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Health Policy Analysis

Do Profit Margins of Pharmaceuticals Influence Reimbursement Decisions? A Discrete Choice Experiment Among Dutch Healthcare Decision Makers

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ABSTRACT

Objectives: This study aimed to investigate whether the profit margins of pharmaceuticals would influence the outcome of reimbursement decisions within the Dutch policy context.

Methods: We conducted a discrete choice experiment among 58 Dutch decision makers. In 20 choice sets, we asked respondents to indicate which of 2 pharmaceutical treatment options they would select for reimbursement. Options were described using 5 attributes (disease severity, incremental costs per quality-adjusted life-year, health gain, budget impact, and profit margin) with 3 levels each. Additionally, cognitive debriefing questions were presented, and for validation debriefing, interviews were conducted. Choice data were analyzed using mixed logit models, also to calculate marginal effects and choice probabilities.

Results: Results indicated that the specified levels of profit margins significantly influenced choices made. Decision makers were less likely to reimburse a product with a higher profit margin. The relative importance of profit margins was lower than that of the included traditional health technology assessment criteria, but not negligible. When asked directly, 61% of respondents indicated that profit margin should play a role in reimbursement decision making, although concerns about feasibility and the connection to price negotiations were voiced.

Conclusions: Our results suggest that if available to decision makers the profit margin of pharmaceutical products would influence reimbursement decisions within the Dutch policy context. Higher profit margins would reduce the likelihood of reimbursement. Whether adding profit margin as an additional, explicit criterion to the health technology assessment decision framework would be feasible and desirable is open to further exploration.

Keywords: discrete choice experiment, health technology assessment, policy, profitability, reimbursement, The Netherlands

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Introduction

Healthcare expenditures are increasing in many countries, leading to questions about financial sustainability of healthcare systems and optimal allocation of resources. Economic evaluations and, more broadly, health technology assessment (HTA) may help to control costs and inform allocation decisions within the healthcare sector.[1] In many countries, including The Netherlands, HTA is used to inform reimbursement and pricing decisions.

Traditionally, pharmaceutical products are relatively often subject to HTA before a decision is made on reimbursement.[2] HTA offers a systematic way of considering whether and under which circumstances pharmaceuticals offer value for money to the health system and society. Given the increase in the number of new pharmaceutical products, which sometimes may be perceived as relatively expensive,[3] a sound assessment of their costs and benefits may be considered necessary, especially given the pressure on overall healthcare budgets. In that context, one of the cost components in an HTA is the (initial, official, "list," or requested) price of the pharmaceutical under evaluation. Together with information on, among other things, target population, clinical effectiveness, and broader cost consequences of using the pharmaceutical, this information on the price of a pharmaceutical is used to assess whether it may offer value for money.

More recently, in several jurisdictions, questions have been raised about the sustainability and "fairness" of the prices asked or set for pharmaceuticals (for an extensive definition of "fair pricing" for pharmaceuticals, we refer to Moon et al[3]).[3,4] These questions seem to pertain to both the general question whether, given prices, some products can be perceived to still offer value for money and, even if this is the case, whether the division of surplus implicitly proposed through these prices can be considered "fair."[3,5] Although the first question is answered through common

economic evaluations (often, by the way, equating prices with costs) and judging an incremental cost-effectiveness ratio (ICER) to a relevant threshold,[6] the second is more difficult to answer for several reasons. Prices will normally need to cover different elements, including components to cover the required research and development costs, the (marginal or average) production costs, distribution costs, and a profit margin.[3] Although the former elements may normally follow from the development, manufacturing, and distribution process, the latter under some circumstances may be determined by the manufacturer (within the boundaries of existing thresholds). By setting the profit margin higher, more of the surplus generated by the pharmaceutical is appropriated by the manufacturer, at the expense of the payer. Nevertheless, commonly, these payers, often government authorities, have limited information on the exact cost components of the pharmaceutical under evaluation in relation to its price. Hence, the division of surplus or the "fairness" of the profit margin or price is not directly observed.

Nonetheless, given the increase in expensive new pharmaceuticals and reports on the relatively high levels of profitability among pharmaceutical companies,[7,8] prices and profit margins are receiving attention. The increased reliance on price negotiations in several jurisdictions, presumably aimed at reducing profit margins and changing the division of surplus, is also relevant to mention here. Moreover, new pricing models have been proposed[3,9,10] and calls for more transparency on cost components have been advocated,[5] to justify prices or to allow cost-based price models.[11] More transparency would allow more insight into profit margins of particular products, which could be relevant for and used within HTA.

At present, profit margins of health technologies are not part of the explicit criteria considered during reimbursement decision making.[12] Obviously, this may reflect the fact that this information is typically not available. Nonetheless, it is interesting to understand how information on profit margins could influence reimbursement and pricing decisions, for at least 2 reasons. First of all, including information on profit margins more systematically in HTA is only relevant if doing so actually is expected to affect final decisions. If it does, profit margins could perhaps be considered as an explicit criterion in HTA. Currently, to the best of our knowledge, direct evidence on this issue is lacking. Second, given the increased attention for profit margins and "fair pricing" of pharmaceuticals and price negotiations and despite the fact that profit margin is not an explicit criterion at present, perceptions of or incidental information on profitability of specific interventions might play a role in reimbursement decisions. Indeed, in the context of some previous reimbursement processes, manufacturer costs in relation to prices seem to have been considered relevant to the reimbursement decision.[13,14] This could suggest that, in some instances, (perceptions of) profit margins may already play a role in (some) decisions.

Currently, it is unknown whether information on profit margins, if available to decision makers, would influence reimbursement decisions when being used alongside more traditional HTA criteria, such as clinical effectiveness, severity of illness, cost-effectiveness, and budget impact. Therefore, this study aimed to assess whether and to what extent actual healthcare decision makers would take information on profit margins into account in hypothetical reimbursement decisions, when presented alongside common information on pharmaceutical products. To investigate this further, in line with previous studies,[15,16] we conducted a discrete choice experiment (DCE) in a sample of Dutch policy makers. Although we also acknowledge the importance of more normative consideration of the desirability and optimal way of presenting information on profit margins in HTA informing reimbursement decisions, this provides first important insights into the potential role of profit margins in such decisions.

Methods

The setup of our study followed Koopmanschap et al,[17] who used a DCE to elicit preferences regarding the applied health priority setting criteria among Dutch healthcare professionals. Koopmanschap et al[17] asked respondents to select 1 of 2 different unlabeled, curative treatment options for reimbursement, using 27 choice sets. Best-practice guidelines were applied for developing and analyzing our DCE.[18-20] Ethical approval for this study was obtained from the Research Ethics Review Committee of the Erasmus School of Health Policy & Management.

Attribute and Level Development

We reused the 4 most influential attributes from Koopmanschap et al,[17] that is, disease severity, incremental costs per quality-adjusted life-year (QALY), individual health gain, and budget impact. Their current relevance was confirmed in a recent description of the Dutch HTA process[2] and by reviewing recent Dutch National Health Care Institute (Zorginstituut Nederland [ZIN]) reimbursement reports. Furthermore, we included the expected level of profitability (profit margin in %) of the pharmaceutical as an additional attribute. Although other criteria may also be relevant in this decision context,[15] we limited the number of attributes to 5 to keep the choice tasks cognitively feasible and in light of our main research aim.

A total of 3 levels were set for each attribute, which were sought to represent a realistic and distinctive range of the respective characteristics in current Dutch reimbursement decision-making practice. This was validated by reviewing recent ZIN reimbursement reports. Levels for disease severity and individual health gain in QALYs were directly extracted from Koopmanschap et al.[17] Level values for incremental costs per QALY (ICER) and budget impact were adjusted upward, to correct for changes since the time of that study. The levels for profit margin were specified to range from 5% to 50%, avoiding values that may be perceived as unrealistically low or excessively high, but still providing a distinct range. Given that values of profit margins on product level from current Dutch (or any other) reimbursement practice are unavailable, the midlevel (20%) was set in relation to the average profit margin on industry level. For the US context, a mean net income margin of 16.2% has been reported[7] whereas in Dutch context a net profit margin of the pharmaceutical industry of 17.5% has been suggested.[8]

Experimental Design

The created attributes and levels (Table 1) were used in a set of 20 unlabeled, pairwise comparisons of hypothetical treatment options. An opt-out option was not included as our main interest concerned eliciting relative preferences and to maximize the amount of information obtained per choice task. To create the choice tasks, we applied a Bayesian D-efficient design, implemented using Ngene software (version 1.2.1) (ChoiceMetrics, Sydney, NSW, Australia). The design was optimized for a standard multinomial logit model, based on a utility function including main effects (the levels themselves) and 2-way interactions between cost-effectiveness and budget impact, which was significant in the DCE performed by Koopmanschap et al,[17] and the level of profitability and all other attributes. Lowest budget impact (€10 million) was prohibited to appear together with the highest QALY gain (4) and the highest ICER (€120 000 per QALY) to prevent unrealistic choice sets considering the context information given

Table 1. Attributes and levels.

Concept	Attribute	Levels
Health gain	Number of gained QALYs per patient	0.5, 2, 4 (QALYs)
Cost-effectiveness	Incremental cost per QALY (ICER)	20 000, 60 000, 120 000 (€ per QALY)
Budget impact	Additional national medical costs per year	10, 50, 100 (million €)
Severity	Disease severity before treatment	Low, moderate, high
Profit margin	Expected level of profit margin of product (in % of price)	5%, 20%, 50%

ICER indicates incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

to respondents (see below). Information on priors necessary for the Bayesian optimization were initially based on expert judgment, supported by the results from Koopmanschap et al,[17] and updated after the first 22 respondents completed their survey. The mean D-error of the updated design reported by Ngene was 0.033 (SD 0.010).

Survey Design and Information Provided to Respondents

Participants were informed that the aim of the survey was to provide insight into the influence of different characteristics of pharmaceuticals on hypothetical reimbursement decisions, without placing particular emphasis on profit margins. Thereafter, respondents provided an informed consent and were acquainted with the choice task format using a simple pairwise comparison of everyday products. Respondents were then asked to imagine being a healthcare decision maker, having to decide about reimbursing 1 of 2 pharmaceutical products in the Dutch health basic benefits package. Each of the 5 attributes and their levels were explained step by step, (re)familiarizing respondents with the concepts of budget impact, disease severity, QALYs, and ICERs, partly using graphical support. It was explained to respondents that the level of profit margin specified is the price minus production costs, which specifically include the research and development costs for this product development cycle. It was mentioned that a certain degree of profitability would be required for manufacturers to not hamper innovation. Moreover, it was indicated that profits are not necessarily used for, for example, distributing profits to shareholders but could also be spent on developing new drugs.

To reduce bias by omitting potentially relevant attributes, we also specified the following scenario context, which was informed by the setup and results from Koopmanschap et al.[17] The respondents were asked to assume that the options related to a pharmaceutical product, which is not already reimbursed for other indications; the treatment recipients were men and women aged 50 to 75 years, with an average socioeconomic distribution; the product would be an addition to existing therapies in the disease area (and therefore to the basic benefits package); and the composition of the health gains (duration and quality of life) and the number of treated patients (specified to be at least 1000 per year) were equal across alternatives. This context information was added to avoid specific considerations (eg, relating to orphan disease status, socioeconomic inequalities, or age profiles) from influencing the choices.[21,22]

After a warm-up choice task with only 2 attributes (instead of 5), the 20 choice tasks were separated into 2 blocks of 10 choice tasks each, intermitted by several background questions to reduce response fatigue. The order of attributes and choice tasks were randomized across respondents to prevent ordering bias. Attribute and scenario descriptions were accessible to respondents during all choice tasks, as shown in Figure 1, which contains an example choice task. The survey ended with some cognitive debriefing questions and an open text question, in which respondents could indicate whether they felt profit margins should play a role in reimbursement decisions (Appendix A1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.08.007 contains an English translation of the survey). The survey was programmed using Sawtooth software version 9.8.1 (Sequim, WA).

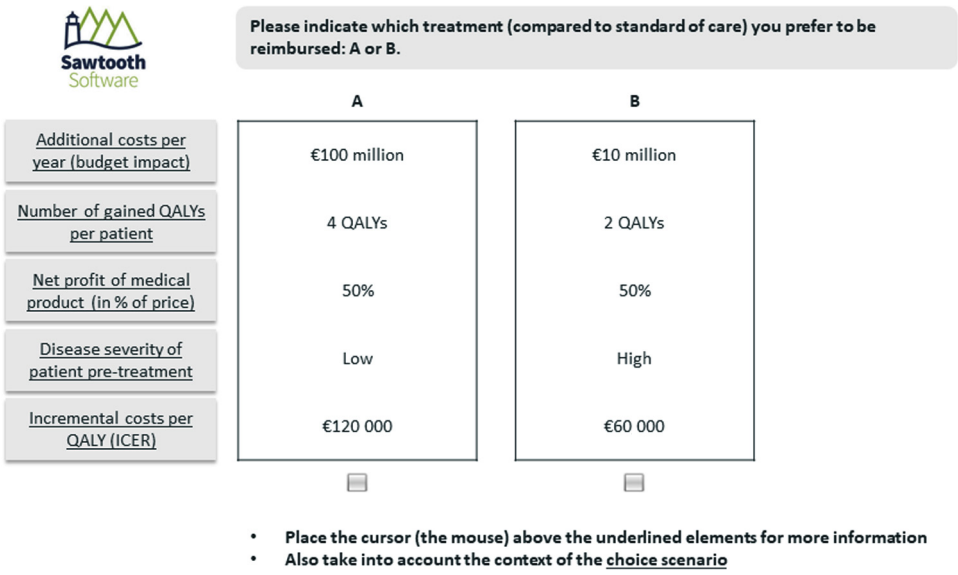
Data Collection

The target population of our survey were individuals employed at ZIN or members of ZIN-related committees (the Insured Package Advisory Committee and the Scientific Advisory Board). Among other tasks, ZIN is responsible for the assessment of health technologies in The Netherlands. A further inclusion criterion was that individuals needed to be familiar with HTA. The number of eligible individuals who were selected (jointly by J.J.E. and S.K.) based on these criteria and were subsequently invited via email to participate in the online survey was 92. Data collection took place in October 2020 and November 2020. The first 22 full responses were used to update the Bayesian priors for generating a more efficient experimental design. Data collection ended upon obtaining responses from roughly 50% of our respondent pool. Of the 67 instances the survey was started, 51 resulted in complete responses and 7 in partial responses (ie, 58 in total). The available choice task responses of the latter were included in the statistical analysis to increase statistical power, leading to a total sample size of 58 decision makers (although the analyses were also run-on complete responses only). This sample size exceeded the calculated sample size (n = 50) required to identify the main effect (Appendix A2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.08.007 describes the sample size calculation).

Statistical Analysis

To account for heterogeneity in preferences toward the HTA criteria included in our experiment, we used mixed logit models to analyze the choice data. Attribute levels were dummy coded, with the (expected) most positive levels as reference categories. The mixed logit models were calculated using 1000 Halton draws. All main effects were set to be random following a normal distribution, because heterogeneity was found for all attributes. A diagonal covariance matrix was specified, implying independence between the random coefficients, because of the low number of observations and therefore a lack of statistical power. Based on model fit and testing for linearity, ICER (in €1000) and level of profitability (in %) were included as linear attributes. Furthermore, we tested the inclusion of the 2-way interactions we optimized our design for. Therefore, an interaction between the level of profitability (as linear term) and the €100 million budget impact level was included in the model. Finding no heterogeneity in preferences toward this interaction, it was set to be a fixed

Figure 1. Example choice task. Translated from Dutch.



ICER indicates incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

parameter. Standard errors were clustered at the respondent level. Mixed logit models were calculated using the mixlogit command in Stata 16 (StataCorp LLC, College Station, TX). Based on the final model, marginal effects and choice probabilities were calculated using the mixlpred command.

Analysis of Open Text Responses, and Debriefing Interviews

An inductive content analysis was conducted for the survey responses to the open text question on whether profitability should play a role in reimbursement decisions according to respondents. Two authors (J.J.E. and S.K.) first independently attached one or more (nonpredetermined) topic labels to each answer. Second, based on these labels, answers were categorized into clusters. Third, the 2 authors jointly selected the 5 most relevant clusters based on their frequency, homogeneity within clusters, and their distinctiveness compared with other clusters.

To validate the results of the choice experiment, short, semi-structured debriefing interviews were conducted with 4 DCE participants within a month after participation. Participants were selected to cover different expertise (cost-effectiveness assessment, effectiveness assessment, and appraisal), and all agreed to an emailed invitation. These short video-assisted personal interviews covered individuals' experiences with the survey, their views on the use of profit margins as an additional HTA criterion in practice, and whether including just 1 additional criterion may have biased the attention toward profitability, and a discussion of the preliminary results of the DCE.

Results

The characteristics of the survey participants providing their demographic and background information (53 of 58) are presented in Table 2. The sample is likely younger and has a higher share of females than the total pool of eligible respondents as invited. We observed a low share of noncompletes (24%) and 76% of respondents completed the survey within a plausible range of 10 to 32 minutes (median 20 minutes). A total of 78% of respondents agreed that the choice tasks were clear and that the number of choice tasks was manageable. Approximately half of respondents (partially) agreed that they based their choices predominantly on just 1 or 2 characteristics.

Preference Estimates

Our main results are based on the full sample of 58 respondents, including 7 respondents who completed the survey partially. Note that a sensitivity analysis showed that excluding these 7 respondents did not lead to noteworthy differences in coefficient estimates. Results from the preferred mixed logit model are presented in Table 3 (Appendix Table A1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.08.007 presents estimates from different model specifications, stepwise progressing from the simplest main effects model to the preferred specification). All attribute coefficients were statistically significant,

Table 2. Characteristics of respondents providing individual information (53 of 58).

Characteristic	N = 53*, n (%)
Age range, years	
<35	16 (30.2)
35-44	16 (30.2)
45-54	9 (17.0)
55-64	10 (18.9)
≥65	2 (3.8)
Gender	
Male	16 (30.2)
Female	37 (69.8)
Self-identified as	
Policy maker/advisor	38 (71.7)
HTA expert	10 (18.9)
Other (eg, medical expert)	5 (9.4)
Mean completion time in minutes	32.6 (median 19.8)

HTA indicates health technology assessment.
*For 5 respondents providing choice task data, no information was available.

Table 3. Preference results of the mixed logit model.

Attributes and levels	Preference estimates				Marginal effect, %
	Coefficient	95% CI	SD	95% CI of SD	
Yearly budget impact					
€10 m	Reference				Reference
€50 m	−1.536†	[−2.060 to −1.011]	0.807*	[1.371-0.244]	−12.0
€100 m	−2.584†	[−3.424 to −1.743]	1.367†	[0.770-1.963]	−20.4
Disease severity					
High	Reference				Reference
Moderate	−1.778†	[−2.394 to −1.162]	1.302†	[0.587-2.017]	−13.4
Low	−4.535†	[−6.032 to −3.038]	1.682†	[0.745-2.620]	−32.1
Cost-effectiveness					
Δ ICER in €1000‡	−0.054†	[−0.072 to −0.035]	0.033†	[0.018-0.047]	−0.3
ICER €20 000	Reference				Reference
ICER €60 000					−15.7
ICER €120 000					−36.3
Health gain in QALYs					
4 QALYs	Reference				Reference
2 QALYs	−2.118†	[−2.895 to −1.341]	1.316§	[0.195-2.436]	−15.3
0.5 QALYs	−5.215†	[−6.454 to −3.976]	1.744†	[1.181-2.307]	−32.1
Level of profitability					
Δ profit 1 %‡	−0.023*	[−0.038 to −0.009]	0.039†	[0.052-0.026]	−0.2
Profit 5%	Reference				Reference
Profit 20%					−3.0
Profit 50%					−9.0
BI100 × profit	−0.021§	[−0.039 to −0.002]			
Log likelihood	−428.9				
AIC	891.8				
Observations	2116				
Respondents	58				

AIC indicates Akaike information criterion; CI, confidence interval; ICER, incremental cost-effectiveness ratio; m, million; QALY, quality-adjusted life-year.
*$P<.05$.
†$P<.01$.
‡Coded as continuous variable in the model. BI100 × profit is an interaction term between the highest budget impact and the linear profitability parameter.
§$P<.1$.

implying that each of the included HTA criteria influenced choices in the experiment. The SDs of all random parameters were significantly different from zero, indicating preference heterogeneity in all dimensions. Finding only negative coefficients is in line with a priori expectations, because the attribute levels we expected to be the most preferred were specified as the reference categories.

The largest coefficients for attribute levels in absolute terms were found for low disease severity and a health gain of 0.5 QALYs (−4.535 and −5.215). These translate to marginal effects, that is, changes in choice probability, compared with their respective reference categories of −32.1% in both cases. The coefficient (−0.054) and marginal effect (−0.3%) of the linear "ICER in €1000" term correspond to differences in choice probabilities between the 2 lowest ICER levels (€20 000 and €60 000) and the lowest and largest ICER levels (€20 000 and €120 000) of −15.7% and −36.3%, respectively. This indicates that cost-effectiveness was the most important HTA criterion in the experiment. The yearly budget impact of a pharmaceutical was less influential, with a marginal effect of the largest level of −20.4%. The coefficient (−0.023) and marginal effect (−0.2%) of a 1% change in profit margin translate to differences in choice probabilities of 3%, moving from 5% to 20% profit margin, and 9% moving from 5% to 50% profit margin. Therefore, the level of profit margin has a lower but non-negligible impact on choices in the experiment. The marginal rate of substitution between the linear ICER and profitability coefficients (−0.023/−0.054 = 0.43) exemplifies this: a 20% increase in level of profit margin is equally weighted as an increase in the ICER of €8600. The interaction term between the highest level of budget impact and profit margin (BI100 × profit) was negative and significant, indicating that given a high budget impact, higher levels of profit margin are evaluated more negatively.

Appendix Figure A1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.08.007 plots preference patterns according to the "seniority" of respondents, showing that older respondents put more weight on cost-effectiveness (ICER) and the profit margin.

To make results more tangible, we calculated the average predicted probabilities of accepting reimbursement for certain hypothetical pharmaceutical scenarios based on the mixed logit coefficients. The first 3 scenarios relate to products with the worst, middle, and best levels for all attributes, respectively (Table 4). The corresponding probabilities of reimbursement were 2.1%, 65.3%, and 94.4%. The last 2 scenarios deviated from the middle levels only in their profit margins. The predicted probability of reimbursement given a profit margin of 50% was 61.0% (67.3% for 5% profit margin).

Insights From Open Text Responses and Debriefing Interviews

A total of 61% of respondents indicated that profit margins should have a role in reimbursement decision making, whereas 39%

Table 4. Choice probabilities of selected reimbursement scenarios.

Attribute	Scenarios				
	Worst	Midpoints	Best	Midpoints + high profit	Midpoints + low profit
Yearly budget impact	€100 m	€50 m	€10 m	€50 m	€50 m
Disease severity	Low	Moderate	High	Moderate	Moderate
Cost-effectiveness (ICER)	€120 000	€60 000	€20 000	€60 000	€60 000
Health gain in QALYs	0.5	2	4	2	2
Profit margin in %	50	20	5	50	5
Probability of reimbursement, %	2.1	65.3	94.4	61.0	67.3

ICER indicates incremental cost-effectiveness ratio; m, million; QALY, quality-adjusted life-year.

indicated they should not. In summarizing the open text responses, containing their substantiations, 5 topic clusters could be formulated, based on 7 and 9 initial clusters formed by 2 authors independently. First, feasibility concerns regarding obtaining valid information on the profit margin of a pharmaceutical product. Second, inclusion of profit margins already during the reimbursement process may interfere with subsequent price negotiations. Third, cost-effectiveness should be leading in decision making, irrespective of profit margins. Fourth, (high) profit margins may be justified as a reward for innovation. Fifth, the use of profitability as a criterion can help to prevent paying too much as society.

The 4 individual debriefing interviews did not raise doubts on survey validity. Respondents expressed to have understood the choice tasks. One respondent doubted reproducibility of answers caused by her indifference in some decisions. When reflecting on their view on profit margins in the context of HTA, 3 respondents expressed to put some weight on profit margin, although less so than to the traditional criteria. A total of 3 respondents could recall a reimbursement dossier in which profit margin had been an issue in practice; these consistently involved a repurposed pharmaceutical with an increased price. One respondent suggested that the structure of the survey (choosing between 2 options) might have increased the attention given to profit margins. Finally, the preliminary results presented in the interviews seemed plausible to participants.

Discussion

This study aimed to investigate whether presenting information on profit margins of pharmaceutical products would influence the outcomes of reimbursement advice or decisions in the Dutch policy context. To investigate this, we conducted a DCE among 58 Dutch healthcare decision makers. Our results indicated that profit margins, at least at the levels specified in the DCE, significantly influenced the choices made in our experiment. In particular, decision makers were less likely to reimburse a product with higher profit margins. The importance of profit margins in comparison with other included HTA criteria (health gain, severity, ICER, budget impact) was relatively low, but certainly not negligible. For instance, an increase in the profit margin of 20% was equally influential as an increase in the ICER of €8600. Arguably, this constitutes a relevant difference within reimbursement decisions. Furthermore, most healthcare decision makers agreed that profit margins should play a role, although not further defined, in reimbursement decisions. Subgroup analyses indicated that older respondents put more emphasis on profit margins.

The open text responses indicated that main concerns in relation to including information on profit margins in the HTA process concerned the feasibility of measuring and obtaining the relevant information on profit margins. The issue of how such inclusion would relate to potential price negotiations (which may take place after the HTA in the Dutch situation) was also mentioned. Moreover, some respondents emphasized that highly effective innovations may justify also high profit margins.

Strengths and Limitations

Our study was based on a unique respondent group, which consisted of persons who work on a day-to-day basis in reimbursement decision making. A further strength of our study is that we undertook several steps to assess the validity of our experiment and its estimates, with generally positive results. This relates to response rate, dropouts, completion time, and cognitive debriefing questions, but also to the conducted individual debriefing interviews. In terms of the external validity, the estimated relative preferences seemed plausible to debriefing interviewees. Moreover, the incremental effects of the attributes compare well to previous estimates from The Netherlands,[17] except for a higher relevance of health gain in this study. Additionally, the results of DCEs among decision makers in other jurisdictions are consistent with our results in the high relative importance they generally attributed to cost-effectiveness, clinical benefits, and disease severity.[23-25]

Nevertheless, some limitations should also be noted. First, we need to acknowledge that we used a stated preference study, based on hypothetical choices, which were different from actual reimbursement decisions (eg, in practice one does not decide between 2 alternatives). Hence, our results may not be directly representative of or transferrable to actual reimbursement decisions. Second, we used healthcare decision makers from the Dutch context, which may hamper the generalizability to other jurisdictions, in which cultural and political context may also play a role. Third, our modest sample size comes with limitations, for example, not allowing for detailed subgroup analysis. Fourth, a more specific limitation of our experiment is that preferences may have been influenced by status quo bias. Respondents may have put more weight on HTA criteria they were more familiar with and that are more prominently used in current Dutch HTA practice. If this was the case, this may have resulted in an underestimation of the importance of profit margins. In contrast, by only including one “new and additional” HTA criterion in the experiment, we may have increased the attention paid to profit margin by respondents. Furthermore, the framing of the choice scenarios and of the presented attributes, although aimed to be neutral and balanced, may have influenced the results of the experiment. This not only relates to the concept and purpose of profit margins, which may be viewed differently by different

respondents, but also to the selected levels of profit margin used in our experiment. More generally, the imposed scenario context information was selected to provide an average approximation of the importance of HTA criteria. This also means that in other contexts profitability could have been more (or less) influential (eg, in the case of first-in-class drugs or repurposed drugs). A last issue in relation to our study design we want to highlight is that we could only provide respondents with limited context information compared with a real-life decision-making context. Additional information on market context (eg, potential competitors) or price negotiations could have influenced respondents view on and weighting of profit margins. In general, prices of pharmaceuticals may be influenced by negotiations, market structure, and other context variables, which could influence the weight placed on them in an HTA. Lacking information on such broader issues, respondents most likely formed their own opinion about this broader context when assessing the choice scenarios.

A general limitation that needs noting is that the type of information we provided in the DCE regarding profitability currently is not generally available. Systematically obtaining information on or estimating profit margins of particular products is not straightforward and would require overcoming many hurdles. For example, nontrivial uncertainties surrounding profit margins may be unavoidable because profits typically depend on market developments unknown at the time of decision making. As long as systematic information on profit margins is lacking, establishing profitability as a criterion may lead to an inconsistent consideration of profit margins in reimbursement decisions, which can have downsides. At the same time, given the feedback of respondents, this may already be the case now.

As an additional subgroup analysis (Appendix Table A2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2021.08.007 presents the stratification output), we examined whether preferences differed between respondents who agreed and disagreed on a role for profit margin in the reimbursement decision by interacting the main effects with this indicator. The profitability coefficient is roughly twice as large in the former group (−0.038) compared with the main analysis (−0.023). This underlines the existence of heterogeneity in preferences related to the role of profit margin, also within an HTA organization.

Implications and Future Research

The results of our study imply that if information on profit margins would be available within the assessment of a health technology, in general healthcare decision makers would take it into account in their decisions. Even though the traditional HTA criteria may receive more weight, the influence of profit margins was shown to be non-negligible in our study. This gives raise to several questions and avenues for future research.

A first question would relate to the desirability of having profitability as an additional criterion. Normative work in this area in relation to new price models and "fair pricing" of pharmaceutical has been performed, but also highlights divergent views on acceptable divisions of surplus (and thus on what is "fair"). Adding this criterion at least requires consensus regarding its general relevance among the responsible decision makers. In The Netherlands, the overall assessment framework, including the basic benefits package criteria, is eventually determined by politicians.[2] Therefore, future research could investigate the normative views of politicians, or maybe more importantly of their constituencies, on the potential role of the level of profitability in the health technology reimbursement decision context.

Related to this point, it also needs to be determined whether using information on profit margins in the context of an HTA would be the appropriate route to take to ensure an optimal division of surplus. Alternative ways of addressing this issue are also conceivable, for example, by conducting price negotiations (potentially guided by a "fair pricing" framework) or through some form of price regulation.[3,11,26]

A second question relates to the feasibility of sufficiently operationalizing this criterion in practice. Can we obtain or estimate the required information within the full reimbursement process? Formulating a structured process to define and measure or estimate profit margins for the purpose of HTA would be a first step. Future research could also consider the complex relationship among reimbursement decision making, price negotiations, and market context, as well as the link between profitability and incentives for innovation.

A final option for future research would be to investigate whether, in specific cases, profit margins already play a role in actual decisions. Although it currently is not an official criterion, our study indicates not only that profit margins would influence outcomes of decisions if they were known but also that in some cases respondents felt that profit margins already played a role.

Conclusions

If available to healthcare decision makers during an HTA process aimed to inform reimbursement decisions, profit margins of pharmaceutical products could be influential, with higher profit margins lowering the likelihood of reimbursement. This highlights the importance of "fair pricing" also in relation to reimbursement decisions. Whether adding "profitability" as an additional explicit criterion to the HTA decision framework is considered feasible or desirable needs further exploration.

Supplemental Material

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.jval.2021.08.007. Data and code used in the study can be accessed on the Open Science Framework: https://osf.io/6d9zs/.

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