BMJ Global Health

The role of the right valuation method in setting the firm's break-even price for mpox (and other) vaccines

Peter-Jan Engelen ,[1,2] Danny Cassimon[3]

To cite: Engelen P-J, Cassimon D. The role of the right valuation method in setting the firm's break-even price for mpox (and other) vaccines. *BMJ Glob Health* 2025;**10**:e018390. doi:10.1136/bmjgh-2024-018390

Handling editor Fi Godlee

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bmjgh-2024-018390).

Received 22 November 2024
Accepted 3 May 2025

[1]Utrecht School of Economics, Utrecht University, Utrecht, Netherlands
[2]Faculty of Business and Economics, University of Antwerp, Antwerpen, Belgium
[3]IOB, University of Antwerp, Antwerpen, Belgium

Correspondence to
Prof Dr Peter-Jan Engelen; peter-jan.engelen@uantwerpen.be

ABSTRACT

Critical voices on unfairly high mpox and other vaccine prices open the debate on the 'right price' to be paid to private vaccine suppliers. We apply compound real options analysis as a more appropriate valuation method to derive a correct firm's break-even price. Real option models are better able to capture the development costs, associated risks and the embedded operational flexibility in vaccine development in a superior way compared with more traditional net present value (NPV) methods. The real option price is lower than standard NPV-based methods, thereby providing a basis to improve the bargaining position of payers in negotiating better vaccine price outcomes. Deeper insights into the correct break-even price will create a more balanced playing field between firms and payers. This can also lead to more equitable access to vaccines in developing countries.

SUMMARY BOX

⇒ Pharmaceutical firms are accused of setting mpox, COVID-19 and other vaccine prices unfairly high for developing countries.
⇒ The debate on the 'right price' will benefit from the appropriateness of the valuation method used to come to a firm's break-even price.
⇒ Using real option valuation methods will lead to lower break-even vaccine prices.
⇒ Deeper insights in the correct break-even price will create a more balanced playing field between firms and payers.

On 18 September, Gavi, the Vaccine Alliance, announced an advance purchase agreement with the Danish firm Bavarian Nordic to secure 500,000 doses of its MVA-BN mpox vaccine (marketed as JYNNEOS or IMVANEX), to complement other recent efforts to rapidly increase supply and help ensure equitable access to countries in Africa impacted by the mpox outbreak; funding will come from Gavi's newly created First Response Fund.[1]

In immediate response to this and other recent supply agreements between public actors and Bavarian Nordic, including one with the US government, critical voices, such as the consumer rights group Public Citizen, accused the firm not only of obstructing the sharing of technology to other manufacturers, but also of a lack of transparency in price setting and unfairly high pricing, mentioning prices that varied from US$55, over US$65, up to even US$141 a dose.[2]

This situation brings us back to a central question in the debate on vaccine public policy, that is, the setting of the 'right price' to be paid to private vaccine suppliers by public actors, given scarce (global) public funds, that could be used for other much-needed purposes when vaccine costs could be brought down. The issue was discussed with respect to the price setting, observed differences between vaccines and regional disparities regarding the COVID-19 vaccines[3 4] and was also prominent in the debate on overcoming the reluctance of private companies to invest in the development of vaccines for tropical diseases. In the latter case, the use of so-called pull financing mechanisms, such as Advanced Market Commitment (AMC), launched in 2009 for pneumococcal vaccines, was often suggested.[5] Recently, AMC-type pull financing has also been suggested as a key instrument for securing affordable and accessible vaccines against COVID-19 and other diseases for the next decade.[6 7]

While the literature focuses on the presence of monopoly power and the lack of intracompany transparency on exact cost structures (and on the use of public funding in early stages of the development of the vaccine) as major causes of the unfairly high price setting by firms, again in the case of the mpox vaccine and Bavarian Nordic, hardly any attention has been paid to one particular dimension of vaccine pricing, which relates to the appropriateness of the valuation method used to come to a correct price. In our view, part of the incorrect price setting and resulting overpricing has to do with the

use of inappropriate methods of valuation, more particularly the continued across-the-board application of the conventional net present value (NPV) approach. In this contribution, we try to show how the use of more appropriate valuation tools, namely a (compound) real options approach, will generally lead to more correct and lower price setting. To show the different price outcomes between the two valuation methods, we will use the AMC-linked pneumococcal vaccine case. Although the prime focus of this article is on the pricing issues surrounding vaccines, the real option model can also be applied to a wider context such as pharmaceutical research and development (R&D), orphan diseases and drug reimbursement where similar pricing issues emerge.[8]

APPLYING DIFFERENT VALUATION METHODS FOR VACCINES

In the pneumococcal case, donors commit to subsidise the purchase of the vaccine at a preagreed price. This AMC mechanism, coordinated and managed by the Global Alliance for Vaccines and Immunisations (GAVI), the intermediating health organisation between donors and vaccine producers, is an example of a pull strategy to incentivise the development of a vaccine. By guaranteeing a minimum viable market demand, it encourages companies to invest in the development or the expansion of manufacturing capacity of vaccines for developing countries. Companies receive this guaranteed price up to a certain number of doses, after which the companies commit to sell the vaccine at a much lower price (ie, the so-called tail price intended to reflect the marginal cost of production).[9] Indeed, the AMC mechanism allows the purchase of vaccines at prices far lower than their typical retail value: contract prices are about 95%–97% lower than retail market prices for *Streptococcus pneumoniae* vaccines.[10] In the case of the pneumococcal vaccine, the total AMC price per dose was set at US$7.0, consisting of a tail price of US$3.50 per dose and a top-up subsidy of US$3.50 paid out of the AMC donor funds for the first 21% of the doses supplied by each company.[11]

Obviously, one of the most difficult (and controversial) steps in this process is determining the correct price for the product. For instance, Médecins Sans Frontières launched a global campaign in 2015 to reduce the price of pneumococcal conjugate vaccine to US$1.66 per dose, while Pfizer claimed that a price of US$3.30 per dose was below the cost of manufacturing.[12] The same pricing issue now resurfaces in the context of COVID-19 and mpox vaccines.

Typically, the standard framework in the pharmaceutical industry to calculate the price is the NPV model. One survey shows that the majority of pharmaceutical firms dominantly rely on NPV-based valuation approaches for evaluating projects.[13] The real option utilisation rate is 6.0% in a survey among Scandinavian firms (19% in healthcare) vs 74% for NPV methods.[14] Another study reports that 14% of healthcare firms use real option methodology.[15] NPV was also the leading method in the pneumococcal vaccine case.[16]

However, an NPV model only looks at cash inflows and outflows, without taking into account any flexibility to adjust, rescale or abandon a project.[17] It assumes a now-or-never decision following a rigid path once the investment decision is taken without possibly adjusting the strategy during the execution of the project.[18] However, in a dynamic environment, projects will often not materialise in the same shape as the decision-maker has initially expected.[17] New information may arrive or particular sources of uncertainty may be resolved, making it thus valuable to modify the project.[19] The added value of real options lies precisely in incorporating such operational flexibilities and strategic dimensions of projects.[20] While the real option model is conceptually superior to an NPV approach, one can also acknowledge some drawbacks. Real option modelling has a higher complexity, requires more data input and often demands programming in a mathematical software program such as Matlab.[14 15]

It is now widely accepted in the economics literature that R&D cannot be accurately valued through an NPV lens.[20] Real option methodology is well suited to handle important resource allocation decisions which require considerable irreversible investments staggered over a prolonged period in combination with highly uncertain future payoffs.[19] The development of a new vaccine is a textbook case of real option analysis.[21]

More specifically, the development of a new vaccine follows a regulated pathway of six distinct phases (see figure 1).[22] Developing a new vaccine starts with a preclinical test phase, followed by three clinical test phases, a supervisory approval phase and ultimately the commercial launch phase. At each transition, a go/no go decision has to be made. This multistaged vaccine development process can be seen as a sequence of real options and can be modelled as a generalised n-fold compound option model. Starting the R&D discovery phase provides a sixfold compound option on future net sales coming from commercialising the vaccine. In contrast to NPV, the compound real option model shows whether the commercial potential of a new vaccine compensates its start-up costs, taking into account the development risks and development costs at each phase.

Due to explicitly considering its optional nature, a crucial insight is that real option logic will lead to a higher project value, compared with the NPV approach.[17 20] This is because the real option model reflects the time value capturing the flexibility of the decision-maker, while the NPV no-flexibility model ignores this value.[18 23] This in turn implies that using this approach may lead to more projects of vaccine development becoming profitable. Consequently, it may also call for a lower preagreed price to render the project profitable to encourage companies to invest.

The real option model (and also the NPV model) calculates the minimum break-even price from the firm's perspective, taking into account its expected costs and

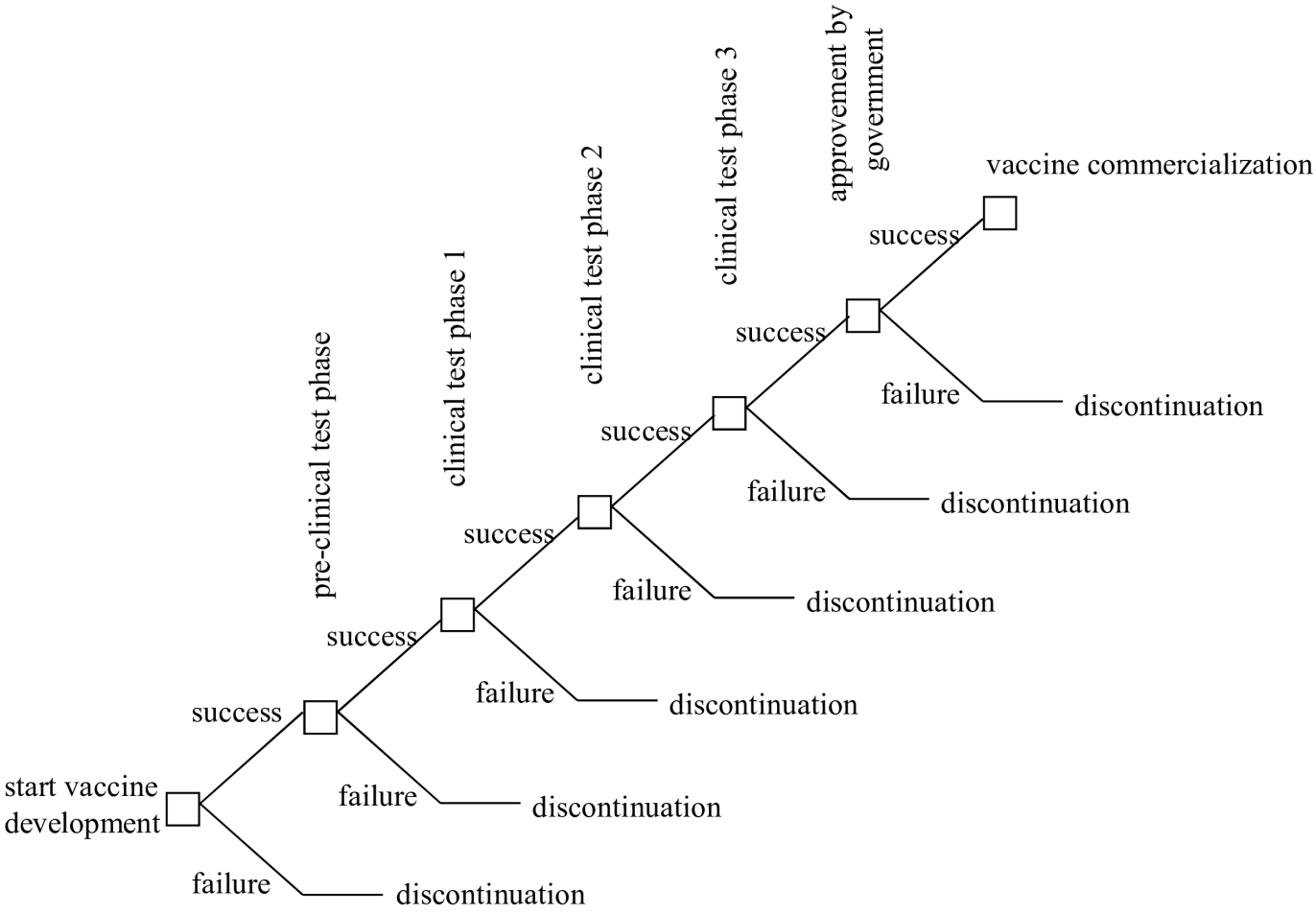

Figure 1 The development process of a vaccine.

benefits/revenues, risks and flexibilities at market conditions.[24] In real life, firms can obviously take into account other elements, such as losses of failed trials elsewhere (portfolio approach), in negotiating a higher price than this break-even price.

Our model on pricing is also related to commonly used approaches in Health Technology Assessment (HTA).[25] Although HTA is a multidisciplinary process that includes not only clinical and economic assessment but also ethical, social and organisational assessments to determine the value of a health technology at different points in its lifecycle, its economic assessment remains an important dimension of HTA, in which a real options approach can provide important additional insights. In terms of economic assessment models used, the real option approach definitely relates to so-called cost-plus methods, where it allows for a more correct inclusion of risk and also includes the value of flexibility (as compared with an NPV-based cost plus method). It can also be perfectly integrated in more value-based assessment methods not only to allow for a better calculation of the cost dimension, but also, more broadly, to incorporate in a more correct way all elements of uncertainty and flexibility that may also be embedded in the societal dimensions of the assessment. As these strategic and uncertainty elements are even more present in early stage HTAs, such as in the case of vaccines, real option models will be particularly useful in this context.[26]

We illustrate the comparison of the real option and NPV model through a stylised example. Table 1 contains detailed information on the timing, development costs and success rates of the six development phases of a fictitious vaccine. For instance, starting up the project (discovery phase) is expected to cost US$9 million, with a probability of success of 98%, while starting the preclinical phase is expected to occur after 1 year at a cost of US$10 million, with a probability of success of 90%, and so on. The target population for the vaccine (the market prospect) is estimated at 100 million doses. We assume that a realistic market price for one vaccine is about US$3.50 per dose, implying an expected incoming cash flow of US$350 million. Launching the vaccine costs US$35 million, leading to a net cash flow of US$315 million. Taking into account the probabilities of success at each phase, one can calculate the expected NPV (ENPV) of the project as −US$38.3 million (see table 1).[27]

The ENPV of the project is calculated as:

$$ENPV = \sum_{i=1}^{7} \rho_i \sum_{t=1}^{T} \frac{ECF_{i,t}}{(1 + wacc)^t} = -38.3\ million$$

Table 1 Calculation of the expected net present value of the vaccine project

Phase	Time	Outgoing CF_{it}	Incoming CF_{it}	Net CF_{it}	p_i	ρ_i	ECF_{it}	CCF_{it}
Discovery	0	–9	0	–9	0.98	0.02	–9.0	–0.2
Preclinical	1	–10	0	–10	0.90	0.098	–18.1	–1.8
Clinical I	2	–13	0	–13	0.88	0.1058	–28.8	–3.1
Clinical II	3	–33	0	–33	0.45	0.4269	–53.6	–22.9
Clinical III	5	–86	0	–86	0.72	0.0978	–107.0	–10.5
Approval	8	–42	0	–42	0.95	0.0126	–126.6	–1.6
Launch	9	–35	350	315	1.00	0.2389	7.0	1.7
							ENPV	–38.3

CCF_{it}, discounted conditional cash flow at time t given that stage i is the end stage given probability ρ_i; CF_{it}, outgoing cash flow (development cost per phase), the incoming cash inflow (the net sales income in the last phase) or the net cash flow (the difference between incoming and outgoing) associated with each development phase i (in million US$); ECF_{it}, discounted total cash flow at time t given that stage i is the end stage; ENPV, expected net present value; Phase, the specific phase in the vaccine development process ; pi, probability of success of stage i ; Time, the maturity date for each phase (expressed in years); ρi, probability that stage i is the end stage for the vaccine.

where i = 1,…,7 represents the seven phases from discovery through commercialisation, ρi is the probability that stage i is the end stage for the drug (put differently, this is the probability that the drug has to be terminated in this stage due to development risks), T is the end stage time for the drug, $ECF_{i,t}$ is the expected discounted total cash flow at time t given that stage i is the end stage, the WACC (or weighted average cost of capital of the firm) is the appropriate discount rate for the expected cash flows (assumed to be 10%).

Clearly, at this price, the NPV model shows that companies will not invest in this vaccine as it turns out to be a loss-making project. To induce companies to develop this vaccine, we can calculate at what price they are prepared to do so. Technically speaking, this is the price that makes the NPV equal to zero. In our example, a price of about US$7.28 will render the project value breakeven and thus acceptable for investment (see upper panel in table 2).

Now we turn to the real option framework. As explained earlier, the value of the compound option has to be compared with the cost of the first phase. Equal to the NPV inputs, at a market price of US$3.50 per dose, the present value of incoming cash flows in the commercialisation phase is estimated to be US$350 million. Similarly, the exercise price of the final phase amounts to US$35 million, the exercise prices of the earlier phases of the compound option amount to US$10 (preclinical), US$13 (clinical I), US$33 (clinical II), US$86 (clinical III) and US$42 (approval) million (see table 1, column 5), while the probabilities of reaching the next phase are 90% (preclinical), 88% (clinical I), 45% (clinical II), 72% (clinical III) and 95% (approval) (see table 1, column 6). Additionally, the real option model assumes that the point estimation of the market potential can vary with an instantaneous SD of the project return of 72.45%. In applying all these parameters to a compound option model, we value the upside potential of the vaccine project at US$7.6 million. In an online supplemental appendix, we present the full n-fold compound option model and its calculations in more detail. Compared with the start-up cost of US$9 million (see table 1), this implies again a rejection of the project as its value becomes negative: –US$1.4 million. Again, we calculate what price per dose is needed to make the project breakeven, a price per dose of about US$3.78 (see lower panel in table 2). This makes the project acceptable for investment.

If one compares the real option value and the NPV, one can see where the additional value of the real option logic comes from. That is,[23]

Table 2 Comparison between NPV and real option logic for price support

	Price per dose (in US$)	Project value (in million US$)	Required support (100 million doses)
NPV logic			
Market price	3.50	NPV=–38.3	
Break-even price	7.28	NPV=0	
Price support	3.78		US$378 million
Real option logic*			
Market price	3.50	ROV=–1.4	
Break-even price	3.78	ROV=0	
Price support	0.28		US$28 million

*The real option model assumes that market risk is measured as the instantaneous SD of the project return and is estimated to be 72.45%. The risk-free interest rate amounts to 2.97%. Source: Aswath Damodaran (New York University) at http://pages.stern.nyu.edu/~adamodar. All other input data for the real option model is identical to the NPV model. A detailed description of the real option model used and the calculations are provided in the online supplemental appendix to this analysis.
NPV, net present value; ROV, real option value.

Real Option Value = Static NPV + Value of Flexibility

Applied to the example this implies that the value of flexibility is the difference between the NPV (−US$38.3 million) and real option value (−US$1.4 million) or US$36.9 million.[23] The added value of the real option logic reflects the full flexibility pharmaceutical firms have at each 'milestone' in the multistage development process (continuation or abandonment). Capturing the full value of this managerial flexibility leads to a higher real option value. Indeed, at each milestone, the firm needs to balance the cost of the focal stage with the potential of continuing the project (real option value beyond that stage).

For instance, suppose one considers the second milestone (clinical I phase). At that moment, the firm needs to compare the real option value of the next stages with the cost of finishing the clinical phase. Only when the real option value is higher than the cost of US$13 million, it is worth for the firm to continue the project, in the opposite case it will abandon the project and avoids being stuck in a loss-making project.

PRACTICAL DATA CHALLENGES

A practical challenge in implementing a real option approach for (mpox and other) vaccines lies in obtaining specific data for different input parameters such as development costs, success rates or market demand. The data requirements are not unique for real option models, they are similar for NPV and similar models in HTA. In fact, real option models share many data points with the other models such as development costs, market demand, time lines and success rates. On top of that real option models require the input of a volatility metric. While many of the data points are often subject to proprietary sources of firms, payers and other outsiders can rely on public proxy data and assumptions based on similar vaccines.

Combining estimates from public clinical trial registries such as ClinicalTrials.gov, expert forecasts,[28] meta-studies,[29] systematic reviews[30] and/or surveys[31] can help in addressing input data. One can combine such historical data with actively tracking mpox vaccine trials such as BioNTech's BNT166[32] and Bavarian Nordic's Jynneos[33] for phase-specific data points and use triangular distributions for missing data.[31] Moreover, one might also consider using data from smallpox vaccine development as a proxy for mpox vaccines.[34]

Estimates for volatility can be estimated using historical data of pharmaceutical companies,[23] implied volatilities of traded options on listed pharmaceutical companies[17] or using a calibrating exercise of matching theoretical probabilities with subjective assessments of managers or experts.[35]

Finally, using sensitivity analysis to analyse the impact of estimation errors for key proxy datapoints gives further insight in the robustness of the approximations (see the online supplemental appendix). While we think that the above approach enables robust investment modelling despite data limitations for payers, we acknowledge this as a potential limitation for the real option approach, but again, this is not different from more traditional methods.

MORE EQUITABLE ACCESS TO VACCINES

While the NPV model calls for a preagreed price per dose of about US$7.28 per dose, the real option model shows that US$3.78 per dose would already suffice to render the project profitable. Table 2 shows the consequences for price support. In the NPV logic about half of the break-even price per dose would need to be sponsored, implying a huge investment of US$378 million, while the real option model shows that a much smaller investment of US$28 million is needed to trigger investment in the vaccine project. Although the gap between the NPV-price per dose and the real option dosage price can vary depending on the specific vaccine, the real option model typically reduces the total price required for profitability.

Our approach also has important consequences for vaccine price negotiations between firms and payers. These negotiations are often characterised by unbalanced power relations, where payers are in the disadvantage, for example, due to asymmetric information on exact parameters of development costs and risks, as well as other factors such as scarcity of alternatives from the payer's perspective.[36–38] Since a real option approach allows for a more correct, and *lower*, firm's break-even price, and all other factors held constant, it improves the bargaining position of the payer as he now has better knowledge of the firm's true break-even price. It typically would provide the payer for a bigger negotiation range between the (now lower) minimal-acceptable price for the firm and the maximum acceptable price for the payer. In case the firm suggests a price that is (considerably) higher than this (real-option-derived) break-even price the payer has a better argument to downplay this claim.

This particular case used may not fully comparable to the Bavarian Nordic mpox vaccine case but was used to make a central argument using a widely known and more transparent case. However, we can safely assume that also Bavarian Nordic uses NPV-type of valuation methods in their pricing models, assuming some overpricing in this sense, making the central argument of this contribution also relevant for this and other cases. Obviously, replication in the case of the Bavarian Nordic mpox case would require more detailed intrafirm cost information and more complete knowledge of the history of the development

of this particular vaccine, including the use of public funding in former stages of its development.

In conclusion, the real option framework not only allows determining the right price for the vaccine R&D program, but also gives detailed insight in the different value drivers of the project to induce pharmaceutical companies to start development. It can be used, as we showed, to determine in more valid ways how much sponsoring is required to compensate a company supplying products at prices affordable in developing countries or to determine how much guaranteed demand is needed to push companies over the threshold value for product development in this domain. Real options are particularly suited to gain important insights in pharmaceutical companies' reluctance to develop vaccines for developing countries and to learn what threshold values are crucial to induce investment. Rigorously applying the real option approach therefore provides a better way to answer the question about the right price of a vaccine, and will typically lead to a reduction of the necessary intervention needed. By shedding light on the appropriate valuation method to come to a correct, transparent price, we hope to improve a more equitable access to vaccines in developing countries.

Contributors PJE is a Professor of Finance specialised in investment decisions under uncertainty and has applied real option modelling to the valuation of pharmaceutical R&D, sustainable energy solutions and human behaviour (crime, refugee flows). He is based at the University of Antwerp, Belgium and Utrecht University, the Netherlands. He is corresponding author for the article. DC is a Professor of Development Finance at the Institute of Development Policy (IOB), University of Antwerp, Belgium. He specialises in global public policy issues such as access to health care, LDC debt relief and development financing mechanisms (debt-for-climate swaps, debt-for-health swaps). CRediT roles: Conceptualisation: PJE and DC. Formal analysis: PJE. Methodology: PJE and DC. Writing–original draft: DC and PJE.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data is available in the additional supplemental material.

ORCID iD

Peter-Jan Engelen http://orcid.org/0000-0003-0578-5460

REFERENCES

1 Gavi signs agreement with bavarian nordic to rapidly secure 500,000 doses of mpox vaccines for africa. 2024. Available: https://www.gavi.org/news/media-room/gavi-signs-agreement-bavarian-nordic-rapidly-secure-500000-doses-mpox-vaccines
2 Nakweya G. Mpox: Africa's response is obstructed by manufacturer's failure to share vaccine technology and unfair pricing, says campaign group. *BMJ* 2024;387:q2174.
3 Ramachandran R, Dhodapkar M, Ross JS, *et al*. Future of covid-19 vaccine pricing: lessons from influenza. *BMJ* 2021;373:n1467.
4 Light DW, Lexchin J. The costs of coronavirus vaccines and their pricing. *J R Soc Med* 2021;114:502–4.
5 Kremer M, Levin J, Snyder CM. Advance market commitments: insights from theory and experience. In AEA Papers and Proceedings 2020.269–73.
6 Snyder CM, Hoyt K, Gouglas D, *et al*. Designing Pull Funding For A COVID-19 Vaccine. *Health Aff (Millwood)* 2020;39:1633–42.
7 Towse A, Chalkidou K, Firth I, *et al*. How Should the World Pay for a Coronavirus Disease (COVID-19) Vaccine? *Value Health* 2021;24:625–31.
8 Johnson PE. Pharmaceutical reimbursement: an overview. *Am J Health Syst Pharm* 2008;65:S4–10.
9 Hargreaves JR, Greenwood B, Clift C, *et al*. Making new vaccines affordable: a comparison of financing processes used to develop and deploy new meningococcal and pneumococcal conjugate vaccines. *The Lancet* 2011;378:1885–93.
10 Hill AB, Kilgore C, McGlynn M, *et al*. Improving global vaccine accessibility. *Curr Opin Biotechnol* 2016;42:67–73.
11 Cernuschi T, Furrer E, Schwalbe N, *et al*. Advance market commitment for pneumococcal vaccines: putting theory into practice. *Bull World Health Organ* 2011;89:913–8.
12 Burki TK. Pricing of pneumococcal conjugate vaccine challenged. *Lancet Respir Med* 2015;3:427.
13 Hartmann M, Hassan A. Application of real options analysis for pharmaceutical R&D project valuation—Empirical results from a survey. *Res Policy* 2006;35:343–54.
14 Horn A, Kjærland F, Molnár P, *et al*. The use of real option theory in Scandinavia's largest companies. *International Review of Financial Analysis* 2015;41:74–81.
15 Block S. Are "Real Options" Actually Used in the Real World? *The Engineering Economist* 2007;52:255–67.
16 Berndt ER, Glennerster R, Kremer MR, *et al*. Advance market commitments for vaccines against neglected diseases: estimating costs and effectiveness. *Health Econ* 2007;16:491–511.
17 Luehrman TA. Investment opportunities as real options: getting started on the numbers. Harvard Business Review; 1998.
18 Shockley R. *An applied course in real options valuation*. Thomson South-Western, USA, 2007.
19 Dixit AK, Pindyck RS. *Investment under uncertainty*. Princeton university press, 1994.
20 Trigeorgis L. *Real options: managerial flexibility and strategy in resource allocation*. USA: The MIT Press, 1996.
21 Cassimon D, Engelen PJ, Thomassen L, *et al*. Valuing new drug applications using n-fold compound options. *Res Policy* 2004;33:41–51.
22 Cassimon D, De Backer M, Engelen PJ, *et al*. Incorporating technical risk in compound real option models to value a pharmaceutical R&D licensing opportunity. *Res Policy* 2011;40:1200–16.
23 Leslie K, Michaels M. The real power of real options. McKinsey Quarterly; 1997.97–108.
24 Damodaran A. *Applied corporate finance*. Wiley, 2015:656
25 Belfiore A, Scaletti A, Lavorato D, *et al*. The long process by which HTA became a paradigm: A longitudinal conceptual structure analysis. *Health Policy* 2023;127:74–9.
26 IJzerman MJ, Koffijberg H, Fenwick E, *et al*. Emerging Use of Early Health Technology Assessment in Medical Product Development: A Scoping Review of the Literature. *Pharmacoeconomics* 2017;35:727–40.
27 Kellogg D, Charnes JM. Real-Options Valuation for a Biotechnology Company. *Financial Analysts Journal* 2000;56:76–84.
28 Kane PB, Moyer H, MacPherson A, *et al*. Expert Forecasts of COVID-19 Vaccine Development Timelines. *J Gen Intern Med* 2020;35:3753–5.
29 Lo AW, Siah KW, Wong CH. Estimating Probabilities of Success of Vaccine and Other Anti-Infective Therapeutic Development Programs. *Harvard Data Science Review* 2020.
30 MacPherson A, Hutchinson N, Schneider O, *et al*. Probability of Success and Timelines for the Development of Vaccines for Emerging and Reemerged Viral Infectious Diseases. *Ann Intern Med* 2021;174:326–34.

31 Gouglas D, Thanh Le T, Henderson K, *et al*. Estimating the cost of vaccine development against epidemic infectious diseases: a cost minimisation study. *Lancet Glob Health* 2018;6:e1386–96.
32 Zuiani A, Dulberger CL, De Silva NS, *et al*. A multivalent mRNA monkeypox virus vaccine (BNT166) protects mice and macaques from orthopoxvirus disease. *Cell* 2024;187:S0092-8674(24)00054-0:1363–73:.
33 Wolff Sagy Y, Zucker R, Hammerman A, *et al*. Real-world effectiveness of a single dose of mpox vaccine in males. *Nat Med* 2023;29:748–52.
34 Christodoulidou MM, Mabbott NA. Efficacy of smallpox vaccines against Mpox infections in humans. *Immunother Adv* 2023;3:ltad020.
35 Cassimon D, Engelen PJ, Yordanov V. Compound real option valuation with phase-specific volatility: A multi-phase mobile payments case study. *Technovation* 2011;31:240–55.
36 Villa F, Tutone M, Altamura G, *et al*. Determinants of price negotiations for new drugs. *The Experience of the Italian Medicines Agency, Health Policy* 2019.
37 Sullivan SD. Medicare Drug Price Negotiation in the United States: Implications and Unanswered Questions. *Value Health* 2023;26:394–9.
38 Grepperud S, Pedersen PA. Positioning and negotiations: The case of pharmaceutical pricing. *Eur J Polit Econ* 2020;62:101853.