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Pharmaceutical pricing and managed entry agreements: An exploratory study on future perspectives in Europe

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ABSTRACT

Objectives: This paper illustrates the results of a research aimed at investigating the opinions collected from selected European payers (HTA organisations, authorities/committees assessing, appraising and negotiating drug prices) and experts (researchers/consultants identified through LinkedIn groups) on drug price regulation, managed entry agreements, transparency and HTA advice.

Methods: Expert and payer opinions were gathered through a structured questionnaire, validated by three potential respondents and self-administered online between July and November 2021.

Results: Respondents totalled 39 (response rate 29%). The response rate was higher among the experts than the payers. Respondents mostly agreed that price regulation should award drug value through a multiple criteria approach (21 respondents) or cost-effectiveness evidence (14). For most respondents the added therapeutic value and the comparative safety profile should be the main drivers of a premium price. A quite high proportion of respondents supported the use of cost-effectiveness, and suggest relying on the perspective of the health care system. Most respondents expect larger diffusion of outcome-based and financial-based managed entry agreements in the future. Finally, respondents advocated for higher transparency of the negotiation process rather than net price transparency, and expressed the belief that HTA advice could be useful in reaching consensus on the level of unmet need, the comparators to consider, and the dimension of the target population.

Conclusions: Despite the limited number of respondents, the paper provides very interesting exploratory insights into much-debated topics related to drug price regulation. The opinions of European payers and experts are very useful for future regulation of drug pricing in Europe.

Public interest summary: Our research aimed at gathering the opinions of payers and experts on drug price regulation. The main findings are that pricing should reflect the value of medicines, that a premium price should be awarded only to those drugs that provide for an added therapeutic value and/o a better safety profile, even if other value dimensions (patient preferences and organisational impact) should be not disregarded. Experts and payers expect a larger role of managed entry agreements in the future, despite they may impose an important administrative burden. Finally, transparency of price negotiation is prioritized compared to net price transparency.

Introduction

Criteria and processes for determining medicine pricing and reimbursement (P&R) have been extensively investigated in the literature [1,2,3]. Together with budget considerations, prices are regulated / negotiated on the basis of two models: value-based model (demand perspective) and cost-plus model (supply perspective) [4]. External reference pricing, i.e., using foreign prices as a reference for the determination of domestic prices, is extensively used to complement other criteria and facilitate the negotiation process [5,6].

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Value-based pricing evaluation can rely on cost-effectiveness analysis or indirect evaluation [4]. The former approach requires that: (i) an incremental cost-effectiveness ratio (ICER) is estimated, i.e., the incremental cost per an additional unit of health; health status is usually measured by integrating survival and quality of life, through the Quality Adjusted Life Years (QALYs); (ii) a threshold value or a threshold range is set for ICER, i.e., the maximum amount of money that society is willing to pay for an extra unit of health.

Indirect evaluation refers to determining value and costs separately and value for money more discretionally. In such a context actual implementation depends on the selection of the value domains, how these domains are integrated and measured, and how they are converted into a price which is consistent with the value [7]. The prevailing approach involves setting the price according to the added therapeutic value of a new product by comparison with existing treatments [8,9]. Other contributions [10] suggested a more holistic approach, including other domains like the burden of disease, level of unmet need, organisational and socioeconomic impact, and patients convenience.

Cost-plus price regulation refers to negotiating prices on the grounds of the costs sustained by pharmaceutical companies for research and development (R&D), production and commercialization of new medicines. Cost-plus price regulation was quite widespread in Europe in the first half of the 1990s. However, it was gradually substituted by a value-based approach due to transparency issues, the sunk and joint nature of R&D costs, and because it rewards the costs sustained and not the output produced [11]. Notwithstanding, high prices are still justified on the grounds of high investment in R&D by the pharmaceutical industry and their sunk nature, thus implicitly advocating for a mixed approach that looks at the value of new medicines but also at the effort to generate this value and the need for recouping this investment.

Price negotiation is often accompanied by market access contracts. These contracts include (hidden) discounts over list prices or more complex Managed Entry Agreements (MEA) [12]. The former were introduced to reduce the financial impact to the advantage of payers, and the impact of cross-reference pricing to the advantage of the pharmaceutical companies. Conversely, the latter have been introduced to manage uncertainty related to the impact of a drug, including its effectiveness and tolerance profile, the duration of treatment and the size of the eligible population. MEA can be financial-based or outcome-based [13]. Financial-based agreements are MEA where reimbursement / price depends on the post-marketing impact of a medicine on the payers' budget (e.g., price-volume agreements, spending cap on medicines). Outcome-based agreements are MEA where reimbursement / price depends on the post-marketing impact of a medicine on health (e.g., coverage with evidence development and performance-linked reimbursement).

Though limited in diffusion compared to financial-based agreements, several recent contributions have highlighted the main pitfalls of outcome-based MEA, including, the associated administrative burden [14]; a main scope of managing affordability rather than collecting real world data [15]; and poor enforcement, which reduced the willingness to collect data [16] and resulted in post-marketing decisions on listing and prices that were not affected by real world data [17].

In P&R regulation, process is relevant as well as the criteria used. The transparency and reproducibility of the P&R regulation process is the first important pillar.

Recent debate has mainly been focused on net price transparency, with some papers advocating for a higher level of transparency ([18,19]) and others highlighting its political unfeasibility [20]. However, a regulatory framework that rewards value through a premium price on the one side and enhances price competition for interchangeable products on the other, requires a transparent and reproducible P&R process as well.

A second pillar is aligning evidence requirements by payers with data collection and analysis by the pharmaceutical industry, to facilitate the P&R negotiation process once a new product is approved. This alignment is facilitated by early interaction between regulatory authorities, payers and industry to design clinical development on the grounds of the needs of both regulatory authorities and payers, including acceptable primary end points, choice and use of surrogate end points, inclusion of an active comparator, use of patient-reported outcomes [21]. A second interaction between payers and industry may occur when the product is approved but better definition is needed for the scope of the assessment (e.g., comparators used and indirect comparison legitimacy) or to address information gaps (e.g., on the dimension of the target population or the long-term durability of the effects of medicines).

The above-mentioned literature has investigated the three pillars (pricing criteria, discounts and MEAs and pricing process) separately. Furthermore, the opinions of key players in these topics have rarely been surveyed (e.g., in [19], on net price transparency; [16], on MEA in Belgium). Our research is aimed at covering this information gap, collecting the opinions of European experts and payers on three pillars: value-based vs cost-plus pricing, the role of discounts and MEA, and transparency of the P&R process.

Methods

We first identified our targeted respondents (experts and payers).

Experts refer to active researchers and consultants on the topics included in our analysis. They were identified from LinkedIn. We prefer LinkedIn to other social media platforms since it's more professional-oriented and there are groups dedicated to the scrutinised topics (Managed Markets Experts - Reimbursement, Pricing and Value Partnerships; Health Economics & Market Access; Oncology Pricing & Reimbursement). Pharmaceutical company employees were excluded.

Payers include Health Technology Assessment (HTA) organisations (e.g., the National Institute for Health and Care Excellence (NICE) in England, the Agency for Health Technology Assessment and Tariff System (AOTMiT) in Poland), authorities / committees that provide for medicine assessment and appraisals (e.g., the Technical-Scientific Committee of the Italian Medicines Agency in Italy (AIFA), and the Transparency Commission at Haute Autorité de Santé (HAS) in France) and price negotiation (e.g., the Price and Reimbursement Committee at AIFA and the Economic Committee in France). Actual payers of drugs, i.e., local, regional and national organisations procuring medicines, were not included since we assumed that reimbursement, pricing and MEA should be managed at the central level.

Participants' opinions were collected through a structured questionnaire (Appendix 1), composed of three sections:

- 9 questions were dedicated to price regulation;
- 8 questions were focused on discounts and MEA;
- 7 questions were dedicated to the assessment and appraisal process.

The questionnaire was validated by three potential respondents and self-administered online (Qualtrics^{XM}). All respondents provided their informed consent and were anonymized, as required by the Ethics Committee of the authors' institution.

Most of the questions require respondents to select one or more choice from several possible options. Some questions required experts and payers to rank options in descending order of importance, with a rank of one as the most important and not allowing any two items to be assigned the same rank. The average score and a concordance index (Kendall Index) were calculated, with 1 and 0 the highest and lowest concordance values, respectively.

The survey was administered between July 5, 2021, and November 15, 2021. Respondents were invited to participate through a letter sent by email explaining the rationale of the research. The same document mentions the sponsors of the study and the sponsors' role in the research. Respondents were also asked to sign the informed consent. Once consent was received, respondents received the link to the questionnaire. The

deadline was postponed twice from the end of September to the middle of November. Three reminders were sent to the list of potential respondents.

Results

A group of 66 experts and 72 payers were identified and invited to participate in the survey, totalling 138. Collected responses numbered 39 (28.7%). The response rate was higher among the experts (28, 42%) than the payers (11, 15.3%). Among non-respondents, 9 payers invoked institutional constraints (they were not allowed to answer the questionnaire) and lack of available time. The 11 payers come from HTA organisations of Austria, Finland, France, Germany, Greece, Italy, Portugal, and Sweden. The international experts come from Austria, France, Germany, Italy, Spain, Switzerland, and United Kingdom and work in consultancy (12), university (11), and independent research centres (5).

Answers to multiple choice questions and rankings are illustrated in Tables and Figures respectively.

The first section of the questionnaire was dedicated to price regulation (Table 1).

Most respondents agreed that price regulation should reward value and be consistent with budget constraints. Only 15/38 respondents thought that price negotiation could be used to push companies to invest in the country where the price is negotiated, i.e. that price negotiation can also be used for industrial purposes.

According to the opinion of most respondents, price regulation and negotiation should rely on a value-based approach alone (23/38) or combined (14/38) with a cost-plus approach. The cost-plus approach was challenged as rewarding costs instead of results and would thus indirectly incentivise inefficiencies in the R&D process. Furthermore, respondents highlighted that allocating R&D costs, which are sunk and joint costs, to each single product is very difficult. A cost-plus approach could be useful, provided it integrates a value-based approach for orphan medicines and advanced therapies. If a cost-plus approach is used, most respondents suggested estimating R&D costs net of incentives provided by public authorities to the industry.

Value-based pricing should be pursued through a multiple criteria approach (21/38) or cost-effectiveness evidence (14/38). For 13 respondents, the multi-criteria pathway should be very structured, in terms of value domains and the way they are converted into a price, whereas 8 of them would prefer a more discretional approach. Most supporters of cost-effectiveness were favourable towards setting a threshold or a threshold range over the ICER.

For most respondents the added therapeutic value (clinical and patient-reported) and the comparative safety profile should be the main drivers of a premium price. However, more than half of respondents suggested considering the organisational impact and patient reported experience as well. Other domains quoted by respondents were disease severity and the unmet (clinical) need.

The largest proportion of respondents supporting the use of ICER advocates for relying on the perspective of the health care system when costs are estimated (22/38). They acknowledged that the social perspective is the most correct to take decisions, provided allocative efficiency is pursued. However, they pointed out that, in general, the health care budget is separate from the budget of other areas of the

Table 1
Answers to the first section of the questionnaire: pricing models.

Do you agree with giving a higher price to products of companies that invest in R&D and production in the country where the product is launched? (38/39)	#		%	
No	23/38		60.5%	
Yes	15/38		39.5%	
Price negotiation should rely on: (38/39)	**#**		**%**	
A value-based approach	23/38		60.5%	
Both value-based and cost-plus approaches	14/38		36.8%	
A cost-plus approach	1/38		2.6%	
If a cost-plus approach is adopted, do you think that R&D incentives provided to pharmaceutical companies should be removed from R&D cost estimates? (37/39)	**#**		**%**	
Yes	25/37		67.6%	
No	12/37		32.4%	
Value-based pricing should rely on: (38/39)	**#**		**%**	
A structured pathway that converts value into a premium price	13/38	21/38	34.2%	55.3%
A more discretional pathway that converts value into a premium price	8/38		21.1%	
An indicator (ICER) with a threshold on ICER or a threshold range on ICER	11/38	14/38	28.9%	36.8%
An indicator (ICER) without a threshold on ICER or a threshold range on ICER	3/38		7.9%	
Other models	3/38	3/38	7.9%	7.9%
If the ICER is not used, which domains should be considered for a premium price? (36/39)	**#**		**%**	
Added clinical value	36/36		100.0%	
Added quality of life	29/36		80.6%	
Lower side-effects	27/36		75.0%	
Advantages from an organisational viewpoint (e.g. oral administration)	22/36		61.1%	
Advantages in the perspective of patients (e.g. treatment-free intervals)	20/36		55.6%	
Other domains	11/36		30.6%	
If the ICER is used, cost of new medicine and comparators should be estimated with the perspective of: (38/39)	**#**		**%**	
Payer of health care	22/38		57.9%	
Society	10/38		26.3%	
Payer of the treatment cost	6/38		15.8%	
Payer of medicine	0/38		0.0%	
Value-based pricing is usually integrated with budget impact consideration (sustainability issues). Price negotiation should rely on: (37/39)	**#**		**%**	
Value for money first and budget impact after	29/37		78.4%	
Budget impact first and value-for money after	8/37		21.6%	

R&D: Research and Development; ICER: Incremental Cost-Effectiveness Ration.

welfare programs and that relying on the health system perspective is useful at least in overcoming a silos budget approach within the health care system.

Sustainability is considered in price negotiation as well as value-for-money. Most respondents think that both criteria should be considered, since a medicine could be cost-effective for each patient treated, but not sustainable for the whole population, if the incremental cost is high and the target population large. However, the majority of respondents think that price negotiation should be grounded in value-for-money first and budget impact afterward.

The comparator(s) eventually used in clinical trials, the selected endpoint(s), and the absence of a head-to-head study were considered the most important obstacles for value-based pricing (Fig. 1).

The second section of the questionnaire was dedicated to MEA. Most respondents expect greater diffusion of both outcome-based and financial-based agreements (Table 2).

According to the opinions of both experts and payers, outcome-based agreements respond to immature evidence on medicines at their market launch (Fig. 2) and are more useful when this evidence is highly uncertain (e.g., for orphan medicines and ATMP - Advanced Therapy Medicinal Products) (Table 2).

On the other side, management of these contracts could be burdensome and result in uncertainty regarding the unit cost / revenue per patient treated (Fig. 2).

Financial-based agreements are very useful to reduce the budget impact of new drugs / indications and easier to manage than outcome-based contracts. However, they do not allow for the collection of real world data and are more complex to manage than simple discounting (Fig. 2). One specific question was dedicated to staged payments, i.e., paying different instalments. Most of respondents stated that these contracts are feasible (Table 2). The minority who challenged their feasibility pointed out that the accounting system in health care organizations does not allow for amortizing current expenditure and that, since the budget is allocated to hospitals on an yearly basis, hospitals cannot take a long-term financial commitment. For most respondents, staged payments should be accompanied by outcome based-agreements (Table 2), in particular for one-shot treatment / ATMP and drugs launched onto the market with notable uncertainty about the dimension and persistence of their effects.

The third and final section of the questionnaire was focused on the assessment and appraisal process, and more specifically on transparency and HTA advice.

Table 2
Answers to the second section of the questionnaire: pricing models.

In your opinion, the frequency of outcome-based agreements in the future will: (39/39)	#	%
Increase	26/39	66.7%
Remain the same	9/39	23.0%
Decrease	4/39	10.3%
In your opinion, the frequency of financial-based agreements in the future will: (38/39)	**#**	**%**
Increase	27/38	71.1%
Decrease	10/38	26.3%
Remain the same	1/38	2.6%
Specify for which medicines outcome-based agreements will be more useful in the future (39/39)	**#**	**%**
ATMP (Advance Therapy Medicinal Products)	35/39	89.7%
Orphan medicines	21/39	53.8%
Others	9/39	23.1%
Combo Therapies	7/39	17.9%
Among MEA, there is a growing attention to staged payment (including annuity payment) for one-shot therapies. Is it feasible? (38/39)	**#**	**%**
Yes	35/39	92.1%
No	3/39	7.9%
If you have flagged 'Yes', should annuity payments be integrated with outcome-based agreements? (35/35)	**#**	**%**
Yes	20/35	57.1%
It depends on medicines	14/35	40.0%
No	1/35	2.9%

MEA = Managed Entry Agreements.

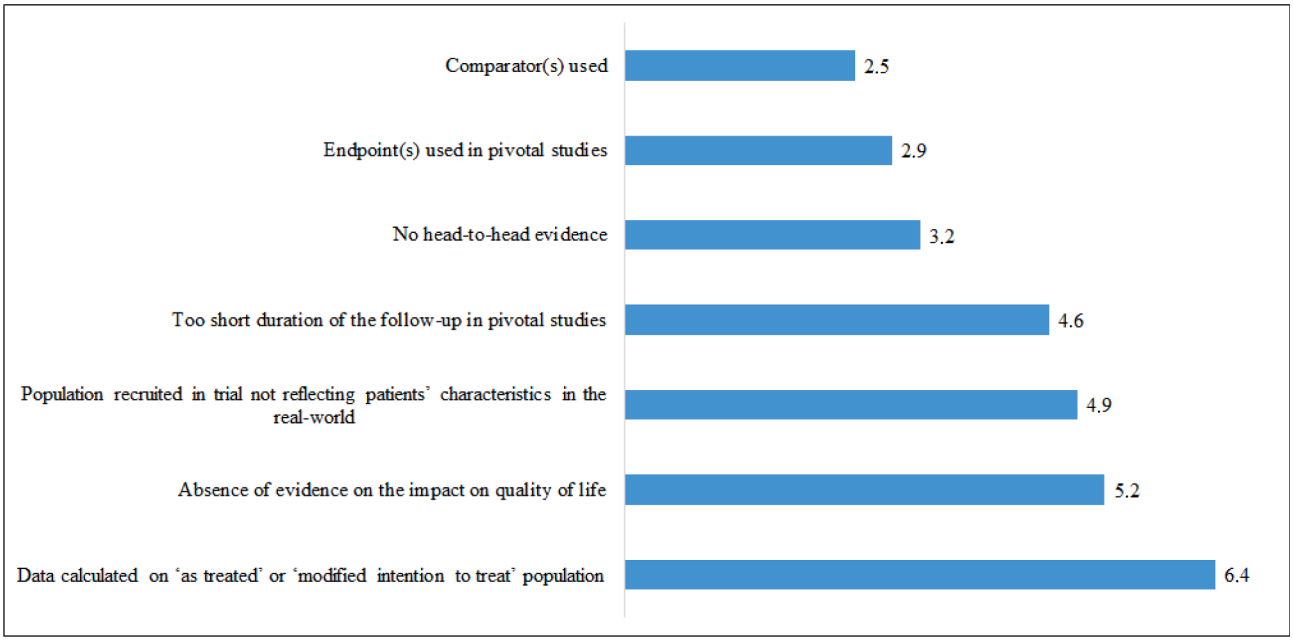

Fig. 1. Average score of critical issues for value assessment*.
* 38/39 answered to this question. Ranking from 1 (most important) to 8 (less important). Kendall Index (min 0; max 1) = 0.3

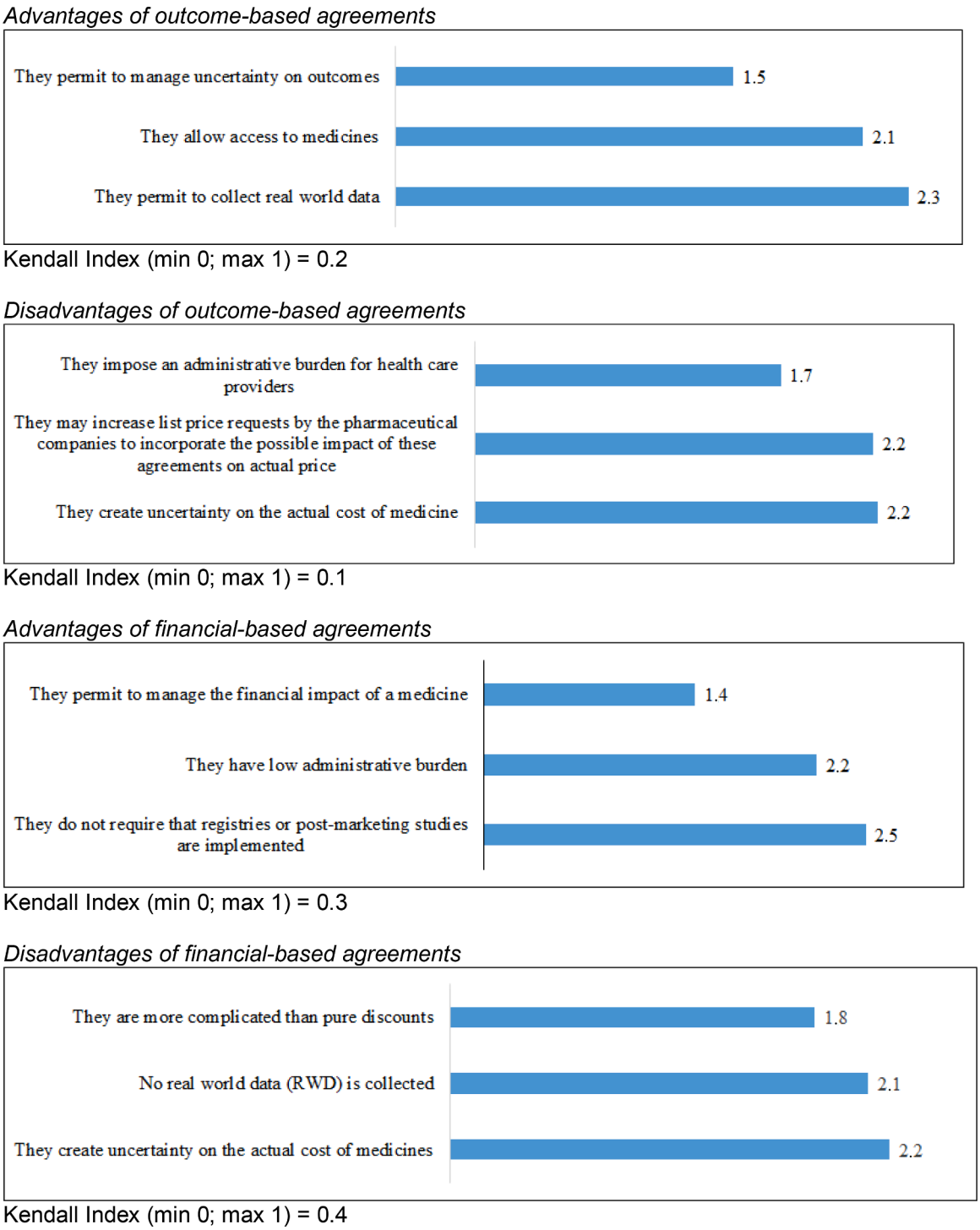

Fig. 2. Average score of advantages / disadvantages of outcome-based and financial-based agreements (ranking from 1 - most important - to 3 - less important) (39/39 answered to these questions).

Most respondents (32/37) recommend publishing the scoping document, i.e., the document – if any – where data needed to negotiate pricing and reimbursement are specified (e.g., the comparator(s) used), the assessment and appraisal reports, and the existence of a MEA. More than a half of responders advocated for rendering transparent the content of the MEA (e.g., endpoint(s) used and time to evaluation) (Table 3).

Only 10/37 respondents were in favor of publishing both the public price and the discount (the proportion was a little higher for payers than for experts). The main reasons cited for not publishing discounts was

Table 3
Answers to the third section of the questionnaire: transparency and HTA Advice.

Which of the following information should be published during the assessment, appraisal and P&R process? (37/39)	#	%
Assessment document (e.g. evidence on benefits)	36/37	97.3%
Appraisal document (e.g. added value score)	34/37	91.9%
Scoping document	32/37	86.5%
Managed Entry Agreement (existence or not)	31/37	83.8%
Managed Entry Agreement (content)	19/37	51.4%
Discount / Actual price	10/37	27.0%
The publication of discounts over list prices is: (36/39)	**#**	**%**
Not desirable, as it will reduce the probability of manufacturers offering discounts	21/36	58.3%
Not desirable, since cross-reference pricing may undermine the launch of new medicines in countries where prices are lower	12/36	33.3%
Desirable, in order to let payers cross-compare actual prices	10/36	27.8%
Is there an HTA Advice in your country? (38/39)	**#**	**%**
Yes	25/38	65.8%
No	13/38	34.2%
Yes, but limited to some specific aspects	8/38	21.1%

HTA = Health Technology Assessment.

that cross-reference pricing would refer to net prices, thus undermining the launch of new medicines in small countries where prices are lower and reducing the probability of manufacturers offering discounts.

More than half of respondents declared that, at least formally, HTA advice is provided by payers to the pharmaceutical industry (Table 3). This advice should be mainly focused on the level of unmet need, the comparators to consider, the dimension of the target population. The perceived benefits of HTA advice are, in order of importance, the possibility to speed up the assessment and appraisal processes, to push both payers and industry to provide more information, and to prepare a MEA. Drawbacks of HTA advice are represented by the additional administrative burden for payers, the absence of data required for the advice, and the addition of another step that may prolong pricing and reimbursement negotiation (Fig. 3). However, the level of agreement on the ranking of negative aspects of HTA advice was very low, which indicates that they are actually equally ranked.

Discussion

This paper illustrates the results of an exploratory research aimed at collecting the opinions of payers and experts on drug pricing criteria, MEA, transparency and HTA advice.

Respondents advocated for a value-based pricing model, possibly integrated with cost considerations for some medicines, e.g., orphan drugs and ATMP. The literature supports a higher price for orphan medicines for reasons other than cost considerations. Prices of orphan medicines are usually higher than for other drugs due to the important unmet need they respond to and the expected limited volume of sales [22,23], whereas their R&D costs have been estimated at 23.4% of those sustained for non-orphan medicines [24]. ATMP, besides being mostly orphan medicines, are one-shot treatments and assumed to have high production costs, but evidence is lacking on this.

Payers and experts also recommended a more structured, transparent and reproducible value-for-money assessment process that should be prioritised with respect to budget impact. Regarding value domains respondents confirmed that the added therapeutic value should be the main driver of a premium price over the comparator(s). However, more than half of respondents cautioned against disregarding the impact on health care organisations (organisational impact) and patient

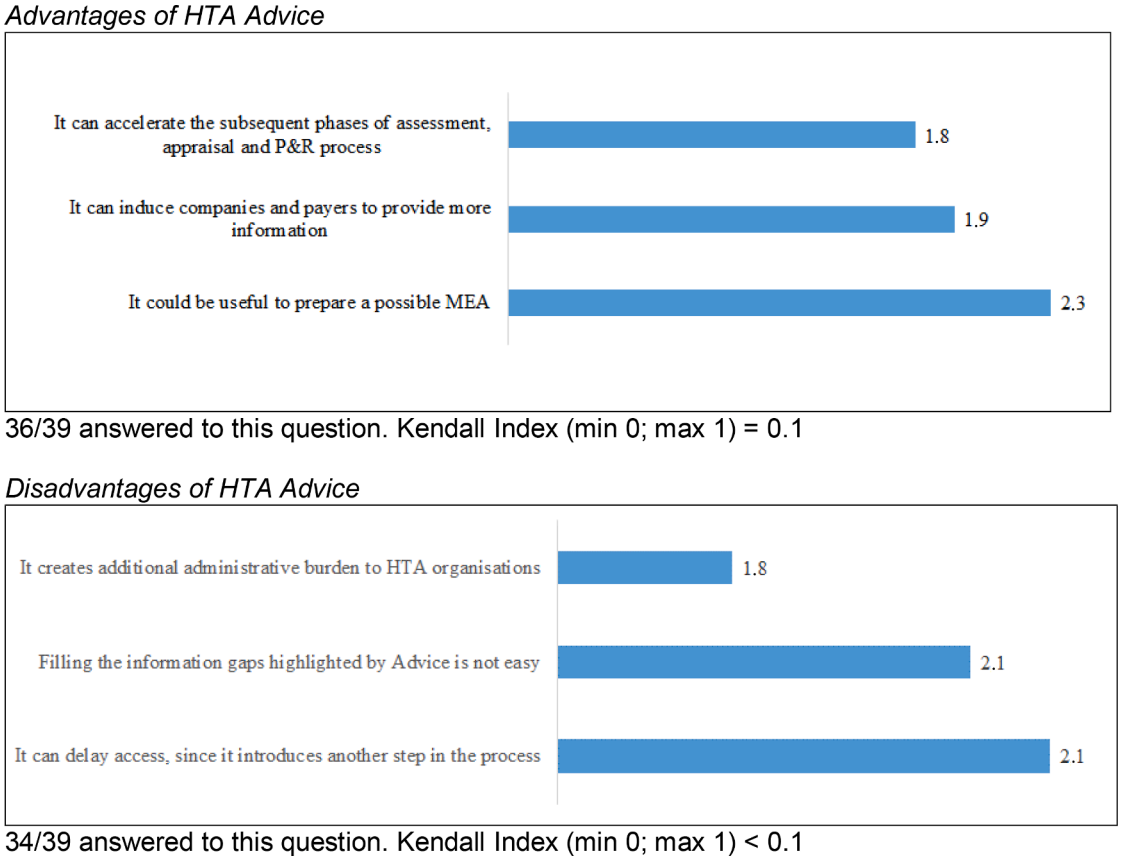

Fig. 3. Average score of advantages / disadvantages of an HTA Advice (ranking from 1 - most important - to 3 - less important).

convenience (e.g., a more comfortable route of administration). This would imply that (i) a new formulation of an existing product that is more convenient for patients or that has a favourable organisational impact (like an oral or sub-cutaneous formulation) is either awarded a premium price or does not have its price reduced if volume increases are foreseen; (ii) cost-effectiveness is gradually overcome by a cost-benefit evaluation, where more outcomes (including patient preferences and organisational impact) are monetized.

In the respondents' view, value-based pricing should be product / indication-specific and, for most of them not tied to pharmaceutical industry investment in the interested country. The former recommendation is aligned with some recent contributions on indication-based pricing [25,26], but requires that use per indication is tracked. The second recommendation is consistent with evidence derived from the literature. Allowing a higher price to companies investing in the relevant country would not be consistent with the value-based approach, and not even useful for making the county attractive for companies' investment: the location of investment by pharmaceutical companies is influenced by the stability and transparency of pricing and reimbursement regulation and not whether these investments are considered in price negotiations [27].

Respondents have foreseen the need for a growing role played by outcome-based and financial-based MEA. However, as for the former, they highlighted critical issues that could undermine their implementation in the future. These critical issues are rather aligned with the literature.

The respondents advocated for higher transparency for the assessment and appraisal process. This would generate an improvement of the evidence produced, a higher reproducibility level for the assessment and appraisal process, and a perception of equity in the way the evidence is used for P&R negotiation purposes. Payers would be favourable towards making prices net of discounts / rebates transparent as well, in line with other publications that have investigated discounts and rebates from the payers' perspective [19]. Experts recommended maintaining confidentiality of discounts and contents of MEA. This would help avoid more aggressive cross-reference pricing that would undermine or delay market launch in countries where net prices are particularly low due to budget constraints. A recent contribution highlighted that for this reason implementing net pricing transparency would be politically unfeasible, since countries where net prices are lower would impede making these prices public [20].

Finally, both experts and payers are in favor of a larger role played by HTA 'late' advice, provided it is prioritised to address those domains likely to have greater impact, in order to avoid an additional burden to HTA organisations. The role of this late HTA advice is intended to discuss, once the registrational trial has been completed, the scope of the HTA (e.g., comparators used and indirect comparison legitimacy) and information gaps (e.g., on the dimension of the target population or the long-term durability of the effects of medicines).

This paper has three major limitations. The first is the low response rate (28.7%) of our targeted respondents, that makes our findings more exploratory than conclusive. The second is that responses are unbalanced, with more experts represented than payers. The limited participation, especially of payers, was possibly motivated by the ongoing pandemic too. It is likely that payers prioritized other activities and had not time to respond to the survey. This has potential impact on the responses to the more sensitive questions, like transparency of net prices and price negotiation for new indications. However, experts better reflect the average opinion of all stakeholders, since they could be either 'pure' researchers, people consulting with the pharmaceutical industry, or professionals supporting HTA authorities. The third limitation is that the opinions could be affected by contingencies of market access regulation. For example, the questionnaire included a question on the future role of the European HTA regulation (Regulation 2021/2282 [28]. At the time the questionnaire was completed it was still unknown whether the Joint Clinical Assessments would be binding or not binding. For this reason, the answers to this question were not reported.

Conclusions

This paper has elicited the opinions of payers and experts in the field of market access in Europe on P&R for medicines. Despite the limited number of respondents, it provides some important exploratory insights into relevant and much-discussed topics, including value-based pricing, transparency issues, and the role played by MEA.

Payers and experts are favourable towards an increasing role for value-based pricing, integrated into budget impact considerations. They support a holistic approach to value and higher transparency of the evaluation process, regardless of whether it is grounded on a direct or indirect link between prices and value. A need for transparency is advocated for price negotiation, whereas net price transparency is much more debated since it could undermine market launch in smaller countries where the availability to pay is lower.

Another clear message is that outcome-based MEA represent an opportunity not to be missed. However, their use should be enforced and optimized to enhance their ability to respond to uncertainties at market launch and minimize their administrative burden.

These considerations are very useful for future regulation of drug pricing in Europe, considering that harmonization of clinical assessment is expected with the application of the new EU HTA Regulation.

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Ethical approval

The survey was approved by the Ethical Committee of Bocconi University (ECR - Submission Report FA000306).

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CRediT authorship contribution statement

Claudio Jommi: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing. **Arianna Bertolani:** Conceptualization, Data curation, Formal analysis, Investigation, Validation. **Patrizio Armeni:** Conceptualization, Methodology, Validation, Writing – review & editing. **Francesco Costa:** Conceptualization, Methodology, Validation, Writing – review & editing. **Monica Otto:** Conceptualization, Funding acquisition, Methodology, Supervision, Validation, Writing – review & editing.

Declaration of Competing Interest

AB reported serving as an advisory board member for Jannsen Cilag and paid speaker for Roche, outside the submitted work.

CJ reported serving as an advisory board member and a paid speaker for Amgen, Astrazeneca, BMS, CSL Behring, Gilead, Incyte, MSD, Roche, Sanofi, Takeda, outside the submitted work.

Other authors have no conflicts to declare

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.hlpt.2023.100771.

References

[1] Garattini L, Cornago D, De Compadri P. Pricing and reimbursement of in-patent drugs in seven European countries: a comparative analysis. Health Policy (New York) 2007;82(3):330–9.

[2] Kleijnen S, Lipska I, Leonardo Alves T, et al. Relative effectiveness assessments of oncology medicines for pricing and reimbursement decisions in European countries. Ann Oncol 2016;27(9):1768–75.

[3] Panteli D, Arickx F, Cleemput I, et al. Pharmaceutical regulation in 15 European countries review. Health Syst Transit 2016;18(5):1–122.

[4] Jommi C, Armeni P, Costa F, Bertolani A, Otto M. Implementation of value-based pricing for medicines. Clin Ther 2020;42(1):15–24.

[5] Gill J, Fontrier AM, Kyriopoulos D, Kanavos P. Variations in external reference pricing implementation: does it matter for public policy? Eur J Health Econ 2019; 20(9):1375–97.

[6] Rand LZ, Kesselheim AS. International reference pricing for prescription drugs: a landscape analysis. J Manag Care Spec Pharm 2021;27(9):1309–13.

[7] Sussex J, Towse A, Devlin N. Operationalizing value-based pricing of medicines: a taxonomy of approaches. Pharmacoeconomics 2013;31(1):1–10.

[8] Garner S, Rintoul A, Hill SR. Value-Based Pricing: l'Enfant Terrible? Pharmacoeconomics 2018;36(1):5–6. Jan.

[9] Vogler S, Paris V, Ferrario A, et al. How can pricing and reimbursement policies improve affordable access to medicines? Lessons learned from european countries. Appl Health Econ Health Policy 2017;15(3):307–21.

[10] Angelis A, Kanavos P. Multiple criteria decision analysis (MCDA) for evaluating new medicines in health technology assessment and beyond: the advance value framework. Soc Sci Med 2017;188:137–56.

[11] Jommi C. Pharmaceutical policy and organisation of the regulatory authorities in the main EU countries. Milano: EGEA; 2001.

[12] Wenzl M, Chapman S. 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 2022;115. https://www.oecd.org/health/health-systems/pharma-managed-entry-agreements.htm. accessed July, 24.

[13] Morel T, Arickx F, Befrits G, 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 2013;24(8):198.

[14] Garattini L, Curto A, van de Vooren K. Italian risk-sharing agreements on drugs: are they worthwhile? Eur J Health Econ 2015;16(1):1–3.

[15] Andersson E, Svensson J, Persson U, Lindgren P. Risk sharing in managed entry agreements-A review of the Swedish experience. Health Policy (New York) 2020; 124(4):404–10.

[16] Neyt M, Gerkens S, San Miguel L, Vinck I, Thiry N, Cleemput I. An evaluation of managed entry agreements in Belgium: a system with threats and (high) potential if properly applied. Health Policy (New York) 2020;124(9):959–64.

[17] Makady A, van Veelen A, de Boer A, Hillege H, Klungel OH, Goettsch W. Implementing managed entry agreements in practice: the Dutch reality check. Health Policy (New York) 2019;123(3):267–74.

[18] Morgan SG, Bathula HS, Moon S. Pricing of pharmaceuticals is becoming a major challenge for health systems. BMJ 2020;368:l4627.

[19] Vogler S, Zimmermann N, Habl C, Piessnegger J, Bucsics A. Discounts and rebates granted to public payers for medicines in European countries. South Med Rev 2012;5(1):38–46. Jul.

[20] Riccaboni M, Swoboda T, Van Dyck W. Pharmaceutical net price transparency across European markets: insights from a multi-agent simulation model. Health Policy (New York) 2022;126(6):534–40.

[21] Wang T, McAuslane N, Liberti L, Leufkens H, Hövels A. Building synergy between regulatory and HTA agencies beyond processes and procedures. Can we effectively align the evidentiary requirements? A survey of stakeholder perceptions. Value Health 2018;21(6):707–14.

[22] Jommi C, Listorti E, Villa F, et al. Variables affecting pricing of orphan drugs: the Italian case. Orphanet J Rare Dis 2021;16(1):439.

[23] Korchagina D, Millier A, Vataire AL, Aballea S, Falissard B, Toumi M. Determinants of orphan drugs prices in France: a regression analysis. Orphanet J Rare Dis 2017; 12(75).

[24] Berdud M, Drummond M, Towse A. Establishing a reasonable price for an orphan drug. Cost Eff Resour Alloc 2020;18:31.

[25] Cole A, Neri M, Cookson G. Payment models for multi-indication therapies. OHE; 2021. https://www.ohe.org. accessed July, 24, 2022.

[26] Pani L, Cicchetti A, De Luca A, et al. Pricing for multi-indication medicines: a discussion with Italian experts. Pharmadvances 2022;4(2):163–70.

[27] Koenig P, Macgarvie M. Regulatory policy and the location of bio-pharmaceutical foreign direct investment in Europe. J Health Econ 2011;30(5):950–65.

[28] Regulation (EU) 2021/2282 of the European Parliament and of the Council of 15 December 2021 on health technology assessment and amending Directive 2011/ 24/EU.https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX: 32021R2282, accessed July, 24, 2022.