# Trends, challenges, and success factors in pharmaceutical portfolio management: Cognitive biases in decision-making and their mitigating measures



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**Effective portfolio management is crucial for innovation and sustaining revenue in pharmaceutical companies. This article holistically reviews trends, challenges, and approaches to pharmaceutical portfolio management and focuses, in particular, on cognitive biases in portfolio decision-making. Portfolio managers strongly rely on external innovation and face increasing competitive pressure and portfolio complexity. The ability to address biases and make robust decisions remains a challenge. Portfolio management practitioners most commonly face confirmation bias, champion bias, or misaligned incentives, which they seek to mitigate through expert input, team diversity, and rewarding truth-seeking. Ultimately, highest-quality portfolio management decision-making could be enabled by three factors: high-quality data, structured review processes, and comprehensive mitigating measures against biases in decision-making.**

**Keywords: portfolio management; decision process quality; cognitive biases; bias mitigating measures; R&D pipeline management; pharmaceutical industry**

## Introduction

Over the past few decades, decision-making has become more complex for pharmaceutical portfolio managers as a result of the increased reliance on external partnerships leading to an increased portfolio complexity,[1] increasing requirements for drug safety and efficacy, growing costs, and a highly competitive environment, which forces organizations to be more flexible, responsive, and efficient.[2] Pharmaceutical companies are facing continuous pressure to innovate to deliver future value sustainably.[3] Yet, portfolio managers are facing the challenge to systematically conduct portfolio reviews, prioritize assets effectively, allocate limited resources flexibly, and terminate projects in a timely fashion.[4,5] Importantly, the total number of projects in the portfolio and the percentage share of priority projects have major implications for the resources required and how they are distributed across programs: Too many backup or low-priority candidates could bind resources, thereby decreasing R&D productivity and risking portfolio success.[5,6]

The success of the portfolio determines the long-term success of a pharmaceutical organization; yet, portfolios appear to only become successful if they are supported by decision processes of high quality and the right decision-making.[1] Cognitive biases impact the quality of pharmaceutical R&D decision-making in general (i.e., confirmation bias, champion bias, storytelling bias, or sunk-cost fallacy), whereas their specific impact on portfolio level decision-making remains unexplored to date.[7] To provide the reader with the relevant context about recent trends and challenges in pharmaceutical portfolio management, we review these two aspects first. Second, we explore portfolio review approaches, mechanisms of asset evaluation, and strategies for asset prioritization to enable portfolio management practitioners to understand the different approaches and, ultimately, to adopt

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best practices to enhance their portfolio management and pharmaceutical R&D process. Third, to address a gap in the existing literature, we research cognitive biases in portfolio management decision-making and their mitigating measures. Our work has four key research contributions to advance the field: (i) specific for portfolio management decision-making during the pharmaceutical R&D process, we present the five most prevalent cognitive biases impacting the quality of decision-making; (ii) for each of the five most prevalent cognitive biases, we present the five most common counter-measures; (iii) additionally, we uncover more hidden cognitive biases, which go beyond data presented in the existing literature; and (iv) finally, we present novel counter-measures against cognitive biases, which were deemed relevant by portfolio management practitioners.

To complement our literature review with perspectives from industry practitioners, we facilitated a global online survey. We collected answers from 92 industry practitioners globally who were responsible for making portfolio-level decisions during technical review meetings, portfolio governance meetings, or for allocating resources across the portfolio projects while working for different large and mid-size pharmaceutical companies and biotech companies. The online survey design was developed based on a comprehensive literature review to identify the most prevalent biases in portfolio decisions and understand what approaches industry practitioners are taking to mitigate them. A detailed overview of the survey approach and the participants' demographics can be found in the Supplemental information online. Overall, our analysis is more granular than the existing literature and presents novel findings beyond standard cognitive biases, which advance the research field.

Finally, to enable practitioners to apply the findings of this work in practice, enhance their portfolio management processes, as well as the quality of decision-making in their organization, we present a new management framework: the 'seven pillars of pharmaceutical portfolio management'.

## Although pharmaceutical companies face intensified competitive pressure and increased portfolio complexity, robust decision-making remains a challenge for portfolio managers

Overall, competition in the pharmaceutical industry is fierce and, between 2006 and 2015, the total worldwide R&D spend of pharmaceutical and biotechnology companies increased from US$108 billion to US$141 billion.[2,8] The increasing complexity of pharmaceutical project portfolios over the past few decades becomes furthermore apparent when analyzing data about mergers and acquisitions, the growing costs of R&D per developed drug, challenges when forming partnerships between academia and industry [e.g., intellectual property (IP) negotiations, change in strategies or restrictions on publications] or other outsourcing and risk-sharing activities during late-stage developments.[2,8,9] To monitor and assess competition, portfolio managers can turn to data relating to patent applications filed, number and types of drugs in R&D pipelines, or products launched to the market.[2]

When managing an R&D pipeline of a pharmaceutical company, portfolio managers face a plethora of challenges and complexities. Often they encounter too many development projects in their portfolios because of a failure to kill projects in a timely manner.[4,5] Moreover the lack of reliable project data and of a systematic review process makes project prioritization for portfolio managers overwhelming.[4,5] Especially during the early development stage, project data are sparse, which increases the risk of biases in portfolio decision-making, such as optimism bias, personal stakes of experts, or groupthink, which can compromise the decision quality.[10–12] Furthermore, continuous reallocation of resources is frequently required to overcome urgent project crises.[4,5] Leveraging optimization algorithms to determine an optimal resource allocation that maximizes the portfolio output or defining priority projects could help portfolio managers to use their limited resources most effectively.[13,14]

In addition, certain trends are strongly shaping the pharmaceutical industry and provide new paradigms for portfolio managers. Pharmaceutical companies are under the burden of an increasingly competitive R&D landscape;[15–20] they work on highly differentiated drugs;[19] and strive to go beyond traditional modalities or to enter new therapeutic areas.[17,20] Lastly, they have a strong reliance on external research partnerships to supplement internal research and gain access to new technologies.[17–19,21,22] This shift toward external innovation introduces the additional complexity of managing both the internal portfolio and that of the partnering company.[1]

To manage these newly introduced complexities and achieve a high-quality decision process, structured frameworks are beneficial tools for portfolio managers when assessing assets, such as AstraZeneca's 5R framework (the right target, the right patient, the right tissue, the right safety and the right commercial potential).[23,24] Next to AstraZeneca's 5R framework other pharmaceutical companies, such as Pfizer or Eli Lilly, have published alternative frameworks.[25] For example, Pfizer published the 'Three pillars of survival' framework (Pillar 1: exposure at the target site of action; Pillar 2: binding to the pharmacological target; Pillar 3: expression of pharmacology), which was based on an analysis of their Phase II clinical trials (2005–2009).[25] Although Pfizer lagged behind the industry benchmark for decades, it achieved an industry-leading clinical success rate by the end of 2020 and syndicated its new management principles. The '3 pillar' framework was developed further into the 'Signs of Clinical Activity (SOCA) paradigm', which leverages proof of mechanism (POM) and early signal of efficacy (ESOE) to enhance early-stage decision-making and attritions when it is most cost effective by embracing a culture shift to objective decision-making.[24] Eli Lilly's Chorus 'quick-win, fast-fail model' is similar to the Pfizer 'SOCA paradigm' because it strives to enable quick and efficient answers to crucial questions, which can lead to 'go/no-go' decision (e.g., by focusing on 'killer experiments', truth-seeking behavior, or deferring investments in downstream activities).[24,26] The described frameworks provide guidelines to practitioners on how to assess and compare pharmaceutical R&D projects at different stages. Yet, they lack dimensions addressing additional process management aspects (e.g., portfolio review cadences, facilitation processes of review meetings, or list of stakeholders involved in review meetings) or decision-making quality (i.e., measures to detect and mitigate cognitive biases in decision-making).[23–26] Therefore, we focus here on reviewing different portfolio review mechanisms and asset prioritization strategies, and survey portfolio management practitioners about cognitive biases and their mitigating measures. To complement the existing framework presented by different pharmaceutical organizations, we synthesized our findings into a new framework (The 'seven pillars of pharmaceutical portfolio management') and present it at the end of this article.

The pharmaceutical industry is characterized by a unique combination of governance requirements, which include regulatory scrutiny, long development timelines, high risk and uncertainty, and ethical considerations.[8,27] Comparing this set of governance requirements to other research and development-intensive sectors, it can be observed that heavily regulated industries, such as the aerospace industry,[28] share certain characteristics with the governance requirements of the pharmaceutical industry, whereas other, less-regulated sectors, such as the technology industry,[28–30] do not. In the aerospace industry, product development cycles are also long and heavy government regulation needs to be implemented.[28] Therefore, the governance model is often formally structured and decision-making is centralized.[31] This approach of centralized decision-making is also a useful approach to pharmaceutical portfolio management.[32] By contrast, the technology industry functions fundamentally differently: often small dynamic teams with flat hierarchies operate in rapid innovation cycles and govern their R&D by decentralized decision-making processes.[29,30]

Overall, portfolio governance bodies have a major role in pharmaceutical portfolio management[27] and their success can be enabled by various factors: to ensure effectiveness of the portfolio governance committee, the roles and responsibilities of each team member need to be clearly defined.[33] One way to accomplish this is to use role cards, which define each team member's job and responsibilities.[33] Furthermore, openness and transparency among stakeholders are identified as key factors for successful portfolio management to promote collaboration and avert silos.[33,34] The usage of rigorous quantitative measures is encouraged as well as truth-seeking behavior to enable transparent and effective portfolio decision-making.[23,33,34] According to the management paradigm 'culture eats strategy for breakfast', portfolio managers identify the corporate culture of an organization as a key enabler or inhibitor to high-quality decision-making and accomplishing strategic goals.[34,35] Thus, it might be beneficial to complement portfolio management frameworks (such as the AstraZeneca 5R framework) by a cultural dimension to foster information sharing and transparent decision-making within the organization and the portfolio governance body.[23]

To further understand how to best compose portfolio governance bodies, approach portfolio review meetings, evaluate and prioritize assets and leverage decision guiding tools, we review these aspects in more detail below.

## Formally structured portfolio reviews build the foundation for efficient portfolio decision-making

Managing a portfolio is a multidimensional challenge; therefore, defining a formally structured process could enable best practices in decision-making.[32] In pharmaceutical companies, it is common for portfolio governance bodies to be cross-functional teams to enable a comprehensive decision-making process.[1] Often clinicians, pharmacologists, statisticians, and regulatory and project management experts are included in portfolio review meetings.[1] Limiting the number of stakeholders involved in regular reviews could help to ensure effectiveness of the portfolio review committee.[33] Overall, the portfolio manager can act as a crucial integrator who enables good communications and quick access to all stakeholders, which could help to ensure alignment, trust, and effectiveness of portfolio management reviews and resolve competing interests.[33] However, it remains unclear and requires further research to understand which stakeholders it is best to involve and when not to involve them (dependent on the portfolio size, pipeline stage, and organizational structure) to achieve effective portfolio decision-making.

Large pharmaceutical companies typically review and rebuild their portfolio on an annual, semi-annual, or quarterly level (one to four portfolio reviews per year).[5,13,36] Yet, the optimal portfolio review cadence depends, for example, on the planning cadences of an organization as well as the lifecycle stages of the projects in the R&D pipeline (early-stage projects carry higher uncertainties) and could vary across organizations.[13,36]

Moreover, clear priorities are at the core of effective portfolio management: candidates with the highest success potential should be prioritized and funded first.[1] Prioritizing and sequencing potential drug candidates in the R&D pipeline effectively could lead to significantly higher return on investments (estimated as up to 28%).[37] Formalizing the asset prioritization process (allocating more resources and accelerating project timeline) could help pharmaceutical companies to address the dilemma of diluting priorities by wanting to include too many or all projects in their portfolio.[5,38] This might be particularly true for early-stage projects with limited data availability, whereas later-stage assets have more clearly defined decision/termination points and more comprehensive project data available.[39] Yet, it remains unclear how to determine which share of prioritized projects to select dependent on the size of an organization and development stage of the drug development pipeline of the company. Answering this question would require further research.

Overall, having more frequent portfolio reviews or switching to more regular review cycles for high-priority projects would provide project teams with more frequent feedback, which could have two benefits. First, it could help to identify problems and motivate teams to find solutions. Second, it could avoid failing late in the development process and promote killing projects early enough.[1,40] Yet, the likelihood of failing R&D projects at early versus late stages depends on further internal practices of a firm: If decision-makers are oriented toward identifying failures, then the projects are more likely to be terminated early.[39] Once a priority project has proven unsuccessful, it is important to execute a portfolio decision quickly to exit the program instead of investing additional resources, holding on to hope for success in another area and, thus, falling into the trap of the progression-seeking bias.[2,41]

Pharmaceutical companies apply key performance indicators (KPIs), such as commercial value of a potential drug, risk and target safety, competitive situation, strategic fit, unmet medical need, and novelty of the drug or therapy, to assess and evaluate pipeline assets.[1,38,42] Quantifying the financial value of

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preclinical assets remains a challenge because of high clinical attrition rates and high rates of market uncertainty.[43] When assets enter the clinical stage, their financial value becomes more easily quantifiable: here, real option analysis (ROA) or the net present value (NPV) calculations are commonly used.[42,44] Given that drug target safety is one of the major causes for project failure, it is recommended to conduct comprehensive safety reviews early during the drug discovery process.[45]

Whereas advanced data analytics and Artificial Intelligence are gaining traction in the drug discovery process, such as for target screening,[46,47] portfolio management decisions still strongly rely on a mix of both qualitative and quantitative measures.[48] Commonly human judgement rather than formal analytical methods are used because decision-making modeling for new product development in the pharmaceutical industry remains challenging.[1,48]

Yet, mathematical models (e.g., integer/mixed integer programming optimization models) could be beneficial to prioritize and select the optimal set of projects for a company portfolio to maximize its value under constrained resources and potential risks of failure.[1,38,49–51] During an earlier stage of the drug R&D pipeline, optimization models could support the *in vitro* screening of potential drug candidates, considering the limited capacity for such experiments and predicted success probabilities of different drug candidates. [51] During late-stage clinical development, when it is known which drug candidates will enter Phase III clinical trials, integer programming optimization models could be used to determine optimal sample sizes and trial schedules. [38,49] Such optimization models comprise a set of formulas that describe the objective function of the model (e.g., maximizing expected net present value), constraints (e.g., budget), and decision variables (design choices portfolio management decision-makers can make).[1,49] Such optimization models take factors such as scheduling constraints (e.g., deadlines), trial sizes, patient enrollment rates, treatment period per patient, uncertainties in the trial process, market sizes, costs, and budget constraints, into account.[49,50] In addition, these optimization models could help to test 'what-if' scenarios to guide strategic decision-making, such as exploring different cost-sharing and partnership models for clinical trials, different timelines, or market uncertainty.[1,49]

However, to be in the position to leverage such mathematical optimization models, data of good quality characterizing each asset are required.[10] Data availability and data harmonization on assets and their R&D pipeline history are often limited.[10] This might constrain the successful application of primarily quantitative metrics when conducting portfolio reviews and introduces the requirement to include expert knowledge from a human.[10] Nonetheless, introducing standardized quantitative KPIs, which could be summarized on score cards, can help portfolio managers to ensure a comparable and structured decision-making process, which could lead to better decision outcomes.[5] Moreover, introducing data quality requirements could help to protect against potential sources of biases and leverage data more effectively for high-quality decision-making.[52].

Overall, a useful tool to guide portfolio prioritization decisions are decision trees, which allow combining both qualitative and quantitative metrics and suggest clear causal relationships.[38,53] However, despite leveraging qualitative and quantitative metrics, decision-makers can be prone to cognitive biases, which can impact the quality of decision-making and risk portfolio success. [7,43,54,55] To equip portfolio managers with a toolkit to be aware and overcome such biases, we review a set of common cognitive biases, validate their relevance, and identify most effective mitigating measures based on a survey of 92 industry practitioners involved in portfolio management decisions in the pharmaceutical industry.

## Pharma companies observe a wide range of cognitive biases in portfolio level decision-making, but mitigating measures have started to gain traction

Although cognitive biases have been subject to research studies for decades, they still remain widely present across domains.[56–58] Cognitive biases are a psychological phenomenon that can be understood as errors in the way in which the mind processes information, which, in turn, compromise human judgement.[56–58] For example, cognitive biases can incentivize individuals to deviate from project goals, filter out alternative perspectives, lead to the discounting of disconfirming information, or result in irrational decision-making.[43,54,55]

Cognitive biases are widely observed across many different fields and organizations. For example: start-ups often neglect the capabilities and plans of competitors, resulting in their optimism bias reducing the amount of market share they can capture; executives overestimate the success of mergers and acquisitions, such that three-quarters of such deals never pay off; or managers fall prey to the planning fallacy when forecasting the outcomes of risky projects, such that they base their go/no-go decisions on delusional optimism instead of objectively weighing gains, losses, and probabilities.[7,43,54–56,59–66] Overall, cognitive biases are particularly relevant to the pharmaceutical industry because the drug discovery process involves many risks and uncertainties and the management of a pharmaceutical R&D pipeline relies strongly on human decision-making.[7] Biased decisions made by portfolio managers can lead to fallacious asset prioritization and investment decisions, which, in turn, can cause suboptimal portfolio outcomes or pipeline failures.[43,54,55]

The range of cognitive biases that can be observed across different domains during real-world decision-making is large.[43,54,55,59–66] Often, biases, such as the confirmation bias,[55] champion bias,[64] misaligned individual incentives,[65] consensus bias,[59,60] groupthink,[43] availability bias,[66] power of storytelling,[43,63] *status quo* bias,[62] anchoring bias,[59] loss aversion,[59] optimism bias,[11] sunk-cost fallacy,[61] or the misaligned perception of corporate goals[67,68] impact human decision-makers. Table 1 summarizes these 13 cognitive biases and provides detailed descriptions for each of them.

To understand which of these biases are predominant in portfolio decision-making during technical review meetings, portfolio governance meetings, or when deciding about resource allocation across assets, we conducted an online survey among 92 industry practitioners working for pharmaceutical and biotech companies. Most of the surveyed experts observed a wide range of biases in portfolio decisions that they were involved with. Overall, the five most frequently observed cognitive biases

**TABLE 1**

**Overview of common cognitive biases impacting decision-making.**

| No. | Bias | Description | Refs |
|---|---|---|---|
| 1 | Confirmation bias | Discounting information that undermines personal believes, past choices and judgments, overweighing evidence supporting personally favored views | [55] |
| 2 | Champion bias | Projecting project champion's previous success on project proposal or overweighing champion's personal view when selecting projects | [64] |
| 3 | Misaligned individual incentives | Incentives creating conflicting interests, e.g., misalignment of executives' compensation plans and shareholder value | [65] |
| 4 | Consensus bias | Leader overestimates similarity between own preferences and preferences of the group (e.g., overestimation of product acceptance in market) | [59,60] |
| 5 | Groupthink | Seeking consensus in group to such an extent that irrational decisions are made | [43] |
| 6 | Availability bias | Tendency to make decisions based on information that readily comes to mind. This leads to bias toward easily recallable options rather than most important options | [66] |
| 7 | Power of storytelling | The way in which information is framed and presented can lead to different conclusions; facts embedded in coherent stories are easier to remember | [43,63] |
| 8 | *Status quo* bias | Change aversion leading to bias toward existing views/options | [62] |
| 9 | Anchoring bias | Rooting of oneself to initial quantitative value that leads to over- or underestimation of subsequent scenarios with differing conditions | [59] |
| 10 | Loss aversion | Tendency to prefer avoiding losses and uncertainty (preferring safe bets with small rewards over risky projects with high rewards) | [59] |
| 11 | Optimism bias | Overconfidence, which makes one believe that project will be successful | [11] |
| 12 | Sunk-cost fallacy | Continuing failing projects because they have already consumed numerous resources (previous expenditures in influence decision making) | [61] |
| 13 | Misaligned perception of corporate goals | For example, focusing on short-term success versus working toward corporate long-term vision | [67,68] |

were: confirmation bias, champion bias, misaligned incentives, consensus bias, or groupthink (Figure 1).

Beyond the set of 13 predefined cognitive biases that were included in our online survey, portfolio management practitioners reported additional cognitive biases, which they had observed within their organizations: gender bias, fear to challenge authorities, fear of social punishment for being critical, fear of punishment for failure, fear of risking career, rejection of external ideas, bias toward hypothesis validation versus rejection, bias toward old methods, and distraction (Table 2).

Frustratingly, gender bias against women remains prevalent across multiple R&D pipeline stages (from lab animals to dose-finding trials), which can cause human suffering and death, and lead to withdrawal of drugs from the market.[69] Accounting for a gender dimension across the R&D pipeline can help prevent life-threatening errors and deliver better treatments to patients.[69]

Interestingly, four out of nine of the additional cognitive biases observed by portfolio management practitioners were related to fear (Table 2). The fear of challenging authorities, fear of social punishment for being critical, fear of punishment for failure, or fear of risking career are all phenomena that are widely observed beyond the pharmaceutical industry (e.g., in the aerospace industry, automotive industry, or energy sector) and can result in people not speaking up or foster a culture of not listening.[70] A culture of silence can lead to catastrophic outcomes; the NASA Space Shuttle Columbia accident on February 1, 2003 would be an example of such an instance.[70] Similarly, a culture of not listening can lead to the ignorance of warnings, leading to avoidable accidents and failures. The nuclear accident in Fukushima in 2011, which was a result of ignored warnings and insufficient implementation of protective measures against natural disasters, is an example of a culture of not listening.[70] Beyond fear leading to tragic accidents, fear can also hinder innovation.[70] Consequently, creating a fearless organization could yield multiple benefits: increasing capacity for innovation and reduction in the incidence of disastrous failures or accidents.[70] For example, pharmaceutical industry practitioners might benefit from adopting Google X's practices of psychological safety that promote an environment safe for failure, reward the killing of unpromising projects, and ensure career advancement regardless of project termination.[70]

Furthermore, practitioners observed that individuals had the tendency to reject ideas that were invented outside of their own group or domain (Table 2). This rejection of external innovation could cause the dismissal of valuable external knowledge and limit further progress on R&D projects. Fundamentally, this cognitive bias is in stark contrast with the practice of external innovation sourcing, on which the pharmaceutical industry strongly relies. Furthermore, the observation that portfolio managers have a bias toward hypothesis validation versus rejection (Table 2) could lead to the tendency to ignore contradictory evidence or dismiss the consideration of alternatives. While bias toward old methods and the tendency to shy away from new approaches could be a barrier to both learning and innovation, the bias to keep searching for weak signals could be a distraction (Table 2). Overall, it becomes clear that such biases would lead to flaws in decision-making, and portfolio management practitioners should create awareness of these biases and adopt dedicated mitigating measures.

Across industries, various mitigating measures against cognitive biases have been suggested or adopted that are expected to enhance the quality of decision-making. These range from musicians auditioning behind curtains to overcome gender bias in the selection process for competitive orchestras, or NASA

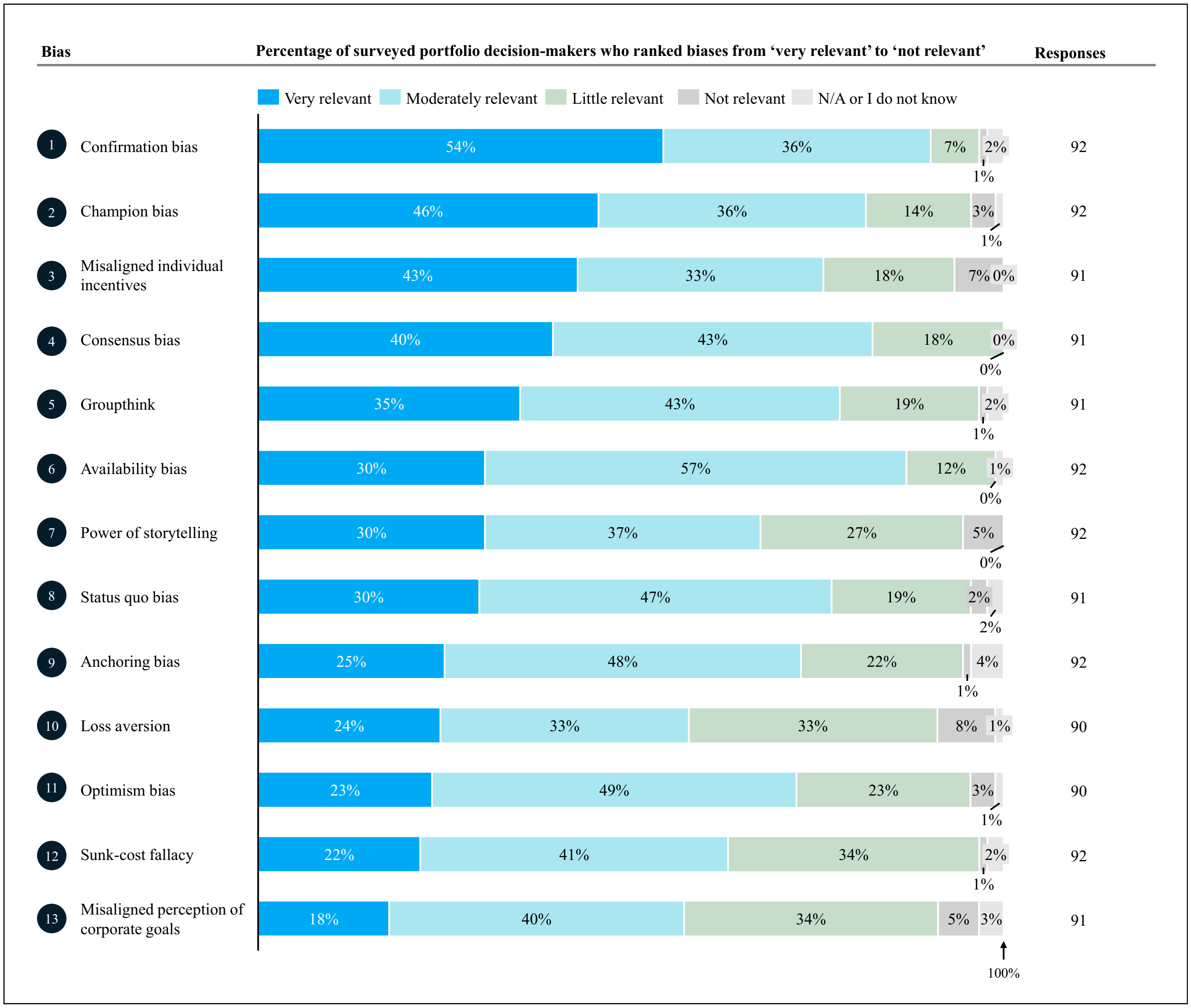


**FIGURE 1**

Cognitive biases and their presence in portfolio management decision-making in the pharmaceutical industry. Insights from a globally facilitated survey of prevalent biases in portfolio-level decision-making in the pharmaceutical industry: 92 industry practitioners who work for globally leading pharmaceutical and biotechnology companies responded to the survey and ranked the biases by their relevance. The five most-relevant biases observed during portfolio level decision-making (during technical review meetings, portfolio governance meetings, or portfolio resource allocation decision) were the confirmation bias, champion bias, misaligned individual incentives, consensus bias, and groupthink.

encouraging engineers to acknowledge their biases before they present a particular engineering design, to sales teams in the entertainment industry using a reference class of movies when forecasting expected revenues.[58,71,72] In particular, in the area of forecasting, multiple approaches have been proposed, such as relying on an 'outside view' or using 'superforecasting'.[56] For example, inside views are often biased to be overly optimistic and often rely on the judgment of one expert, whereas outside view forecasts examine a set of reference projects, provide a distribution of possible outcomes, and locate the current project within that distribution. This outside view approach draws upon more information and is expected to yield a more objective and accurate forecast.[56] The accuracy gain in forecasting through the outside view is expected to be largest in situations in which companies undertake initiatives that they have never attempted before (e.g., implementing a new manufacturing process or entering a new market). Of course, choosing the right set of reference projects as the forecasting basis is difficult in situations in which no precedents are easily found.[56] Moreover, superforecasting describes the idea of leveraging a network of diverse forecasters to embrace the principle of the wisdom of crowds in situations in which uncertainty is high.[73,74] For example,

**TABLE 2**

**Nine additional cognitive biases observed by portfolio management practitioners in the pharmaceutical industry.**[a]

| Additional cognitive biases observed by the portfolio management practitioners | | | | |
|---|---|---|---|---|
| **#** | **Cognitive bias** | | **Detail description of cognitive bias observed by experts** | **Comments** |
| 1 | **Gender bias** | “” | ‘Falling back on existing behaviors’. . . ‘You **don't consider dosing pregnant women** and children until later in development process’ | Gender bias remains prevalent **across all R&D pipeline stages**[69] |
| 2 | **Fear to challenge authorities** | “” | ‘**Fear of speaking up** against authority’ | Leaders need to shape an organizational culture that **provides psychological safety** and positively rewards **to challenge authorities, think critically** and learn through mistakes[70,79]<br>Moreover, career incentives need to be aligned to **enable risk taking, failure, learning**, and **innovation**[70] |
| 3 | **Fear of social punishment for being critical** | “” | ‘Perception that being **labeled as pessimistic** when alternative less optimistic scenarios are considered’ | |
| 4 | **Fear of punishments for failure** | “” | ‘Cultural factors that **punish mistakes** or failures – perception (not reality) of career exposure’ | |
| 5 | **Fear of risking career** | “” | ‘Project versus **career trade-off**’ | |
| 6 | **Rejection of external ideas** | “” | ‘Not invented here. The initial stimulus for the **development occurred outside the group** responsible for developing it’ | |
| 7 | **Bias towards hypothesis verification versus rejection** | “” | ‘Instead of trying to falsify a hypothesis, **people try to verify**’ | |
| 8 | **Bias towards old methods/aversion to learn** | “” | ‘**Missing understanding** of **new methodologies**’ – ‘only using methods or relying on data, which are well understood’ | |
| 9 | **Distraction** | “” | ‘Keep **searching** for **weak signals**’ | |

[a] Insights from a globally facilitated survey of prevalent biases in portfolio-level decision-making in the pharmaceutical industry: 92 industry practitioners who work for globally leading pharmaceutical and biotechnology companies responded to the survey and shared cognitive biases that they observed in their organization impacting portfolio-level decision-making.

having a large collective of individuals engaging in the forecasting of expected peak sales of new drugs could reduce the impact of cognitive biases, counter high project uncertainty resulting from limitations in available project data, and, therefore, lead to more realistic and accurate forecasts.[74]

The presence of a wide range of cognitive biases can be concerning and alarming to portfolio decision-makers. Fortunately, there is a plethora of opportunities available to them to mitigate biases during the drug discovery process, such as rotation of project leadership to enable a new perspective,[75] introduction of standardized quantitative KPIs to ensure comparability across assets,[76] seeking of external expert input to have a critical outside perspective,[77–79] practicing of red versus blue teaming (pro/contra teams) to encourage critical thinking and intended falsification,[79] or usage of anonymous voting,[76] having a personal stake in the project,[80] or checking bias in data visualizations.[81] The ‘right culture’ is a crucial factor for successful decision-making[6]: encouraging truth-seeking behavior versus setting volume targets was found to be a key enabler of high R&D productivity and effective portfolio decision-making.[23,34,82] Moreover, presenting multiple options instead of a single one,[77] ensuring team diversity by getting the right balance of decision-makers across functions,[83] training decision-makers in bias awareness,[84] or signing a pre-committed contract that guides portfolio decision-makers [such as a target product profile (TPP) that lists clear ‘go’ versus ‘no-go’-criteria][85] are identified as bias-mitigating measures.

These techniques have only started to gain traction among the surveyed industry experts and could be an enabler for a higher decision process quality, more effective portfolio decision-making, and, ultimately, improved R&D pipeline success. Among the top techniques adopted by portfolio decision-makers in the pharmaceutical industry to counteract the most common cognitive biases are seeking expert input, ensuring team diversity, and rewarding truth-seeking behavior (Figure 2).

Beyond this set of most frequently adopted mitigating measures, the surveyed portfolio management practitioners reported additional effective strategies to counter the top five cognitive biases impacting their decision-making (confirmation bias, champion bias, misaligned incentives, groupthink, or consensus bias). Table 3 summarizes the diverse set of alternative mitigating measures that could enable portfolio managers to enhance the quality of their decision-making. For example, to counter confirmation bias, practitioners suggest identifying and evaluating all assumptions underlying decision-making, challenging evidence provided in existing publications, or inducing changes to the work environment and work culture that people operate in. How to best counter champion bias remains unclear to practitioners, whereas multiple approaches to mitigate misaligned incentives were suggested. These include focusing on aligning incentives across the organizational hierarchy, particularly rewarding value-increasing milestones that would not necessarily be the immediate next milestone, or implementing a reward system rooted in long-term versus short-term performance.

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| Bias | % Share of experts ranked as top 5 bias | Description | Top 5 mitigating measures applied by portfolio decision-makers | |
|---|---|---|---|---|
| Confirmation bias | 68% | Discounting information that undermines personal believes, past choices and judgments, overweighting evidences supporting personally favoured views[55] | External expert input | 54% |
| | | | Multiple options approach | 44% |
| | | | Quantitative deliverables per project | 41% |
| | | | Awareness about biases | 25% |
| | | | Intended falsification | 22% |
| Champion bias | 57% | Projecting project champion's previous success on project proposal or overweight champion's personal view when selecting projects[64] | External expert input | 69% |
| | | | Team diversity | 46% |
| | | | Multiple options approach | 35% |
| | | | Quantitative deliverables per project | 33% |
| | | | Rotations of leadership positions | 29% |
| Misaligned individual incentives | 46% | Incentives creating conflicting interests, e.g., misalignment of executives' compensation plans and shareholder value[65] | Rewarding truth-seeking behavior | 55% |
| | | | Quantitative deliverables per project | 33% |
| | | | Rotations of leadership positions | 33% |
| | | | Signing a pre-committed contract | 31% |
| | | | External expert input | 29% |
| Consensus bias | 45% | Leader overestimates similarity between own preferences and group's preferences (e.g., overestimation of product acceptance in market)[59, 60] | Multiple options approach | 44% |
| | | | Team diversity | 39% |
| | | | External expert input | 39% |
| | | | Quantitative deliverables per project | 32% |
| | | | Rotations of leadership positions | 33% |
| Groupthink | 41% | Seeking consensus in group to such an extent that irrational decisions are made [43] | External expert input | 55% |
| | | | Team diversity | 42% |
| | | | Intended falsification | 39% |
| | | | Multiple options approach | 37% |
| | | | Quantitative deliverables per project | 32% |

Percentage share of surveyed experts who selected this bias counter-measure

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**FIGURE 2**

Top five cognitive biases in pharmaceutical portfolio management and their most common mitigating measures. Insights from a globally facilitated survey of the top five biases in portfolio-level decision-making in the pharmaceutical industry and their most-effective mitigating measures: 92 industry practitioners who work for globally leading pharmaceutical and biotechnology companies responded to the survey, ranking their five most-important biases and indicating the most-effective mitigating measure. To mitigate the five dominating biases (confirmation bias, champion bias, misaligned individual incentives, consensus bias, and groupthink), industry practitioners commonly seek expert input, apply a multiple options approach, define quantitative deliverables, enhance bias awareness, use intended falsification, rotate leadership positions, or ensure team diversity.

Furthermore, to mitigate groupthink, portfolio management practitioners use strategies, such as positively rewarding critical thinkers, aiming at making everyone's voice heard by using voting mechanisms (weights of votes could vary), or seeking to create a culture of accountability. Finally, pharmaceutical portfolio management practitioners identify and evaluate informal influencing mechanisms, which could bias formal decision-making, encourage a speak-up culture to break a culture of

**TABLE 3**

**Additional effective mitigating measures against cognitive biases used by industry practitioners.**[a]

| # | Cognitive bias | Mitigation measure | Detailed perspectives shared by industry experts |
|---|---|---|---|
| | **Additional mitigation measures for the five top ranked cognitive biases provided by portfolio management practitioners** | | |
| 1 | Confirmation bias | Monitor external information | "Requiring **in-depth** landscaping **assessment of external world**, with refreshes on an ongoing basis" |
| | | Review and validate assumptions | "Identification and **evaluation of all assumptions** in decision-making, including those that are based on medical opinion" |
| | | Induce cultural change | "**Changing** the environment/**culture** that the person(s) work in" |
| | | Question evidence provided in existing publications | "**Confirmation bias can occur** at early and late phase. In early phase, evidence confirming certain published results in e.g., the biomarker space can create a sense of confirmation. However, the validity and utility of such biomarkers may not be questioned - i.e., the **original publication is not questioned**." |
| | | Calibrate *P* value or use Bayesian statistics | "In later phase, a 'positive' Phase II **trial** in the sense of small**/borderline *P*-value** can create a false indication of efficacy, as evidence in many failed attempt of replicating the results in phase 3. **P-value calibration or a Bayesian approach** can alleviate this problem" |
| 2 | Champion bias | Effective strategies remain unclear to practitioners | "**Not seen** very much in this regard in general" |
| 3 | Misaligned incentives | Align individual incentives to company mission | "**Align incentives** to key **overarching organizational ambitions** (e.g., positive PoCP)" (proof-of-concept project) |
| | | Align incentives across organizational hierarchy | "**Align incentives** with the above' (i.e., **senior colleagues**)" |
| | | Use compound success rate (versus volume) as KPI | "Drug development is a long-term process. Incentivize R&D productivity, not by the number of compounds produced, rather the **number of successful compounds**. There is a challenge of how practically this can be implemented (e.g., shared long-term financial incentives)" |
| | | Reward value-increasing milestones | "**Rewarding** a **relevant milestone** (not necessarily the next one to come)" |
| | | Track and reward long-term performance (versus short-term) | "Make **individual rewards** more reliant on **long-term** outcomes of projects' |
| | | | 'Tracking of **long-term performance** of Project Leaders and **'Deciders'.'** |
| | | | 'Tracking of **long-term performance** of **business areas** or focus topics." |
| 4 | Groupthink | Reward critical thinkers and challengers | "**Reward** and incentivize those that **challenge** the **group-think mentality.'** |
| | | | 'The 'final decision maker' **developing a culture of purposeful dissent** without penalty." |
| | | Make everyone's voice heard | "**Everyone has a vote**/voice but might be weighted differently" |
| | | Create a culture of accountability | "Creating a **culture of accountability**. Often in groups, it's easy to follow the herd than to truly think independently and voice differing opinions. A format, or culture of **voicing opinions should be encouraged**." |
| 5 | Consensus bias | Review informal influencing, which could bias formal decision-making | "A **systemic appreciation of how decisions are influenced prior to** the public 'taking' of a **decision by** a **governance process** may need to be appreciated" |
| | | Foster a speak-up culture | "True and valued speak-up culture and opportunities, leaders/**decision makers don't speak first**, rather last. Empowering the team to come up with a decision/proposal that they stand behind." |
| | | Use mathematical algorithms to unbias decision-making | "How might the 'human' aspects of the decision-making process be further reduced - **applying behavioral economics algorithms"** |
| | | Repeatedly quantitatively assess risks and benefits | "**Ongoing quantitative evaluation of risk–benefit** /cost-effectiveness including review of profiles with regulatory agencies and HTAs" |

[a] Insights from a globally facilitated survey of prevalent biases in portfolio-level decision-making in the pharmaceutical industry: 92 industry practitioners who work for globally leading pharmaceutical and biotechnology companies responded to the survey and shared the bias-mitigating measures used for the five most common cognitive biases.

silence, leverage mathematical models, or repeatedly quantitatively assess risks and benefits of projects to counter consensus bias.

It becomes clear that a broad range of practical strategies is available to portfolio managers to create awareness of cognitive biases, mitigate their impact, and make portfolio management



POST-SCREEN (GREY)

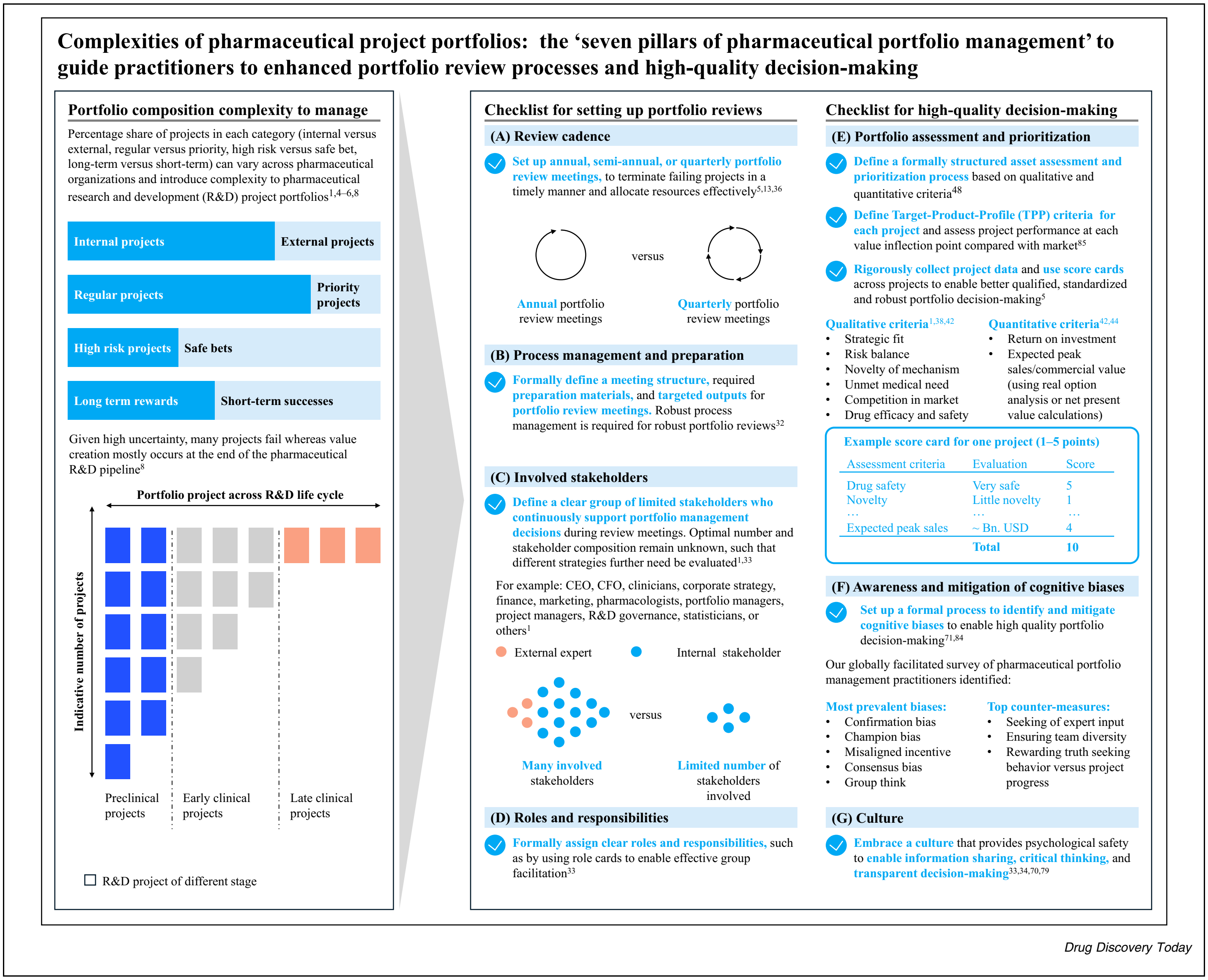


**FIGURE 3**

The 'seven pillars of pharmaceutical portfolio management'. A framework developed for portfolio management practitioners in the pharmaceutical industry to manage complexity in their portfolio, set up formally structured review processes, and achieve high quality unbiased and robust decision-making. The framework is intended to complement existing frameworks and serve as a guide for practitioners.

decision more robust, ultimately strengthening the success of the R&D pipeline of their organization. Therefore, we conclude that approaches to create awareness and implement mitigating measures of cognitive biases should be included in portfolio management frameworks. Given that the existing frameworks presented above [5Rs,[23,24] the '3 pillar' framework,[25] or the 'Signs of Clinical Activity (SOCA) paradigm'[24]] fall short along this dimension, we have developed a new framework that complements these existing approaches.

## To manage the complexity of pharmaceutical portfolios, we introduce the 'seven pillars of pharmaceutical portfolio management' framework, which complements existing ones

To manage complex portfolios that include internal and external projects, regular and priority projects, high-risk projects or safe bets, and to strike a balance of long-term success versus short-term rewards, we propose the 'seven pillars of pharmaceutical portfolio management' framework (Figure 3), which embraces unbiased and robust decision-making. This framework can serve as a guide for portfolio management practitioners to set up structured portfolio reviews and achieve high quality decision-making. It addresses seven key dimensions:

(A) Portfolio review cadence;
(B) Process management and preparation;
(C) Stakeholder group to involve;
(D) Roles and responsibilities;
(E) Strategies towards portfolio assessment and prioritization;
(F) Approaches to creating awareness of cognitive biases and implementing mitigating measures;
(G) Culture.

We suggest the application of this framework in combination with the existing frameworks to complement their gaps and leverage synergies between them.

## Concluding remarks

We conclude that effective portfolio management in the pharmaceutical industry could be enabled by three key factors: high-quality project data; structured portfolio review processes; and the application of mitigating measures against biases in portfolio decision-making. Data of high quality could help to reduce ambiguity in decision-making and protect against potential sources of biases. However, rigorous data quality requirements often still need to be established in pharmaceutical companies. Moreover, to address challenges introduced by an intensified competitive pressure, the strong reliance on external innovation, and the rapidly changing external conditions in the pharmaceutical industry, the introduction of rigorous portfolio review processes could be beneficial for portfolio managers of pharmaceutical companies to drive innovation, prioritize assets effectively, allocate resources efficiently, and terminate failing projects in a timely fashion. In particular, the usage of both quantitative and qualitative review criteria, which are differentiated for preclinical and clinical development stages, could be beneficial to the portfolio governance body. Finally, given that our review finds that a wide range of cognitive biases was observed by the 92 surveyed industry partitioners, company leaders could benefit from enforcing formally defined techniques to mitigate bias in portfolio decision-making, which, in turn, could contribute to achieving better portfolio decisions and enhance portfolio performance.

Finally, these approaches can only enhance robust portfolio decision-making, but will never make it perfect. Uncertainty will remain in the drug discovery process given the limited data availability (i.e., during early project stages), rapidly changing market environments, and a dynamic competitor landscape.

## Declaration of interests

L.B., M.Z., and F.D. participated in this project while on academic leave from a large international consulting firm. H.T. is employed by AiCuris AG, which engages in anti-infective new drug development. He is also the founder of The Knowledge House GmbH, which focuses on the exchange of knowledge around pharmaceutical and MedTech R&D. The study was executed during the authors' personal time. Neither the consulting firm nor any of the mentioned other companies were involved at any point in the research and no funding was provided by them.

## Data availability

Data will be made available on request.


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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.drudis.2023.103734.


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