PAYMENT MODELS FOR FUTURE HEALTH TECHNOLOGIES IN CENTRAL AND EASTERN EUROPE

PhD thesis

Ildikó Ádám

Semmelweis University Doctoral School

Pharmaceutical Sciences and Health Technologies Division

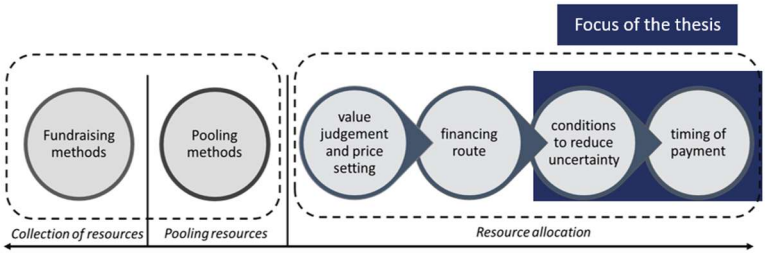
Supervisor:	Zoltán Kaló, Ph.D
Official reviewers:	Fanni Rencz, D.Sc Balázs Babarczy, Ph.D
Head of the Complex Examination Committee:	Romána Zelkó, D.Sc
Members of the Complex Examination Committee:	Zoltán Vokó, D.Sc Marcell Csanádi, Ph.D

Budapest
2025

1. Introduction

Pharmaceutical research and development (R&D) have undergone a profound transformation over recent decades with notable successes in addressing unmet medical needs, especially in orphan diseases. Discovering potential solutions to medical problems alone is insufficient; it does not automatically attract pharmaceutical developers to invest into areas with unmet medical need. Hence, public incentives are essential. The public incentives can be categorized into two groups: push and pull mechanisms. Push mechanism reduce necessary investment to R&D. Pull mechanisms are targeted to increase the return on R&D investment.

High upfront costs of new therapies burden global healthcare systems with affordability and efficacy uncertainties. In Central and Eastern Europe (CEE) where resources are scarce, these challenges are even more acute. Due to the high upfront costs health care payers need to find a solution for two different problems: (1) how to manage the uncertainty around whether long-term effects will be realized, and (2) how to overcome challenges of managing the short-term budget impact of these therapies. In my thesis I focused on these aspects of health care financing as illustrated below.



Health care financing of new health technologies

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.

2. Objectives

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

	Phase 1	**Phase 2**	**Phase 3**
Research Objectives	Overview pharmaceutical R&D incentives available in 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 in European level?	2.a) How countries in the CEE region can 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?

Summary of research objectives and research questions divided by research phases

3. Methods

3.1. Policy tools for supporting pharmaceutical R&D in 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 European Union (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 in the thesis.

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 therapies (Vreman, 2020). To understand the barriers of introducing outcome-based payment models and delayed payment models, and formulate recommendations thereto, a targeted literature review, a survey, several expert sessions, and two parallel workshops were conducted in the frame of the EU-funded Next Generation Health Technology Assessment (HTx) project. 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; Egypt, Jordan, and Lebanon; and the Netherlands, Sweden and the United Kingdom. The methods for identifying barriers and recommendations are summarized in the below figure.

Summary of identifying barriers and recommendations

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

A targeted literature review (TLR) was conducted to map the existing scientific literature on public reimbursement strategies for DHTs. The search strategy and results are summarized in the thesis based on the work in collaboration with Máté Pálfi (Pálfi, 2023). The search strategy is summarized in the below table.

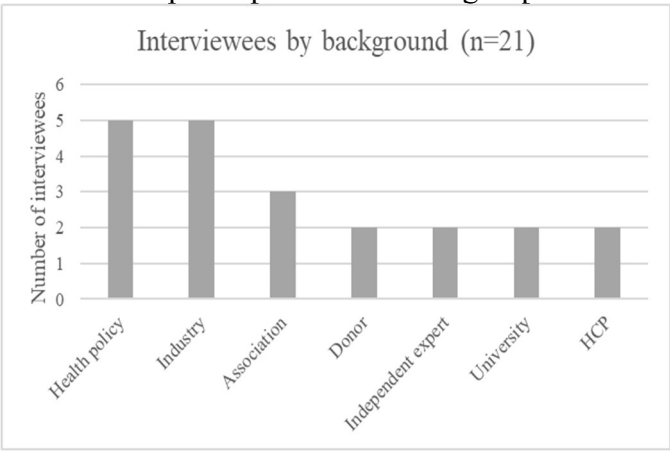
First search term group	(((Digital health technologies[Title/Abstract]) OR (Digital health applications[Title/Abstract])) OR (Health app policy[Title/Abstract])) OR (DiGA[Title/Abstract])
Boolean operator	AND
Second search term group	((Reimbursement[Title/Abstract]) OR (Financing[Title/Abstract])) OR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

Search term applied for TLR (Pálfi, 2023)

I participated in the working group organized by the Hungarian Chapter of ISPOR, which evaluated international practices in Health Technology Assessment (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 in the thesis. 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

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. Interviewees were carefully chosen to reflect a range of perspectives. We successfully conducted 21 interviews. The following chart summarizes the respondents' background and the number of participants from each group.



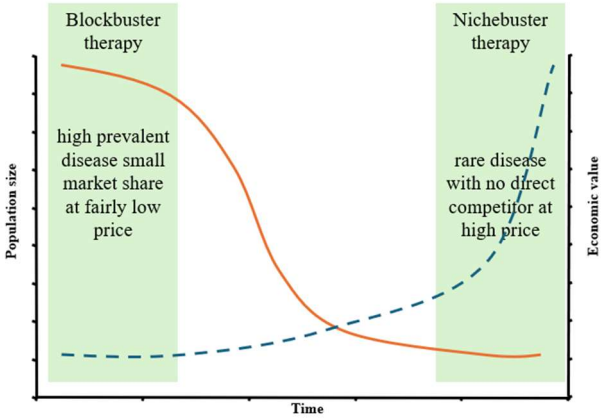
Number and background of interviewees

For the interviews, we followed widely accepted best practices and principles in qualitative research methodology. 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.

4. Results

4.1 Policy tools for supporting pharmaceutical R&D in European level (Objective 1)

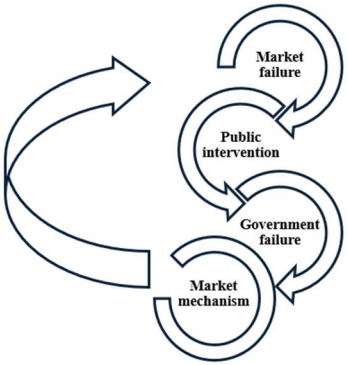
Given that unmet medical needs are often greater in diseases affecting smaller populations, public policymakers have had to incentivize pharmaceutical companies to invest in these areas. This has led to a paradigm shift in pharmaceutical R&D, moving from blockbuster therapies to "nichebuster" therapies - treatments for rare diseases without a competition, offered at high prices. The below figure illustrates that the justifiable price as determined by economic value and disease rarity, is inversely proportional.



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

An example of the influence of public financial and non-financial incentives on addressing health care challenges can be observed in the realm of rare diseases. The below figure illustrates the sequence of events in this domain. The decision into investing in a new drug candidate is fundamentally a business decision, made only in the expectation of a positive net

present value. The unmet medical need is usually higher in small patient population. Consequently, in the absence of public initiatives, the field of rare diseases experienced a market failure (first circle). Coordinated public interventions at the largest pharmaceutical markets have encouraged pharmaceutical companies to pursue therapies for rare diseases (second circle). This has led to a paradigm shift in pharmaceutical R&D, moving from blockbuster therapies to "nichebuster" therapies - 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 therapies while also protecting the health care budgets (third circle). The emergence of "nichebuster" therapies as blockbuster drugs is attributable to the reinforcement of market mechanism (fourth circle). This success has also led to a new form of market failure, including limited patient access due to unjustifiably high pharmaceutical prices and limited evidence about the clinical benefits and safety of new orphan medicines. The situation necessitates further public interventions to improve the evidence base of orphan drugs and control pharmaceutical prices (left arrow).



Impact of R&D incentives in pharmaceutical industry based on the example of rare diseases

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 table of barriers and recommendations is presented below.

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 health care providers to collect data	1) Health care institutions should opt-in to prescribe medicines in outcome-based schemes

Group of barriers	Barriers	Recommendations
		2) Involve leading centres 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 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 health care delivery

Group of barriers	Barriers	Recommendations
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 health care system limit the scope of outcomes to hard endpoints 2) Promote national platform for outcome based agreements with system based incentives even in fragmented health care 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 health care 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

Group of barriers	Barriers	Recommendations
	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
	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 centres	1) Consider that no agreement would result in no patient access to new technologies 2) Extend the scope of prescribing centres when renegotiating the agreement
	No improvement in the evidence based 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

Group of barriers	Barriers	Recommendations
		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 to implement value-based health care, as due to confidentiality of actual prices, true cost-effectiveness of any health care 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

Summary of barriers & recommendations for health care payers for the implementation of outcome-based reimbursement models in CEE (Ádám, 2022)

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

Barriers and recommendations were categorized into four groups from the perspective of public health care 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. A table below summarizes the barriers and recommendations for delayed payment models.

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 health care 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 the 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 health care 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
	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

Summary of barriers & recommendations of delayed payment models in CEE from the perspective of health care payers (Ádám, 2022)

4.4 Payment models for DHTs in Hungary (Objective 3)

Based on the TLR and scoping review performed, although there is no EU level framework for adopting DHTs to health care 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. Following the international regimes, as described previously, due to the lack of widely used international framework for adopting DHTs to the health care system, the thesis focused on the case of Hungary. We focused on understanding the status quo of DHTs in the Hungarian health care system and identifying the barriers for adopting public reimbursement scheme for DHTs in Hungary in the frame of interviews with different stakeholders. The barriers are summarized in the Political, Economic, Social, Technological, Legal and Environment (PESTLE) framework.

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

Barriers of adopting DHTs in Hungary summarised in PESTLE framework

5. Conclusions

A variety of public push and pull mechanisms are available to support the R&D of health technologies. The case of orphan medicines demonstrates that public interventions are crucial. 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 lack of 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.

Lower-income countries (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) 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 Advanced Therapy Medicinal Product (ATMPs), by introducing delayed payment models. While there are numerous barriers, this research offers several practical recommendations.

Hungary could benefit from adopting international public payment models for DHTs. 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-harmonised frameworks, if there would be any.

6. Bibliography of the candidate's publications

Publications related to the thesis:

1. **Ádám I.**, Kaló, Z. (2021). Development of public financing initiatives in pharmaceutical R&D – is it the key to the future of medicine? Kaleidoscope Művelődés-, Tudomány-, és Orvostörténeti Kiadványok, 2021/22, 316-324.
   IF: -
2. **Ádám I**, Callenbach M, Németh B, Vreman RA, Pontén J, Strbad T, Dawoud D, Kostyuk A, Seyam A, Nagy L, Goettsch WG and Kaló Z (2022) Delayed payment schemes in Central-Eastern Europe and Middle-East. Front. Med. 9:940371.
   IF: 3.9
3. **Ádám I**, Callenbach M, Németh B, Vreman RA, Tollin C, Pontén J, Dawoud D, Elvidge J, Crabb N, van Waalwijk van DoornKhosrovani SB, Pisters-van Roy A, Vinczickzki Á, Almomani E, Vajagic M, Oner ZG, Matni M, Fürst J, Kahveci R, Goettsch WG and Kaló Z (2022) Outcome-based reimbursement in Central-Eastern Europe and Middle-East. Front. Med. 9:940886.
   IF: 3.9
4. Marcelien H.E. Callenbach, **Ildikó Ádám**, Rick A. Vreman, Bertalan Németh, Zoltán Kaló, Wim G. Goettsch (2023) Reimbursement and payment models in Central and Eastern European as well as Middle Eastern countries: A survey of their current use and future outlook, Drug Discovery Today, Volume 28, Issue 1, 103433.
   IF: 6.5
5. Mezei F, Horváth K, Pálfi M, Lovas K, **Ádám I** and Túri G (2023) International practices in health technology assessment and public financing of digital health

technologies: recommendations for Hungary. Front. Public Health 11:1197949. **IF: 3.0**

∑ **IF: 17.3** (as of 12 May 2025)