From the analyst's couch

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Mitigating bias in pharmaceutical R&D decision-making

Hubert Truebel & Mark Seidler

Decisions made during the pharmaceutical research and development (R&D) process involve many risks and uncertainties. With the emergence of behavioural economics, substantial literature has accumulated regarding biases and their impact on the quality of decision-making. However, the overall prevalence and roles that these biases play in decision-making have largely been studied on an individual level, and have not been scrutinized as much in more complex drug R&D settings.

Here, we discuss findings from a survey of senior decision-makers across the pharmaceutical landscape to understand relevant biases and indicate countermeasures that could help mitigate resulting flaws in decision-making in pharmaceutical R&D. We also discuss the current level of awareness and the potential for more systematic application of mitigation measures.

Survey and analysis

We surveyed senior decision-makers across the pharmaceutical landscape about their assessment of the relevance of a range of biases and mitigation measures to pharmaceutical R&D decision-making on a four-level scale (very relevant, moderately relevant, of little relevance, not relevant). Each participant was also then asked to identify their top five biases and match them with mitigation measures, which enabled a ranking of the top five biases overall based on cumulative responses. Details of the survey respondents and their characteristics, the biases and mitigation measures, and the survey questions are provided in Supplementary Box 1.

A total of 117 survey respondents provided the information required (with 100 fully complete data sets), of which ~60% came from companies with >10,000 employees. The distribution of the perceived relevance of the 13 listed biases and 11 mitigation measures was analysed across the full sample.

Overall, the respondents generally considered all of the biases listed, as well as all mitigation measures, but at different rates and in different combinations, as indicated by the different colours in the heat map in Fig. 1 (see Supplementary Box 2 for details). In this heat map, biases and mitigation measures, as ranked by the respondents, were plotted against each other to visualize their relative importance to the respondents, as well as how they matched biases and mitigation measures to each other. Biases and mitigation measures that featured most frequently in the responses from the survey participants are in the green areas of the heat map, whereas biases and mitigation measures that featured less frequently are in the red areas.

Some biases were particularly prominent in the responses from the group overall. Confirmation bias — the overweighting of evidence consistent with a favoured belief and underweighting of evidence against a favoured belief — was considered very relevant by the largest proportion of respondents (57%) in the first part of the survey (Supplementary Box 2), and ranked highest in the second part of the survey (Fig. 1). Champion bias, which is the tendency to evaluate a plan or proposal based on the track record of the person presenting it, was also highly ranked in both parts of the survey. For both biases, the top ranked mitigation measure was clearly input from experts who have no stake in the project (Fig. 1).

Other biases that at least 25% of participants considered very relevant in the first part of the survey (Supplementary Box 2) were less prominent in the second part of the survey, such as the storytelling bias (the tendency to remember and to believe more easily a set of facts when they are presented as part of a coherent story) and the sunk-cost fallacy (the tendency to invest further in projects because they already have consumed a lot of resources). In addition, there was not an obvious distinction between the possible mitigation measures for these two biases.

Discussion

Although it is not possible to judge from this survey how good or bad decision-making is in the pharmaceutical industry, or whether awareness of biases and mitigation methods have already (partially) addressed issues with poor decision-making owing to various biases, the wide range of performance across R&D organizations in the pharmaceutical industry gives reason to believe that more could be done.

In this respect, the results of our analysis have implications for further improving decision quality in pharmaceutical R&D. All biases in the survey list were broadly recognized by participants, but we observed differences in perceptions about how to effectively mitigate them. Input from external experts, which ranked as the most relevant mitigation measure overall, is already frequently used in many settings in pharmaceutical R&D. However, further mitigation measures seem less well understood. Moreover, with a few exceptions — such as the use of input from external experts to address confirmation bias — a broad range of mitigation measures was proposed for each bias, with no clear indication of which ones are generally considered effective.

A more systematic approach — searching for both frequently and less frequently considered or poorly addressed biases, and planning decision processes in such a way that their implicit nature is turned into an explicit understanding and awareness — could help to improve decision-making quality further. Indeed, in the context of pharmaceutical R&D, there are examples of systematic approaches to aspects of decision-making that have been reported to lead to improved productivity, such as AstraZeneca's 5R framework (*Nat. Rev. Drug Disc.* **17**, 167–181; 2018) and Pfizer's three pillars of candidate survival (*Drug Disc. Today* **17**, 419–424; 2012). There are also examples in other industries, such as entertainment, financial services and aerospace (see references in Supplementary Box 1). However, it seems the reported specific productivity examples in pharmaceutical R&D focused primarily on mitigation of biases through using the mitigation measure of 'defining quantitative deliverables'. We suggest that recognizing less-well-known biases could increase the application of mitigation measures in general, and thereby contribute to more robust decisions that further improve the productivity of the pharmaceutical industry.

Consider, for example, the storytelling bias, which is not highly ranked in Fig. 1. For this bias, intentionally trying to disprove a story (intended

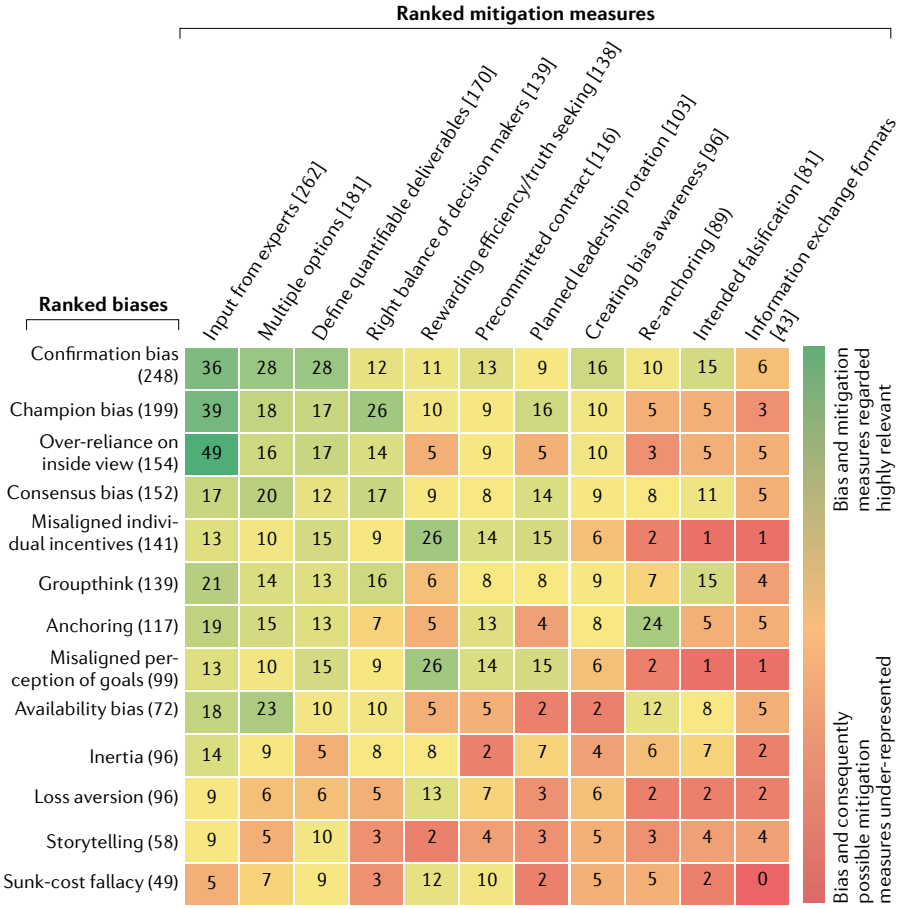

Fig. 1 | Rankings of biases and mitigation measures in R&D decision-making. In the survey, 117 senior decision-makers in pharmaceutical R&D identified their top five biases and matched them with mitigation measures. The biases were ranked using a sum score: a bias was assigned 5 points for being the 'number 1' bias, 4 points for 'number 2' and so on, such that the cumulative score per bias (shown in brackets) reflects both the frequency of a bias being selected and how important it was regarded to be by participants who selected it. The number of times the mitigation measures were mentioned for each bias was counted and the sum of mentions is shown in square brackets. The figure was generated by mapping the number of times a particular mitigation measure was chosen for a particular bias, as shown in each coloured square, with green indicating a mitigation measure that was often considered as relevant for the bias, and red indicating that such combinations of mitigation measure and bias were rarely chosen. See Supplementary information for details.

falsification) or routinely asking for a counter-position are mitigation measures that could help to rebalance a decision-making process.

Another example of an under-represented bias in Fig. 1 is the sunk-cost fallacy. One way to mitigate this bias could be the application of quantitative precommitted contracts — for example, in the form of a target product profile that includes clear 'go' or 'no go' criteria for further development, thereby gating funding decisions. Both the sunk-cost fallacy and the storytelling bias could also be countered by re-anchoring; that is, by seeking a more nuanced or multiperspective view and not relying on a single reference point.

Overall, we draw the following conclusions. First, decision-makers in industry need help to become aware of biases and mitigation measures as an initial step towards systematically addressing blind spots. Second, addressing biases is not only a personal leadership skill but foremost a task to be actively supported by senior leadership. Reflecting on the examples from AstraZeneca and Pfizer, as well as from other industries, it seems necessary to drive rigorous debiasing efforts from the top level of management and put them into a broader cultural change context. Third, the organizational bias mitigation toolbox could benefit from more equipment. Mitigation measures such as input from experts are already considered a powerful tool to mitigate the risk of flawed decision-making owing to biases that are widely perceived as important, such as confirmation bias. However, our survey also raises the question of whether more practical measures, such as interdisciplinary teams whose task it is to play 'devil's advocate', or simple tools, such as checklists, would be easier to implement or could be added to existing measures to also address less frequently considered biases. Similarly, in high-stake settings in which personal incentives might run counter to the best interests of the company, concerted measures to identify, transparently communicate, and apply a company's decision criteria and priorities are needed.

How could these needs start to be addressed? As we are all naturally biased, bias awareness and proficiency in the application of mitigation tools need to become core aspects of leadership development efforts and management training. Given that strong support from senior leadership is essential, perhaps even more rigour could be introduced by having a 'decision quality officer' at the highest level of the company (comparable to the compliance officers' role), whose role is to watch out for biases — essentially an independent "decision observer" as proposed by Kahneman et al. (see Supplementary Box 1). Finally, given the complexity of decision-making in pharmaceutical R&D, intuition (system 1, or fast, thinking according to Kahneman et al.) should not be ignored. Rather, better decision-making processes could be established to augment our system 1 and system 2 (rational, or slow) thinking with systematic bias mitigation measures based on tools, data and diverse input from others.

Hubert Truebel[1,2] ✉ **& Mark Seidler**[3]
[1]University of Witten/Herdecke, Witten, Germany. [2]The Knowledgehouse GmbH, Düsseldorf, Germany. [3]Strategic Decisions Group, Düsseldorf, Germany.
✉e-mail: hubert.truebel@uni-wh.de

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Additional information
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