ELSEVIER

Feature

Reimbursement and payment models in Central and Eastern European as well as Middle Eastern countries: A survey of their current use and future outlook

Marcelien H.E. Callenbach [1], Ildikó àdám [2], Rick A. Vreman [1,3], Bertalan Németh [4], Zoltán Kaló [2,4], Wim G. Goettsch [1,3,*]

There is growing interest in innovative reimbursement and payment models in Central and Eastern European (CEE) and Middle Eastern (ME) countries. A questionnaire was sent to payers from CEE and ME countries regarding the current use of, future preferences for and perceived barriers with these models. Twenty-seven healthcare payers from 11 countries completed the survey. Results showed participants preferred using outcome-based reimbursement models and delayed payment models more often; however, currently they are rarely applied. Barriers hindering implementation were mostly related to IT and data infrastructure, measurement issues, transaction costs and the administrative burden. Given these barriers highlighted in our study, policymakers should focus on the development of an implementation framework with contract templates for the preferred reimbursement and payment schemes to aid the feasibility of a successful implementation.

Keywords: outcome-based reimbursement; managed entry agreements; Central and Eastern Europe; delayed payment; Middle East; pharmaceutical reimbursement

Reimbursement and payment models in CEE and ME countries

Pharmaceutical interventions associated with high prices and large uncertainties are increasingly challenging the sustainability of healthcare reimbursement systems.[1–6] Given that healthcare budgets are restricted, competent authorities for pricing and reimbursement (CAPR), such as healthcare payers, governmental organisations or health technology assessment (HTA) agencies, are challenged to find solutions for optimising expenditure of, and access to, medicines.[2–4,7–8] Consequently, innovative arrangements between CAPR and drug manufacturers aiming to enable access to new medicines, while sharing risks due to uncertainty, are gaining relevance.[4,7,9–13].

These arrangements can exist in a variety of forms and combinations and are often referred to as 'managed entry agreements' (MEAs) and/or 'risk-sharing arrangements.[2,13–15] They can be defined as "arrangements between drug manufacturers and CAPR that ensure access to coverage or reimbursement of a drug under specified conditions".[2,13–15] Such agreements can be further divided into arrangements that relate to pricing and reimbursement status (reimbursement models) and the way payments are organised (payment models). Reimbursement

https://doi.org/10.1016/j.drudis.2022.103433

models are usually broken down into two main categories: purely financial agreements (e.g., discounts); and outcome-based agreements (e.g., pay-for-performance).[2,16–19] Payment models can be structured such that the therapy is paid upfront (i.e., before the treatment is delivered it is agreed that full payment will be made before or after delivery, possibly with rebates when a result is not achieved) or with a delayed or spread-out payment [possibly only after certain (prespecified) results have been achieved].[2,16–18].

To mitigate high upfront payments and to answer remaining uncertainties that often go hand in hand with the introduction of innovative therapies, outcome-based reimbursement models and delayed payment models have especially been seen as promising alternatives to the more commonly used finance-based and upfront agreements.[2,18,20] However, there is considerable variation between countries regarding how payment and reimbursement systems are organised.[21] Research shows that the applicability of these models might therefore differ between countries.[3,8,18,21]

Much attention has been given to different models and their implementation feasibility in high-income countries.[9–10,18–19,22–24] Nevertheless, little is known about how transferable these models are to lower-income countries such as those in Central and Eastern Europe (CEE)[25] and the Middle Eastern (ME)[26] that are facing the same challenges as high-income countries.[1,27–28] The population health status in these countries is generally poorer compared with high-income countries and healthcare resources are more limited. Most CEE and ME countries often do not have a clear roadmap for HTA implementation and have a much greater social opportunity cost of adopting inappropriate health technologies and introducing inappropriate decisions on pricing and reimbursement.[1,29–31] Given that the way in which countries organise their healthcare systems and funding and the way decisions are made have an impact on the success of the implementation of payment and reimbursement models, a greater understanding is required of the compatibility and transferability of these models to CEE and ME countries because there can be considerable concerns with funding and reimbursing new biological medicines.

This study was designed to gain an understanding of the implementation of innovative payment and reimbursement models in CEE and ME countries and to provide future directions that might be followed. Through a survey, the experiences and barriers experienced in pricing and reimbursement by stakeholders from CEE and ME countries were investigated, as well as their preferences regarding the current and future use of innovative payment and reimbursement models.

The view of relevant payer experts

The survey was aimed at experts in pricing and reimbursement, most notably those with current or former payer experience or involvement in CAPR processes from multiple CEE and ME countries. Depending on their jurisdiction, the stakeholders fell into the following categories: current or former members of regional or national healthcare payers and health technology assessment agencies; academic experts; or consultants in healthcare financing. Selecting the response group across these categories allowed opinions from different perspectives and experiences to be captured. The specific stakeholder representatives were selected based on their seniority and their involvement in pricing and reimbursement mechanisms and were approached through purposeful sampling. The targeted stakeholders were invited to take part through a standardised email between May and July 2021. The invitation included a Word document of the survey as well as an online link. To secure that all participants had the same definition in mind when answering the survey, a knowledge clip was shown when opening the survey and a definition list of the different payment and reimbursement models was included (see Supplementary Material online). The survey was followed up by a workshop for which the results are reported elsewhere.[32] The survey and the workshop are part of the HTx project. HTx is a Horizon 2020 project supported by the European Union lasting for 5 years from January 2019. The main aim of HTx is to create a framework for the Next Generation HTA to support patient-centred, societally oriented, real-time decision-making on access to and reimbursement for health technologies throughout Europe.[33]

Out of the 37 stakeholders invited to fill out the survey a total of 27 participants completed the survey (response rate 73%). In total, stakeholders from 11 different countries (17 countries were invited) completed the questionnaire (Table 1). More than half of the stakeholders who filled out the survey were current members of regional or national healthcare payers (n = 15). The other stakeholders were mainly former members of regional or national healthcare payers who now have a position at a health technology assessment agency (n = 4) or work as consultants in healthcare financing (n = 5) or academia (n = 3). Most respondents indicated they came from a country with a centralised HTA institution (n = 12). Additionally, most HTA institutions have a weak influence on health-decision-making (n = 13), according to the respondents. In over half of the countries there are multiple payer organisations to provide a basic benefit package (n = 15).

The questionnaire was divided into two parts according to the split of managed entry agreements into reimbursement models as well as payment models. The first part questioned the current use of, future preferences for and perceived barriers with reimbursement models; whereas the second part questioned these three elements for payment models. These questions were asked for in- and out-patient pharmaceuticals to identify whether differences exist between them for these three elements. To supplement the two main sections of the survey, information was gathered about the individual stakeholders and the healthcare systems, and there was room for additional comments. Thus, in total, the questionnaire included 22 questions arranged according to five domains: (i) the role of the respondent within the healthcare system; (ii) how the healthcare system of the respondent is organised; (iii) the use of reimbursement models; (iv) the use of payment models; and (v) arrangements beyond those included in this survey (questionnaire available, see Supplementary Material online). The included reimbursement and payment models and taxonomy were based on previous work,[17] with minor adaptations to reflect the setting of lower-income countries (see Supplementary Material online for definitions). The developed survey was tested on content and construct valid-

TABLE 1

Respondent nations and healthcare system descriptions.

Description	Number of descriptions (overall *n* = 27)
Nations	
Jordan	4
Turkey	4
Kazakhstan	3
Poland	3
Slovakia	3
Croatia	2
Egypt	2
Slovenia	1
Serbia	1
Hungary	1
Czech Republic	1
Ukraine	1
Romania	1
Centralized HTA institution	
No	6 (22%)
Yes	12 (44%)
No HTA institution exists	9 (33%)
Influence of HTA institutions on healthcare decision-making	
Strong HTA institution	5 (19%)
Weak HTA institution	13(48%)
No HTA institution exits	9 (33%)
Number of payer organizations to provide basic benefit package	
One	12 (44%)
Multiple	15 (56%)
Difference between inpatient and outpatient pharmaceuticals regarding types of reimbursement models applied	
Yes	15 (56%)
Difference between inpatient and outpatient pharmaceuticals regarding types of payment models applied	
Yes	14 (52%)

ity by the authors and was pilot tested to verify the format, clarity, length and usability of the survey for the setting in question.[34,35] Any comments were used to make revisions. The survey instrument was programmed in LimeSurvey. The results were generated from completed surveys; however, if some answers were missing but the survey was still completed to the end those responses were included.

The collected information was of a qualitative and quantitative nature. Quantitative questions included reimbursement and payment models currently used and which models are preferred to be used more often for in- and out-patient pharmaceuticals by indicating this using Likert scales. If no large differences were found between the results for in- and out-patient pharmaceuticals the results were combined and presented in one figure. Country characteristics were questioned using multiple-choice questions where the results were analysed individually. Qualitative information focused specifically on the introduction of innovative models (i.e., the perceived barriers with outcome-based reimbursement models and delayed payment models). These open questions were analysed using NVivo 12 Pro (QRS International).[36] Where a node structure was used to structure the barriers that were perceived (see Supplementary Material online). The basis of this node was inductive and deductive because the main categories were based on previous literature[18,37,38]; but if mentioned barriers fell outside these predefined categories new categories were added. The results are presented by first discussing the current use of reimbursement and payment models, followed by the preferred use and perceived barriers.

The current use of reimbursement and payment models

Current use of reimbursement models

In Figure 1 we merged data on in- and out-patient pharmaceuticals because, overall, no large differences were seen between those two categories. In the experience of the stakeholders, the finance-based reimbursement models are more often applied compared with the outcome-based reimbursement models – specifically, discounts and/or rebates are applied most. The outcome-based reimbursement models with evidence development and pay-for-outcome and outcome-guarantee models are currently used very little with ~60% of the stakeholders indicating that these reimbursement models are currently never applied in their countries.

Current use of payment models

Again, no large differences in the current use of payment models between in- and out-patient pharmaceuticals were reported and therefore the results were combined in Figure 2. It shows that upfront payment is the most applied payment model, whereas more than half of the respondents indicated that in their experience the different delayed payment models are currently rarely-to-never applied. Only for the countries where an HTA institution exists, annuity payments and health leasing are sometimes, or in a few cases rarely,

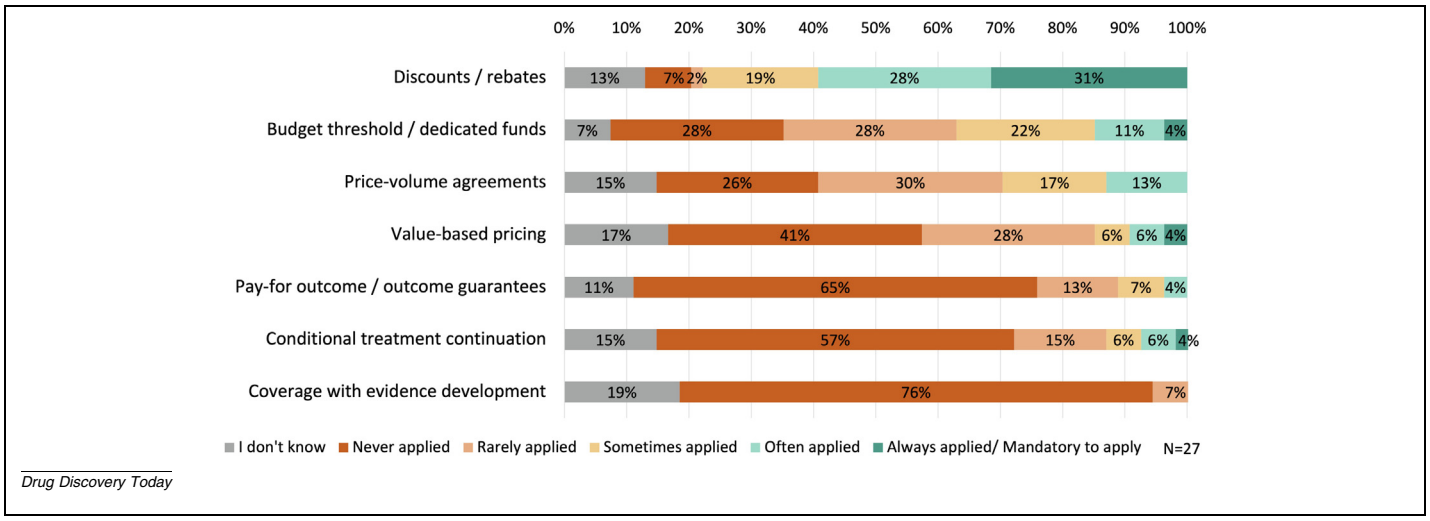

FIGURE 1

Current use of reimbursement models for inpatient and outpatient pharmaceuticals. The horizontal axis indicates the percentage of how respondents indicated the current use of the reimbursement model on a Likert scale.

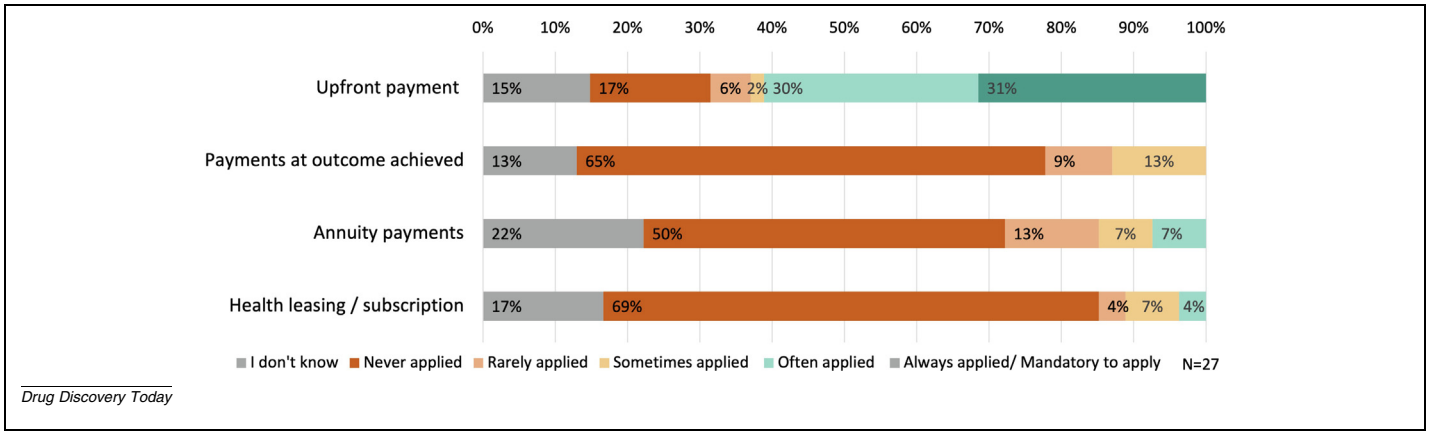

FIGURE 2

Current use of payment models for outpatient and inpatient pharmaceuticals. The horizontal axis indicates the percentage of how respondents indicated the current use of the payment model on a Likert scale.

applied. In countries where no HTA institution exists only upfront payment models are applied.

Future preferences for reimbursement and payment models

Preferences for reimbursement models

The respondents were asked to indicate which models they would prefer to be applied more often in 5 years from now. No large differences were found, and the results were combined. The majority of the stakeholders indicated that they would prefer the outcome-based reimbursement model pay-for-outcome and outcome-guarantee to be applied more often (Figure 3). A majority would also prefer value-based pricing to be applied more often.

Preferences for payment models

Stakeholders indicated a clear preference for certain payment models to be applied more often than currently. For in- and out-patient pharmaceuticals, almost 80% of the stakeholders indicated that they prefer the payments at outcomes achieved to be applied more often (n = 24). Stakeholders from CEE and ME countries show similarities in their preferences for payment at outcome achieved, with 80% of the stakeholders from these countries indicating this.

Perceived barriers with the implementation and use of outcome-based reimbursement models and delayed payment models

Perceived barriers with the implementation and use of outcome-based reimbursement models

To gain insight into what is currently preventing outcome-based models to be applied more often, the respondents were asked to elaborate on which barriers are currently encountered with pay-for-outcome, conditional treatment continuation and coverage with evidence development (Table 2). The most often mentioned barriers experienced with pay-for-outcome reimbursement models are

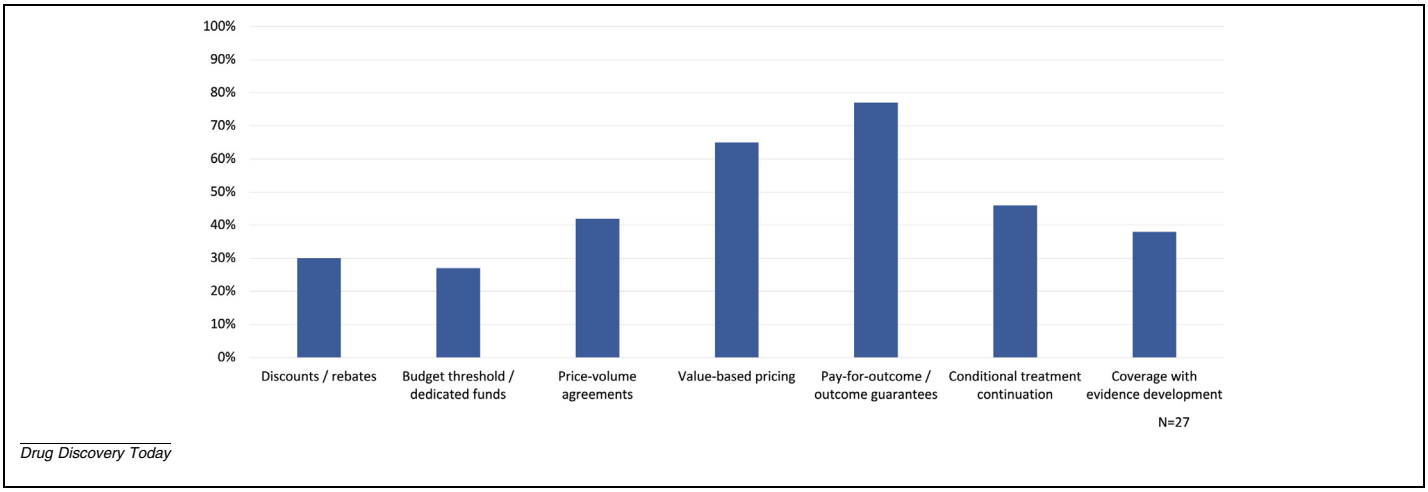

FIGURE 3

Percentage of stakeholders that indicated per reimbursement model whether they preferer the reimbursement models (Yes/No) to be applied more often 5 years from now.

related to 'IT and data infrastructure', where especially "the failure to capture the necessary data to reduce uncertainty within the current infrastructure" was frequently mentioned. Additionally, barriers regarding 'transaction costs and administrative burden' were raised often with, specifically, the complex and timely negotiations on contractual terms with drug manufacturers. 'Measurement issues' given a lack of health economic and outcome research expertise to define hard endpoints were also perceived as a main barrier. For the 'conditional treatment continuation' of the reimbursement model, this measurement issue was also the most mentioned barrier. Hereafter the most perceived barrier for conditional treatment continuation was related to 'transaction costs and administrative burden' where especially "the lack of resources to organise and implement the reimbursement model" such as lacking personnel, budget and capacities were mentioned as barriers hindering a more frequent use. However, the most barriers were perceived for coverage with evidence development reimbursement models. Especially, barriers around 'IT and data infrastructure' again were mentioned often as a reason why this model is not implemented more often. Barriers surrounding the failure to capture the necessary data to reduce uncertainty within the current infrastructure were perceived most, followed by a limited uptake of patient registries. Another mentioned barrier was related to 'governance', wherein the experiences of the respondents regarding the regulatory framework of CEE and ME countries do not support coverage with evidence development models to be implemented more often.

Perceived barriers to the implementation and use of delayed payment models

When asked to elaborate on what the greatest barriers are that prevent delayed payments to be applied more often in their country, the stakeholders mentioned the most barriers with the payment-at-outcome-achieved models (Table 2). The greatest barriers with this payment model were perceived with its "transaction costs and administrative burden" where respondents especially mentioned the costly implementation and the complexity of the contracts as barriers hindering the implementation of payments-at-outcome-achieved in models more in the future. Barriers with the 'IT and data infrastructure' were also mentioned frequently, especially the lacking infrastructure to monitor patient statuses, in addition to barriers with the 'payment schedule', owing to limited experience with determining the optimal amount and/or duration of payments. Looking at the delayed payment model annuity payments and health leasing, the most perceived barrier relates to the 'payment schedule' where difficulties are experienced with conflicting financial flows of both parties involved owing to 12-month budgetary cycles.

Implications of the observed current use of, future preferences for and perceived barriers with the different reimbursement and payment models

Our inquiry shows that the stakeholders from CEE and ME countries report that finance-based reimbursement models, specifically discounts, are currently applied most in CEE and ME countries. The respondents indicated a preference for using outcome-based reimbursement models more in the future, where particularly pay-for-outcome models were preferred. Upfront payments are currently the most frequently applied payment model in CEE and ME countries. However, delayed payment models are preferred to be applied more often. The respondents especially preferred payment at outcome-achieved models to be applied more often in the future. A type of payment model that goes hand in hand with the preferred pay-for-outcome reimbursement model enforces the moment of payment for the therapy to be only after certain results have been achieved. The barriers of implementing outcome-based agreements were mostly related to IT and data infrastructure for payment-at-outcome-achieved models and coverage with evidence-development models, whereas the perceived barriers for conditional treatment continuation mostly related to measurement issues. Barriers preventing a more frequent implementation of delayed payments are mostly related to transaction costs, IT and data infrastructure when applying

TABLE 2

The most frequently perceived barriers with outcome-based reimbursement and delayed payment models.

Outcome-based reimbursement barriers		Delayed payment barriers	
IT and data infrastructure	Failure to capture the necessary data	*IT and data infrastructure*	Lacking infrastructure to monitor patient statuses
Transaction costs and administrative burden	Complex and timely negations on contractual terms The lack of resources to organize and implement the reimbursement model	*Transaction costs and administrative burden*	Costly implementation and the complexity of the contracts
Governance	Regulatory framework of CEE and ME countries does not support	*Payment structure*	Conflicting financial flows of both parties due to 12-month budgetary cycles Limited experience with determining the optimal amount and/or duration of payments.
Measurement issues	Lack of expertise to define hard endpoint and to capture them		

payment-at-outcome-achieved models. Barriers concerning the payment structures were perceived most often for annuity payments and health leasing. Considering that there is still a limited amount of available literature surrounding payment and reimbursement models in CEE and ME countries, the gained insights into which payment and reimbursement models are currently applied in CEE and ME countries, in addition to exploring future preferences and barriers perceived by current and former healthcare payers, are of added value. The presented overview can provide stakeholders from CEE and ME countries with future direction when implementing innovative reimbursement and payment models.

The results are in line with previously reported findings from CEE and ME countries and Western countries, where various studies confirm that finance-based reimbursement models and upfront payments are currently applied more often than outcome-based reimbursement models and delayed payments.[8,27,39–42] Ferrario *et al.* showed that the most common managed entry agreements (MEAs) in CEE countries are confidential discounts, a conclusion that was also found by Rotar *et al.* where finance-based MEAs are used frequently but performance-based MEAs are scarce and used to a limited extent in CEE countries.[28,38] Similar results are shown for ME and North African countries. The study by Maskineh *et al.* concluded this as well. Given the complexities typically involved in outcome-based and delayed payment models, as well as the necessary infrastructure to undertake such models, these results are not surprising.[22,37,41,43] Many countries, including CEE and ME but also Western countries, appear to still be in their infancy when it comes to the necessary preconditions for such models, for example a mature information infrastructure.[14,27,39–41] Multiple studies argue that the best practices for more-complex reimbursement and payment models, such as outcome-based agreements and delayed payments, are developed in countries with solid government mechanisms for reimbursement decisions and health outcomes research.[14,19,27,40,44] Given that more than half of the stakeholders from different CEE and ME countries indicated having a weak or absent HTA organisation, it is understandable that finance-based models are being applied most often.

Several studies illustrate a similar preference for outcome-based reimbursement models over finance-based models and delayed payment models over upfront payment.[9,27,37,45] Previous literature shows that these models are seen as promising alternatives to improve and ensure patient access, diminish the budget impact, reduce uncertainty, manage utilisation and address payer concerns regarding affordability in the pharmaceutical market.[14,37,46] Nevertheless, other studies show increasing use of more finance-based reimbursement models and upfront-payment models owing to the administrative burden and complexity of outcome-based agreements and delayed payments.[44,47]

Consistent with previous literature, we found that barriers relating to IT and data infrastructure, transaction costs and governance hinder the implementation of outcome-based reimbursement models.[9,19,24,38,41,44,47,48] However, other literature highlighted more concerns about bureaucracy and burdens mainly for clinical personnel.[19,24,49] In the recent literature review by Michelsen, the different barriers hindering spread payments are outlined in detail.[41] In this review, it is concluded that the main identified barriers for the implementation of spread payments reach an agreement on financial terms while considering 12-month budget cycles and the possible violation of corresponding international accounting rules. These results differ somewhat from ours where also other barriers preventing a more frequent implementation of delayed payments were mentioned, which related to the transaction costs, the IT and data infrastructure and the limited experience with determining the optimal amount and/or duration of payments. Given that the included countries in this study are lower-income countries compared with the countries in previous studies, it is explainable that these perceived barriers play a more prominent part in CEE and ME countries owing to more-restricted resources.

Recommendations

Some preliminary recommendations can be made on how to overcome these barriers and provide future direction. Firstly, a greater dialogue between experts in pricing and reimbursement, clinical opinion leaders, industry, governmental organisations, HTA agencies and patient representatives capturing different perspectives is encouraged at the initiation and follow-up of agreements stages. Through enhanced insight into each other's perspectives, more awareness is created about what the feasible options are and how each stakeholder group can contribute. This includes dialogues at the national and international levels. Through more European collabora-

tion and by joining international initiatives, learnings can be taken from each other's best practices. Secondly, if difficulties are expected with the data collection within the current infrastructure, a pilot phase to compare and evaluate different methods could be considered. Given that the stakeholders experienced barriers with how the current IT and data infrastructure support the implementation of the preferred outcome-based reimbursement models and delayed payment models, a lot could be gained by investigating how the existing infrastructure could be optimally used. Finally, the promotion of a national platform for outcome-based reimbursement models and delayed payment models could aid to overcome barriers related to the transaction costs and administrative burden. By providing country-specific implementation frameworks, contract templates for the most common reimbursement and payment schemes and legal guidance, the implementation of the preferred models would be more accessible.

Further research

Our findings could lead to some areas for further research. By including a broader range of involved stakeholders, such as stakeholders from pharmaceutical companies, clinicians or patient organisations, a more comprehensive overview can be given of the current situation, future preferences and perceived barriers. Given that it is still debated[19,28,46] about how much is exactly gained by implementing more-complex outcome-based reimbursement and delayed payment models, a frequent update on current use and experiences of CAPR stakeholders is of value to provide future direction in successfully implementing the most feasible models. Better knowledge of the effects of these agreements would help to improve the design of future agreements. Therefore, it is necessary to analyse whether the agreements are fit-for-purpose, while keeping the characteristics of governmental structures of CEE and ME countries in mind. This could be achieved by initiating pilot studies to systematically review the consequences of implementing outcome-based and delayed payment models in CEE and ME countries. Additionally, a pilot could also be initiated to review whether the additional data collected with these reimbursement and payment agreements could aid possible re-evaluations of the cost-effectiveness and recalculation of a value-based price.[50] This could enable the possibility of making better-informed reimbursement decisions and protect healthcare systems from a possible considerable loss of resources. Moreover, a pilot could also focus on what the consequences are when the medicine used as the reference in the calculations of the cost-effectiveness in reimbursement decision becomes available at a low-cost generic or biosimilar, appreciably altering the potential value the new medicine.[45] Finally, the application of the studied models is not mutually exclusive, therefore future research should focus on the possibility to combine elements in the same agreement and address different issues at the same time (e.g., budget impact and use, access and cost-effectiveness), specifically for CEE and ME countries.[18,37,51]

Limitations

The survey targeted stakeholders from CAPRs in CEE and ME countries; but it was not possible to contact stakeholders from all CEE and ME countries. Given that stakeholders were invited based on purposeful sampling, selection bias should be taken into account. Additionally, the general response rate from some countries was low. Furthermore, the presented results do not differentiate between countries that are part of the European Union and those that are not. These factors emphasise that caution should be taken with generalising the results to the entire CEE and ME region. However, our outcomes show a high level of homogeneity, and we aimed to invite key stakeholders with a vast knowledge of their fields, therefore they provide an adequate representation of the experiences and preferences for these models in these countries.

Concluding remarks

Despite the preference healthcare payers have for using outcome-based reimbursement models and delayed payment models more often in the future, they are currently rarely applied. For future use, stakeholders have indicated a specific preference for applying pay-for-outcome reimbursement models and payment-at-outcome-achieved models more often. These insights can provide stakeholders from CEE and ME countries with a future direction when implementing innovative reimbursement and payment models. Attention should be paid to which barriers are currently perceived because this could aid successful implementation. Further research is required and should focus on how to overcome the perceived barriers best and on exploring which combinations of reimbursement and payment models are most likely to be successful in CEE and ME countries.

Data availability

Data will be made available on request.

Acknowledgements

Funding

The HTx project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement no. 825162. The content of this paper reflects only the HTx group's views, and the European Commission is not liable for any use that might be made of the information contained herein. The article was prepared with the professional support of the Doctoral Student Scholarship Program of the Co-operative Doctoral Program of the Ministry of Innovation and Technology financed from the National Research, Development and Innovation Fund, Hungary. This project was funded by the Dutch National Health Care Institute as part of the Academic Living Lab for Health Technology Assessment.

Disclaimer

The views expressed in this article are the personal views of the authors and may not be understood or quoted as being made on behalf of or reflecting the position of the agencies or organisations with which the authors are affiliated.

Appendix A. Supplementary material

Supplementary material to this article can be found online at https://doi.org/10.1016/j.drudis.2022.103433.

References

1 L. García-Mochón, J. Espín Balbino, A Olry de Labry Lima, A. Caro Martinez, E. Martin Ruiz, V.R. Pérez, HTA and decision-making processes in Central, Eastern and South Eastern Europe: Results from a survey, Health Policy (New York) 123 (2019) 182–190, https://doi.org/10.1016/J.HEALTHPOL.2017.03.010.

2 M. Wenzl, S. Chapman, Performance-based managed entry agreements for new medicines in OECD countries and EU member states: How they work

and possible improvements going forward, OECD Health Working Papers 115 (2019), https://doi.org/10.1787/6e5e4c0f-en.
3 Vogler S, Paris V, Ferrario A, et al. How can pricing and reimbursement policies improve affordable access to medicines? Lessons learned from European countries Article (Accepted version) (Refereed) Original citation. Published online 2017. doi: 10.1007/s40258-016-0300-z.
4 A. Ferrario, P. Kanavos, Dealing with uncertainty and high prices of new medicines: A comparative analysis of the use of managed entry agreements in Belgium, England, the Netherlands and Sweden, Soc Sci Med 124 (2015) 39–47, https://doi.org/10.1016/j.socscimed.2014.11.003.
5 V.J. Wirtz, H.V. Hogerzeil, A.L. Gray, et al., Essential medicines for universal health coverage, The Lancet 389 (2017) 403–476, https://doi.org/10.1016/S0140-6736(16)31599-9.
6 D. Tordrup, H.A. van den Ham, J. Glanville, A.K. Mantel-Teeuwisse, Systematic reviews of ten pharmaceutical pricing policies - A research protocol, J Pharm Policy Pract 13 (2020) 22, https://doi.org/10.1186/s40545-020-00228-0.
7 C. Davis, H. Naci, E. Gurpinar, E. Poplavska, A. Pinto, A. Aggarwal, Availability of evidence of benefits on overall survival and quality of life of cancer drugs approved by European Medicines Agency: Retrospective cohort study of drug approvals 2009–13, BMJ (Online) 359 (2017), https://doi.org/10.1136/bmj.j4530.
8 J.C. Bouvy, C. Sapede, S. Garner, Managed entry agreements for pharmaceuticals in the context of adaptive pathways in Europe, Front Pharmacol 9 (2018) 280, https://doi.org/10.3389/FPHAR.2018.00280/BIBTEX.
9 T. Nazareth, J.J. Ko, R. Sasane, et al., Outcomes-based contracting experience: Research findings from U.S. and European stakeholders, J Manag Care Spec Pharm 23 (2017) 1018–1026, https://doi.org/10.18553/jmcp.2017.23.10.1018.
10 W.C.N. Dunlop, A. Staufer, P. Levy, G.J. Edwards, Innovative pharmaceutical pricing agreements in five European markets: A survey of stakeholder attitudes and experience, Health Policy (New York) 122 (2018) 528–532, https://doi.org/10.1016/j.healthpol.2018.02.008.
11 World Health Organisation (WHO). *WHO Guideline on Country Pharmaceutical Pricing Policies (Web Annex B)*.; 2020. https://apps.who.int/iris/bitstream/handle/10665/335705/9789240011908-eng.pdf.
12 T. Morel, F. Arickx, G. Befrits, et al., Reconciling uncertainty of costs and outcomes with the need for access to orphan medicinal products: A comparative study of managed entry agreements across seven European countries, Orphanet J Rare Dis 8 (2013) 1–15, https://doi.org/10.1186/1750-1172-8-198.
13 A. Ferrario, P. Kanavos, O. Dabbous, et al., Managed entry agreements for pharmaceuticals: the European experience, Ecancermedicalscience 12 (2013) 1–151. http://www.oecd.org/health/health-systems/Pharmaceutical-Innovation-and-Access-to-Medicines-Executive-Summary-ENGLISH.pdf%0Ahttps://www.duo.uio.no/bitstream/handle/10852/58667/Peters_Marjolein_Master_Thesis_EuH, https://doi.org/10.1016/j.jval.2018.11.010%0A.
14 F. Antonanzas, C. Juárez-Castelló, R. Lorente, R. Rodríguez-Ibeas, The Use of Risk-Sharing Contracts in Healthcare: Theoretical and Empirical Assessments, Pharmacoeconomics 37 (2019) 1469–1483, https://doi.org/10.1007/s40273-019-00838-w.
15 L.P. Garrison, A. Towse, A. Briggs, et al., Performance-based risk-sharing arrangements - Good practices for design, implementation, and evaluation: Report of the ISPOR good practices for performance-based risk-sharing arrangements task force, Value in Health 16 (2013) 703–719, https://doi.org/10.1016/j.jval.2013.04.011.
16 E. Hanna, M. Toumi, C. Dussart, et al., Funding breakthrough therapies: A systematic review and recommendation, Health Policy (New York) 122 (2018) 217–229, https://doi.org/10.1016/j.healthpol.2017.11.012.
17 J.J. Carlson, S.D. Sullivan, L.P. Garrison, P.J. Neumann, D.L. Veenstra, Linking payment to health outcomes: A taxonomy and examination of performance-based reimbursement schemes between healthcare payers and manufacturers, Health Policy (New York) 96 (2010) 179–190, https://doi.org/10.1016/j.healthpol.2010.02.005.
18 R.A. Vreman, T.F. Broekhoff, H.G.M. Leufkens, A.K. Mantel-Teeuwisse, W.G. Goettsch, Application of Managed Entry Agreements for Innovative Therapies in Different Settings and Combinations: A Feasibility Analysis, Int J Environ Res Public Health 17 (2020) 1–20, https://doi.org/10.3390/IJERPH17228309.
19 J. Adamski, B. Godman, G. Ofierska-Sujkowska, et al., Risk sharing arrangements for pharmaceuticals: Potential considerations and recommendations for European payers, BMC Health Serv Res (2010) 10, https://doi.org/10.1186/1472-6963-10-153.
20 Maes I, Boufraioua H, Dyck W van, Schoonaert L. Innovative funding solutions for paradigm changing advanced therapy medicinal products (ATMP) in Belgium Multi-stakeholder consensus on gene therapy funding solutions Policy report. Published online 2019.
21 N. Allen, F. Pichler, T. Wang, S. Patel, S. Salek, Development of archetypes for non-ranking classification and comparison of European National Health Technology Assessment systems, Health Policy (New York) 113 (2013) 305–312, https://doi.org/10.1016/J.HEALTHPOL.2013.09.007.
22 A. Makady, A. van Veelen, A. de Boer, H. Hillege, O.H. Klungel, W. Goettsch, Implementing managed entry agreements in practice: The Dutch reality check, Health Policy (New York) 123 (2019) 267–274, https://doi.org/10.1016/j.healthpol.2018.09.016.
23 S.G. Morgan, P.A. Thomson, J.R. Daw, M.K. Friesen, Canadian policy makers' views on pharmaceutical reimbursement contracts involving confidential discounts from drug manufacturers, Health Policy (New York) 112 (2013) 248–254, https://doi.org/10.1016/j.healthpol.2013.05.022.
24 N. Bohm, S. Bermingham, F. Grimsey Jones, et al., The Challenges of Outcomes-Based Contract Implementation for Medicines in Europe, Pharmacoeconomics (2021) 1–17, https://doi.org/10.1007/S40273-021-01070-1/TABLES/4. Published online September 4, 2021.
25 OECD Glossary of Statistical Terms – Central and Eastern European Countries (CEECs) Definition. Accessed August 11, 2022. https://stats.oecd.org/glossary/detail.asp?ID=303.
26 MENA – Organisation for Economic Co-operation and Development. Accessed August 11, 2022. https://www.oecd.org/mena/.
27 C. Maskineh, S.C. Nasser, Managed Entry Agreements for Pharmaceutical Products in Middle East and North African countries: Payer and Manufacturer Experience and Outlook, Value Health Reg Issues 16 (2018) 33–38, https://doi.org/10.1016/j.vhri.2018.04.003.
28 A. Ferrario, D. Arāja, T. Bochenek, et al., The Implementation of Managed Entry Agreements in Central and Eastern Europe: Findings and Implications, Pharmacoeconomics 35 (2017) 1271–1285, https://doi.org/10.1007/s40273-017-0559-4.
29 B. Tubic, V. Marković-Peković, S. Jungić, E. Allocati, B. Godman, Availability and accessibility of monoclonal antibodies in Bosnia and Herzegovina: Findings and implications, https://doi.org/101177/23992026211027692 5 (2021), https://doi.org/10.1177/23992026211027692. 239920262110276.
30 D.C. Baumgart, L. Misery, S. Naeyaert, P.C. Taylor, Biological therapies in immune-mediated inflammatory diseases: Can biosimilars reduce access inequities?, Front Pharmacol 10 (2019) 279, https://doiorg/10.3389/FPHAR.2019.00279/BIBTEX.
31 P. Putrik, S. Ramiro, T.K. Kvien, et al., Inequities in access to biologic and synthetic DMARDs across 46 European countries, Ann Rheum Dis 73 (2014) 198–206, https://doi.org/10.1136/ANNRHEUMDIS-2012-202603.
32 I. àdám, M. Callenbach, B. Németh, et al., Delayed payment schemes in Central-Eastern Europe and Middle-East, Front Med (Lausanne) (2022) 2380, https://doi.org/10.3389/FMED.2022.940371.
33 HTx Project | Next Generation Health Technology Assessment. Accessed August 8, 2022. https://www.htx-h2020.eu/.
34 Validity and reliability of questionnaires. Accessed July 30, 2021. https://www.slideshare.net/Venkitachalam/validity-and-reliability-of-questionnaires.
35 Bolarinwa, Principles and methods of validity and reliability testing of questionnaires used in social and health science researches, Nigerian Postgraduate Medical Journal. 22 (2015) 195, https://doi.org/10.4103/1117-1936.173959.
36 Qualitative Data Analysis Software | NVivo. Accessed September 8, 2021. https://www.qsrinternational.com/nvivo-qualitative-data-analysis-software/home.
37 K. Pauwels, I. Huys, S. Vogler, M. Casteels, S. Simoens, Managed entry agreements for oncology drugs: Lessons from the European experience to inform the future, Front Pharmacol 8 (2017), https://doi.org/10.3389/fphar.2017.00171.
38 A.M. Rotar, A. Preda, O. Löblová, et al., Rationalizing the introduction and use of pharmaceutical products: The role of managed entry agreements in Central and Eastern European countries, Health Policy (New York) 122 (2018) 230–236, https://doi.org/10.1016/J.HEALTHPOL.2018.01.006.
39 C. Zampirolli Dias, B. Godman, L.P. Gargano, et al., Integrative Review of Managed Entry Agreements: Chances and Limitations, Pharmacoeconomics 38 (2020) 1165–1185, https://doi.org/10.1007/s40273-020-00943-1.
40 K.M. Facey, J. Espin, E. Kent, et al., Implementing Outcomes-Based Managed Entry Agreements for Rare Disease Treatments: Nusinersen and Tisagenlecleucel, Pharmacoeconomics (2021), https://doi.org/10.1007/s40273-021-01050-5. 0123456789.
41 S. Michelsen, S. Nachi, W. van Dyck, S. Simoens, I. Huys, Barriers and Opportunities for Implementation of Outcome-Based Spread Payments for High-Cost, One-Shot Curative Therapies, Front Pharmacol 11 (2020) 1, https://doi.org/10.3389/fphar.2020.594446.
42 M. Phelan, C. Cook, A treatment revolution for those who can afford it? Hepatitis C treatment: new medications, profits and patients, BMC Infect Dis 14 (Suppl 6) (2014), https://doi.org/10.1186/1471-2334-14-S6-S5.
43 M. Neyt, S. Gerkens, L. San Miguel, I. Vinck, N. Thiry, I. Cleemput, An evaluation of managed entry agreements in Belgium: A system with threats and (high) potential if properly applied, Health Policy (New York) 124 (2020) 959–964, https://doi.org/10.1016/J.HEALTHPOL.2020.06.007.
44 A. Makady, S. van Acker, H. Nijmeijer, et al., Conditional Financing of Drugs in the Netherlands: Past, Present, and Future—Results From Stakeholder Interviews, Value in Health 22 (2019) 399–407, https://doi.org/10.1016/j.jval.2018.11.016.
45 B. Godman, A. Hill, S. Simoens, et al., Potential approaches for the pricing of cancer medicines across Europe to enhance the sustainability of healthcare systems and the implications, Expert Rev Pharmacoecon Outcomes Res 21 (2021) 527–540, https://doi.org/10.1080/14737167.2021.1884546.

46 Goodman C, Villarivera C, Gregor K, van Bavel J. *Regulatory, Policy, and Operational Considerations for Outcomes-Based Risk-Sharing Agreements in the U.S. Market: Opportunities for Reform*. Vol 25; 2019. www.jmcp.org.
47 Garrison LP, Carlson JJ, Bajaj PS, et al. Private Sector Risk-Sharing Agreements in the. 2015; 21 (September): 632–640.
48 L. Coulton, L. Annemans, R. Carter, et al., Outcomes-based Risk-sharing Schemes: Is There a Potential Role in the Asia-Pacific Markets?, Health Outcomes Res Med 3 (2012) e205–e219, https://doiorg/10.1016/J.EHRM.2012.07.002.
49 A. Clopes, M. Gasol, R. Cajal, et al., Financial consequences of a payment-by-results scheme in Catalonia: gefitinib in advanced EGFR-mutation positive non-small-cell lung cancer, J Med Econ 20 (2016) 1–7, https://doi.org/10.1080/13696998.2016.1215991.
50 A. Pisana, B. Wettermark, A. Kurdi, et al., Challenges and Opportunities With Routinely Collected Data on the Utilization of Cancer Medicines. Perspectives From Health Authority Personnel Across 18 European Countries, *Front Pharmacol* 13 (2022) 1, https://doi.org/10.3389/FPHAR.2022.873556.
51 Kanavos P, Ferrario A, Tafuri G, Siviero P. Managing Risk and Uncertainty in Health Technology Introduction : The Role of Managed Entry Agreements Special Issue Article. 2017; 8: 84–92. doi: 10.1111/1758-5899.12386.

Marcelien H.E. Callenbach [1], Ildikó àdám [2], Rick A. Vreman [1,3], Bertalan Németh [4], Zoltán Kaló [2,4], Wim G. Goettsch [1,3,*]

[1] Division of Pharmacoepidemiology & Clinical Pharmacology, Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University, Utrecht, The Netherlands
[2] Center for Health Technology Assessment, Semmelweis University, Budapest, Hungary
[3] National Health Care Institute (ZIN), Diemen, The Netherlands
[4] Syreon Research Institute, Budapest, Hungary

* *Corresponding author: Goettsch, W.G.*