - impede the direct applicability of these cost-saving estimates to emerging markets, particularly within the clinical research landscape of Central and Eastern Europe (de Jong et al., 2024). This non-transferability is even more pronounced in Hungary, where clinical research is predominantly concentrated in university centres and public hospitals (Orosz, 2022). The specific systemic and regulatory characteristics of this national framework create substantial barriers to the seamless adoption of international methodologies. This situation has led to an underutilisation paradox regarding the EESZT. Although Hungary boasts one of the most sophisticated centralised digital health data infrastructures, which theoretically provides an ideal foundation for retrospective patient screening and RWE generation, its operational potential remains largely untapped. This limitation is largely due to a lack of interoperability between the EESZT and international clinical trial platforms, further complicated by overlapping legal, data protection (GDPR), and technical restrictions. Systemic capacity deficits and widespread digital fatigue exacerbate these structural challenges. Within the strained public healthcare sector, investigator-physicians, already facing excessive

workloads, often resist the adoption of new digital tools. They view these innovations as additional administrative and technical burdens rather than as solutions that enhance efficiency. Additionally, domestic pharmaceutical authorities and ethics committees tend to adopt a more conservative stance towards the approval of fully decentralised (siteless) trial models compared to their counterparts in Western Europe and the United States, thereby hindering the local implementation of contemporary trial paradigms.

In the rapidly evolving technological landscape of clinical research and development, the challenge of patient recruitment has led to a decline in the number of clinical trials conducted in Hungary. Concurrently, the emergence of data-driven trials and the transformation of global resource allocation have precipitated a shift in research activity to Eastern Europe. The economic and practical feasibility of DCTs in this region is fundamentally determined by the readiness of the local infrastructure and the willingness of patients to cooperate. In view of the aforementioned, the domestic market should prioritise the implementation of hybrid models that balance physical surveillance and digital data collection to ensure patient safety.

The methodological limitations of the current research findings are primarily attributable to the sample, the interpretative nature of the qualitative methods, and the context-dependent results. Consequently, contemporary economic appraisals of DCTs should be approached with a degree of circumspection.

To enhance the methodological and practical rigour of future research, it is essential to make concerted efforts in ensuring the consistent application of mixed methods, with a focus on explicit data integration and the strategic utilisation of convergence matrices. In alignment with the integration recommendations put forth by Fetters et al. (2013), newly identified contradictions should form the basis for developing targeted follow-up research questions. Decision-makers would also benefit from the implementation of joint displays, which offer a concise overview of the available evidence and pinpoint specific areas that require further empirical investigation. To facilitate this process, cost accounting frameworks should be established that are standardised, transparent, and empirically grounded. These frameworks should be supported by ongoing data collection across a diverse range of clinical trial portfolios, encompassing both multicentre and multicomprehensive studies.

6.5 Presentation of further research directions

One possible direction for further extending the research is to expand the sample through in-depth interviews or structured questionnaire data collection, which would allow for a broader validation of the findings. In addition, using clinical trial databases, it may be worthwhile to conduct analyses examining trends and proportions related to the use of DCTs. Although these data sources typically do not contain specific cost items, they may be suitable for comparative analysis of the use and prevalence of DHTs at national, EU and global levels. A further potential avenue for data collection is to re-engage with regulatory authorities, as although they generally do not possess direct cost information, data on regulatory approval rates and regulatory experiences regarding DCTs can contribute to a more comprehensive understanding of the phenomenon.

6.5.1 Opportunities for developing the research methodology

Given the complexity of the topic under investigation and the rapidly changing environment of DCTs, the research methodology can be further developed in several directions. The following recommendations, building on one another, can contribute to increasing the validity, generalisability and practical relevance of the findings.

6.5.1.1 Incorporation of empirical, primary data collection

The current approach, based on narrative and secondary sources, could be supplemented with primary empirical data, such as an analysis of the cost structures of sponsors, CROs or trial sites. Structured questionnaire surveys or semi-structured interviews could provide a more accurate picture of actual expenditure, the time-series of costs, and the real cost-benefit ratios of individual DHT components.

6.5.1.2 Application of standardised cost definitions and categories

The methodology could be improved by introducing a uniform cost category system that distinguishes between fixed and variable, direct and indirect, and one-off and recurring costs. This would reduce the distortions arising from the differences in definitions frequently found in the literature and enable comparability between different studies.

6.5.1.3 Phase-, indication- and geography-specific analyses

The accuracy of the research would be significantly enhanced by a stratified analysis that examines Phase I-IV trials, different therapeutic areas (e.g. oncology, neurology, rare diseases), and different geographical and regulatory environments separately. This would help avoid generalisations in cases where the cost-effectiveness of DCTs varies markedly.

6.5.1.4 Application of quantitative cost-benefit and life-cycle analysis

The methodology could be further developed through quantitative cost-benefit analysis and a life-cycle cost approach. This would enable quantification of the extent to which initial technological and compliance investments are recouped over the entire duration of the trial, or at a portfolio level spanning multiple trials.

6.5.1.5 Integration of outcome and quality indicators

The current focus is primarily on cost structure; the methodology could be strengthened by incorporating data quality, patient safety and retention indicators. Linking these to costs would make it possible to examine whether DCTs are not only cheaper or more expensive, but also more effective in scientific and clinical terms.

6.5.1.6 Longitudinal and portfolio-level approaches

Future research could benefit from the analysis of longitudinal data that tracks changes in cost structure across multiple consecutive trials or over a period of several years. This would be particularly suitable for exploring the economic impacts of scalability and institutional learning.

6.5.1.7 Sensitivity and design analyses

The robustness of the methodology could be enhanced by applying sensitivity analyses that examine how changes in key parameters (e.g. patient numbers, dropout rates, technology licence fees, regulatory requirements) affect total costs. In parallel, a comparison of different trial designs (conventional, hybrid, fully decentralised) would also be warranted.

6.5.1.8 Incorporating a multi-stakeholder perspective

Finally, the methodology could be enhanced by explicitly incorporating a multi-stakeholder perspective. Sponsors, CROs, trial sites, patients and regulatory authorities have differing perceptions of costs and value; therefore, a parallel examination of these could provide a more nuanced picture of the true economic and social impacts of DCTs.

In summary, the direction of methodological developments clearly points away from a narrative, descriptive approach towards more structured, quantitative and empirically supported analyses. Such a strengthened methodology would enable the cost structure of DCTs to be not merely the subject of conceptual comparison, but to become a well-founded decision-support tool in the formulation of clinical development strategies.

References

235/2009. (X. 20.) Korm. Rendelet Az Emberen Végzett Orvostudományi Kutatások, Az Emberi Felhasználásra Kerülő Vizsgálati Készítmények Klinikai Vizsgálata, Valamint Az Emberen Történő Alkalmazásra Szolgáló, Klinikai Vizsgálatra Szánt Orvostechnikai Eszközök Klinikai Vizsgálata Engedélyezési Eljárásának Szabályairól (2025). <https://njt.hu/jogszabaly/2009-235-20-22>

536/2014/EU rendelet, 158 OJ L (2014). <http://data.europa.eu/eli/reg/2014/536/oj/hun>

2005. Évi XCV. Törvény Az Emberi Alkalmazásra Kerülő Gyógyszerekről És Egyéb, a Gyógyszerpiacot Szabályozó Törvények Módosításáról (2005). <https://net.jogtar.hu/jogszabaly?docid=a0500095.tv>

Adedinsewo, D., Morales-Lara, A. C., Hardway, H., Johnson, P. W., Young, K. A., Douglass, E. J., Butler Tobah, Y. S., Rose, H., Burnette, D. P., Attia, Z. I., Lopez-Jimenez, F., Friedman, P. A., Carter, R. E., & Noseworthy, P. A. (2023). Implementing artificial intelligence-based cardio-obstetric screening in a diverse patient population: A prospective study. *European Heart Journal*, Volume 44(Issue Supplement_2). <https://doi.org/https://doi.org/10.1093/eurheartj/ehad655.2730>

Adshead, F., Holmes, S., Nathalie, P., & Mitan, A. (2025, March 4). Sustainable Clinical Trials: Reducing Greenhouse Gas Emissions. *DIA Global Forum*. <https://globalforum.diaglobal.org/issue/march-2025/sustainable-clinical-trials-reducing-greenhouse-gas-emissions/>

Aiyegbusi, O. L., Rivera, S. C., Kamudoni, P., Anderson, N., Collis, P., Denniston, A. K., Harding, R., Hughes, S., Khunti, K., Kotecha, D., Krumholz, H. M., Liu, X., McMullan, C., Molony-Oates, B., Monteiro, J. F. G., Myles, P., Rantell, K., Soltys, K. M., Verdi, R., ... Calvert, M. (2024). Recommendations to promote equity, diversity and inclusion in decentralized clinical trials. *Nature Network Boston*. <https://doi.org/10.1038/s41591-024-03323-w>

Ananthakrishnan, N., & Shanthi, A. K. (2012). ICMR's ethical guidelines for biomedical research on human participants: Need for clarification. *Indian Journal of Medical Ethics*, 9(3), 207–209. <https://doi.org/10.20529/IJME.2012.067>

Beauroyre. (2025, June 25). Clinical Trial Costing: Phase-By-Phase Budget Guide. <https://www.abacum.ai/blog/clinical-trial-costing>

Berenyi, L., Deutsch, N., Pinter, E., Bago, P., & Nagy-Borsy, V. (2021). Technology Adoption Propensity Among Hungarian Business Students. *European Scientific Journal*, ESJ, 17(32), 1–1. <https://doi.org/10.19044/esj.2021.v17n32p1>

Bhatt, A. (2010). Evolution of clinical research: A history before and beyond james lind. *Perspectives in Clinical Research*, 1(1), 6–10.

Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology*, 3(2), 77–101. <https://doi.org/10.1191/1478088706qp063oa>

Brinkmann, S., & Kvale, S. (2018). *Doing Interviews*. SAGE Publications Ltd. <https://doi.org/10.4135/9781529716665>

British Medical Journal. (1948). Streptomycin Treatment of Pulmonary Tuberculosis. *British Medical Journal*, 2(4582), 769–782.

British Medical Journal. (1996). The Nuremberg Code (1947). *BMJ*, 1996;313:1448, 313(7070), 1448. <https://doi.org/10.1136/bmj.313.7070.1448>

Brixner, D., Kaló, Z., Maniadakis, N., Kim, K., & Wijaya, K. (2018). An Evidence Framework for Off-Patent Pharmaceutical Review for Health Technology Assessment in Emerging Markets. *Value in Health Regional Issues*, 16, 9–13. <https://doi.org/10.1016/j.vhri.2018.01.003>

Brøgger-Mikkelsen, M., Ali, Z., Zibert, J. R., Andersen, A. D., & Thomsen, S. F. (2020). Online Patient Recruitment in Clinical Trials: Systematic Review and Meta-Analysis. *Journal of Medical Internet Research*, 22(11), e22179. <https://doi.org/10.2196/22179>

Bull, J. (1951). *A study of the history and principles of clinical therapeutic trials*. MD Thesis, University of Cambridge. The James Lind Library. <https://www.jameslindlibrary.org/articles/bull-jp-1951/>

Center for Information and Study on Clinical Research Participation. (2023). *Perceptions and Insights Study*. CISC RP. <https://www.ciscrp.org/professional-services/perceptions-and-insights-studies>

Center for Information and Study on Clinical Research Participation. (2025). *2025 Perceptions and Insights Study*. CISC RP. <https://www.ciscrp.org/2025-perceptions-and-insights-study>

Chalmers, I., Milne, I., Tröhler, U., Vandenbroucke, J., Morabia, A., Tait, G., Dukan, E., & James Lind Library Editorial Team. (2008). The James Lind Library: Explaining and illustrating the evolution of fair tests of medical treatments. *The Journal of the Royal College of Physicians of Edinburgh*, 38(3), 259–264.

Chesbrough, H. W. (2003). *Open Innovation: The New Imperative for Creating and Profiting from Technology*. Harvard Business School Press, Boston. https://books.google.hu/books/about/Open_Innovation.html?id=4hTRWStFhVgC&redir_esc=y

Clemons, Pacino, A., & Rodriguez-Chavez, I. R. (2025, March 3). Top 10 Challenges and Solutions for Decentralized Clinical Trials: Technology, Diversity, and Regulations in 2025 and Beyond. *DIA Global Forum*. <https://globalforum.diaglobal.org/issue/march-2025/top-10-challenges-and-solutions-for-decentralized-clinical-trials-technology-diversity-and-regulations-in-2025-and-beyond/>

ClinicalConnection. (n.d.). *The First Recognized Clinical Trials*. ClinicalConnection. Retrieved 26 October 2025, from <https://www.clinicalconnection.com/blogs/987e4a5f-289e-4a31-be7b-695380ce2fe0/the-first-recognized-clinical-trials>

Collier, R. (2009). Legumes, lemons and streptomycin: A short history of the clinical trial. *CMAJ: Canadian Medical Association Journal*, 180(1), 23–24. <https://doi.org/10.1503/cmaj.081879>

Council of Europe. (2023). Compass: Manual for Human Rights Education with Young people. Manual for Human Rights Education with Young People. <https://www.coe.int/en/web/compass/the-international-covenant-on-civil-and-political-rights>

Creswell, J. W., & Plano Clark, V. L. (2018). Designing and Conducting Mixed Methods Research (3rd edn). <https://collegepublishing.sagepub.com/products/designing-and-conducting-mixed-methods-research-3-241842>

Creswell, J. W., & Poth, C. N. (2018). Qualitative Inquiry and Research Design: Choosing among Five Approaches. SAGE Publications. <https://uk.sagepub.com/en-gb/eur/qualitative-inquiry-and-research-design/book266033>

Csedő Z., Gábor P., & Máté Z. (2021). Az innovációs tudáshálózatok a felsőoktatásban: egy power-to-gas innovációs ökoszisztéma fejlődésnek tapasztalatai. *Pro Publico Bono – Magyar Közigazgatás*, 9(3), 6–31. <https://doi.org/10.32575/ppb.2021.3.1>

Csedo, Z., Kovacs, K., & Zavarko, M. (2017). How does Digitalization Affect Change Management: Empirical Research at an Innovative Industrial Group. *European Journal of Business and Management*, 9(36), 1–5.

Csedő, Z., Magyari, J., & Zavarkó, M. (2022). Dynamic Corporate Governance, Innovation, and Sustainability: Post-COVID Period. *Sustainability*, 14(6), 3189. <https://doi.org/10.3390/su14063189>

Csedő, Z., Zavarkó, M., & Sára, Z. (2018). A vállalati innováció által indukált szervezeti változások a magyar energiaszektorban. *Vezetéstudomány - Budapest Management Review*, 49(2), 53–62.

Csedő, Z., Zavarkó, M., & Sára, Z. (2019). Innováció-e a digitalizáció? A digitális transzformáció és az innovációmenedzsment tanulságai egy pénzügyi szolgáltatónál. *Vezetéstudomány - Budapest Management Review*, 50(7–8), 88–101.

Cserti, R. (2024, February 14). What is the train-the-trainer model? SessionLab. <https://www.sessionlab.com/blog/train-the-trainer-model/>

Daly, B., Brawley, O. W., Gospodarowicz, M. K., Olopade, O. I., Fashoyin-Aje, L., Smart, V. W., Chang, I.-F., Tendler, C. L., Kim, G., Fuchs, C. S., Beg, M. S., Zhang, L., Legos, J. J., Duran, C. O., Kalidas, C., Qian, J., Finnegan, J., Pilarski, P., Keane, H., ... Li, B. T. (2024). Remote Monitoring and Data Collection for Decentralized Clinical Trials. *JAMA Network Open*, 7(4), e246228. <https://doi.org/10.1001/jamanetworkopen.2024.6228>

D'Arcy Hart, P. (1999). A change in scientific approach: From alternation to randomised allocation in clinical trials in the 1940s. *BMJ (Clinical Research Ed.)*, 319(7209), 572–573. <https://doi.org/10.1136/bmj.319.7209.572>

DayOne. (2025, May 28). How digital tools can maximize sustainability in clinical trials. DayOne. <https://www.dayone.swiss/blog-post/how-digital-tools-can-maximize-sustainability-in-clinical-trials/>

de Bruin, A., Masullo, J., Sine, S., & Getz, K. (2025). Promoting Diversity through an Understanding of Barriers and Drivers for Inclusive Clinical Trials. *Therapeutic Innovation & Regulatory Science*. <https://doi.org/10.1007/s43441-025-00751-9>

de Jong, A. J., Zuidgeest, M. G. P., Santa-Ana-Tellez, Y., de Boer, A., & Gardarsdottir, H. (2024). Regulatory readiness to facilitate the appropriate use of innovation in clinical trials: The case of decentralized clinical trial approaches. *Drug Discovery Today*, 29(11), 104180. <https://doi.org/10.1016/j.drudis.2024.104180>

De Sario Velasquez, G. D., Borna, S., Maniaci, M. J., Coffey, J. D., Haider, C. R., Demaerschalk, B. M., & Forte, A. J. (2024). Economic Perspective of the Use of Wearables in Health Care: A Systematic Review. *Mayo Clinic Proceedings: Digital Health*, 2(3), 299–317. <https://doi.org/10.1016/j.mcpdig.2024.05.003>

Deutsch, N., & Berényi, L. (2023). Technology and Strategy: Towards Strategic Techno-Management. *Theory, Methodology, Practice – Review of Business and Management*, 19(01), 41–51. <https://doi.org/10.18096/TMP.2023.01.04>

Deutsch N., Hoffer I., Berényi L., & Nagy-Borsy V. (2019). A technológia szerepének stratégiai felértékelődése. Corvinus University of Budapest. http://unipub.lib.uni-corvinus.hu/http://unipub.lib.uni-corvinus.hu/4081/1/Deutsch_Hoffer_konyv.pdf

DiMasi, J. A., Grabowski, H. G., & Hansen, R. W. (2016). Innovation in the pharmaceutical industry: New estimates of R&D costs. *Journal of Health Economics*. <https://doi.org/10.1016/J.JHEALECO.2016.01.012>

DiMasi, J. A., Smith, Z., Oakley-Girvan, I., Mackinnon, A., Costello, M., Tenaerts, P., & Getz, K. A. (2023). Assessing the Financial Value of Decentralized Clinical Trials. *Therapeutic Innovation & Regulatory Science*, 57(2), 209–219. <https://doi.org/10.1007/s43441-022-00454-5>

Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the Approximation of the Laws, Regulations and Administrative Provisions of the Member States Relating to the Implementation of Good Clinical Practice in the Conduct of Clinical Trials on Medicinal Products for Human Use (2001). <https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX%3A02001L0020-20090807>

Directive 2001/83 of the European Parliament and of the Council of 6 November 2001 on the Community Code Relating to Medicinal Products for Human Use (2001). <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A02001L0083-20250101>

Directive 2005/28/EC of 8 April 2005 Laying down Principles and Detailed Guidelines for Good Clinical Practice as Regards Investigational Medicinal Products for Human Use, as Well as the Requirements for Authorisation of the Manufacturing or Importation of Such Products (2005). <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32005L0028>

docs24. (n.d.). Guidance on Environmental Impact Mitigation in Decentralized Clinical Trials. Retrieved <chrome-extension://efaidnbmnnnibpcajpgclclefindmkaj/https://docs24.co.uk/wp-content/uploads/2024/07/Guidance-on-Environmental-Impact-Mitigation-in-Decentralized-Clinical-Trials.pdf>

Dodgson, S. (2006). The evolution of clinical trials. *The Journal of the European Medical Writers Association*, Vol 15.(No 1.). https://www.researchgate.net/publication/242561119_The_evolution_of_clinical_trials

Ebenso, B., Namisango, E., Abejirinde, I.-O., & Allsop, M. J. (2025). Editorial: The scale-up and sustainability of digital health interventions in low- and middle-income settings. *Frontiers in Digital Health*, 7, 1634223. <https://doi.org/10.3389/fdgth.2025.1634223>

EFPIA. (2022, October 24). 60,000 fewer clinical trial places for Europeans, despite global surge in research projects. <https://www.efpia.eu/news-events/the-efpia-view/statements-press-releases/60-000-fewer-clinical-trial-places-for-europeans-despite-global-surge-in-research-projects/>

Ernstmeyer, K., & Christman, E. (2023). Pharmacokinetics & Pharmacodynamics. In *Nursing Pharmacology* [Internet]. 2nd edition. Chippewa Valley Technical College. (PMID: 37748008). <https://www.ncbi.nlm.nih.gov/books/NBK595006/>

European Commission. (n.d.-a). Clinical trials—Regulation EU No 536/2014. Retrieved https://health.ec.europa.eu/medicinal-products/clinical-trials/clinical-trials-regulation-eu-no-5362014_en

European Commission. (n.d.-b). EudraLex—Volume 10—Clinical trials guidelines. Retrieved https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-that-will-be-authorised-under-regulation-eu-no-5362014-once-it-becomes-applicable

European Commission. (2012). Proposal for a Regulation of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC. <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex:52012PC0369>

European Commission. (2022, December 14). Recommendation paper on decentralised elements in clinical trials. https://health.ec.europa.eu/latest-updates/recommendation-paper-decentralised-elements-clinical-trials-2022-12-14_en

European Commission. (2025, October 30). New and updated documents—EudraLex Volume 10: Clinical trials guidelines. https://health.ec.europa.eu/latest-updates/new-and-updated-documents-eudralex-volume-10-clinical-trials-guidelines-2025-10-30_en

European Commission, European Medicines Agency, & Heads of Medicines Agencies. (2022, August). ACT EU multi-annual Workplan 2022-2026. https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/accelerating-clinical-trials-eu-act-eu-delivering-eu-clinical-trials-transformation-initiative_en.pdf

European Commission, European Medicines Agency, & Heads of Medicines Agencies. (2023, November). ACT EU workplan for 2023-2026. https://accelerating-clinical-trials.europa.eu/newsroom/news/act-eu-workplan-2023-2026-published-2023-11-10_en

European Commission, European Medicines Agency, & Heads of Medicines Agencies. (2024). ACT EU workplan for 2025-2026. https://accelerating-clinical-trials.europa.eu/newsroom/news/act-eu-workplan-2025-2026-published-2025-01-20_en

European Medicines Agency. (2013, April 9). European Medicines Agency publishes report on patient recruitment and geographical location of clinical trials | European Medicines Agency (EMA). <https://www.ema.europa.eu/en/news/european-medicines-agency-publishes-report-patient-recruitment-geographical-location-clinical-trials>

European Medicines Agency. (2020, June 29). Implications of coronavirus disease (COVID-19) on methodological aspects of ongoing clinical trials—Scientific guideline. <https://www.ema.europa.eu/en/implications-coronavirus-disease-covid-19-methodological-aspects-ongoing-clinical-trials-scientific-guideline>

European Medicines Agency. (2022a, February 10). Updated document—Guidance on the management of clinical trials during the COVID-19 (Coronavirus) pandemic. https://health.ec.europa.eu/latest-updates/updated-document-guidance-management-clinical-trials-during-covid-19-coronavirus-pandemic-2022-02-10_en

European Medicines Agency. (2022b, May 23). Questions and answers—Complex clinical trials. https://health.ec.europa.eu/latest-updates/questions-and-answers-complex-clinical-trials-2022-06-02_en

European Medicines Agency (Director). (2022c, October 31). ACT EU multi stakeholder workshop on Decentralised Clinical Trials [[Video]]. <https://www.youtube.com/watch?app=desktop&v=QUGmhHmjGh4>

European Medicines Agency. (2025, July 23). ICH E6(R3) Guideline on good clinical practice (GCP). <https://www.ema.europa.eu/en/ich-e6-good-clinical-practice-scientific-guideline>

European Medicines Agency. (2026). Report to monitor the European clinical trials environment. https://accelerating-clinical-trials.europa.eu/documents_en?f%5B0%5D=document_title%3Amonitor&f%5B1%5D=priority_actions_priority_actions%3A2

European Medicines Agency, & Heads of Medicines Agencies. (2015, March 31). European medicines agencies network strategy (EMANS). <https://www.ema.europa.eu/en/about-us/how-we-work/european-medicines-regulatory-network/european-medicines-agencies-network-strategy>

Exemplars In Global Health. (n.d.). What are the core challenges of scaling and sustaining digital health interventions? Retrieved 3 April 2026, from <https://www.exemplars.health/topics/digital-health/what-are-the-core-challenges-of-scaling-and-sustaining-digital-health-interventions>

Fehérváry, I. A., Stubnya, G. R., & Pörzse, G. F. (2024). Enhancing National Clinical Trials Ecosystems: The Examples of Hungary and Spain. *Kaleidoscope History*, 14(29), 471–485. <https://doi.org/10.17107/KH.2024.29.52>

Fetters, M. D., Curry, L. A., & Creswell, J. W. (2013). Achieving integration in mixed methods designs-principles and practices. *Health Services Research*, 48(6 Pt 2), 2134–2156. <https://doi.org/10.1111/1475-6773.12117>

Fu, Z., Liu, X., Zhao, S., Yuan, Y., & Jiang, M. (2023). Reducing Clinical Trial Monitoring Resources and Costs With Remote Monitoring: Retrospective Study Comparing On-Site

Versus Hybrid Monitoring. *Journal of Medical Internet Research*, 25(1), e42175. <https://doi.org/10.2196/42175>

Gallese, C. (2024). The Risks of Health Data Commodification in the EU Digital Market. *Yearbook of Antitrust and Regulatory Studies*, 17, 89–126. <https://doi.org/10.7172/1689-9024.YARS.2024.17.29.3>

Gassmann, O., Enkel, E., & Chesbrough, H. (2010). The future of open innovation. *R&D Management*, 40(3), 213–221. <https://doi.org/10.1111/j.1467-9310.2010.00605.x>

Geels, F. W. (2002). Technological transitions as evolutionary reconfiguration processes: A multi-level perspective and a case-study. *Research Policy*, NELSON + WINTER + 20, 31(8), 1257–1274. [https://doi.org/10.1016/S0048-7333\(02\)00062-8](https://doi.org/10.1016/S0048-7333(02)00062-8)

Geels, F. W. (2011). The multi-level perspective on sustainability transitions: Responses to seven criticisms. *Environmental Innovation and Societal Transitions*, 1(1), 24–40. <https://doi.org/10.1016/j.eist.2011.02.002>

Gefenas, E., Cekanauskaite, A., Lekstutiene, J., & Lukaseviciene, V. (2017). Application challenges of the new EU Clinical Trials Regulation. *European Journal of Clinical Pharmacology*, 73(7), 795–798. <https://doi.org/10.1007/s00228-017-2267-6>

Gomez, M. B., Joel. (2023, November 20). Integrating healthcare apps and data with FHIR + HL7 | IBM. <https://www.ibm.com/think/insights/hl7-fhir-integration>

Guest, G., Bunce, A., & Johnson, L. (2006). How Many Interviews Are Enough? An Experiment with Data Saturation and Variability. *Field Methods*, Volume 18(Issue 1), 59–82. <https://doi.org/https://doi.org/10.1177/1525822X052799>

Hariton, E., & Locascio, J. J. (2018). Randomised controlled trials—The gold standard for effectiveness research. *BJOG: An International Journal of Obstetrics and Gynaecology*, 125(13), 1716. <https://doi.org/10.1111/1471-0528.15199>

Harmon, D. M., Noseworthy, P. A., & Yao, X. (2023). The Digitization and Decentralization of Clinical Trials. *Mayo Clinic Proceedings*. <https://doi.org/10.1016/j.mayocp.2022.10.001>

Hinkson, I. V., Madej, B., & Stahlberg, E. A. (2020). Accelerating Therapeutics for Opportunities in Medicine: A Paradigm Shift in Drug Discovery. *Frontiers in Pharmacology*, 11, 770. <https://doi.org/10.3389/fphar.2020.00770>

Hummel, J. P., Leipold, R. J., Amorosi, S. L., Bao, H., Deger, K. A., Jones, P. W., Kansal, A. R., Ott, L. S., Stern, S., Stein, K., Curtis, J. P., & Akar, J. G. (2019). Outcomes and costs of remote patient monitoring among patients with implanted cardiac defibrillators: An economic model based on the PREDICT RM database. *Journal of Cardiovascular Electrophysiology*, 30(7), 1066–1077. <https://doi.org/10.1111/jce.13934>

Integra IT. (2022, August 26). Achieving Interoperability Between Clinical Trials Software. <https://www.integrat.co/achieving-interoperability-between-clinical-trials-software/>

IntuitionLabs. (n.d.). Clinical Trial Start-Up Costs: A Breakdown & Benchmarks. IntuitionLabs. Retrieved 17 January 2026, from <https://intuitionlabs.ai/articles/clinical-trial-start-up-costs>

IQVIA. (2022a). DCTs Deliver Big ROI. <https://www.iqvia.com/library/white-papers/dcts-deliver-big-roi>

IQVIA. (2022b, September 7). New IQVIA Study Demonstrates Cost and Time Savings of Decentralized Trials. <https://www.iqvia.com/newsroom/2022/09/new-iqvia-study-demonstrates-cost-and-time-savings-of-decentralized-trials>

Jean-Louis, G., & Seixas, A. A. (2024). The value of decentralized clinical trials: Inclusion, accessibility, and innovation. *Science*, 385(6711), eadq4994. <https://doi.org/10.1126/science.adq4994>

Jiang, Y., Leng, Y., Wu, Q., Hou, Y., Dong, X., Zeng, C., Wu, D., Fang, H., Tang, Y., Huang, H., & Li, N. (2025). Understanding the gap between expectations and reality in decentralized clinical trials. *Npj Digital Medicine*, 8(1), 408. <https://doi.org/10.1038/s41746-025-01811-y>

Johnson, R. B., Onwuegbuzie, A. J., & Turner, L. A. (2007). Toward a Definition of Mixed Methods Research. *Journal of Mixed Methods Research*, Volume 1(Issue 2), 112–133.

Jong, A. J., Rijssel, T. I., Zuidgeest, M. G. P., Thiel, G. J. M. W., Askin, S., Fons-Martínez, J., Smedt, T. D., Boer, A., Santa-Ana-Tellez, Y., Gardarsdottir, H., & Consortium, the T. (2022). Opportunities and Challenges for Decentralized Clinical Trials: European Regulators' Perspective. *Clinical Pharmacology & Therapeutics*, 112(2), 344–352. <https://doi.org/10.1002/cpt.2628>

Joshi, A., Kale, S., Chandel, S., & Pal, D. K. (2015). Likert Scale: Explored and Explained. *Current Journal of Applied Science and Technology*, 396–403. <https://doi.org/10.9734/BJAST/2015/14975>

Kaló, Z., Petrova, G., Németh, B., Bonča, P. D., Delnoij, D., Bennett, A., Tachkov, K., Zhang, Y., Kreif, N., Knies, S., Lipska, I., Tesar, T., Mitkova, Z., Ponten, J., Viberg, A., Paveliu, M.-S., Piniaskho, O., Turcu-Stiolica, A., Doležal, T., ... Manca, A. (2026). Transferability of Real World Evidence to Support HTA Recommendations in Lower Income European Countries. *Health Science Reports*, 9(2), e71534. <https://doi.org/10.1002/hsr2.71534>

Kaló, Z., Petykó, Z. I., Fricke, F.-U., Maniadakis, N., Tesař, T., Podrazilová, K., Espin, J., & Inotai, A. (2021). Development of a core evaluation framework of value-added medicines: Report 2 on pharmaceutical policy perspectives. *Cost Effectiveness and Resource Allocation: C/E*, 19(1), 42. <https://doi.org/10.1186/s12962-021-00296-2>

Kamusheva, M., Németh, B., Zemplényi, A., Kaló, Z., Elvidge, J., Dimitrova, M., Pontén, J., Tachkov, K., & Mitkova, Z. (2022). Using real-world evidence in healthcare from Western to Central and Eastern Europe: A review of existing barriers. *Journal of Comparative Effectiveness Research*, 11(12), 905–913. <https://doi.org/10.2217/cer-2022-0065>

Keserű G. M. (2015). A gyógyszerkutatás kémiája. Akadémiai Kiadó. https://mersz.hu/dokumentum/gyogysz__43/

Kijewski, S., McBride, C., Owens, E., Bernheim, E., & Vayena, E. (2026). Decentralized clinical trials: A comprehensive analysis of trends, technologies, and global challenges. *PLOS Digital Health*, 5(1), e0001191. <https://doi.org/10.1371/journal.pdig.0001191>

King, S., Trabanino, S., Azizi, Z., & Rodriguez, F. (2024). Leveraging Social Determinants of Health to Enhance Recruitment of Underrepresented Populations in Clinical Trials. *Methodist DeBakey Cardiovascular Journal*, 20(5), 81–88. <https://doi.org/10.14797/mdcvj.1447>

Kohl, S. H., & Schmidt-Lucke, C. (2023). Clinical trials to go green—A sustainable argument for decentralised digital clinical trials. *PLOS Digital Health*, 2(10), e0000366. <https://doi.org/10.1371/journal.pdig.0000366>

Krenyácz, E., & Révész, É. E. (2025). Consequences of centralized healthcare systems: Changing role and autonomy of hospital managers – insights from a Hungarian case. *Journal of Health Organization and Management*, Vol. 39(No. 9 pp.), 177–191. <https://doi.org/https://doi.org/10.1108/JHOM-08-2024-0358>

Kvale, S. (1996). *InterViews: An Introduction to Qualitative Research Interviewing*. SAGE Publications.

Laurent, A. (2026, April 3). Decentralized Clinical Trials (DCTs): How They Work & Benefits. IntuitionLabs. <https://intuitionlabs.ai/articles/decentralized-clinical-trials-guide>

Ledesma, P. (2024, January 12). How an EDC System Saves Costs in Clinical Trials. Klindat. <https://klindat.com/how-an-edc-system-saves-costs-in-clinical-trials/>

Likert. (1932). A technique for the measurement of attitudes—National Library of Medicine Institution. The Science Press. https://catalog.nlm.nih.gov/discovery/fulldisplay/alma9916816193406676/01NLM_INST:01NLM_INST

Lo, B., Field, M. J., & Institute of Medicine (US) Committee on Conflict of Interest in Medical Research, E. (2009). *The Pathway from Idea to Regulatory Approval: Examples for Drug Development. In Conflict of Interest in Medical Research, Education, and Practice*. National Academies Press (US). <https://www.ncbi.nlm.nih.gov/books/NBK22930/>

Mackillop, N., Shah, J., Collins, M., Costelloe, T., & Öhman, D. (2023). Carbon footprint of industry-sponsored late-stage clinical trials. <https://doi.org/10.1136/bmjopen-2023-072491>

Magyarországi Klinikai Vizsgálatszervezők Társasága. (n.d.). Klinikai vizsgálati fázisok [Text]. mkvt.hu. MKVT. Retrieved 6 October 2025, from <https://mkvt.hu/betegeknek/mi-a-klinikai-vizsgalat-klinikai-vizsgalati-fazisok>

Malik, S., Dorothea, Z. P., Argyropoulos, C. D., Themistocleous, S., Macken, A. J., Valdenmaier, O., Scheckenbach, F., Bardach, E., Pfeiffer, A., Loens, K., Ochando, J. C., Cornely, O. A., Demotes-Mainard, J., Contrino, S., & Felder, G. (2025). Data Interoperability in COVID-19 Vaccine Trials: Methodological Approach in the VACCELERATE Project. *JMIR Medical Informatics*, 13, e65590. <https://doi.org/10.2196/65590>

Malone, S., Prewitt, K., Hackett, R., Lin, J. C., McKay, V., Walsh-Bailey, C., & Luke, D. A. (2021). The Clinical Sustainability Assessment Tool: Measuring organizational capacity to

promote sustainability in healthcare. *Implementation Science Communications*, 2(1), 77. <https://doi.org/10.1186/s43058-021-00181-2>

Mayor, S. (2011). EU must reform clinical trial regulation, warn medical research bodies. *BMJ*, 343(sep28 1), d6215. <https://doi.org/10.1136/bmj.d6215>

Miles, M. B., Huberman, A. M., & Saldana, J. (2014). *Qualitative Data Analysis: A Methods Sourcebook*. SAGE Publications. <https://www.scirp.org/reference/referencespapers?referenceid=1977773>

Millstone Medical, i. (2025, March 10). What Is the Price of Developing Medical Devices? Millstone Medical. <https://millstonemedical.com/resources/blog/what-is-the-price-of-developing-medical-devices>

Moore, J., Goodson, N., Wicks, P., & Reites, J. (2022). What role can decentralized trial designs play to improve rare disease studies? *Orphanet Journal of Rare Diseases*. <https://doi.org/10.1186/s13023-022-02388-5>

Móricz, P., Marciniak, R., & Baksa, M. (2022). Excellence and Renewal: Digital Transformation Patterns in the Hungarian Business Services Sector. *Vezetéstudomány / Budapest Management Review*, 53(5), 32–44. <https://doi.org/10.14267/VEZTUD.2022.05.03>

Moseson, H., Kumar, S., & Juusola, J. L. (2020). Comparison of study samples recruited with virtual versus traditional recruitment methods. *Contemporary Clinical Trials Communications*, 19, 100590. <https://doi.org/10.1016/j.conctc.2020.100590>

Nag, S., Baidya, A. T. K., Mandal, A., Mathew, A. T., Das, B., Devi, B., & Kumar, R. (2022). Deep learning tools for advancing drug discovery and development. *3 Biotech*, 12(5), 110. <https://doi.org/10.1007/s13205-022-03165-8>

Nair, B. (2019). Clinical Trial Designs. *Indian Dermatology Online Journal*, 10(2), 193–201. https://doi.org/10.4103/idoj.IDOJ_475_18

Németh, B., Goettsch, W., Kristensen, F. B., Piniashko, O., Huić, M., Tesař, T., Atanasijevic, D., Lipska, I., & Kaló, Z. (2020). The transferability of health technology assessment: The European perspective with focus on central and Eastern European countries. *Expert Review of Pharmacoeconomics & Outcomes Research*, 20(4), 321–330. <https://doi.org/10.1080/14737167.2020.1779061>

Németh, B., Kamusheva, M., Mitkova, Z., Petykó, Z. I., Zemplényi, A., Dimitrova, M., Tachkov, K., Balkányi, L., Czech, M., Dawoud, D., Goettsch, W., Hren, R., Knies, S., Lorenzovici, L., Maravic, Z., Piniashko, O., Zerovnik, S., & Kaló, Z. (2023). Guidance on using real-world evidence from Western Europe in Central and Eastern European health policy decision making. *Journal of Comparative Effectiveness Research*, 12(4), e220157. <https://doi.org/10.57264/cer-2022-0157>

NNGYK. (2023). Forgalmába hozatali engedélyezés. Országos Gyógyszerészeti és Élelmezés-egészségügyi Intézet. https://ogyei.gov.hu/forgalomba_hozatal

Noy, C. (2008). Sampling Knowledge: The Hermeneutics of Snowball Sampling in Qualitative Research. *International Journal of Social Research Methodology*, Vol 11(No 4). <https://doi.org/https://doi.org/10.1080/13645570701401305>

Nurmsoo, S., & Hayes, M. (2015). Awareness of risks of biobank research may affect public attitudes toward consent. *Journal of Community Genetics*, 6(2), 181–182. <https://doi.org/10.1007/s12687-015-0215-7>

Orosz, É. (2006). Egészségügy: Kihívások és lehetséges válaszok. In *A társadalmi kohézió erősítése*. (pp. 190–220). Új Mandátum Könyvkiadó (UMK).

Orosz É. (2022). Miért buktak el a szervezeti innovációk a magyar egészségügyben? *ESÉLY: TÁRSADALOM ÉS SZOCIÁLPOLITIKAI FOLYÓIRAT*, 33(1), 3–39.

Otte, A., Maier-Lenz, H., & Dierckx, R. A. (2005). Good clinical practice: Historical background and key aspects. *Nuclear Medicine Communications*, 26(7), 563–574. <https://doi.org/10.1097/01.mnm.0000168408.03133.e3>

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., ... Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ*, 372, n71. <https://doi.org/10.1136/bmj.n71>

Palinkas, L. A., Horwitz, S. M., Green, C. A., Wisdom, J. P., Duan, N., & Hoagwood, K. (2015). Purposeful sampling for qualitative data collection and analysis in mixed method implementation research. *Administration and Policy in Mental Health*, 42(5), 533–544. <https://doi.org/10.1007/s10488-013-0528-y>

Park, J. J. H., Sharif, B., Harari, O., Dron, L., Heath, A., Meade, M., Zarychanski, R., Lee, R., Tremblay, G., Mills, E. J., Jemai, Y., Mehta, C., & Wathen, J. K. (2022). Economic Evaluation of Cost and Time Required for a Platform Trial vs Conventional Trials. *JAMA Network Open*, 5(7), e2221140. <https://doi.org/10.1001/jamanetworkopen.2022.21140>

Patton, M. Q. (2015). Sampling, Qualitative (Purposeful). In *The Blackwell Encyclopedia of Sociology*. John Wiley & Sons, Ltd. <https://doi.org/10.1002/9781405165518.wbeoss012.pub2>

PharmaOnline. (2024, July 30). Uniós szabályozás: Biztonságosabb és átláthatóbb klinikai vizsgálatok. Pharma Online. <https://pharmaonline.hu/cikk/kutatas/unios-szabalyozas-biztonsagosabb-es-atlathatobb-klinikai-vizsgalatok>

Polhemus, A. M., Kadhim, H., Barnes, S., Zebrowski, S. E., Simmonds, A., Masand, S. N., Banner, J., & Dupont, M. (2018). Accelerating Adoption of Patient-Facing Technologies in Clinical Trials: A Pharmaceutical Industry Perspective on Opportunities and Challenges. *Therapeutic Innovation & Regulatory Science*, 53(1), 8–24. <https://doi.org/10.1177/2168479018801566>

Pörzse, G., Csedő, Z., & Zavarkó, M. (2021). Disruption Potential Assessment of the Power-to-Methane Technology. *Energies*, 14(8), 2297. <https://doi.org/10.3390/en14082297>

Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the Protection of Natural Persons with Regard to the Processing of Personal Data and on the Free Movement of Such Data, 119 OJ L (2016). <http://data.europa.eu/eli/reg/2016/679/oj>

Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on Medical Devices (2017). <https://eur-lex.europa.eu/eli/reg/2017/745/oj/eng>

Regulation (EU) 2025/327. (2025). Regulation (EU) 2025/327 of the European Parliament and of the Council of 11 February 2025 on the European Health Data Space. https://eur-lex.europa.eu/legal-content/HU/TXT/?uri=OJ:L_202500327

Resnik, D. B. (n.d.). Research Ethics Timeline. National Institute of Environmental Health Sciences. Retrieved 26 October 2025, from <https://www.niehs.nih.gov/research/resources/bioethics/timeline>

Richter Gedeon Nyrt. (2025, September 17). Pontosan 10 éve kapta meg az FDA engedélyét a Richter originális készítménye, a cariprazine. [gedeonrichter.com. https://www.gedeonrichter.com/hu-hu/media/250917](https://www.gedeonrichter.com/hu-hu/media/250917)

Rodriguez-Chavez, I. R. (2021, March 29). Linking Regulations with Diversity, Inclusion, and New Opportunities in Decentralized Clinical Trials. DIA Global Forum. <https://globalforum.diaglobal.org/issue/april-2021/linking-regulations-with-diversity-inclusion-and-new-opportunities-in-decentralized-clinical-trials/>

Rosa, C., Marsch, L. A., Winstanley, E. L., Brunner, M., & Campbell, A. N. C. (2021). Using digital technologies in clinical trials: Current and future applications. *Contemporary Clinical Trials*, 100, 106219. <https://doi.org/10.1016/j.cct.2020.106219>

Saldana, J. (2016). *The Coding Manual for Qualitative Researchers*. SAGE Publications. <https://www.scirp.org/reference/referencespapers?referenceid=3154174>

Santa-Ana-Tellez, Y., Lagerwaard, B., de Jong, A. J., Gardarsdottir, H., Grobbee, D. E., Hawkins, K., Heath, M., & Zuidgeest, M. G. P. (2023). Decentralised, patient-centric, site-less, virtual, and digital clinical trials? From confusion to consensus. *Drug Discovery Today*, 28(4), 103520. <https://doi.org/10.1016/j.drudis.2023.103520>

Saunders, B., Sim, J., Kingstone, T., Baker, S., Waterfield, J., Bartlam, B., Burroughs, H., & Jinks, C. (2018). Saturation in qualitative research: Exploring its conceptualization and operationalization. *Quality & Quantity*, 52(4), 1893–1907. <https://doi.org/10.1007/s11135-017-0574-8>

SciencePharma. (n.d.). The History of Clinical Trials. SciencePharma. Retrieved 3 August 2025, from <https://www.sciencepharma.com/blog/changing-face-of-clinical-trials-history/>

Semmelweis Egyetem. (n.d.). A klinikai vizsgálatok fázisai. Retrieved 12 February 2025, from <https://semmelweis.hu/klinikai-vizsgalatok/a-vizsgalatokrol/a-klinikai-vizsgalatok-fazisai/>

Sertkaya, A., Beleche, T., Jessup, A., & Sommers, B. D. (2024). Costs of Drug Development and Research and Development Intensity in the US, 2000-2018. *JAMA Network Open*. <https://doi.org/10.1001/jamanetworkopen.2024.15445>

Shah, J., Rajgor, D., Pradhan, S., McCready, M., Zaveri, A., & Pietrobon, R. (2010). Electronic Data Capture for Registries and Clinical Trials in Orthopaedic Surgery: Open Source versus Commercial Systems. *Clinical Orthopaedics and Related Research*, 468(10), 2664–2671. <https://doi.org/10.1007/s11999-010-1469-3>

Simmons, L. A., Phipps, J. E., Whipps, M., Smith, P., Carbajal, K. A., Overstreet, C., McLaughlin, J., De Lombaert, K., & Noonan, D. (2022). From hybrid to fully remote clinical trial amidst the COVID-19 pandemic: Strategies to promote recruitment, retention, and engagement in a randomized mHealth trial. *Digital Health*, 8, 20552076221129065. <https://doi.org/10.1177/20552076221129065>

Sinha, S. D., Chary Sriramadasu, S., Raphael, R., & Roy, S. (2024). Decentralisation in Clinical Trials and Patient Centricity: Benefits and Challenges. *Pharmaceutical Medicine*, 38(2), 109–120. <https://doi.org/10.1007/s40290-024-00518-x>

Sparks, J. (2002). Timeline of laws related to the protection of human subjects. Office of History, National Institutes of Health. history.nih.gov/about/timelines_laws_human.html

Stern, A. D., & Trusheim, M. (2024). Transformation of the Clinical Trial Enterprise: Lessons Learned from the COVID-19 Pandemic: Final Report. Office of the Assistant Secretary for Planning and Evaluation (ASPE). <http://www.ncbi.nlm.nih.gov/books/NBK609006/>

Sustainable Carbon Coalition. (2026). iLCCT Calculator. <https://clinicaltrialcarbon.org/>

Szent Biblia. (n.d.). Magyar Bibliatársulat újfordítású Bibliája (1990)—Mózes első könyve—1Móz 1,29. Retrieved 13 January 2025, from <https://szentiras.hu/biblia/ruf/1m%C3%B3z/1,29>

Tambe, A. R. (2025). Digital transformation of clinical research: Facilitating decentralized clinical trials in India. *International Journal of Clinical Trials*, 12(3), 262–269. <https://doi.org/10.18203/2349-3259.ijct20252205>

Teece, D. J. (2007). Explicating dynamic capabilities: The nature and microfoundations of (sustainable) enterprise performance. *Strategic Management Journal*, 28(13), 1319–1350. <https://doi.org/10.1002/smj.640>

Teece, D. J. (2018). Business models and dynamic capabilities. *Long Range Planning*, 51(1), 40–49. <https://doi.org/10.1016/j.lrp.2017.06.007>

Tenti, E., Basile, G., Giorgetti, C., Sangiorgi, D., Mikus, E., Sebastiani, G., Bolcato, V., Tronconi, L. P., & Tremoli, E. (2025). Decentralized Clinical Trials: Governance, Ethics and Medico-Legal Issues for the New Paradigm of Research with a Focus on Cardiovascular Field. *Medical Sciences*, 13(4), 222. <https://doi.org/10.3390/medsci13040222>

Tornatzky, L. G., & Fleischer, M. (1990). *Technological Innovation as a Process*. Lexington Books.

Twyman, R. (2004). A brief history of clinical trials. *The Human Genome*. 2004. Sep. http://genome.wellcome.ac.uk/doc_WTD020948.html

United Nations. (2015). *Transforming our world: The 2030 Agenda for Sustainable Development*. Department of Economic and Social Affairs. <https://sdgs.un.org/2030agenda>

U.S. Department of Health, Education, and Welfare, O. for H. R. (1979, April 18). The Belmont Report: Ethical principles and guidelines for the protection of human subjects of research [Page]. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. <https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html>

Vayena, E., Blasimme, A., & Sugarman, J. (2023). Decentralised clinical trials: Ethical opportunities and challenges. *The Lancet. Digital Health*, 5(6), e390–e394. [https://doi.org/10.1016/S2589-7500\(23\)00052-3](https://doi.org/10.1016/S2589-7500(23)00052-3)

Wang, H., Daizadeh, N., Shen, Y., Chen, J., Rockhold, F. W., Pang, H., & Lee, H. (2025). Decentralized Clinical Trials in the Era of Real-World Evidence: A Critical Assessment of Recent Experiences. *Clinical and Translational Science*, 18(9), e70328. <https://doi.org/10.1111/cts.70328>

Wax, P. M. (1995). Elixirs, diluents, and the passage of the 1938 Federal Food, Drug and Cosmetic Act. *Annals of Internal Medicine*, 122(6), 456–461. <https://doi.org/10.7326/0003-4819-122-6-199503150-00009>

Weber, K. (2021, November 11). Decentralized or Traditional? Clinical Trials in Comparison. <https://climedo.de/en/blog/decentralized-or-traditional-clinical-trials-in-comparison/>

Weiner, B. J. (2009). A theory of organizational readiness for change. *Implementation Science*, 4(1), 67. <https://doi.org/10.1186/1748-5908-4-67>

Westra, A. E., Bos, W., & Cohen, A. F. (2014). New EU clinical trials regulation. *BMJ : British Medical Journal*, 348(jun05 6), g3710. <https://doi.org/10.1136/bmj.g3710>

World Bank Group. (n.d.). Middle Income Countries. Retrieved 2 May 2026, from <https://www.worldbank.org/ext/en/region/mic>

World Health Organization. (2020). Global strategy on digital health 2020-2027. <https://www.who.int/publications/i/item/9789240116870>

World Medical Association. (2016, October 22). Declaration of Taipei on Ethical Considerations regarding Health Databases and Biobanks. <https://www.wma.net/policies-post/wma-declaration-of-taipei-on-ethical-considerations-regarding-health-databases-and-biobanks/>

World Medical Association. (2024, October 19). WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects – WMA – The World Medical Association. <https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/>

Yang, A. (2025, March 27). Regulatory Opportunities for Decentralized Clinical Trials: Insights from the SHASTA Project. DIA Global Forum. <https://globalforum.diaglobal.org/issue/april-2025/regulatory-opportunities-for-decentralized-clinical-trials-insights-from-the-shasta-project/>

Zhang, D. S., Millet, L., Bellows, B. K., Lee, S., & Mann, D. (2025). Program Cost and Return on Investment of a Remote Patient Monitoring Program for Hypertension Management. medRxiv, 2025.01.29.25321334. <https://doi.org/10.1101/2025.01.29.25321334>

Acknowledgements

I would like to take this opportunity to thank everyone who contributed to the completion of this doctoral thesis through their support, professional assistance and encouragement.

First and foremost, I am deeply grateful **to my family**, who provided childcare and thus created the peaceful working conditions necessary for my research. Their patience, understanding and constant emotional support saw me through the long and often demanding period of my doctoral research. Without their encouragement and unconditional support, this work could not have been completed.

I would like to express my heartfelt thanks **to my supervisor**, who guided me through the research process with his professional guidance, constructive criticism and consistent support. His reliable professional presence, methodological advice and stimulating questions contributed significantly to the development of the thesis's academic standard and structural coherence.

I am grateful **to my colleagues and professional partners**, who supported the research by sharing their experience in the fields of clinical trials and pharmaceutical practice, and by offering valuable insights through professional discussions and interviews. I am grateful to all those who, through their openness, cooperation and constructive feedback, contributed to establishing and refining the empirical section.

Finally, I would like to thank all my colleagues and lecturers at **the Institute of Strategy and Management** for their help and inspiration; whether through a conversation or a timely piece of advice, they all contributed to the progress of this research.

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Appendices

1. Appendix: Comparative table of the structure of traditional clinical trials and the structure of digital clinical trials

Dimension	Aspect	Traditional clinical trial	Digital clinical trial
Patient access and recruitment	Patient reach	Limited access, dependent on geographical proximity and travel options	Geographically diverse population; patients in rural areas and those with limited mobility can also be included
	Method of inclusion	On-site recruitment, face-to-face interviews; slower recruitment, higher dropout rates	Online registration, digital advertisements, automated/AI-based pre-screening; faster and more cost-effective recruitment
Patient communication and experience	Patient communication	Telephone appointments, face-to-face meetings	Mobile apps, video calls, chat functions
	Patient experience and retention	Time-consuming and travel-intensive, high participation burden	Greater convenience and flexibility, improved satisfaction and retention
On-site and organisational structure	Study sites	Centralised clinical centres, hospitals	decentralised model: patient's home, telemedicine, partially or fully <i>trial-at-home</i>
	Logistics	Transport of samples between sites	Home sampling kits, digital data transmission
Study methodology	Test procedures	Physical examinations, on-site laboratory sampling	Remote monitoring, teleconsultations, wearable devices
Data collection and data management	Data collection	On-site measurements, paper-based CRF or EDC; episodic data points	Continuous or high-frequency data collection (ePRO, DHTs, wearables)
	Data management method	Paper-based documentation, manual data entry	Electronic data collection, cloud-based storage, automated processing
	Data quality	Controlled environment, less frequent measurements; 'white-coat' effect and missing data	More frequent/continuous measurement; fewer missing data points, but risks associated with technical and device variability
Monitoring and safety	Monitoring	Scheduled on-site monitoring visits	Remote monitoring, hybrid or fully virtual model
	Safety assessment	Periodic, pre-planned assessments	Real-time monitoring based on connected devices

Technology infrastructure	Technology used	Core software, limited integration	Integrated platforms (EDC, eCOA, eConsent), wearables, API-based processes
Human resources and costs	Staff	On-site researchers and coordinators	decentralised teams, remote carers, virtual support
	Cost structure	High on-site overheads (infrastructure, staff, monitoring)	Lower site overheads, new cost elements: technology, logistics, remote monitoring
Time dimension	Duration of the study	On average 6-8 years (Phases I-III)	On average 4-6 years (faster recruitment and data processing)
Regulatory environment	Regulatory compliance	Stable, well-established requirements; on-site audits, GCP inspections	Evolving guidelines (FDA, EMA DCT guidance), data protection and IT audit requirements

Source: own compilation

2. Appendix: Factors influencing the sustainability of DCTs

Sustainability category	Key factors	Characteristics
Social / Equity	Patient trust and ethical issues	Trust and transparency in the secure handling of personal and health data.
	Digital access and equality	Ensuring access to devices and the internet; reducing the digital divide.
	Health and digital literacy	The ability of participants and communities to use digital platforms.
	User-friendly design	Influences social acceptance.
	Social determinants, technology provision	Addressing local economic, educational, linguistic and infrastructural disadvantages; providing the means for participation.
Economic	Community engagement, integration	Community partnerships, cultural fit, inclusive recruitment.
	Long-term ROI and operational efficiency	Larger-scale trials have high potential for ROI.
	Scalability	The global and LMIC adaptability of digital solutions.
	Sustainable funding model	Multi-year funding, milestone-based resource allocation.
	Initial technology investments	Significant upfront costs for infrastructure, data security and training.
Infrastructure / Technology	Interoperability and data standards	Uniform, validated, harmonised systems; prevention of fragmentation.
	Digital infrastructure and internet access	Stable network environment, device provisioning, data centre infrastructure.
	Ongoing technical support	Ensuring reliable operation.
	Training and capacity-building needs	Local skills development, long-term training programmes.
Regulatory	Regulatory alignment and harmonisation	Addressing FDA-EMA differences; uniform operational frameworks.
	Data quality assurance	Continuous validation, audits, transparent data flow.
	Transcultural and regional adaptability	Adapting guidelines to demographic and contextual differences.

Environmental	Reducing the carbon footprint	Reducing travel, logistics and administrative burdens, and significantly reducing CO ₂ emissions.
	Logistical trade-off ¹⁴	Home delivery may increase transport emissions; optimisation is required.
	Energy requirements of digital infrastructure	Operational emissions from data centres and servers.
	Sustainable technological solutions	Green data centres, renewable energy, full life-cycle management of equipment.
Organisational / Institutional	Political and institutional commitment	Long-term strategic vision and stable support framework.
	Expert capacity	Ensuring a workforce of trained researchers and data managers.
	Partnership networks and system integration	Integration at the level of the healthcare system; avoiding the pilot project syndrome.
	Context-specific infrastructure assessment	Design and adaptation tailored to the local environment.

Source: own compilation

¹⁴ logistics trade-off: when making a logistics decision, achieving one objective (e.g. cost reduction) may come at the expense of another (e.g. faster delivery, better quality), as resources in logistics systems are finite and it is not possible to maximise multiple objectives simultaneously; therefore, a compromise must always be struck between different performance objectives - such as cost, speed, quality and flexibility - to find the optimal balance.

3. Appendix: Comparative table of the main cost categories determining traditional and digital clinical trials

Cost category	Traditional clinical trial	Digital clinical trial	Main structural difference
Planning and regulation	Traditional protocol, site-based design; multiple local authorisations and ethical approvals	Supplementary DCT design, data protection and digital process descriptions; fewer physical sites	Planning complexity is shifting towards technology
Site structure and start-up	Many physical sites; high site start-up, training and contractual costs	Fewer or virtual sites; lower site fixed costs, platform roll-out required	Physical infrastructure ↓, digital infrastructure ↑
Trial operations (site and investigator fees)	Frequent on-site visits, significant administration; ~30% of the budget	Fewer on-site visits, partly remote care; new service fees emerge	On-site operations reduced, hybrid operation
Monitoring and quality control	Regular on-site monitoring, high travel and staff costs	Remote and risk-based monitoring; less frequent physical visits	Monitoring costs significantly reduced
Patient recruitment	Relies on medical networks and site screening; slower, high per-patient costs	Digital campaigns, direct online recruitment; faster enrolment	10-25% cost reduction, shorter recruitment
Patient visits and compensation	On-site visits requiring travel, significant reimbursement and logistics	More telemedicine and home data collection; lower travel costs	Reduced burden and costs for patients
Sampling and logistics	Site-specific sampling, central laboratory	Home health nurse, local laboratories, direct-to-patient logistics	May be more expensive per unit, but fewer site-specific costs
Data collection and data management	EDC + paper-based elements; more manual data entry and cleaning	Integrated EDC, eCOA, eDiary; higher platform fees, less manual work	Increased automation, faster data processing
Technology and IT security	Minimal digital tools; low licensing costs, high human resource requirements	DHTs, wearables, eConsent; increased GDPR and cybersecurity costs	Significant initial and ongoing technology costs
Project management and overhead	Coordination of many sites; high administrative overhead	Fewer sites, more vendors and technology partners	Overheads are being restructured

Source: own compilation

4. Appendix: List of participants in expert interviews

	Expert's name	Place of work	Position	Relevant experience	Date of interview
1.	Dr Zsolt Szombathelyi	Richter Gedeon Plc. (Sponsor)	Advisor to the CEO	40+ years	23 September 2025, 10:00
2.	Dr Balázs Szatmári	Richter Gedeon Plc. (Sponsor)	Chief Medical Officer	14+ years	3 October 2025, 09:30
3.	Dr Tamás Joó	Semmelweis University EKK Centre for Healthcare Management (Expert)	Deputy Director, Associate Professor, data-driven healthcare expert	14+ years	22 October 2025, 10:00
4.	Dr Borbála Szepes	Richter Gedeon Plc. (Sponsor)	Early Phase Clinical Project Team Lead	7+ years	29 October 2025, 14:00
5.	Dr Ágota Barabássy	Richter Gedeon Plc. (Sponsor)	Medical Affairs CNS Team Lead	Ages 13 and over	13 November 2025, 10:00
6.	Dr Zoltán Hujber	Richter Gedeon Plc. (Sponsor)	Late Phase Clinical Project Team Lead	6+ years	18 November 2025, 13:00
7.	Dr Judit Harsányi	Richter Gedeon Plc. (Sponsor)	Manager of Global Clinical Operations	10+ years	21 November 2025, 09:30
8.	Zsuzsanna Bojtor	RIROSZ (Patient organisation)	Professional Coordinator		25 November 2025, 09:00
8.	Dr Gábor Pogány	RIROSZ (Patient organisation)	President	20+ years	25 November 2025, 09:00

9.	Dr István Kerekes	Richter Gedeon Plc. (Sponsor)	Senior Clinical Project Manager	11+ years	2 December 2025, 09:00
10	Dr Klára Hajnal	Participant	Retired university lecturer	has had a rare condition for over 13 years	13 January 2026, 13:00
11	Dr Szilvia Harsányi	Research Professionals CRO	decentralised Clinical Trial Operations Manager	5+ years	29 January 2026, 09:00
12	Dr Bálint Hajduska-Dér	Semmelweis University, Department of Psychology and Psychotherapy (PI)	Specialist psychiatrist, psychotherapist	9+ years	10 March 2026, 10:00
13	Dr Róbert Takács	Albert Szent-Györgyi Clinical Centre, Department of Internal Medicine (PI)	Senior Consultant, Diabetologist, Endocrinologist, Internist, Hypertension Specialist, Obesity Specialist, Clinical Pharmacologist	20+ years	18 March 2026, 13:00

The regulatory authority is an unrepresented group (n= 0). Based on their response to the inquiry, they do not have the requested data.

5. Appendix: Standard set of questions for expert interviews

The use of digital health technologies (DHTs) has now become commonplace; consider the countless health apps, home patient monitoring and wearable devices, telemedicine, or the use of electronic health records (EHR). In addition to software supporting digital therapies, the range of virtual modelling and design, advanced diagnostic capabilities, and predictive analytics-such as AI/VR/AR-based solutions-is growing ever longer. The use of remote solutions outside the clinical trial site has become possible in connection with the so-called decentralised clinical trial approach. By utilising the technologies listed above, DCTs can be conducted more efficiently, enabling the remote involvement of participants, more accurate and continuous data collection, and the faster and more cost-effective conduct of trials.

1. What disruptive technological developments would you mention that, in your experience, have revolutionised the field of clinical trials? Which of these have been a great success because they have become widespread/popular/easy to use etc. worldwide, and which have fallen short of expectations?
2. What is your experience with the use of DHT in clinical trials?
3. Could you give an example of a case where digitalisation improved a traditional clinical trial, or one where the trial was made possible specifically because of digitalisation and something new was achieved as a result?
4. If you used DHT in any aspect of a digital clinical trial, what was the primary problem you were trying to solve? What benefits did you experience during its use?
5. What challenges and obstacles did you identify when integrating this type of technology into a clinical trial?
6. What further benefits and challenges might arise in digital clinical trials compared to traditional clinical trials?
7. In your experience, will the structure of digital clinical trials be a key focus in 2026? To what extent does this manifest itself during the planning phase (e.g. willingness to invest/monopolistic service providers/selection of region/selection of principal investigators/regulatory compliance, etc.) and during implementation (e.g. patient recruitment/willingness to participate/data processing, etc.)?
8. From a scientific and/or innovation perspective, is it more obvious or popular today to conduct digital clinical trials, or is there any indication of such expectations or pressure from competitors? Do you see any risks in this regard, and if so, what are they?

9. In your opinion, how can the aforementioned risks be mitigated?
10. Do you think the trial could place a greater burden on digital clinical trial stakeholders? If so, how can these burdens be reduced, or perhaps eliminated?
11. How do the cost structures of digital and traditional clinical trials differ? How do DHTs affect the costs of clinical trials?
12. Which costs can be reduced or optimised using DHT solutions? What hidden costs do you see in digital clinical trials?
13. In your experience, what short- and long-term financial impacts might the use of DHT have?
14. Please give an example of a DHT solution or service that has led to significant cost savings, even though this was not expected, or one where savings were expected but did not materialise.
15. How can the financial benefits of a digital clinical trial be measured? What key performance indicators (KPIs) would you mention? What are the advantages and disadvantages of the metrics used?
16. How do you think the cost-benefit/cost-effectiveness profile of the DHT used in the trial can be determined?
17. How would you assess the return on investment (ROI) of a digital clinical trial?
18. Could you share any examples where DHTs have increased the profitability of a clinical trial? What strategies were used in these cases that helped to increase profitability?
19. In your view, is there a common best practice among them, or are the cases unique? What lessons can be drawn from these examples for future clinical trials?
20. What would you recommend to ensure that the potential of DHT solutions is exploited as widely as possible?
21. What do you expect from DHT in the longer term? How do you expect it to reshape the market? Could new players enter the market?
22. Please rate your agreement with the following statements on a scale of 1 to 4 (strongly disagree - strongly agree).

In my experience, the use of the digital clinical trial concept has a positive impact on....:

	I strongly disagree	I tend to disagree	I tend to agree	I completely agree
on the clinical applicability/acceptance of DHT				
the design of the trial protocol				
the selection of the principal investigator				
the regulatory approval process				
compliance with regulations				
reducing the number of protocol amendments				
to improve the screening error rate/the inclusion process				
patient engagement / trust				
patient retention rates				
ensuring data security				
the volume of data collected				
the quality / reliability / information content of the data collected				

the usability / processability of the collected data				
patient-centred care				
doctor-patient communication / relationship				
the process of reporting adverse events				
the duration of the investigation				
to reduce testing costs / improve cost-effectiveness				
to ensure a return on testing costs				

23. In your opinion, what important factors were not mentioned in the interview but would be worth discussing?

24. Who do you think would be worth interviewing on this topic?

6. Appendix: MAXQDA code frequency matrix and heat map showing subcategories

Code System	1. inte...	2. inte...	3. inte...	4. inte...	5. inte...	6. inte...	7. inte...	8. inte...	9. inte...	10. inte...	11. int...	12. int...	13. int...
▼ Economic & Business Impacts													
▼ Time & Performance Measurement									1				
KPIs		4			1	4			4	8	3	4	3
Efficiency Improvements	7	4	7		1	7	4	4	8	7	3	7	6
▼ Costs & Return on Investment													
Cost-Effectiveness / ROI	7	2	1		3	11	2	10	7	11	8	8	14
New Costs / Cost Structure		5	2		9	7	1	1	11	4	2	7	5
> Clinical Operations & Trial Management	19	3	9		8	15	9	9	13	1	11	8	7
▼ Strategy, Innovation & Vision		1		1					1		2	1	
▼ Technological Advancements													
Trends	4		4		1		3	3	1		4	5	2
▼ Market Directions													
Vision	6	5	6		1	2	8	1	3	3	5	9	2
▼ Stakeholder Impacts & Burden													
▼ Human Resources & Change Manag													
Training / Education	3		1			2	7			2			5
Physician Attitude / Change Ma	8	6	3		3	8				2	4	6	1
▼ Clinical & Operational Burden													
Overuse	1							1	3	2	1	1	
Physician & Site Burden		2	1		2	3		4	1	3	1	5	
Patient Burden					4	1	1		4				
Patient Experience	4	5	1		7	6	3	1	12	6	5	3	6
> Regulatory Environment		5	9	2	7	7	9	3	3	7	24	3	8
▼ Data Management & Quality													
More Data										1	1	1	2
Data Quality	1	2	1		3	1	1	1	3	2	2	6	4
Data Integrity						4		2	2	5		6	3
Data Security			2		2	1	2		2	1			3
▼ Patient-Centeredness & Access	1		1					2			2		2
▼ Environmental Impacts & Sustainab	1		1										3
Travel Burden		4	1	1	2		1	2	1	2	3	6	4
▼ Equal Access		3	4	1	1		1			1	1		
Remote Regions & Rare Disease		1				1	1		2	1			2
▼ Disruptive Digital Technologies					1	4		2	1	1	8		1
▼ Technological Challenges / Platform	1				6	3	6		2	5	12	6	4
Technological Challenges	4		7	2	2	2	2		1	1	6		1
Platforms & CRO System Challen	1				3			4	6	3	2	6	1
AI	4	1	3	2			4	2	4	1	1	1	
▼ Clinical Systems													
EPRO / eConsent / EDC		2			1	15		11	5	7	4	7	3
Databases / EESZT			3	2		6	7				2	4	
▼ Digital Healthcare Technologies													
VR / Avatars	5		5				4				3		1
Home visit / Telemedicina		6		1	3	7	4	10	1	2	4	5	8
Wearables	1		3		1		5	1			4	1	5
Apps	2		3		1		1						1
Digital Clinical Trials		10	1		16	4		1		4	3		2
▼ Social & Demographic Challenges							6		1	3	1		
Patient Distrust			4		2	1	1	2	2	2	1		
Digital Divide (Age-Related Barriers)		1	1		1	1	5	1	1	1		4	2
Digital Illiteracy		2	1									2	2

7. Appendix: MAXQDA code relation matrix with subcodes

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119	120	121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136	137	138	139	140	141	142	143	144	145	146	147	148	149	150	151	152	153	154	155	156	157	158	159	160	161	162	163	164	165	166	167	168	169	170	171	172	173	174	175	176	177	178	179	180	181	182	183	184	185	186	187	188	189	190	191	192	193	194	195	196	197	198	199	200	201	202	203	204	205	206	207	208	209	210	211	212	213	214	215	216	217	218	219	220	221	222	223	224	225	226	227	228	229	230	231	232	233	234	235	236	237	238	239	240	241	242	243	244	245	246	247	248	249	250	251	252	253	254	255	256	257	258	259	260	261	262	263	264	265	266	267	268	269	270	271	272	273	274	275	276	277	278	279	280	281	282	283	284	285	286	287	288	289	290	291	292	293	294	295	296	297	298	299	300	301	302	303	304	305	306	307	308	309	310	311	312	313	314	315	316	317	318	319	320	321	322	323	324	325	326	327	328	329	330	331	332	333	334	335	336	337	338	339	340	341	342	343	344	345	346	347	348	349	350	351	352	353	354	355	356	357	358	359	360	361	362	363	364	365	366	367	368	369	370	371	372	373	374	375	376	377	378	379	380	381	382	383	384	385	386	387	388	389	390	391	392	393	394	395	396	397	398	399	400	401	402	403	404	405	406	407	408	409	410	411	412	413	414	415	416	417	418	419	420	421	422	423	424	425	426	427	428	429	430	431	432	433	434	435	436	437	438	439	440	441	442	443	444	445	446	447	448	449	450	451	452	453	454	455	456	457	458	459	460	461	462	463	464	465	466	467	468	469	470	471	472	473	474	475	476	477	478	479	480	481	482	483	484	485	486	487	488	489	490	491	492	493	494	495	496	497	498	499	500	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525	526	527	528	529	530	531	532	533	534	535	536	537	538	539	540	541	542	543	544	545	546	547	548	549	550	551	552	553	554	555	556	557	558	559	560	561	562	563	564	565	566	567	568	569	570	571	572	573	574	575	576	577	578	579	580	581	582	583	584	585	586	587	588	589	590	591	592	593	594	595	596	597	598	599	600	601	602	603	604	605	606	607	608	609	610	611	612	613	614	615	616	617	618	619	620	621	622	623	624	625	626	627	628	629	630	631	632	633	634	635	636	637	638	639	640	641	642	643	644	645	646	647	648	649	650	651	652	653	654	655	656	657	658	659	660	661	662	663	664	665	666	667	668	669	670	671	672	673	674	675	676	677	678	679	680	681	682	683	684	685	686	687	688	689	690	691	692	693	694	695	696	697	698	699	700	701	702	703	704	705	706	707	708	709	710	711	712	713	714	715	716	717	718	719	720	721	722	723	724	725	726	727	728	729	730	731	732	733	734	735	736	737	738	739	740	741	742	743	744	745	746	747	748	749	750	751	752	753	754	755	756	757	758	759	760	761	762	763	764	765	766	767	768	769	770	771	772	773	774	775	776	777	778	779	780	781	782	783	784	785	786	787	788	789	790	791	792	793	794	795	796	797	798	799	800	801	802	803	804	805	806	807	808	809	810	811	812	813	814	815	816	817	818	819	820	821	822	823	824	825	826	827	828	829	830	831	832	833	834	835	836	837	838	839	840	841	842	843	844	845	846	847	848	849	850	851	852	853	854	855	856	857	858	859	860	861	862	863	864	865	866	867	868	869	870	871	872	873	874	875	876	877	878	879	880	881	882	883	884	885	886	887	888	889	890	891	892	893	894	895	896	897	898	899	900	901	902	903	904	905	906	907	908	909	910	911	912	913	914	915	916	917	918	919	920	921	922	923	924	925	926	927	928	929	930	931	932	933	934	935	936	937	938	939	940	941	942	943	944	945	946	947	948	949	950	951	952	953	954	955	956	957	958	959	960	961	962	963	964	965	966	967	968	969	970	971	972	973	974	975	976	977	978	979	980	981	982	983	984	985	986	987	988	989	990	991	992	993	994	995	996	997	998	999	1000
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