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PAYMENT MODELS FOR FUTURE HEALTH TECHNOLOGIES IN CENTRAL AND EASTERN EUROPE

PhD thesis

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List of Abbreviations

AI	Artificial Intelligence
ATMP	
BfArM	Bundesinstitut für Arzneimittel und Medizinprodukte
CE	Conformité Européenne
CEE	Central and Eastern Europe
DHT	Digital Health Technology
DiGA	Digitale Gesundheitsanwendungen
DNDi	Drugs for Neglected Diseases initiative
EFPIA	European Federation of Pharmaceutical Industries and Associations
EU	European Union
EY	Ernst & Young Consulting Limited
FDA	U.S. Food & Drug Administration
GNI	Gross National Income
GP	General Practitioner
HCP	Health Care Professional
HIC	Higher-income countries
HTA	Health Technology Assessment
HTx	Next Generation Health Technology Assessment
ISPOR	The Professional Society for Health Economics and Outcomes Research
IQVIA	Legacy company from the merger of IMS Health and Quintiles
IT	Information Technology
LICs	Lower-income countries
MDR	Medical Device Regulation
MDSW	Medical Device Software
MEDLINE	Medical Literature Analysis and Retrieval System Online
MENA	Middle East and North Africa
MEA	Managed Entry Agreements
mHealth	Mobile Health Technologies

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NICE	National Institute for Health Care and Excellence, UK
PDP	Product development partnership
PESTLE	Political, Economic, Social, Technological, Legal and Environment
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
R&D	Research and Development
SMA	Spinal muscular atrophy
TLR	Targeted Literature Review
UK	United Kingdom
US	United States of America
USD	the United States Dollar
W.A.I.T.	Waiting to Access to Innovative Therapies
WE	Western Europe
WHO	World Health Organization
ZIN	National Health Care Institute, Netherlands

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1. Introduction

The significance of pharmaceutical research and development (R&D) remains unquestioned as long as incurable diseases persist. Thanks to significant advances in pharmaceutical R&D, treatment options exist for several specialty diseases, such as those in oncology, hematology, and autoimmune disorders. At the same time, the issue of patient access to these treatment options got into the spotlight, driven by the substantial disparities observed, even within the European Union (EU). Upon closer examination, one of the main blockers of patient access to specialty treatments proved to be the availability of public healthcare financing schemes covering these treatments.

Pharmaceutical R&D underwent a profound transformation over recent decades. It has become clear that discovering potential solutions to medical problems alone is insufficient; it does not automatically attract pharmaceutical developers to invest into areas with material unmet medical need, especially in cases with limited potential for return on investment. Governments identified this issue, and public incentives have played a pivotal role in tackling this challenge, achieving notable success stories in addressing unmet medical needs, particularly in rare diseases. These public incentives typically fall into two categories: push mechanisms, which reduce the necessary investment in the R&D phase, and pull mechanisms, which offer an increased return on investment.

The increasing number of health technologies with high upfront costs entering the market are placing a significant burden on the financing of healthcare systems globally. The key concerns are the affordability and the uncertainty regarding long-term health benefits of these health technologies. To maintain pull incentives for the continuous development of such technologies, alternative payment models are needed, which can address these concerns.

In Western Europe (WE) innovative payment models such as outcome-based risk-sharing agreements between payers and pharmaceutical companies and delayed payment options have emerged to address these issues. In Central and Eastern Europe (CEE), where healthcare budgets are more limited, these pull incentives are limitedly applied, as high technologies with upfront cost exacerbate the pressure on the sustainability of healthcare

financing. The literature focuses mostly on pull incentive models applicable to wealthier nations, while there was a gap in understanding the CEE applicability of already existing and used payment models. To bridge this gap the barriers of transferring these payment models to CEE should be explored and recommendations should be made to overcome them.

The lack of pull incentives through innovative payment models is even a more rate limiting challenge for digital health technologies (DHT), which may benefit the most from new technological platforms, such digitalization of health records and availability of artificial intelligence methods. Consequently, patient access to these rapidly growing market segments remains unresolved. Some Western European countries, such as Germany and Belgium, have taken the lead by establishing special health technology assessment (HTA) frameworks and payment models for DHTs, but a unified EU-level framework is still absent, although efforts are underway to create one. Most of the literature is focusing on evaluating the transferability of the German payment model to other EU countries and comparing different HTA framework proposals. In Hungary, DHT usage in the public healthcare system is heterogenous, there is no HTA practice or payment model for DHTs apart from telemedicine. Currently, the inclusion of DHTs into the system of public healthcare financing is not prioritized, despite recognition of their potential benefits by most stakeholders.

Considering the above-described paradigm shift in pharmaceutical R&D, my thesis aims to facilitate discussions among relevant stakeholders by putting the spotlight on the challenges faced by pull incentives of public healthcare financing in the case of high upfront cost technologies. Alternative payment models are analyzed – such as outcome-based and delayed payment models, to identify solutions to the challenges around these technologies' affordability and uncertainty in health gain. The aim is to identify barriers in applying WE payment models in the CEE region, and to propose recommendations to overcome these barriers. Furthermore, considering that DHTs represent the next prevailing challenge in public healthcare financing, this thesis also includes an entry barrier mapping for alternative payment models as part of public reimbursement of DHTs on the local, Hungarian market.

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1.1 Paradigm shift in public incentives for pharmaceutical R&D: the case of orphan diseases

Note: This subchapter references the publication Ádám, 2021. Where other references are applicable, they are noted.

Historically, pharmaceutical companies concentrated on developing solutions for common diseases with high prevalence, a strategy that mitigated financial risks associated with drug development but necessitated strong promotional activities to maximize profits. This period is often referred to as the 'blockbuster technology' era of pharmaceutical R&D, where even a modest market share in a large patient population could generate annual sales exceeding United States Dollar (USD) 1 billion, the benchmark of blockbuster medicines. (Schuhmacher, 2022)

A significant milestone in transforming pharmaceutical R&D was the enactment of the Orphan Drug Act in the United States in 1983. A response from the EU followed in 2000. These legislative frameworks demonstrated that public incentives could accelerate pharmaceutical R&D in areas where standard market forces are insufficient to promote research, such as orphan diseases. The Orphan Drug Act defines orphan drugs as "one with efficacy against a disease affecting less than 200,000 people or one that will not be profitable for seven years". Hence, orphan drugs are either to treat rare diseases or drugs that are too expensive to develop (Aronson, 2006). After this, the landscape of pharmaceutical R&D has undergone a significant transformation, changing from drug development geared towards blockbusters - therapeutic areas with high prevalence and low unmet medical need, towards rare diseases. This focus shift was influenced by both market demand and public incentives, such as those included in the Orphan Drug Act.

Public incentives adapted to the above-described paradigm shift, new approaches being created, which can be categorized into two groups: push and pull mechanisms. Push mechanisms reduce necessary investment into R&D by reducing the risks and costs of developing investigational medical technologies. Pull mechanisms are targeted to increase the return on R&D investment with a special focus on financial revenues after market authorization. (Wilson, 2010) Further examples for both push and pull incentives are detailed in *Figure 1.* In *Figure 1.* under push mechanisms, PDP stands for Product Development Partnerships, which is a collaborative arrangement between different

stakeholders, such as pharmaceutical companies, research institutions, and non-profit organizations aimed at developing new technologies.

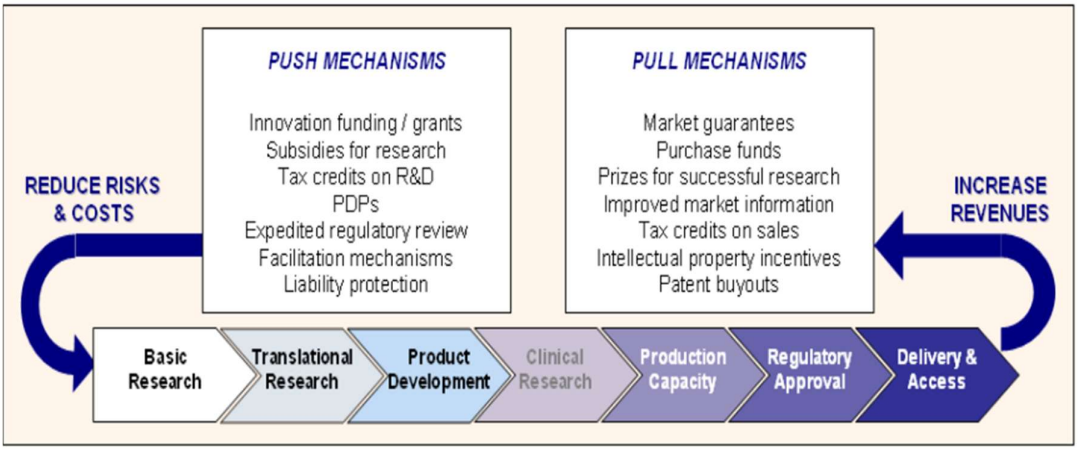

Figure 1. Push and pull mechanisms (Wilson, 2010)

Public interventions at various stages of the R&D lifecycle can be further stratified in financial and non-financial incentives, as shown in Table 1 below.

Table 1. Categorization of financial and non-financial push and pull incentives (own work)

	Push	Pull
Financial	• Public research grants • Establishment of patient registries from public resources	• Higher price premium due to increased cost-effectiveness thresholds • Innovative payment models to ensure earlier reimbursement
Non-financial	• Scientific advice for protocol design of pivotal trials • Registration based on small scale phase II studies	• Accelerated market authorization • Extended market exclusivity

The introduction of public incentives brought on new challenges, which are described in the next chapters.

1.2 Managing the uncertainty of realized health gain: Health technology assessment (HTA) for high upfront cost technologies

While market authorization based on small scale Phase 2 studies reduces the necessary investment and R&D risks, the evidence base of newly launched health technologies has

been reduced (Pontes, 2018). In the clinical assessment of new technologies only preliminary scientific evidence is available in those cases, where due to the accelerated market authorization process Phase III clinical trials are bypassed. This situation results in insufficient evidence for healthcare payers to judge the value-based price of new technologies. Sharing risks with pharmaceutical companies and necessitating the collection of real-world evidence in outcome-based conditional payment models can reduce the uncertainty of health care payers.

1.3 Affordability of high upfront cost technologies: The challenges faced by public healthcare financing

New technologies with significant premium price challenge the sustainability of health care financing. The affordability constraints are especially relevant for technologies with high upfront costs, such as advanced therapy medicinal products (ATMPs) or new generation vaccines (Hampson, 2018). These new health technologies are single shot interventions with significant short-term budget impact, which may be compensated for by long-term health gain and avoided future healthcare costs (Salzman, 2018; Hampson, 2018). (Ádám, 2022)

Due to the high initial costs, the timing of payment is a critical question for healthcare payers to manage their budget. Instead of the standard upfront payment methods, in which pharmaceutical companies receive the payment from healthcare payers at the time of delivering the treatment, an urgent need emerged for alternative payment models.

1.4 Alternative payment models: Linking payment to realizing value – is it a reality?

Note: This subchapter references the publication Ádám, 2022. Where other references are applicable, they are noted.

Concluding from subchapters 1.2 and 1.3, healthcare payers need to find a solution for the below two different problems to maintain the pull incentives for high upfront cost technologies:

(1) how to reduce the uncertainty around long-term health benefits,
(2) and how to manage the short-term budget implications (Farrington, 2019; Ádám, 2022)

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At this point it is important to narrow the focus area of my research within the full scope of health care financing. *Figure 2.* illustrates the main components of healthcare financing, including (1) collection of resources, (2) pooling resources and (3) resource allocation. My thesis focuses solely on the aspect of resource allocation.

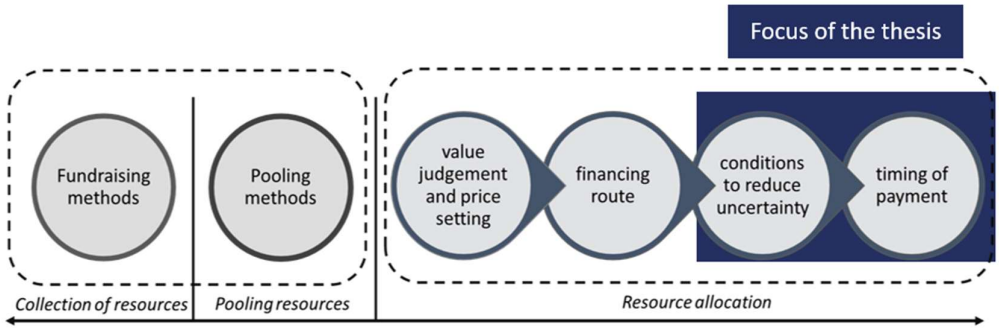

Figure 2. Healthcare financing of new health technologies (Resource allocation part published in Ádám, 2022, and partly own work)

We are not addressing expectations on increasing the collection of resources for new technologies (i.e. fundraising), or enhanced efficiency of pooling resources, because the major question for healthcare financing of new health technologies in publicly funded EU healthcare systems is selecting the appropriate payment models for the allocation of healthcare resources.

As healthcare payers need to address multiple challenges, in the frame of resource allocation, they may apply complex payment models, as described in *Figure 2.* The first component of complex payment models (value judgement and price setting) may include extended evaluation frameworks, which cover patient centric and societal value criteria in addition to traditional value judgement based on incremental health gain and healthcare costs. The second component (financing route) may be the consideration of a special financing route as opposed to the positive reimbursement list, such as joint international procurement, financing only in hospitals, or reimbursement on a named-patient basis. The third component of innovative payment models (conditions to reduce uncertainty) may describe special conditions for public financing of new technologies, such as financial or outcome-based risk-sharing agreements, or restricted prescription only in specialty healthcare centers. The fourth component (timing of payment) may improve the sustainability of healthcare financing by introducing delayed payment models.

There are several practical applications for reducing uncertainty and for timing of payments, the third and fourth components described above, respectively. Existing research summarized that uncertainty can be reduced through managed entry agreements (MEA) and innovative payment models for new health technologies, including those that might be able to manage the market access of potentially curative health technologies (Vreman, 2020). Potentially curative health technologies are those which have the potential to be cost-effective, as they might prevent chronic treatments and negative clinical outcomes in the long run.

In terms of timing of payments, delayed payment options should be considered. Different types of delayed payment options were described by Vreman et al. (Vreman, 2020). These include (a) paying treatment costs only after results have been achieved, or (b) annuity or staggered payment methods, in which payments are spread over multiple years with an agreement upon amount of treatment or outcomes delivered, and (c) health leasing or subscription methods, in which payment is made for the unlimited use of technology within a predefined period. All these delayed payment options can be implemented at patient or population level. Outcome-based agreements are a subtype of MEAs (Carlson, 2010; Wenzl, 2019), that link payments through various ways to the health benefits that patients realize due to the use of the novel health technology. Some examples of outcome-based MEAs include pay-for-outcome, conditional treatment continuation, and coverage with evidence development.

The alternative payment models presented above can effectively reduce the risk of payers in cases when there is significant uncertainty or heterogeneity regarding the clinical value of the pharmaceutical in question (Inotai, 2019).

1.5 Challenges of financing new health technologies in Central and Eastern Europe (CEE)

European countries can be divided into two groups: higher income countries (HICs) are mainly located in WE, while lower income countries (LICs) are mainly located in CEE. LICs are defined as countries with nominal gross domestic product (GDP) per capita below the European median GDP value. (Németh, 2022)

LICs are not only less affluent countries from a financial perspective, but generally they also have a poorer health status compared to wealthier nations, according to various

metrics (Marmot, 2012; Boncz, 2014; Bowry, 2015; Stanifer, 2016; Bertuccio, 2019). Further specific constraints to LICs are detailed in Németh at al., 2022, such as limited purchasing power, limited availability of high-quality healthcare data, and lack of an efficient HTA system in LICs. (Németh, 2022)

The disparity between health and economic status is often accompanied by financial constraints, resulting in restricted access to costly, innovative health technologies (Adam, 2012; Hollis, 2016; Pejcic, 2018; Ozawa, 2019). When exploring the availability of technologies, the European Federation of Pharmaceutical Industries and Associations (EFPIA) and IQVIA's W.A.I.T. indicator (Waiting to Access to Innovative Technologies) provides insights into the situation within the EU. The latest report indicates that a product is assessed as available under public reimbursement if that product is added to a reimbursement list, even if the given product's actual availability is limited by additional selection criteria. From 2019 to 2022, the average product availability rate in the EU stood at 43%, while Hungary and other CEE countries were below the EU average, with the exception of the Czech Republic, which stood at 62%. (Newton, 2024) The robustness of these statistics may be questioned due to varying interpretations of reimbursement status across countries (e.g. whether named-patient program can be considered as reimbursed status). Nonetheless, the data highlights the challenges faced by healthcare payers, particularly in the CEE region.

In situations where there is a recognized unmet medical need, patient groups and the public may strongly advocate for access despite the significant financial burden on the healthcare budgets in LICs. This is expected to be prevalent in geographies ranging from the CEE region to the Middle East (ME) and the broader Middle East and North Africa (MENA) regions. One potential strategy to address the disparity between the recognized unmet medical needs and the limited healthcare budgets, while also supporting the usage of alternative payment models, is the implementation of confidential agreements (e.g. MEAs) between payers and manufacturers (Klemp, 2011; Kanavos, 2017; Fens, 2020). MEAs represent a potential middle ground for the two stakeholder groups (Németh, 2020) and have demonstrated success in facilitating access to innovative pharmaceuticals in WE countries for instance (Pauwels, 2017; van Waalwijk van Doorn-Khosrovani, 2019; van Waalwijk van Doorn-Khosrovani, 2021). (Ádám, 2022)

Outcome-based MEAs play an important role in the health care financing of several HICs, for example in Italy (Xoxi, 2021). However, their uptake in LICs seems to be lagging (Ferrario, 2017) as these countries often rely more on simpler methods, such as financial MEAs and volume restrictions (e.g. price-volume agreement, manufacturer funded initial treatment period, utilization cap), without accomplishing the potentially increased patient access due to outcome-based agreements (Inotai, 2019). One of the main barriers for adopting alternative payment models is that in most cases pharmaceutical companies and payers reach an agreement on financial terms (Michelsen, 2020). Outcome based risk-sharing agreements to manage the uncertain effectiveness and delayed payment methods to manage the affordability of new health technologies with high upfront costs were mainly described in developed countries. (Ádám, 2022)

1.6 The next challenge: digital health technologies (DHT)

While the implementation of innovative payment models is still being heavily worked on for high upfront cost technologies, DHTs are already emerging as the next challenge in public healthcare financing. The necessity for innovative pharmaceutical technologies is widely recognized, and similarly, the importance of developing digital solutions for healthcare is also evident. Since the introduction of the iPhone 3.0 operating system in 2008, medical mobile applications have emerged as a distinct category (Dolan, 2010). With the increased accessibility of smartphones and tablets, the demand for connectivity to healthcare services has become a natural requirement for both patients and healthcare providers (HCPs) (Gotadki, 2024). This phenomenon is commonly referred to as DHT.

The precise definition of DHT falls outside the scope of this thesis. Also, considering that the definition and regulation of DHTs varies globally, the regulatory expectations in different jurisdictions were not addressed in this thesis. The US and EU have relatively broad definitions for DHTs. The U.S. Food & Drug Administration (FDA) defines digital health to encompass mobile health (mHealth), health information technology (IT), wearable devices, telehealth, telemedicine, and personalized medicine, including software that supports medical decisions and mobile medical apps. DHT is recognized for its potential to enhance medical decisions, aid in diagnosis, and even treat diseases (U.S. Food & Drug Administration, 2020). In the EU, the medical device regulation

(MDR) and the medical device software (MDSW) regulation address the definition of DHTs.

Considering the wide variety of DHT definitions, it is crucial to clarify that in this thesis, the purpose and the method of use of DHTs are the primary determinants of inclusion in the research scope. Commonly, DHTs are utilized for care coordination, diagnostics, and therapeutic purposes. The use of DHTs can vary, depending on whether they are employed independently or in combination with a medication or medical device. The categories relevant to this thesis are selected based on purpose and method of use. In terms of cost-effectiveness there are two important considerations: (i) possibility for independent use, and (ii) whether the technology is applied in diagnostics or therapy. The in-scope instances are indicated in Table 2. below with 'xx'. (Pálfi, 2023)

Table 2. Classification of DHTs according to the purpose and method of use (Pálfi, 2023)

Purpose of use → / Methods of use ↓	Care coordination	Diagnostics	Therapy
Independent use		xx	xx
Combination: medicine + app			xx
Combination: medical device + app			

The diversity of DHTs is evidenced by the existence of over 350,000 mHealth apps across various platforms (Katariya, 2024). Nonetheless, as with pharmaceuticals, patient access to these technologies remains a challenge. Access to public reimbursement for DHTs could also stimulate the development of additional technologies, like the impact observed with pharmaceutical technologies. We are observing the rise of new DHTs throughout various healthcare domains, fueled by innovations from the private sector. However, EU regulators often find themselves lagging slightly behind these advancements. It is essential for the healthcare industry to work closely with regulatory agencies, establishing a consistent framework for the evaluation and public reimbursement of these technologies. The successful commercialization of innovations is crucial for driving further innovation, which is a vital element of competitiveness in advanced economies (Mezei, 2023).

Several EU countries are in the process of adopting specialized HTA frameworks for DHTs, however, this is expected to be a difficult process, considering the experience that

standardizing HTA is challenging even for well-established technology types, which have the advantage of decades of accumulated experience and established evaluation methods. Some countries, where patients already have access to DHTs in the public healthcare system, such as Germany and Belgium, are at the forefront in adopting DHT specific HTAs. (Mezei, 2023)

Looking at the local market, considering that DHTs represent the next prevailing challenge in public healthcare financing, the introduction of public incentives for the development of DHTs could be an appropriate target for expediting R&D in the healthcare sector in Hungary. One way to incentivize the R&D of DHTs in Hungary would be a special reimbursement pathway in the Hungarian public health care financing system, as this would generate earlier return on investment and reference for reimbursement applications of local innovators in other countries. To support this process, the first step is to map the entry barriers for alternative payment models for DHTs in Hungary is required.

2. Objectives

This thesis covers some tools by public reimbursement that can facilitate the development process of future health technologies. My thesis and the underlying research work were divided into three phases. The objectives and research questions presented here also follow this structure.

The objective of the first research phase was to overview the pharmaceutical R&D incentives available in the past for rare diseases and generally for pharmaceuticals at a European, supranational level. The underlying research question was the following: 1) Which policy tools were available to support the R&D of pharmaceuticals at the European level?

The second research phase was covering that new types of health technologies required new payment models. The research topic is quite broad, so it was divided into two subtopics. My thesis involves a comprehensive review and summary of how public reimbursement can support R&D activity in CEE, particularly in scenarios where there is uncertainty regarding health gains, such as orphan medicines (subtopic a), and/or when affordability is in question, especially concerning curative ATMPs, including cell and

gene technologies (subtopic b). My thesis concentrates on the 3rd and 4th components of complex payment models, as indicated by the dark blue rectangle in Figure 2. These components include tools to mitigate uncertainty in health gain and the uncertainty in affordability by deferring the timing of payment. The objective was in this phase to identify barriers and potential solutions for payment models for new types of technologies in CEE. We phrased the research questions as per the following. 2.a) How countries in the CEE region can reduce the uncertainty in clinical outcomes for technologies with limited clinical trial evidence (e.g., orphan medicines, technologies in urgent periods – such as pandemic) by introducing outcome-based payment models? 2.b) How countries in the CEE region can facilitate the affordability of medicines with high upfront costs, such as ATMPs by introducing delayed payment models?

In the third research phase the geographic and therapeutic scope was narrowed down to DHT and Hungary. This thesis concentrates on the potential integration of DHTs into the public healthcare system within a public reimbursement framework. The research objective was to identify the status quo of public payment models for DHTs in Hungary based on international examples and address the barriers of adopting public reimbursement for DHTs in Hungary. A critical component of the research was to review and summarize European practices for the public reimbursement of DHTs, including the identification of barriers and opportunities for the public reimbursement of DHTs in Hungary. The research questions in Phase 3 were phrased as per the following: 3.a) How can Hungary learn from international public payment models for DHTs? 3.b) Is it a realistic expectation to implement such payment models in Hungary in the next 2-3 years?

The research and the thesis were divided into three phases. The following table (Table 3.) summarizes the research objectives and research questions divided into three phases.

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Table 3. Summary of research objectives and research questions divided by research phases (own work)

	Phase 1	**Phase 2**	**Phase 3**
Research Objectives	Overview pharmaceutical R&D incentives available at a European level in the past.	Identify barriers and potential solutions for payment models for new types of technologies in CEE.	Identify the status quo and barriers of adapting public reimbursement for DHTs in Hungary.
Research Questions	1.) Which policy tools were available to support R&D of pharmaceuticals at a European level?	2.a) How can countries in the CEE region reduce the uncertainty in clinical outcomes for technologies with limited clinical trial evidence by introducing outcome-based payment models?	3.a) How can Hungary learn from international public payment models for DHTs?
		2.b) How countries in the CEE region can facilitate the affordability of medicines with high upfront costs by introducing delayed payment models?	3.b) Is it a realistic expectation to implement it in the next 2-3 years?

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3. Methods

3.1 Public incentives for supporting pharmaceutical R&D at a European level (Objective 1)

To establish a foundation for my thesis, I reviewed the public incentives available to pharmaceutical companies engaged in R&D activities for rare diseases and at the EU, at supranational level. This thesis also encompassed an analysis of trends in public financing. The scoping review drew upon current legislation and state aid framework programs available at the EU level in 2020. This scoping review is presented in detail in a separate manuscript (Ádám, 2021), with key points summarized herein.

The search strategy involved searching the Google Scholar database, as the scope of my thesis was to identify pharmaceutical R&D-specific incentive programs available at the EU level in 2020, with an overview of a major public incentive program introduced for orphan drugs. The keywords used during the search were 'pharmaceutical R&D incentives', 'public funding' and 'EU'. I included results that were specifically related to the pharmaceutical industry. State aid programs targeting R&D in general were excluded. As most of the programs were described in EU legislation and documents, my search mostly relied on grey literature and legislation. The scoping review was performed in January-February 2021.

3.2-3.3 Reducing uncertainty: outcome-based payment models (Objective 2.a) and Facilitating affordability: delayed payment models (Objective 2.b)

This thesis builds upon a prior overview of various MEAs and payment mechanisms for innovative technologies (Vreman, 2020). The initial phase involved gathering information from relevant literature and the Next Generation Health Technology Assessment (HTx) project about potential barriers and solutions for implementing outcome-based reimbursement models in CEE and in the ME. (Ádám, 2022) HTx is a Horizon 2020 project funded by the EU. It was established in January 2019 and lasted for 5 years. The formation was underpinned by the need to develop methodologies to deliver more customized information on the effectiveness and cost-effectiveness of complex and personalized combinations of health technologies. The main aim of the HTx project was to create a framework for the Next Generation Health Technology Assessment. The HTx

project was a consortium consisting of several universities (e.g., Utrecht University, Medical University of Sofia), health technology assessment agencies (e.g., National Institute for Health Care and Excellence (NICE) from the UK, National Health Care Institute (ZIN) from the Netherlands) and research institutes (e.g., Syreon Research Institute). (HTx, 2025) My involvement into this large EU-funded project helped me gain access to multiple stakeholders, including representatives of HTA bodies, healthcare payers and academic experts, and ensured funding for studying the feasibility of special payment models, especially orphan drugs and ATMPs. We shared a common goal to support the development of flexible funding and reimbursement models for complex health technologies. That was the connection of Phase 2 of my thesis to the work of HTx project.

Data collection proceeded in parallel with three different sources. A survey was conducted to ascertain the status of the utilization of outcome-based agreements and delayed payment models and the perceived barriers in these regions, encompassing four topics related to outcome-based reimbursement and payment models, including the use of reimbursement models such as discounts and pay for outcome. The method of the survey is summarized in a separate manuscript. (Callenbach, 2023) Simultaneously, a targeted review of both scientific and grey literature was undertaken to further identify and examine barriers and potential solutions. Additionally, iterative discussions with HTx project members, representing diverse stakeholders in the HTA field, enriched the list of barriers and recommendations with their expert insights. There were 10 meetings held with the consortium members. The information was continuously reviewed to minimize redundancy in the barriers list and to refine the corresponding recommendations. (Ádám, 2022)

Given the parallel and iterative nature of the exploratory process for these barriers and related recommendations, the clear backtracking to identify the various sources would be cumbersome as well as irrelevant for the next steps. The second step in our approach was to review the draft list of barriers and recommendations identified in the earlier step, with representatives of healthcare payers and with healthcare financing experts (advisers of healthcare payers or former payers) from CEE and ME countries during a policy workshop. Considering the travel restrictions related to the COVID-19 pandemic, the workshop was organized as a virtual meeting. The virtual workshop took place in June

2021 with 16 members of the HTx project and 14 payer experts, from Bulgaria, Croatia, Hungary, Poland, Ukraine, Serbia, Slovakia, Slovenia, and Turkey (9 CEE countries); Egypt, Jordan, and Lebanon (3 MENA countries); and the Netherlands, Sweden and the United Kingdom (3 WE countries). In the first part of the workshop, participants received an introduction of relevant experiences in Sweden, United Kingdom, and Netherlands. This was followed by a presentation of the draft list of barriers and recommendations created by the research team. Participants were then allocated into working groups, consisting of four payer experts and four representatives from the research team in each group. Finally, the rapporteurs summarized the findings of each working group, providing feedback to workshop participants, identifying common themes, and clarifying all emerging questions. (Ádám, 2022)

As part of the third and final step of our approach, the research team summarized their findings in a draft report containing the consolidated list of barriers and recommendations identified. Workshop participants were given an opportunity to make final comments and amendment suggestions to the report. After the workshop, we reached out to participating experts to confirm their inputs provided during the workshop. The outcome of the research carried out within the HTx project was a list of barriers and potential solutions for outcome-based reimbursement and delayed payment models, based on a consensus among the research team and workshop participants. (Ádám, 2022) Figure 3. below summarizes the sequence of steps of the methodology.

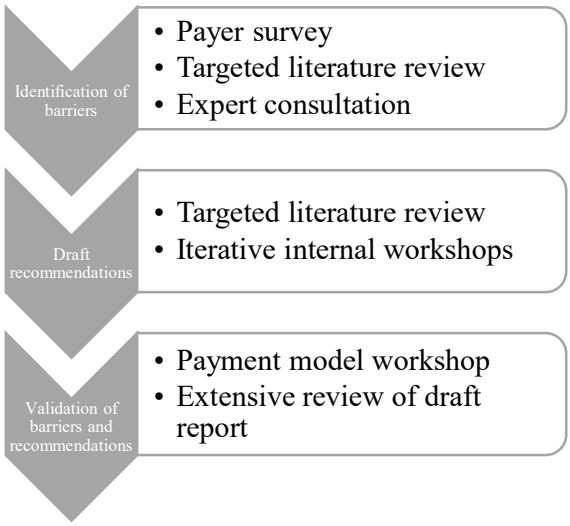

Figure 3. Summary of identifying barriers and recommendations (Ádám, 2022)

While the methods for identifying barriers and recommendations for both outcome-based and delayed payment models were identical, the targeted literature review (TLR) and subsequent discussions were conducted separately.

3.4 Public payment models for DHTs in Hungary (Objective 3)

Upon finalizing the list of barriers and recommendations for implementing innovative payment models in CEE and addressing affordability challenges, the focus of the thesis shifted to explore the emerging field of DHTs in Hungary.

Given that no DHT is currently included in the public reimbursement system in Hungary - unlike some pioneering countries that have already integrated such technologies -, the review of international examples was imperative. A TLR was conducted to map the existing scientific literature on public reimbursement strategies for DHTs. Collaborating as a co-supervisor with a pharmacy student completing his graduate studies at Semmelweis University, we jointly conducted portions of the research, with part of the study described in his thesis. (Pálfi, 2023)

The search strategy was grouped into two parts. The first search term group was concerning DHT and its relevant synonyms or other relevant phrases. The second search term group was about reimbursement and its associated synonyms. Within each search term group, ‘OR’ Boolean operator was used to enhance the search’s sensitivity. The search term groups were connected by ‘AND’ Boolean operator to filter for articles that referenced both DHT and reimbursement. We assumed that the existing search filters would not be applicable in our case. Hence, we did not use any validated or existing search filters. We experimented with several search strategies before concluding on the final one as presented in the thesis. The search term is outlined in Table 4. Search term applied for TLR (Pálfi, 2023) below. The search was carried out on 9 September 2022, using the Medical Literature Analysis and Retrieval System Online (MEDLINE) database through PubMed. (Pálfi, 2023) PubMed was chosen as the primary source for the TLR due to its comprehensive coverage of biomedical and life sciences literature. We decided to use only the MEDLINE database through PubMed due to the novelty of our research topic. Extending the search to additional white paper-based databases would not likely have resulted in relevant papers.

Table 4. Search term applied for TLR (Pálfi, 2023)

First search term group	(((Digital health technologies[Title/Abstract]) OR (Digital health applications[Title/Abstract])) OR (Health app policy[Title/Abstract])) OR (DiGA[Title/Abstract])
Boolean operator	AND
Second search term group	((Reimbursement[Title/Abstract]) OR (Financing[Title/Abstract])) OR (market access[Title/Abstract])

The search results were filtered to include only articles from the last 5 years (2018-2022) written in English. During the screening phase, we excluded articles based on the following exclusion criteria: (1) No English Abstract available, (2) No DHT included, (3) No information on reimbursement or adaptation, (4) Exclusive focus on a single therapeutic area. Articles that did not meet any exclusion criteria were selected for a full-text review. One article was not retrievable in its entirety, however its absence likely does not impact the quality of the TLR, as it pertained to the German system, which was well-represented in other publications. (Pálfi, 2023). To ensure comprehensive coverage of relevant literature, including non-peer-reviewed 'grey' literature, a reference tracking method was applied. We reviewed the references cited in the articles identified during TLR. None of the articles included implications specific to Hungary.

I participated in the working group organized by the Hungarian Chapter of ISPOR, which evaluated international practices in HTA and public reimbursement of DHTs to derive implications for Hungary. The methodology of this research is elaborated in a separate manuscript (Mezei, 2023), with key points summarized below. The need to conduct a separate literature review for the ISPOR Hungarian Chapter's working group arose because the aim and scope was different. The ISPOR Hungarian Chapter's working group focused not only on international practices in public financing of DHTs but also on the classifications of DHTs and HTA methodology, which were outside the scope of the TLR performed together with Máté Pálfi (Pálfi, 2023). Moreover, our study focused specifically on DHTs that were used and accessed also by patients for therapeutic purposes and not only by HCPs for diagnostic purposes. In July 2023, a scoping review was conducted to examine country-specific classifications of DHTs. The literature search

focused on five European countries, with established frameworks for DHT financing: Germany, France, Belgium, the United Kingdom, and Finland. Additionally, a separate literature review assessed the Hungarian approach to DHT financing. We have examined the practices of various European nations and synthesized the primary attributes of their approaches in a comprehensive manuscript (Mezei, 2023).

After reviewing international practices, and in parallel with the ISPOR Hungarian Chapter's efforts, we interviewed Hungarian experts to determine whether lessons could be learned from countries already incorporating DHTs into public reimbursement. The interview may not be the best study design to explore DHT use in Hungary in the public reimbursement context. We considered alternative approaches. We assessed the feasibility of conducting a survey, using the Delphi method, and conducting focus group discussions. Considering the novelty of the topic of public reimbursement of DHTs, the lack of a widely used scheme for public reimbursement of DHT use in Hungary, the conflict of interests between different market domains and the limited number and availability of experts, we decided to use the interview method despite its disadvantages, e.g., potential bias due to respondents' background, region, and specialty.

Instead of targeting many potential interviewees, who may be involved in healthcare and/or DHT but has no information in the context of public payment models, or is not interested in this topic, we focused on targeting individuals from diverse healthcare sectors for interviews on three topics: (i) the status of DHTs in Hungary, (ii) the potential benefits of integrating DHTs into the Hungarian healthcare system (iii) potential barriers to implementing public reimbursement for DHTs. For selecting the interviewees, we created a long list of individuals based on the ISPOR Hungarian Chapter's working group, where several different perspectives were present. Then, based on those interviews, we followed a snowball method and requested the interviewees' recommendations on who else could provide relevant input in the field. Based on those suggestions we concluded the final list of 24 individuals with my supervisor. Interviewees were carefully chosen to reflect a range of perspectives, including health policy, industry, associations, universities, HCPs and donors for developing DHTs in Hungary. We successfully conducted 21 interviews. The following chart (Figure 4.) summarizes the respondents' background and the number of participants from each group.

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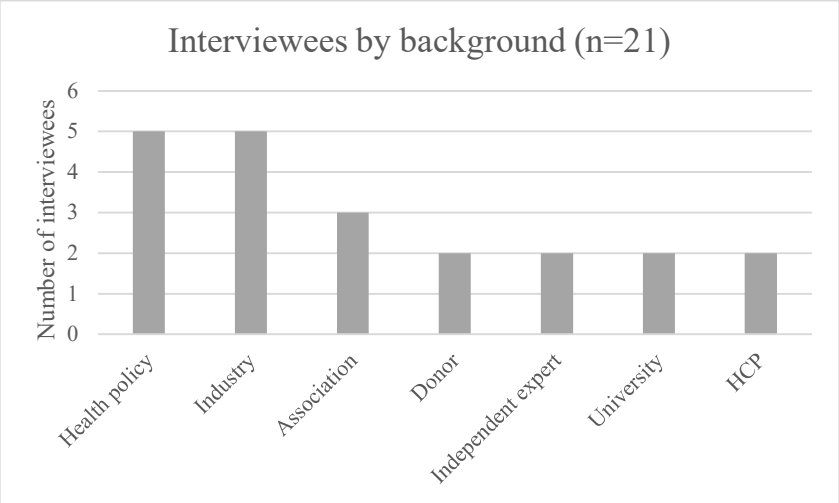

Figure 4. Number and background of interviewees (own work)

For the interviews, we followed widely accepted best practices and principles in qualitative research methodology. Namely, the following were the qualitative guidelines for the respective study:

1. **Research design and planning**
    - Define objectives: as detailed under Section 2, Phase 3 in this thesis
    - Choose interview type: structured interviews
    - Develop the interview guide: Annex 1 of the thesis
    - Pilot the interview: with my supervisor
2. **Participant selection**
    - Sampling strategy: cover all domains of the market, start with inviting individuals from the ISPOR Hungarian Chapter's working group, and then use the snowball method
3. **Conducting interviews**
    - Build rapport: encourage open and honest responses, ensure confidentiality
    - Active listening
    - Aim neutral stance
    - Record all interviews: based on the consent of participants

4. **Data management**
    - Store the recordings: the interviews stored in a secure cloud to prevent loss of access
    - Transcribe: with the AIrite software which is very useful in Hungarian language compared to other similar solutions (AIrite, 2025)
5. **Data analysis**
    - Thematic analysis: in a separate excel file, based on the topics and questions received to identify patterns, analysis performed instantly following each interview
6. **Ethical considerations**
    - Confidentiality: anonymizing data in the separate excel file and not disclosing names of individuals in this thesis either
7. **Dissemination**
    - Transparency: Report the research process transparently, including the background for methodology, participant selection, data analysis.
    - Limitations: potential bias influencing the research process and findings

We defined data saturation as the point when no new information was received in the study. When all relevant parties were represented and no new information was obtained during the interview of the next individual from the same background, we considered that domain complete. We ensured that we tracked the data saturation point by checking in parallel with processing the information received in each complete interview. Once all domains were complete, we considered the study complete. We concluded the interview phase with my supervisor once we reached the data saturation point, i.e., when no new information was received.

The interview questionnaire is detailed in Annex 1. Given the scarcity of therapeutic DHTs in the system of public healthcare financing, we explored the obstacles to DHT adoption in Hungary during the interviews. Upon completing the interviews, we summarized the main insights regarding the public reimbursement of DHTs in Hungary. The identified barriers and opportunities were organized and summarized in the Political, Economic, Social, Technological, Legal and Environment (PESTLE) framework.

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4. Results

4.1 Public incentives for supporting pharmaceutical R&D at a European level (Objective 1)

The public incentives available, their focus areas, associated opportunities, and the shortcomings of these incentives are detailed in a separate research paper, the key findings of which are summarized in this chapter (Ádám, 2021).

The first finding was that as a result of public incentives R&D efforts pivoted towards rare diseases, characterized by low prevalence but high unmet medical need. Figure 5. illustrates that the justifiable price, as determined by economic value and disease rarity, is inversely proportional.

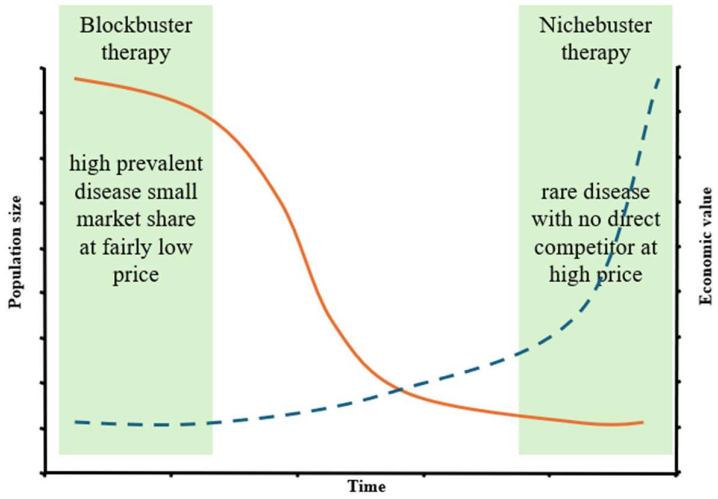

Figure 5. Shift in pharmaceutical R&D in the dimension of population size and economic value (Ádám, 2021)

In the private sector, the decision to invest in the development of a new drug is fundamentally a business one. R&D commences only if the drug is projected to be profitable, that is, if it has a positive expected net present value. Given that unmet medical needs are often greater in diseases affecting smaller populations, public policymakers have had to incentivize pharmaceutical companies to invest in these areas.

The shift towards an increased number of high-priced medicines in niche areas has introduced new challenges, such as limited patient access to novel technologies and substantial burden on healthcare budgets. Consequently, the traditional model of

financing new technologies has become unsustainable. Persistent challenges abound in many therapeutic areas, such as antimicrobial resistance, where prevalent issues remain unresolved. This calls for additional public interventions, including both push and pull mechanisms. Hence, it is important to understand the applicability of alternative payment models as part of these additional public interventions.

An example of the influence of public financial and non-financial incentives on addressing healthcare challenges can be observed in the space of rare diseases. Figure 6 illustrates the sequence of events in this domain.

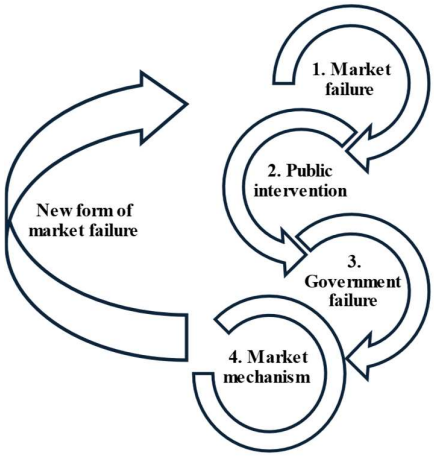

Figure 6. Impact of R&D incentives in the pharmaceutical industry based on the example of rare diseases (own work)

As mentioned above, the decision to invest in a new drug candidate is fundamentally a business decision, made only in the expectation of a positive net present value. At the same time, unmet medical needs are usually higher in small patient population diseases. Consequently, in the absence of public initiatives, the field of rare diseases experienced a market failure, as depicted in the first circle of Figure 6.

Coordinated public interventions in the largest pharmaceutical markets – including the US, the EU, and Japan – have encouraged pharmaceutical companies to pursue technologies for rare diseases, as shown in the second circle of Figure 6. This led to a paradigm shift in pharmaceutical R&D, moving from blockbuster technologies to “niche” technologies - treatments for rare diseases without a competition, offered at high prices. This transition poses a dilemma for governments: they must maintain incentives for

pharmaceutical companies to develop new technologies while also protecting the healthcare budgets from the unproportional burden of highly priced niche technologies, to avoid government failures, as highlighted in the third circle of Figure 6.

Those niche technologies which reach the revenue threshold of blockbuster drugs are called "nichebusters". The emergence of an increasing number of nichebuster technologies is attributable to the reinforcement of the market mechanism (the fourth circle in Figure 6), where public intervention catalyzed the development of such technologies by leveraging the market's financial incentive mechanism. However, this success has also led to a new form of market failure (as indicated by the ascending arrow on the left of Figure 6), including limited patient access due to unjustifiably high pharmaceutical prices especially in LICs (Szegedi, 2018), and limited evidence about the clinical benefits and safety of new orphan medicines due to registration without large scale randomized controlled trials (Nestler-Parr, 2018). At this moment, the cycle starts again, the situation necessitating further public intervention to improve the evidence base of orphan drugs and control pharmaceutical prices.

Reflecting on the above, Table 5. below summarizes some examples of blockbuster and nichebuster technologies. These examples are selected randomly, only for illustration purposes. The data below exemplifies that nichebuster technologies can reach very large market sizes, comparable to blockbuster technologies. At the same time, the target population is significantly smaller in the case of nichebuster technologies, resulting in significantly larger therapy prices. This trend is illustrated in Figure 6 above with the ascending arrow linking the market mechanism and the market failure steps, representing the fact that while the market mechanism supported the development of niche technologies, their outstandingly high prices lead to a market failure, since the technologies cannot be broadly accessed by the target population.

Table 5. Specific examples of blockbuster and nichebuster technologies (own work)

Technologies	**Blockbuster**	**Nichebuster**
Example No. 1		
Active ingredient	Atorvastatin	Nusinersen
Indication	High cholesterol	Spinal muscular atrophy (SMA)
Short description	Atorvastatin is used to lower cholesterol and reduce the risk of heart disease.	Nusinersen is an antisense oligonucleotide that treats SMA by increasing the production of survival motor neuron protein.

Technologies	**Blockbuster**	**Nichebuster**
Example No. 1		
Prevalence	According to the World Health Organization (WHO), the prevalence of raised cholesterol among adults was 39% in 2008. (WHO, 2025)	Affecting 1 in 10,000 live births. (Sarv, 2021)
Market size	USD 4.55 billion in 2022 (global market) (Yahoo, 2023)	USD 2.7 billion in 2023 (data covering only the 7 major markets: France, Germany, Italy, Japan, Spain, the United Kingdom, (UK) and the US) (GlobalData, 2024)
Example No. 2		
Active ingredient	Adalimumab	Palbociclib
Indication	Rheumatoid arthritis, Crohn's disease, psoriasis, and other autoimmune conditions	HR-positive, HER2-negative breast cancer
Short description	Adalimumab is a monoclonal antibody that targets TNF-alpha, helping to reduce inflammation in various autoimmune diseases. (Business Research, 2025)	Palbociclib is a targeted therapy that inhibits cyclin-dependent kinases 4 and 6, used in combination with hormone therapy for specific types of breast cancer.
Prevalence	18 million people worldwide living with rheumatoid arthritis in 2019 (WHO, 2025)	70% of all breast cancer (Cleveland, 2025) is this type of breast cancer. In 2022 2.3 million women were diagnosed with breast cancer, so approx. 1.6 million women worldwide. (WHO, 2024)
Market size	USD 2.41 billion in 2024 (Business Research, 2025)	USD 2.4 billion in 2024 (Verified Market Reports, 2025)
Example No. 3		
Active ingredient	Etanercept	Ivacaftor
Indication	Rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis	Cystic fibrosis with specific genetic mutations
Short description	Etanercept is a biologic that helps manage symptoms of autoimmune diseases by inhibiting TNF.	Ivacaftor targets the underlying cause of cystic fibrosis in patients with specific mutations, improving lung function and overall health.
Prevalence	18 million people worldwide living with rheumatoid arthritis in 2019 (WHO, 2025)	Approximately 100,000 people worldwide. (American Lung Association, 2024)
Market size	USD 16.1 billion in 2022 (Zion, 2023)	USD 1.5 billion in 2023 (DataIntelo, 2024)

It is important to note that certain technologies do not fall in the above two categories. For example, new immunological and oncological drugs that target sufficiently large populations (e.g. psoriasis, lung cancer), which are still smaller than the population of a hypertension drug and larger than the population of a gene technology for an inherited disease, would not qualify as either nichebuster or blockbuster technologies. The reason is that those areas do not require push and pull incentives, as the return on investment is already sizeable, even without public intervention.

4.2 Reducing uncertainty: outcome-based payment models (Objective 2.a)

In total, 20 barriers were identified and organized into five groups: (1) transaction costs and administrative burden, (2) measurement issues, (3) IT and data infrastructure, (4) governance, and (5) perverse policy outcomes. A series of recommendations were developed to overcome these obstacles. Comprehensive description of each barrier group and the associated recommendations are provided in a separate manuscript (Ádám, 2022). A summary of barriers and recommendations is presented in Table 6 below. As the results below were obtained within the framework of the HTx project, it was group research. The own contributions are detailed in Annex 3.

Table 6. Summary of barriers & recommendations for healthcare payers for the implementation of outcome-based reimbursement models in CEE (Ádám, 2022)

Group of barriers	Barriers	Recommendations
Transaction costs and administrative burden	Complex and resource intensive negotiations on contractual terms (including the first agreement and renegotiations)	1) Consider transferring the structure of existing agreements from higher income countries 2) Develop contract archetypes for most common schemes 3) Include re-opener clause into the agreements 4) When agreements are renegotiated, the latter agreement should be simpler than the first
	Costly collection of outcomes data without appropriate funding mechanism for data collection	If feasible, 1) rely on existing infrastructure 2) reuse of existing medical or claims data 3) cost of incremental data collection should be covered by pharmaceutical manufacturers
	Administrative burden on healthcare providers to collect data	1) Healthcare institutions should opt-in to prescribe medicines in outcome-based schemes 2) Involve leading centers in a network to publication of real-world data
Measurement issues	Lack of HE&OR expertise to specify and determine treatment effects in nonrandomized and observational settings (especially in rare diseases)	Capacity building in HE&OR (including education and collaboration in international initiatives)
	Long-time frame to capture hard endpoints, however, in surrogate outcomes may not guarantee improvement in hard endpoints	1) Greater dialogue between clinical opinion leaders, HE&OR experts, payers and patient representatives capturing different perspectives both at the initiation and follow-up of agreements 2) Surrogate endpoints should be valid predictors of patient outcomes. If such validation is not available upfront, additional

Group of barriers	Barriers	Recommendations
Measurement issues		data collection within the agreement can be considered to validate the surrogate outcome
	Treatment success is affected by confounding factors that cannot be controlled (e.g., inefficient health systems, local practice patterns, or poor treatment adherence)	Outcome based agreements provide incentives to manufacturers to address inefficiencies of healthcare delivery
IT and data infrastructure	Failure to capture the necessary data to reduce uncertainty within current infrastructure	1) If difficulties to collect data is expected, consider a pilot phase with adjustment according to early experiences 2) Terminate the agreement, if there is no better solution
	Fragmentation of healthcare financing and service provision makes it difficult to undertake outcome-based schemes	1) In fragmented healthcare system limit the scope of outcomes to hard endpoints 2) Promote national platform for outcome-based agreements with system-based incentives even in fragmented healthcare systems
	Limited compatibility of medical, pharmacy and payer data systems restrict meaningful retrospective analysis	Invest into building pragmatic MEA implementation frameworks by 1) linkage of databases 2) reuse of existing data
	Limited uptake of patient registries	Facilitate the establishment of patient registries with incentives to all stakeholders
Governance	Lack of regulation	1) Consider the implementation of pilot cases 2) Consider rationale selection mechanism when to apply outcome-based agreements 3) Prepare regulatory legal framework based on experiences in the pilot phase
	Incentives of healthcare professionals, patients and manufacturers to improve patient access limits their compliance to keep agreements	Outcomes should be objective, clearly defined, reproducible, and difficult to manipulate
	Unknown consequences of better results than expected (e.g. can prices be increased?)	No special action is needed 1) similarly to current practice outside outcome-based agreements 2) such situation rarely happen, as clinical benefits measured in clinical trials can hardly be replicated in real world
	Limited trust between payers and manufacturers	1) Outcomes data should be made available for independent audit 2) Sales are frozen and be made available depending on the outcome to the payer or to the manufacturer

Group of barriers	Barriers	Recommendations
	Difficulties for health authorities to delist health technologies or renegotiate prices	1) Clear legal foundation to support delisting of medicines due to limited efficacy (similarly to existing safety issues) 2) Involve clinical and patient representatives into delisting decisions
Perverse policy outcomes	Equity in patient access may be compromised when the new technology is available only in selected centers	1) Consider that no agreement would result in no patient access to new technologies 2) Extend the scope of prescribing centers when renegotiating the agreement
	No improvement in the evidence bases of health technologies, if real world data in outcome-based schemes remains unpublished	1) Evidence-gathering efforts can be shared and implemented jointly by countries to improve information quality and completeness and to counter potential information bias 2) Evidence about the effectiveness of health technologies should be considered a global public good. Publication of real-world evidence in outcome-based agreements should be an international standard
	Non-transparency of policy decisions due to confidential nature of data captured in agreements	Increase transparency around key components of the scheme
	Difficulties implementing value-based healthcare, as due to confidentiality of actual prices, true cost-effectiveness of any healthcare interventions cannot be calculated	1) Public availability of HTA documents 2) Two-way sensitivity analysis for the prices of compared technologies in economic evaluations
	LICs may pay more for medicines, as higher income countries potentially have greater economic power when negotiating about confidential discounts	1) Strengthen HTA system to calculate the local value-based price 2) Consider joint procurement by LICs

4.3 Facilitating affordability: delayed payment models (Objective 2.b)

Barriers and recommendations were categorized into four groups from the perspective of public healthcare payers: (1) transaction costs and administrative burden, (2) payment schedule, (3) IT and data infrastructure, and (4) governance. A total of 15 recommendations were articulated. The comprehensive description of each barrier group and corresponding recommendation is detailed in a separate manuscript. The table below summarizes the barriers and recommendations for delayed payment models (Table 7). Some barriers relate to the limited capacities of healthcare payers in CEE and ME countries implementing complex payment models. Five barriers pertain to enhancing the affordability of technologies with high upfront cost, which are also thoroughly examined within the context of outcome-based reimbursement. The remaining barriers are specific to the challenges associated with delayed payment models. (Ádám, 2022). As the results

below were obtained within the framework of the HTx project, it was group research. The own contributions are detailed in Annex 3.

Table 7. Summary of barriers and recommendations of delayed payment models in CEE from the perspective of healthcare payers (Ádám, 2022)

Group of barriers	Barriers	Recommendations
Transaction costs and administrative burden	Complex and resource intensive negotiations on contractual terms (including the first agreement and renegotiations)	1) Consider transferring the structure of existing agreements from higher income countries 2) Develop contract archetypes for most common schemes 3) When agreements are renegotiated, the latter agreement should be simpler than the first 4) Re-opener clauses of agreements after entry of competitive product
	Costly implementation of agreements with delayed payment	1) Rely on existing infrastructure 2) Reuse of existing claims or medical data 3) In the long run, adjust payer's data infrastructure to such agreements
Payment schedule	Limited experience with determining the optimal amount and/or duration of payments	1) Greater dialogue between payers and HE&OR experts 2) Consider transferring the structure of existing agreements from higher income countries 3) Develop contract archetypes for most common schemes 4) When agreements are renegotiated, the latter agreement should be simpler than the first 5) Consider that upfront payment has higher present value than delayed payment
	Conflicting financial flows for both parties (i.e. public healthcare payers and manufacturers) due to 12-month budgetary cycles	Propose changes to European and national accounting rules (e.g., to allow accruals over several years)
IT and data infrastructure	Failure to monitor patient status with current infrastructure	1) If difficulties to collect data is expected, consider a pilot phase with adjustment according to early experiences 2) In the long run adjust data infrastructure of healthcare payers to such agreements
	Limited uptake of patient registries	Facilitate the establishment of patient registries
Governance	Lack of regulation	1) Review regulatory frameworks in higher income countries 2) Consider the implementation of pilot cases, and prepare regulatory legal framework based on experiences in the pilot phase

Group of barriers	Barriers	Recommendations
	Weakness of public sector to efficiently negotiate with multinational industry	1) Consider transferring the structure of existing agreements from higher income countries 2) Strengthen HTA system to promote value for money and affordability concepts 3) Joint procurement by smaller countries to increase the purchasing power

4.4 Public payment models for DHTs in Hungary (Objective 3)

There are 3 types of DHTs, including i) administrative tools to manage or facilitate access to healthcare data, ii) diagnostic tools to assist HCPs in making more informed treatment decisions and iii) therapeutic tools, which aim to treat or at least assist the treatment or patients with certain conditions. Numerous countries are exploring the integration of DHTs into their healthcare systems. However, only a select few have implemented payment models to facilitate the inclusion of DHTs in public reimbursement schemes (Mezei, 2023).

While this research was not a systematic literature review or meta-analysis, the process of TLR can be visualized through a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram (Figure 7).

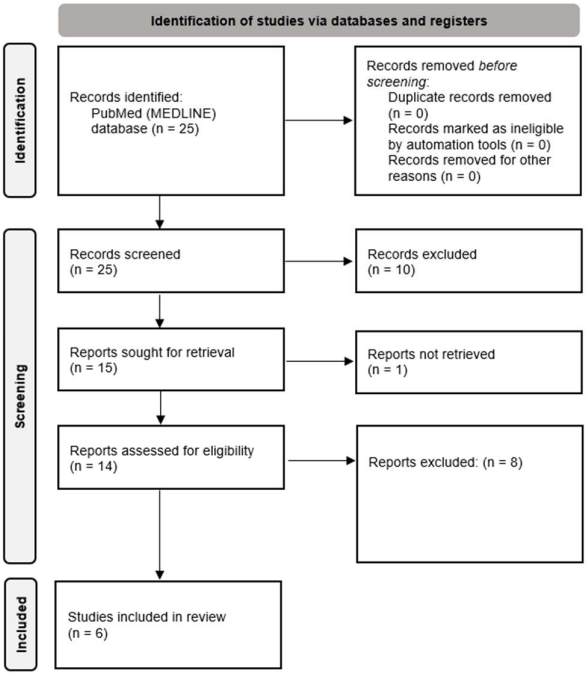

Figure 7. PRISMA flow diagram of TLR (Pálfi, 2023)

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At the end, only 6 studies were included from TLR. It may trigger a question whether the search strategy was too narrow. As described in the Methods section, we experimented with several search strategies before concluding on the final one. Due to the specific focus of the study, a broader search strategy resulted in irrelevant hits. For example, most of the hits were DHTs associated with a specific drug and not in the public reimbursement context.

Based on the TLR and scoping review performed, although there is no EU level framework for adopting DHTs to healthcare systems, many EU countries are dealing with experimenting adoption of DHTs to the public reimbursement system. Among that countries, Germany and Belgium are pioneers with already existing DHTs in public reimbursement. The results of the TLR can be accessed in detail in the publication of (Pálfi, 2023). The results of the scoping review can be read in the publication of (Mezei, 2023). In this thesis, only a summary of the main results from the international experiences is provided, focusing on Germany and Belgium as the most developed countries from the perspective of DHT public reimbursement.

Germany's DHT public reimbursement system, often abbreviated as DiGA (Digitale Gesundheitsanwendungen) is the most developed. In this DiGA framework, HCPs can prescribe DHTs to patients under public reimbursement scheme since 2020. There is a special definition for DiGA, where an important element is that only DHTs falling under the risk categories Class I and IIa can be part of the public reimbursement scheme. The Class I risk category designates the lowest risk health devices that do not pose a threat to human health (e.g., blood pressure monitor). According to EU legislation, the Class IIA risk category designates medium-risk health devices, where the risk associated with these devices is higher than that of Class I devices, but still manageable (e.g., pacemaker) (EU, 2017). In the German system, there is also an option for getting interim reimbursement while gathering further health data on the application of DHTs. As of 10 May 2025, 69 DHTs are recorded in the DiGA directory as permanently or temporarily reimbursed, of which 10 DHTs have been withdrawn. These DHTs are used in several therapeutic areas, e.g. psychiatry, oncology, quitting smoking, cardiovascular diseases, metabolic diseases, hearing disorders, etc. (BfArM, 2025).

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Belgium has also a concept for integrating DHTs to the public healthcare system, which is different from Germany. They aim to integrate DHTs rather as part of the healthcare process, instead of reimbursing stand-alone DHTs. This also means that the adoption of DHTs requires significantly more time and revisions in protocols of the existing setting in healthcare. The tool for admitting DHTs to the Belgian healthcare system is the so called mHealth pyramid. This pyramid classifies applications in four levels, depending on the reimbursement status. The lowest category is Level 1, where the DHT is required to have a Conformité Européenne (CE) certification and there is no reimbursement component at this level. The highest level is Level 3^{+} where the DHT is reimbursed permanently, since the DHT's socio-economic value is fully proven. As of 10 May 2025, there are 28 DHTs registered in all levels, of which 8 DHTs reached Level 3^{+}. These DHTs target to transform several therapeutic areas, such as sleeping disorders, cardiovascular diseases, etc. (mHealth, 2025)

Following the international regimes, as described previously, due to the lack of widely used international framework for adopting DHTs to the healthcare system, the thesis focused on the case of Hungary. In response to the COVID-19 pandemic, Hungary implemented a public payment scheme for certain telemedicine procedures, ensuring patient care continuity when in-person doctor visits were restricted. These measures remain active and are legally upheld by *Section 85 of Act LVIII of 2020 on the transitional rules related to the end of the state of emergency and on epidemic preparedness*. Otherwise, no guideline or framework is in use for public reimbursement of DHTs in Hungary. We focused on understanding the status quo of DHTs in the Hungarian healthcare system and identifying the barriers for adopting public reimbursement scheme for DHTs in Hungary in the frame of interviews with different stakeholders as detailed in Section 3.4. Following the structure of the interview questionnaire, the interviewees' opinions are summarized below. The interview guide and full questionnaire are presented in Annex 1.

1. Question to the interviewees: "*What role do you currently attribute to DHTs (e.g., therapeutic health mobile applications) in the present and future of the Hungarian healthcare system?*"

The vast majority of respondents attribute marginal role to DHTs in the present Hungarian healthcare system. As for the future, the expectations are also moderate, although the benefits are undeniable. Some of the interviewees mentioned that "*DHTs could contribute to tackle the challenges of lacking HCPs and limited access to healthcare in the countryside*.". Although, another interviewee added that "*most probably DHTs will spread in the private sector first. The attitude of public healthcare system towards DHTs is not likely to change in the close future*.".

2. Question to the interviewees: "*Do you know of any cases where digital technologies have been integrated into Hungarian patient care (e.g., applications for treating panic disorder or depression)? In which areas do you see the greatest potential for breakthroughs?*"

Based on the interviews there are contradictory opinions about whether the current legislative background is sufficient to initiate the public reimbursement of any DHTs. On one hand, based on the legislation there is no explicit exclusion for DHTs (*Government Decree 180/2010. (V. 13.) on the Principles, Conditions, and Detailed Rules for the Inclusion of Healthcare Technologies in Health Insurance Financing, and on the Review and Amendment of the Range of Technologies Already Included*). On the other hand, in case of a positive decision on the public reimbursement of any DHTs, legislative amendments would be necessary to create a reimbursement category for DHTs.

Health policy experts indicated that there has been only one instance of a public reimbursement claim for a DHT in Hungary, which was withdrawn before a decision was reached.

In addition to the Electronic Health Data Space (Hungarian: Elektronikus Egészségügyi Szolgáltatási Tér, abbreviated: EESZT), interviewees cited several diagnostic tools, including:

- An application that monitors blood glucose level for Type II diabetes patients and providing general practitioners (GPs) with real-time data access.

- A software that analyses patient-taking photographs of dermatological symptoms, with artificial intelligence (AI) offering diagnostic suggestions to dermatologists.
- An application designed for migraine patients to log headache occurrences, which was associated with a specific migraine medication.
- An application that tracks the progression of Parkinson's disease, used in combination with drug therapy.
- Brainomix's AI stroke imaging software utilized by Hungarian stroke centers to enhance stroke care by supporting HCPs in the real-time interpretation of brain scans. (Brainomix, 2022)

These examples are already in use in the Hungarian healthcare system sporadically. The interviewees summarized that "*the adoption of a DHT to the healthcare is depending on an agile HCP or a healthcare center where the management is committed to the application of DHTs*".

Currently no therapeutic DHTs are included in the public healthcare financing system in Hungary. Most interviewees, however, could identify administrative or diagnostic DHTs, which were adopted into the Hungarian healthcare system. All respondents (n=19) referenced the EESZT, which is accessible to both patients and HCPs.

A single example of a therapeutic application was referenced by interviewees. This application, typically initiated by a hospital center or a group of doctors for their patients, was not included in public reimbursement, but was offered at no cost. The application, aimed at preventing complications and amputations in patients with diabetes or vascular stenosis, has been in use since 2019. The application's name is Limb Saver (in Hungarian: *Végtagmentő)*. (Pauska, 2019)

3. Question to the interviewees: "*If digital health technology is developed in Hungary, what is the communication like between the financier of the development and the development team during the process? In your experience, does the validation of unmet (domestic or international) healthcare needs occur for the financier of the development?*"

For this question only the donors and industry representatives could provide any insights. All the other domain participants were not sure about the communication channels and

mechanisms. The experts agreed that based on their experience, the validation of unmet healthcare is secondary, if it happens at all. A donor stressed that "*For now, the 'brilliance of brainstorming' is primary, and the need is secondary*". One interviewee added that "*the communication between universities and private sector is not in the same level, like private sector designs projects for a year, while universities are usually thinking on a 2-3 year-long horizon. It is very rare that they can cooperate due to these timing differences.*". Hence, based on the answers received in the interviews, there is no direct connection between validating unmet medical need and channeling public funds for developing DHTs. Donors stressed that the main reason for not validating unmet medical needs is that "*Very few people work with us who have any real understanding of the healthcare industry beyond that they quickly learn on the job. But this is typical of public administration, where the generalist nature means you don't hire specialized people, but rather a bunch of humanities graduates or economists, and then they somehow figure it out*.". They also added that in the past there were industry specialists involved on a subcontractor basis, but that practice was no longer applicable.

4. Question to the interviewees: "*Would it be justified for certain digital health technologies to receive public reimbursement in Hungary? If so, what factors would justify this?"*

Most of the respondents agreed on the rationale to adopt DHTs to the public reimbursement system. The mostly cited reasoning was the lack of proper human resources capacity. Another interesting argument by a health policy representative was that *"the DHTs that received public funding (such as cash grants, tax incentives) for development, those could be integrated into the public healthcare system. That could make a precedent case and be a motivation to DHT developers to integrate their solutions into the healthcare system in Hungary*.". Hungarian market is a small market, so it is not in the focus of developers. Although, by introducing public reimbursement aspect could make them motivated to introduce the technologies developed in Hungary in the Hungarian healthcare system, even if there were certain state aid provided to that from the budget of Hungarian state.

5. Question to the interviewees: *"In which therapeutic area would the greatest health gain be expected from the application of digital technologies?*

    - *Oncology*
    - *Cardiology*
    - *Psychiatry*
    - *Metabolic Diseases (diabetes, etc.)*
    - *Dermatology*
    - *Other: …"*

Most respondents mentioned cardiology and oncology. Some of them also added psychiatry in addition to that. Only one respondent mentioned dermatology and another the metabolic diseases. As for the other therapeutic areas, not specified in the question, one interviewee added rehabilitation as an area where application of DHTs could result in greatest health gain since "*people easily forget things that are long-term but still schedulable*".

6. Question to the interviewees: *"What health policy measures are necessary for digital health technologies to spread more widely in Hungary?"*

First of all, "*healthcare should be a priority"* according to the views of interviewees. Currently, all respondents admit that healthcare is not the focus of policy and politics. Including DHTs for public reimbursement is not the first challenge to tackle. There is a need for education of both HCPs and patients about the benefits of DHTs and the way that can be beneficial for healthcare purposes. Furthermore, a wide spectrum communication strategy should be necessary about integrating DHTs into the healthcare setting, highlighting the underlying benefits, but also commenting on the most frequent concerns and how the government would make sure that those are overcome. There are several regulatory aspects that should be addressed, such as accessing patient data while using DHTs and there are no specific IT standards prescribed by law. Furthermore, it was also a consensus between the participants that the definition of non-pharmaceutical technologies is mixed, and stakeholders get puzzled about finding the right definition and rules applicable to a specific technology, including DHTs. There was a valuable comment from a health policy representative, who stressed that there should be an industry policy

for integrating solutions "*so that we develop with public funds, that should later be able to appear in public reimbursement as well*".

7. Question to the interviewees: *"Do you think Hungarian doctors and patients would accept and use the mentioned digital solutions?"*

At this question the responses were heavily mixed. Some of them emphasized that "*if there is a will, there is a way*". Meaning that if it would be decided centrally that adopting DHTs is beneficial for the Hungarian healthcare system, and it would be introduced along with obligations to adopt it by HCPs and patients, it would work. An example referenced here by everyone is the mandatory use of EESZT. Although, many interviewees highlighted that the currently used capacities of HCPs are beyond their limits, so they have no capacity to adopt more responsibilities. As for the patients, the picture was also mixed. Digital literacy is a topic where there was a huge difference between arguments: many argued that the elder population is capable of handling DHTs if it were given to them, several respondents stressed lack of digital literacy. So even if there were DHTs, many patients could not benefit from that unless they provided proper support to learn using the DHTs.

8. Question to the interviewees: *"Recently, a European Union working group was formed to facilitate the development of a system for the public financing of digital health technologies in EU member states. The expert team does not include a Hungarian delegate, although the development of digital health technologies is also a priority for healthcare companies. What do you think is the reason for the lack of Hungarian participants in the EU initiative, and what could be the consequences? Would you consider Hungarian participation in such international working groups necessary?"*

At the EU level, a working group was formed to establish public reimbursement guidelines for DHTs (*The External Advisory Group to the European Taskforce for Harmonised Evaluation of Digital Medical Devices*), but Hungary did not participate. When asked about the potential reasons for that, the majority of experts cited a lack of priority (n=8), while others (n=5) pointed to insufficient capacity within the public administration to engage in such initiatives. Except for two experts, remaining

respondents (n=17) agreed in the importance of participating in these working groups to help shape a European-level system that also addresses Hungary's specific needs.

Based on the interviews, a total of 21 barriers were identified across six categories. That was summarized below in Table 8.

Table 8. Barriers of adopting DHTs in Hungary summarized in PESTLE framework (own work)

External factors	Barriers
Political	1) Health care is not prioritised among policies 2) Health policy decision makers are not informed about DHTs 3) Health policy decision makers do not consider the public reimbursement of DHTs important 4) Weak sign of willingness to transfer state-funded DHTs to health care
Economic	1) Small market 2) Increasing budget pressure 3) Uncertain return on investment 4) No specific requirement for validating the market access criteria in state aid programs 5) No capacity available at HCPs 6) Specific payment models are not in use
Social	1) Scepticism of HCPs and patients 2) Digital literacy level is low among elder patients 3) Uncertain health gain
Technological	1) Uncertain cyber security requirements 2) No widespread interoperability framework for different DHTs and interfaces of HCPs 3) No standardised infrastructure
Legal	1) No clear regulatory framework to provide DHTs under public reimbursement 2) Overlap in definitions of non-pharmaceutical technologies in regulation 3) Not sufficiently detailed IT standards 4) Uncertain data protection framework
Environmental	1) Environmental footprint of health care

Interviewees indicated that Hungary is not fully leveraging its potential in the development of DHTs. Furthermore, even when a DHT is developed in Hungary and receives public grant for the R&D, it remains inaccessible for patients within the Hungarian public healthcare system. The provision of public grants for the R&D of DHTs has not been contingent upon validating an unmet medical need. Additionally, awarding such grants does not align with health policy priorities. While most interviewees believe that push interventions are not essential for developing DHTs, they advocated for stronger emphasis on pull financing, particularly in areas with high unmet medical need, such as psychiatry.

Given that Hungary is viewed as a small market, DHT developers typically regard the country as a source of talented innovators or supporting experts and only in some cases as a venue for pilot project launches. Despite the high unmet medical needs and the absence of an established public payment model (especially for therapeutic) DHTs, it is

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reasonable to consider for Hungary joining supranational efforts to navigate the path to public payment models for DHTs.

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5. Discussion

Over the past decades, there has been a significant increase in public funding for pharmaceutical R&D within the EU, steering innovators towards areas aligned with public health priorities. Nonetheless, the ongoing issue of antimicrobial resistance demonstrates that public funding alone may not always yield timely solutions. In such instances, a broad range of public incentives could offer more effective resolutions, like the approach taken with orphan drugs. (Ádám, 2021) In light of market failures and the emergence of 'nichebuster' technologies, it is important for policy makers and governments to respond promptly to market dynamics to maintain motivation within the pharmaceutical industry, while also ensuring the efficient stewardship of public finances.

The health of a population is linked to a country's economic prosperity. Thus, the opportunity to capitalize on advanced technologies might be more significant in developing countries such as Hungary. Nevertheless, the disparity in health outcomes between less wealthy and more affluent nations cannot be narrowed unless decision-makers in the healthcare sector of LICs prioritize the reimbursement of technologies that yield substantial overall improvements in health. Two types of uncertainty will be more relevant in the foreseeable future for technologies with high upfront costs, including i) uncertainty in the health gain – especially in rare diseases and ii) uncertainty in affordability – especially in common diseases. Uncertainty in the health gain can be managed by outcome-based payment models. The opportunity costs associated with selecting high-cost technologies could be reduced through outcome-based reimbursement models, where health gains are assured. Essentially, healthcare payers would purchase health outcomes rather than merely paying for health technologies. (Ádám, 2022)

Yet, the adoption of outcome-based reimbursement models presents challenges, particularly in LICs, with limited healthcare budgets. These challenges could be mitigated if healthcare providers commit to evaluating technologies within the framework of outcome-based reimbursement models through pilot agreements. The advantages of outcome-based reimbursement models can be realized by all stakeholders, albeit for different reasons. Patients may gain earlier access to treatments under such agreements. Healthcare payers can reduce the uncertainty in their decision-making. Clinicians can confirm the real-world benefits of technologies. Pharmaceutical companies can provide

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tangible real-world evidence to healthcare payers, addressing concerns about data uncertainty in a real-world setting, which can lead to faster market access and support the high price of technologies. (Ádám, 2022)

Uncertainty in the affordability – which is a critical concern for LICs - can be managed by delayed payment models. This thesis has identified a range of barriers and provided practical suggestions for overcoming them. While some recommendations are tailored specifically to LICs, others have universal applicability. Specific solutions of delayed payment models in higher-income countries may not be directly transferable to LICs. Furthermore, it is essential to reiterate the difference between the health status of people among populations, which leads to a higher demand for potentially curative ATMPs in LICs. (Ádám, 2022)

The recommendations outlined in this thesis should be viewed as preliminary steps in a broader multistakeholder dialogue, and the continuation of this work is strongly advised. That need is supported by the trend appearing in the field of oncology. In the most recent years, several players in the pharmaceutical industry started transforming blockbusters to nichebuster drugs by narrowing down the indication group. This means that they are targeting smaller, more specific patient population groups, such as those with a particular type of breast cancer. The rationale behind this strategy is that it allows the pharmaceutical industry to justify higher prices due to the specialized nature of the treatment. This approach is sometimes referred as “salami slicing” or personalized medicine, depending on the perspective of the stakeholder. Hence, implementation of outcome-based payment models and delayed payment models should follow to address the price increase trend in already existing therapeutic fields as well.

Like outcome-based reimbursement and delayed payment models, there are pioneering countries in WE that have already adopted frameworks to integrate DHTs into their healthcare financing systems. However, there is no straightforward solution that can be directly transferred to CEE and Hungary, as several barriers exist. One such barrier is Hungary’s absence from the European task force dedicated to harmonizing evaluation procedures for DHTs across Europe. Interviews with Hungarian experts from all relevant stakeholder groups indicate that integrating DHTs is not currently a priority for the

Hungarian healthcare financing system, despite recognition of DHTs' potential to address human resource shortages and budget constraints.

In Hungary, DHTs are primarily used for diagnostic or administrative purposes, and the only area that exists for therapeutic DHTs is telemedicine, which emerged during the COVID-19 pandemic. There is a debate over whether the current legislation has the potential for the adoption of DHTs into the public healthcare financing system. At present, there are no reimbursement requests for therapeutic DHTs, even though several DHTs developed in Hungary have received public grants during the R&D phase. The next step could involve recognizing the necessity of DHTs in addressing the challenges faced by the Hungarian healthcare system. Subsequently, a framework that enables the integration of DHTs into the public healthcare financing system should be developed. Moreover, the concept of pull financing mechanisms could be advantageous, as the current push financing tools appear to have little effect on widespread use of DHTs. Prioritizing these barriers was beyond the scope of my thesis. However, that could be an opportunity for further research.

5.1 Limitations

In Phase 1 reviewing available policy tools to support pharmaceutical R&D focused on supranational programs. A tailored search strategy to overview national examples could have been added for review. Moreover, the timeline was specific, a broader scope review may have resulted in more examples. The market size and population data can vary between different databases and research companies. Hence, as noted in the relevant subchapter, the data included in this thesis is only for illustration purposes. Thorough data validation is suggested prior to working further with this data.

In Phase 2 identifying barriers and recommendations for outcome-based payment models and delayed payment models were performed in parallel, i.e. the survey, the targeted literature review and the expert sessions. Hence, clear backtracking of sources for each barrier and recommendation would be cumbersome. The primary limitation of my thesis is the inclusion of only a select number of CEE and ME countries in the workshop and survey that explored the challenges and recommendations for delayed payment schemes and outcome-based reimbursement models. Despite the limited number of experts at our workshops, they possessed extensive knowledge of the healthcare financing system in

their respective countries. My thesis concentrated on identifying barriers and recommendations that are significant to the LICs within the CEE and MENA regions. These recommendations were developed from the perspective of healthcare payers from various countries. The broader implications and practicality of these recommendations at the country level should be explored in further research. While the barriers and recommendations were deemed applicable across all participating countries, they were not prioritized in terms of importance. Such prioritization needs to be tailored to each country's specific context, presenting an opportunity for additional research in this field. (Ádám, 2022)

As for Phase 3, we used only PubMed for the targeted literature review considering the novelty of the research topic. Extending the search to additional white-paper-based databases would not likely result in further relevant studies. As for identifying barriers of adopting DHTs to the Hungarian public reimbursement system, interview may not be the best study design. Considering the novelty of the topic of public reimbursement of DHTs, the lack of a widely used scheme for public reimbursement of DHT use in Hungary, the conflict of interests between different market domains and the limited number and availability of experts, we decided to use the interview method despite its disadvantages, e.g. potential bias due to respondents' background, region, and specialty. There were a small number of interviewees, however, we made the decision to launch a pilot first, i.e. focus rather on people who really understand the topic instead of asking large number of non-experts. Following the pilot interview phase, conducting wider research is suggested to confirm results. As data saturation was validated throughout the interview process, and once no new information was received within a domain (min. 2 interviews), we finished that domain. It may be possible that further insights could be retrieved in other study designs, such as the Delphi method. As the interviewees were selected in a snowball method, it is a concern that like-minded people were selected for the interviews from different domains. In a follow-up research these limitations could be tackled.

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6. Conclusions

The main conclusions for the research questions are summarized below.

Firstly, a variety of public push and pull mechanisms are available to support the R&D of health technologies. The case of orphan medicine demonstrates that public interventions are crucial to facilitate R&D in neglected disease areas. However, government failures may arise when market mechanisms are overactivated, potentially leading to market failure. The concept of pull financing incentives is already motivating the pharmaceutical industry and could be adapted for the DHTs. Currently, the process of developing DHTs lacks validating unmet medical needs. Introducing pull financing incentives in larger markets, such as the EU, could implicitly validate and address the unmet medical needs within the DHT field.

LICs, particularly in the less affluent regions of the CEE and the ME, can mitigate the uncertainty of clinical outcomes for technologies with limited clinical trial evidence (e.g., orphan medicines, technologies during urgent periods like the pandemics) by adopting outcome-based payment models. Several barriers exist, but the most effective implementation could be through pilot agreements in specific therapeutic areas.

Countries in the CEE region can address the affordability of potentially curative technologies with high upfront costs, such as ATMPs, by introducing delayed payment models. While there are numerous barriers, this research offers several practical recommendations.

Hungarian innovators could benefit from adopting international public payment models for DHTs. Various frameworks provide insights from pilot programs and real-world implementations. Initially, it is crucial to recognize DHTs as a potential area for public payment to prevent legal ambiguities. Regrettably, the expectation of implementing such payment models in Hungary within the next 2-3 years is not realistic. The necessary framework is absent, and Hungary has not been participating in international working groups. It is more likely, that Hungary will adopt EU-harmonized frameworks, if there would be any.

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7. Summary

Introduction: Pharmaceutical research and development (R&D) have transformed significantly over recent decades, with notable success in addressing unmet medical needs, especially in orphan diseases. However, discovering solutions alone does not ensure patient access. High upfront costs of new technologies burden global healthcare systems with affordability and efficacy uncertainties. In Central Eastern Europe (CEE), where resources are scarce, these challenges are even more acute. While no gold standard exists for addressing these issues, digital health technologies (DHT) are rapidly entering the market, though payment models for patient access remain unresolved.

Objectives: (1) Overview of the pharmaceutical R&D incentives available in the past in European, supranational level. (2) Identify barriers and potential solutions for payment models for new types of technologies in CEE, focusing on outcome-based payment models and delayed payment models. (3) Identify the status quo of public payment models for DHTs in Hungary.

Methods: (1) Scoping review. (2) Targeted literature review, survey, expert sessions, workshops. (3) Targeted literature review, individual expert interviews.

Results: (1) Impact of R&D incentives in pharmaceutical industry based on the example of rare diseases. (2) For implementing outcome-based payment models, 20 barriers were identified and organized into five groups: transaction costs and administrative burden, measurement issues, IT and data infrastructure, governance, and perverse policy outcomes. A series of recommendations were developed to overcome these obstacles. Barriers and recommendations for delayed payment models were categorized into four groups from the perspective of public healthcare payers: transaction costs and administrative burden, payment schedule, IT and data infrastructure, and governance. A total of 15 recommendations were articulated. (3) 21 barriers were identified for implementing payment models for DHTs, summarized in the PESTLE framework.

Discussion: Under certain limitations, CEE countries should focus on pull incentives (facilitate reimbursement). Further research could explore the impact of introducing the outcome-based and delayed payment models in CEE countries. Integration of DHTs into the public healthcare financing system should be developed.

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11. Annexes

Annex 1 – Interview questionnaire

Integrating digital health technologies into public healthcare system in Hungary

– Interview –

The pandemic has further accelerated the already intense digitalization of healthcare systems. This process has raised the question of integrating digital health technologies into publicly funded healthcare systems in many countries. Accordingly, physicians could prescribe certain phone applications or online platforms, and the cost of using these (like reimbursed medications) could be partially or fully financed by health insurers.

Germany and Belgium were the first in Europe to introduce a public reimbursement system for digital health technologies and its methodology. In Hungary, there is no developed system for the public financing of these technologies; independent digital health technologies cannot receive NEAK (National Health Insurance Fund of Hungary) funding, and digital applications supporting medication adherence do not result in a price premium or special advantage in medication price reimbursement.

Digital health technologies can be categorized into several groups based on their application and use. **The interview focuses on digital technologies used independently or in combination with medication for therapeutic or diagnostic purposes, as illustrated in the following table with xx.**

	Care coordination	Diagnostics	Therapy
Independent use		xx	xx
Combination: medicine + app			xx
Combination: medical device + app			

The following interview seeks to gather information on the topic from your professional opinion and experiences.

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I. Present

9. What role do you currently attribute to digital health technologies (e.g., therapeutic health mobile applications) in the present and future of the Hungarian healthcare system?
10. Do you know of any cases where digital technologies have been integrated into Hungarian patient care (e.g., applications for treating panic disorder or depression)? In which areas do you see the greatest potential for breakthroughs?
11. If digital health technology is developed in Hungary, what is the communication like between the financier of the development and the development team during the process? In your experience, does the validation of unmet (domestic or international) healthcare needs occur for the financier of the development?

II. Prospects

12. Would it be justified for certain digital health technologies to receive public reimbursement in Hungary? If so, what factors would justify this?
13. In which therapeutic area would the greatest health gain be expected from the application of digital technologies?

    - Oncology
    - Cardiology
    - Psychiatry
    - Metabolic Diseases (diabetes, etc.)
    - Dermatology
    - Other: …

III. Barriers

14. What health policy measures are necessary for digital health technologies to spread more widely in Hungary?
15. Do you think Hungarian doctors and patients would accept and use the mentioned digital solutions?

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16. Recently, a European Union working group was formed to facilitate the development of a system for the public financing of digital health technologies in EU member states. The expert team does not include a Hungarian delegate, although the development of digital health technologies is also a priority for healthcare companies. What do you think is the reason for the lack of Hungarian participants in the EU initiative, and what could be the consequences? Would you consider Hungarian participation in such international working groups necessary?

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Annex 2 – Summary of the Candidate's contributions to the publications

Contribution / Publication	Ádám et al. (2021)	Ádám et al. (2022)	Ádám et al. (2022)	Callenbach et al. (2023)	Mezei et al. (2023)
Conceived the ideas or the design of the study	L	P	P	P	P
Performed data collection	L	L	L	L	P
Data analysis and interpretation	L	L	L	P	P
Primary author (wrote most of the paper or drafted the paper)	L	L	L	P	P
Provided revision to scientific content of the manuscript	L	P	P	L	L
Implemented revisions based on comments and/or requests of independent reviewers	L	L	L	P	P

Legend:

P: The candidate actively participated in carrying out these tasks

L: The candidate led the task, or carried out the task on his, or mostly on his own

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Annex 3 – Summary of own contributions

Own contributions

Phase 1

- All research tasks were planned and performed on my own under the supervision of my supervisor.

Phase 2

It was a complex research phase, including research within the HTx project. The following tasks were carried out on my own:

- TLR, including
    - Compiling the search terms for MEDLINE database
    - Running trial searches
    - Identifying grey literature sources, compiling search terms, and running these searches in Google Scholar
    - Running the final search terms in MEDLINE, extracting bibliographic records
    - Screening by title and abstract, full-text screening
    - Primary data extraction and data verification
- Preparing the first draft of the list of barriers and recommendations for outcome-based payment models and delayed payment models
- Organizing expert sessions and taking detailed notes during internal and external expert sessions and validation workshop in June 2021
- Participating in the final validation workshop in June 2021, preparing detailed notes of the discussion within the working group (in a breakout room due to the virtual nature) to discuss barriers and recommendations created by the HTx project team
- Preparing the first version of the first (Ádám et al. 2021) and second manuscript (Ádám et al. 2021) (both text content and figures/tables)
- Liaising with co-authors about the manuscripts, implementing the comments received from them prior to submission
- Finalizing the manuscripts
- Handle the submission procedure for both manuscripts

- Revisioning the scientific content of the manuscripts based on the comments and requests of the independent reviewers
- Processing the results of the survey in parallel with Marcelien Callenbach, who was the first author of the manuscript (Callenbach et al. 2023) describing the results of the survey
- Reviewing and suggesting modifications as a co-author to the fourth manuscript (Callenbach et al. 2023)

Phase 3

- Conceive the ideas and the design of the research
- Putting together the list of interviewees for discussion and approval of my supervisor
- Performing the pilot interview with my supervisor based on the interview guide and questions approved
- Checking data saturation throughout the whole research
- Putting together the list of barriers based on the interviews, including removing duplications
- Organizing barriers to the PESTLE framework
- Carrying out the second TLR of international practices of public reimbursement of DHTs in Belgium in July 2023
- Writing part of the fifth manuscript (Mezei et al. 2023), the part specifically related to Belgium, including review of the full manuscript and providing responses to the independent reviewer's comments

Candidate's work in the research group

Phase 2

- Overview of classification of different types of MEAs and payment models for innovative technologies
- Reviewing and commenting on the questions of the survey
- Inviting experts from different backgrounds and countries to participate in the surveys

- Preparing for and attending expert sessions where interim status was discussed and further research areas
- Grouping and deduplicating the extracted barriers and recommendations, then forming groups
- Resolving conflicts arise during the grouping of barriers and recommendations
- Modifying the list of barriers and recommendations between validation steps
- Prepare a detailed description of each barrier and recommendation

Phase 3

- Supervising the work of Máté Pálfi, undergraduate pharmacist student, writing his thesis in the subject, including
    - Reviewing the initial search term compiled by Máté Pálfi for the TLR
    - Reviewing the results of trial searches, suggesting amendments to the search term
    - Reviewing data extraction prepared by Máté Pálfi
    - Reviewing and modifying interview questions prepared by Máté Pálfi
- Preparing the list of questions for the interview
- Carrying out some interviews together with Máté Pálfi (some of them on my own)
- Identify patterns based on the inputs received in the interviews
- Processing the interview transcripts