
Supplementary information

Mitigating bias in pharmaceutical R&D decision-making

In the format provided by the authors

Survey participants

Survey participants were chosen from senior ranks of pharmaceutical and biotech companies to ensure sufficient experience in decision making in pharmaceutical research and development. Participants were encouraged to share the survey within their professional networks, with the same selection prerequisites.

Figure S1 shows the baseline characteristics of the 117 survey participants and the sectors of the biopharmaceutical industry in which they have been involved in decision-making. The group has a high proportion of participants from larger companies. Of note is the fact that several answers per respondent were possible and most respondents worked in different roles and settings across the R&D value chain during their careers, consistent with the level of seniority and experience in the group.

Figure S1a. Characteristics of the survey participants group—organization type and size

How large is the organization where you participated in decision making?

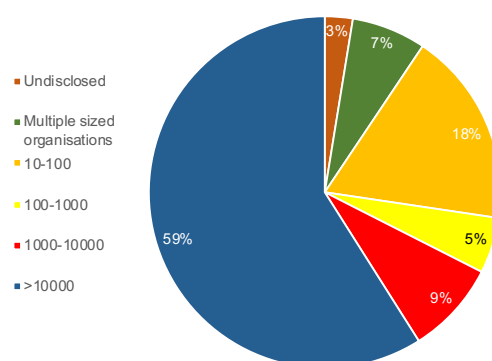


Figure S1b. Characteristics of the survey participants group & decision-making involvement

In what type of decision(s) are/were you involved?

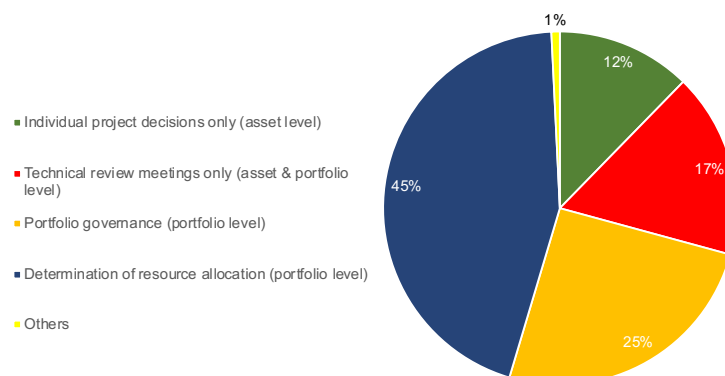


Figure S1c. Characteristics of the survey participants group & decision-making involvement

In which part(s) of the value chain did you participate in decision making?

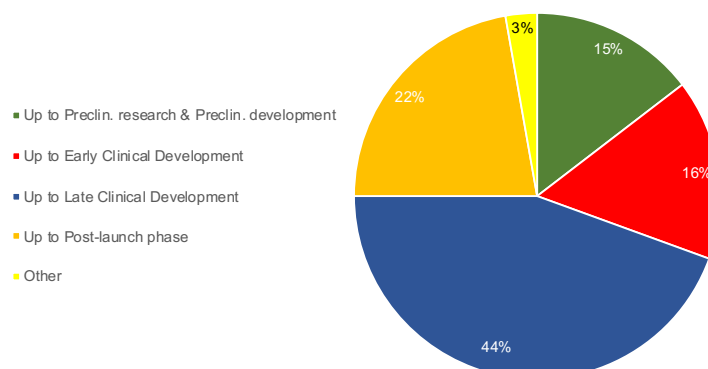


Figure S1 | **Baseline characteristics of survey respondents ($n=117$; 100 full data sets; questions 8-10 in the online survey).** **a** | Size of organizations where participants have been involved in R&D decision-making. **b** | Types of R&D decisions survey participants report to have been involved in and scope of decisions; for example, regarding asset, technical review and/or on a portfolio level. **c** | Position of decision-taker in relation to the R&D value chain (for example, decisions pertaining to early- and/or late-stage R&D).

Survey development

To reduce the overall number of biases and mitigation measures that could be realistically surveyed and that are most relevant to the drug development process, a modified Delphi approach was used. Starting with a collection of biases and mitigation measures [1-6], we generated two lists: one for biases and one for countermeasures, respectively. Further input was solicited from contributors' networks regarding biases or mitigation methods that might have been missed, needed rephrasing, or were closely related and could thus be merged into one entry. The final lists contained 13 biases and 11 mitigation measures, each with a short description (Table S1).

Subsequently, these terms and their descriptions (Table S1) were transferred into an anonymous online survey tool (Qualtrics™; <https://www.qualtrics.com>) and a link (https://corexms34sj5pn9rvyqc.qualtrics.com/jfe/form/SV_6rOcRVKa0vTXXP8) was sent to participants.

Table S1 | Overview of biases and mitigation measures as used in online survey [1–6, 23–33]

Name of bias	Short description
Anchoring	Anchoring and insufficient adjustment is the rooting of oneself to an initial value, leading to insufficient adjustments for uncertainty
Availability bias	Availability bias (related: recency bias or representativeness) is not making sufficient accounting of alternative views
Champion bias	Champion bias is the tendency to evaluate a plan or proposal based on the track record of the person presenting it
Inertia	Inertia/stability bias/status quo bias = change aversion
Confirmation bias	Confirmation bias, i.e., the overweighting of evidence consistent with a favored belief and underweighting of evidence against a favored belief
Consensus bias	Consensus bias or sunflower management (refers to the way a decision is reached, e.g., if a group follows the opinion of its leader)
Groupthink	Groupthink (also sometimes called “herd mentality”)
Loss aversion	Loss aversion is the tendency to prefer avoiding losses to acquiring equivalent gains
Misaligned perception of corporate goals	Misaligned perception of corporate goals, e.g., short-term focus
Misaligned individual incentives	Misaligned individual incentives (example: executive compensation plans can be misaligned with the fiduciary duties toward shareholders. Similarly, project champions can try to get a project to a certain short-term stage without looking at the larger picture due to this bias). The bias of "inappropriate attachment" can be seen in a similar way, maybe with a strong element of emotional attachment
Over-reliance	Over-reliance on an (e.g.) overoptimistic, or overconfident inside view
Storytelling	Power of storytelling is the tendency to remember and to believe more easily a set of facts when they are presented as part of a coherent story

Sunk-cost fallacy	Sunk-cost fallacy (explanation: In everyday life, previous expenditures can influence future decisions, e.g., hanging on to projects that have consumed a lot of resources)
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Name of mitigation measure	Short description
Input from experts	Input from experts who have no stake in a project, e.g., through external polling or consensus-seeking methods. Potentially as a blinded assessment or in the form of simply asking "What would the outside world think?"
Defined quantitative deliverables	Defined quantitative deliverables per project along the stage-gate process. Examples: Advanced checklist, model-informed drug development
Multiple options approach	Multiple options approach (i.e., presenting different options with pros & cons instead of a single preferred option)
Intended falsification	Intended falsification (e.g., via a Red vs. a Blue team approach, each one tasked with coming up with opposing views or via a "Devils' advocate" approach) or premortems
Precommitted contract	Precommitted contract, e.g., in the form of a Target Product Profile (TPP) that could also list clear "go" (green flag) vs. "no-go" criteria (red flag)
Planned rotations of leadership positions	Planned rotations of leadership positions in a project or governance body
Re-anchoring	Re-anchoring, i.e., seeking a more nuanced or multiperspective view and not relying on a single reference point or aspect (e.g., one risk factor or cost comparator)
Rewarding efficiency	Rewarding efficiency in getting to a decision point as opposed to getting just to an advancement of a project (truth-seeking behavior instead of progression seeking)
Get the right balance of decision-makers	Get the right balance of decision makers, e.g., ensuring diversity in governance groups across functions and regions
Information exchange formats	Information exchange formats and meeting facilitation (e.g., intended ask for the counter-position or dashboards to track certain deliverables)
Creating bias awareness	Creating bias awareness and how biases negatively impact decision-making

Online survey that was sent out via Qualtrics

QUESTION 1: Please judge the relevance of biases below (e.g., according to your observation) with respect to decision making in the drug discovery & development process. "Relevance judging" is achieved via choosing 1 of 4 options. Furthermore, you can choose "no opinion / do not know" when unsure and add additional biases that we might have missed and judge their relevance accordingly. (List of biases see Table S1)

QUESTION 2: According to your judgement in the above question, what are the 5 most prevalent biases that you observed during decision making in the drug discovery & development process? Please order these 5 in respect to their relevance by dragging them to their respective rank with the most important bias being at the top. No ranking needed for the remaining biases #6 and downward!

QUESTION 3: What have you observed as mitigation measure(s) that could be used to mitigate the BIAS RANKED No.1 by you in question 2 (multiple answers possible)?
(List of mitigation measures see Table S1)

QUESTION 4: What have you observed as mitigation measure(s) that could be used to mitigate the BIAS RANKED No.2 by you in question 2 (multiple answers possible)?
(List of mitigation measures see Table S1)

QUESTION 5: What have you observed as mitigation measure(s) that could be used to mitigate the BIAS RANKED No.3 by you in question 2 (multiple answers possible)?
(List of mitigation measures see Table S1)

QUESTION 6: What have you observed as mitigation measure(s) that could be used to mitigate the BIAS RANKED No.4 by you in question 2 (multiple answers possible)?
(List of mitigation measures see Table S1)

QUESTION 7: What have you observed as mitigation measure(s) that could be used to mitigate the BIAS RANKED No.5 by you in question 2 (multiple answers possible)?
(List of mitigation measures see Table S1)

QUESTION 8: Your answer(s) here should reflect present or past involvement in decision-making: In which part(s) of the pharmaceutical value chain are/were you involved in decision making?
(Possible answers: Preclinical research, preclinical development; early clinical development; late clinical development; post-launch; others: Text entry possible)

QUESTION 9: When reflecting on the questions above, which size of an organization do you reference your answers to?
(Possible answers: 10-100; 100-1000; 1000-10000; >10000)

QUESTION 10: In what type of organisation did you participate in decision making with respect to the drug discovery and development process?
(Possible answers: Academia; big pharma; biotech; others: Text entry possible)

QUESTION 11: In what type of decision(s) are/were you involved?

(Individual project decisions only (asset level); technical review meetings (portfolio level); portfolio governance (portfolio level); portfolio resource allocation (portfolio level); others: Text entry possible)

QUESTION 12: Are there any additional comments that you'd like to share with us?
(Text entry possible)

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Supplementary Box 2 | Visualization of survey results

One hundred and seventeen survey respondents provided their assessment (with 100 full data sets) of each bias based on its relevance to pharmaceutical R&D decision making. The responses (from “very relevant” to “not relevant”) were aggregated to identify the biases considered to be of highest relevance, i.e., “confirmation bias” was considered by 90% of respondents as very relevant or moderately relevant while 61% of respondents felt that “loss aversion” or “misaligned perception of corporate goals” should be placed in this category (see Figure S2 and Table S1). Survey participants could highlight any biases they were not familiar with, and those responses were not included in the analysis.

The distributions of perceived relevance of biases and mitigation measures were analyzed across the full sample. Quantitative analyses were supplemented with an investigation of comments shared by survey participants, in which they pointed to some additional bias mitigation opportunities specific to the most frequently encountered biases and shared additional observations on the fallacies caused by biases and on the adoption of mitigation measures (Figure S2).

Figure S2

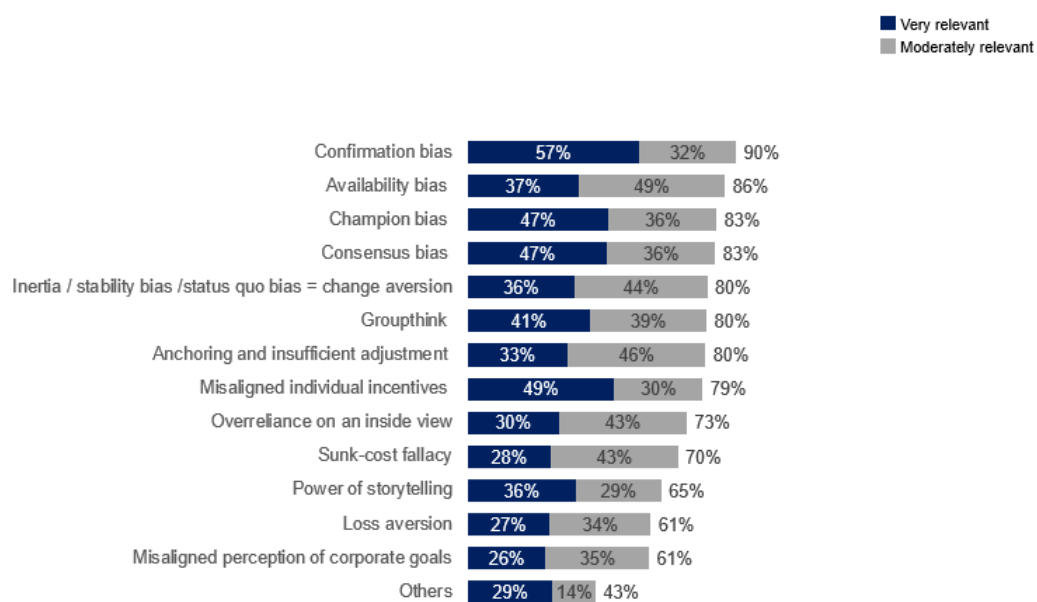


Figure S2 | **Biases considered most relevant by responding pharma decision makers ($n = 117$; question 1 in the online survey).** The figure shows the percentage of responses, excluding respondents not familiar with a particular bias. The number of responses per bias ranged between 100 and 107 (depending on a bias; possible answers: "Very relevant", "Moderately relevant" (not shown: "Little relevance," "Not relevant," "N/A or do not know"; question 1 in the online survey).

In a subsequent part of the survey, each participant was asked to identify their top 5 biases and match them with relevant mitigation measures (multiple choices were allowed; examples depicted in Figure S3 a–c; questions 2–7 in the online survey).

Figure S3a: "Champion bias" and corresponding mitigation measures

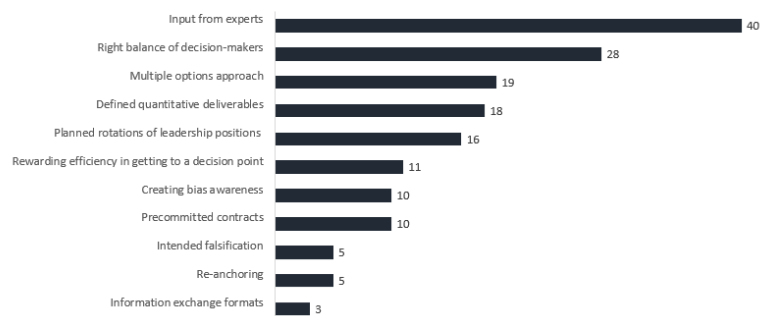


Figure S3b: "Confirmation bias" and corresponding mitigation measures

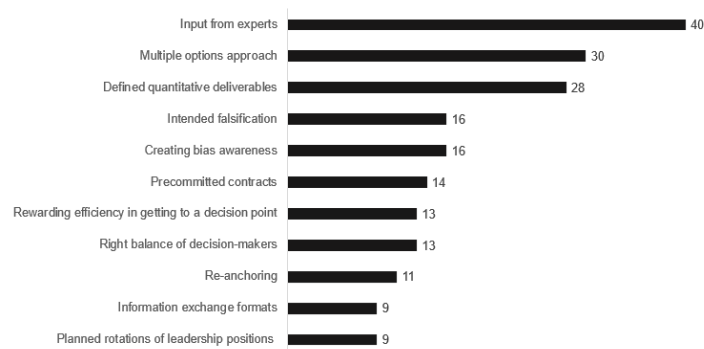


Figure S3c: "Availability bias" and corresponding mitigation measures

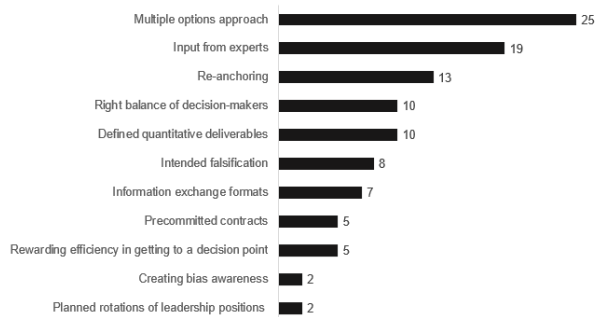


Figure S3 | Top-voted biases and potential mitigation measures as decision-makers selected them. Each respondent could pick multiple mitigation measures per bias.

The biases were then ranked according to a sum score: A bias was assigned 5 points for being the “top 1”-bias, 4 points for “top 2” and so on, such that the cumulative “score” per bias reflects both the frequency of a bias being selected and how important it was regarded by participants who selected it. This score (for example, 248 for “confirmation bias”) led to the ranking that is shown in Figure 1 in the main article. We found that each of the 13 biases on our list has been identified as being in the top 5 by at least several respondents, offering sufficient inputs across all biases. The respective mitigation measures per bias were then counted and their sum was plotted against the ranked biases, thereby generating the heat map in Figure 1. For example, “input from experts” was mentioned the most — a total of 262 times.