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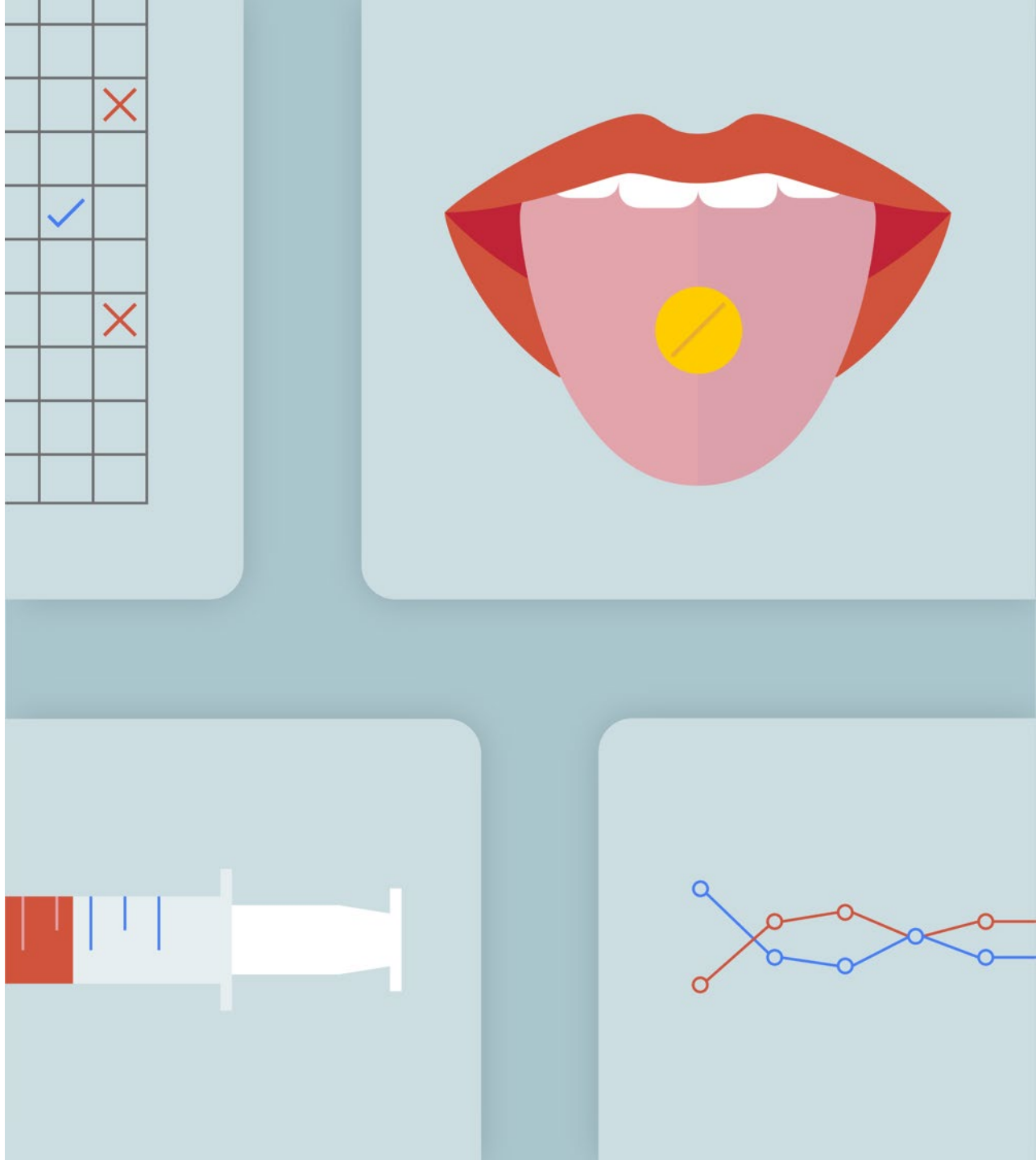
Factors affecting the feasibility of post-authorization RCTs for conditionally authorized anticancer medicines

– a multistakeholder perspective from a qualitative focus group study



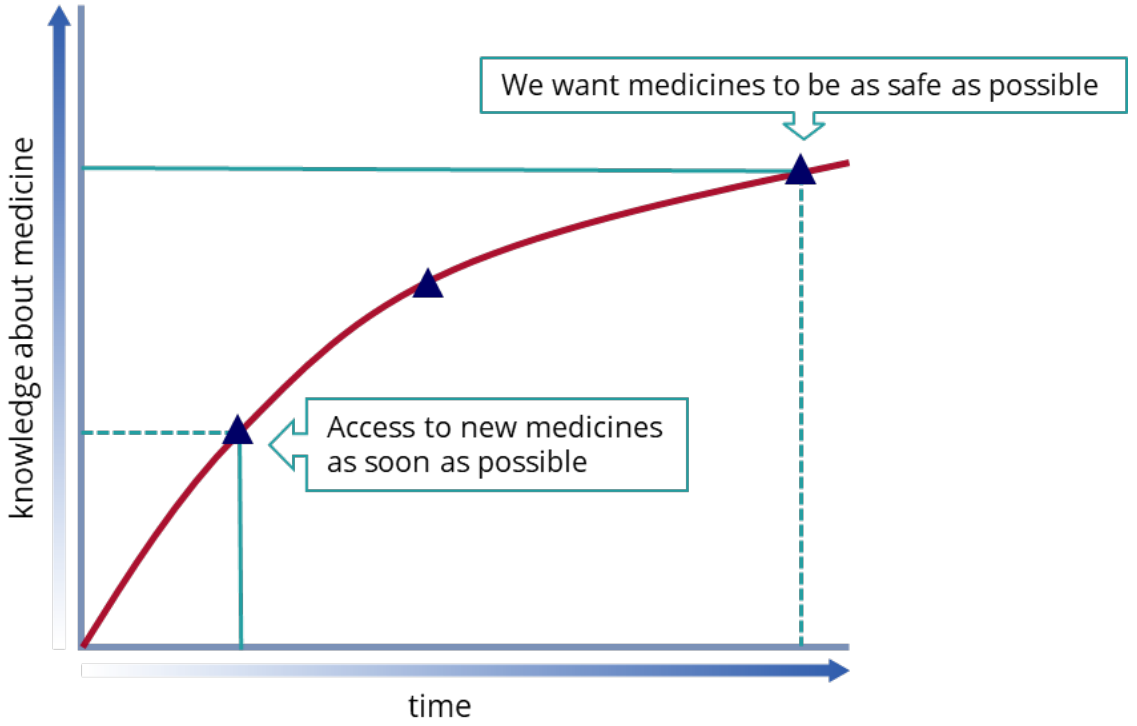
CBG MEB MEDICINES EVALUATION BOARD

Outline

- Background
- Aim
- Methods
- Results
- Discussion & key takeaways

Development of anticancer medicines

- Expedited pathways
- Conditional marketing authorization (CMA)
  - Non-comprehensive evidence ➔ more uncertainties
  - Increasing number CMAs based on single-arm trial data



Adapted from pharmaphorum.com

Conditional marketing authorization (CMA)

Requirements:

- Positive benefit-risk balance;
- Medicine fulfills unmet medical need;
- **Comprehensive evidence** will become available in a timely manner while the medicine is marketed;
- Benefits of timely market access outweigh risks of incomprehensive data

→ Additional evidence through post-authorization randomized controlled trials (RCTs)

Comprehensive data: delays & incomplete

➔ Questions raised about feasibility of post-authorization RCTs

Feasibility assessments by CHMP:

- Limited guidance through regulatory guidelines
- Details rarely described in EPARs

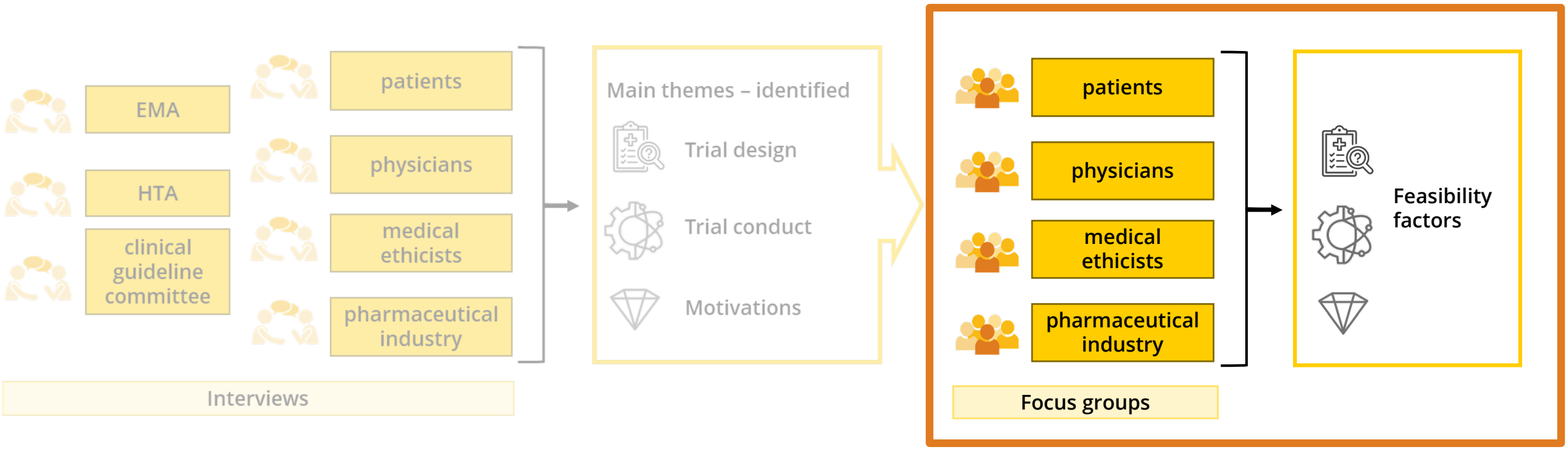
➔ Which feasibility factors should be evaluated?

Aim

To identify factors that facilitate or impede the feasibility of post-authorization RCTs for anticancer medicines that are conditionally authorized based on non-comprehensive data from SATs.

➔ Exploratory qualitative study
➔ Multi-stakeholder perspective

Methods – qualitative research

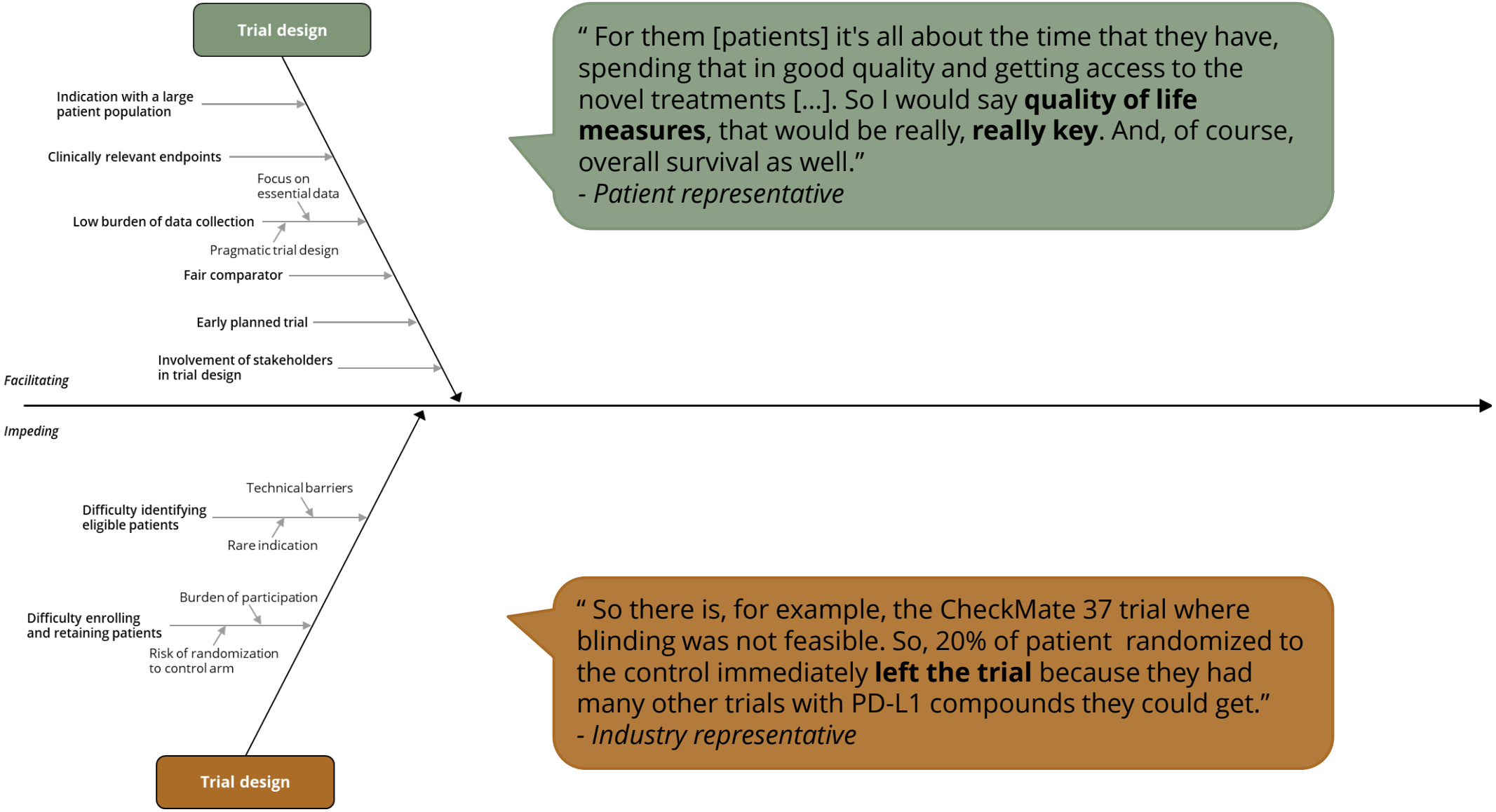


Results – respondent characteristics

	Patient representatives	**Physicians**	**Medical ethicists**	**Industry representatives**
No. respondents (n)	5	6	6	11
Experience in role (median (range) - years)	4 (3 - 5)	15 (5 - 19)	25.5 (8 - 40)	25 (8 - 35)
Understanding of regulatory system (1-5 (median(range))	4 (3 - 5)	3 (3 - 4)	4 (3 - 5)	4 (2 - 5)

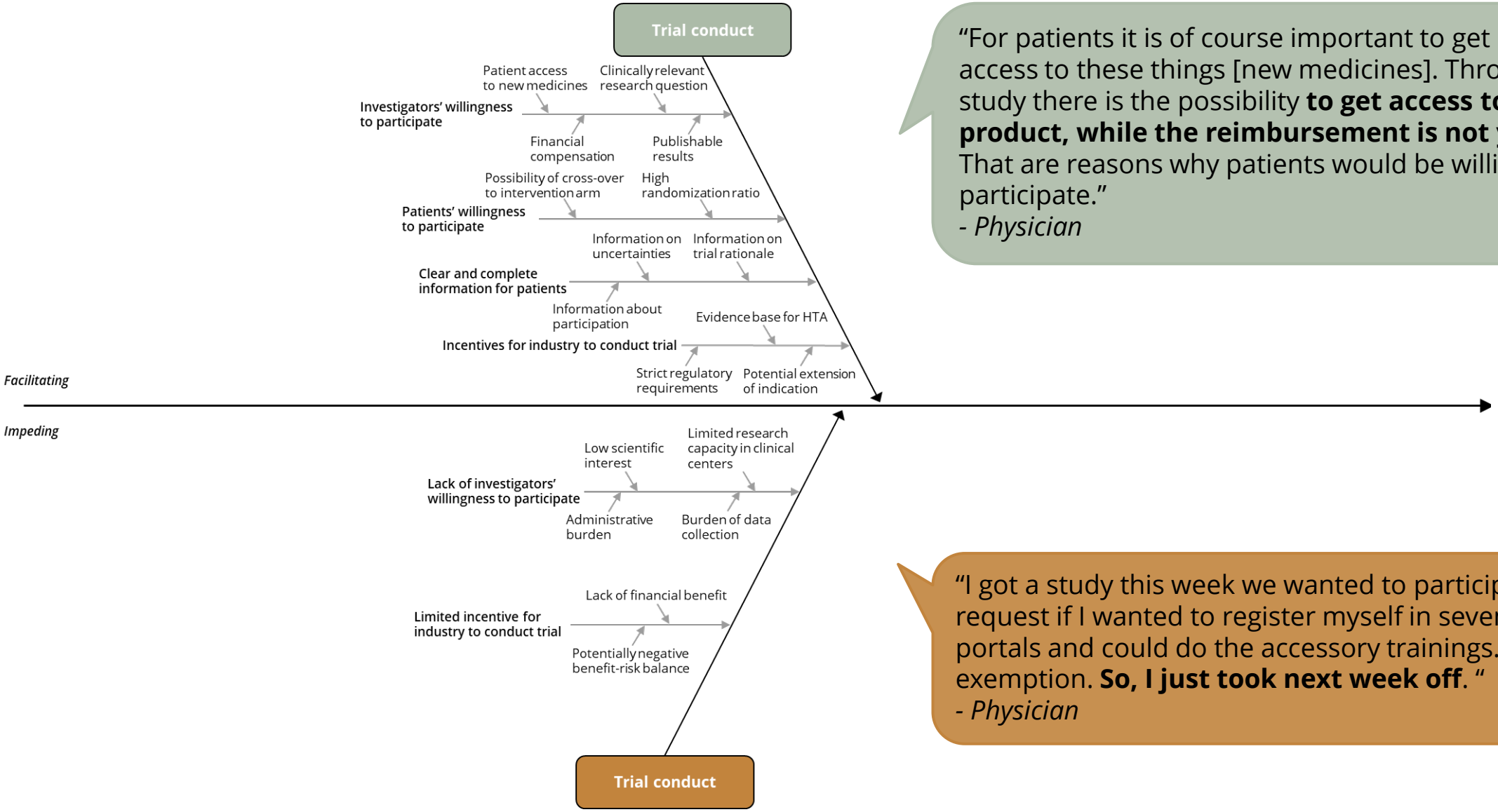
Results were categorized under 4 themes

- Trial design
- Trial conduct
- External factors
- Post-authorization discussion with regulators



" For them [patients] it's all about the time that they have, spending that in good quality and getting access to the novel treatments [...]. So I would say **quality of life measures**, that would be really, **really key**. And, of course, overall survival as well."
- *Patient representative*

" So there is, for example, the CheckMate 37 trial where blinding was not feasible. So, 20% of patient randomized to the control immediately **left the trial** because they had many other trials with PD-L1 compounds they could get."
- *Industry representative*

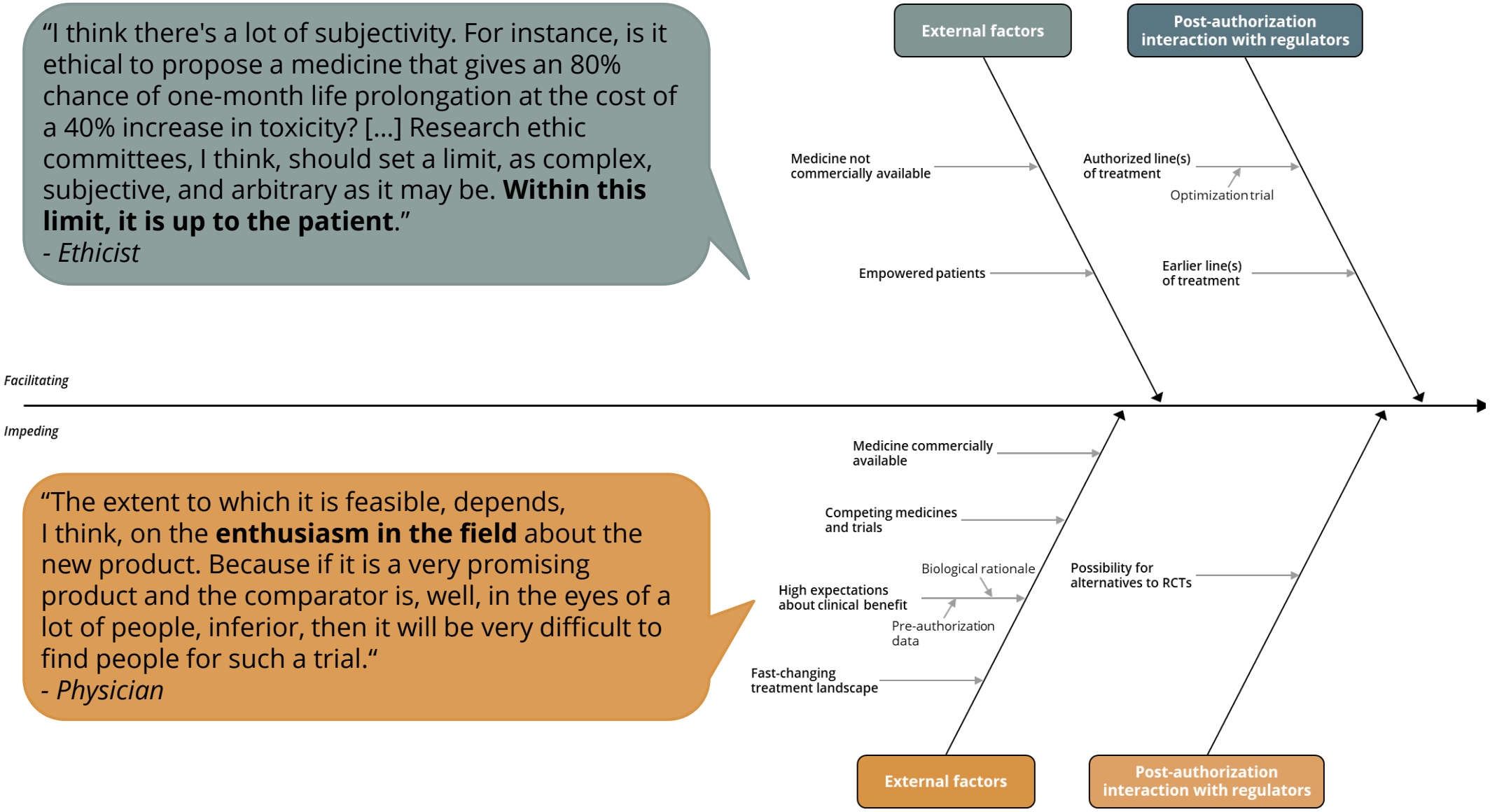


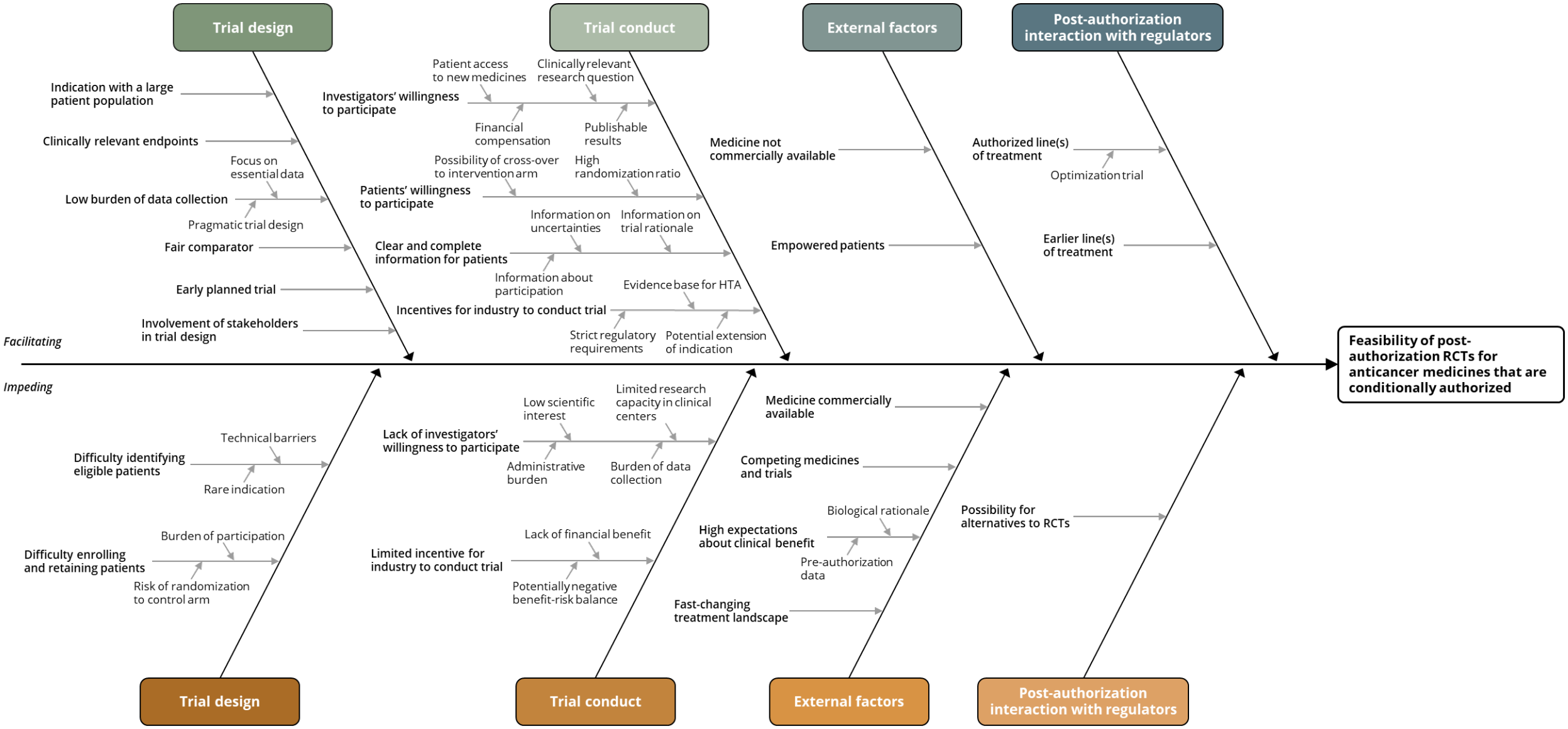
"For patients it is of course important to get access to these things [new medicines]. Through such a study there is the possibility **to get access to the new product, while the reimbursement is not yet arranged**. That are reasons why patients would be willing to participate."
- Physician

"I got a study this week we wanted to participate in, with the request if I wanted to register myself in seven different portals and could do the accessory trainings. And this is no exemption. **So, I just took next week off**. "
- Physician

"I think there's a lot of subjectivity. For instance, is it ethical to propose a medicine that gives an 80% chance of one-month life prolongation at the cost of a 40% increase in toxicity? […] Research ethic committees, I think, should set a limit, as complex, subjective, and arbitrary as it may be. **Within this limit, it is up to the patient**."
- *Ethicist*

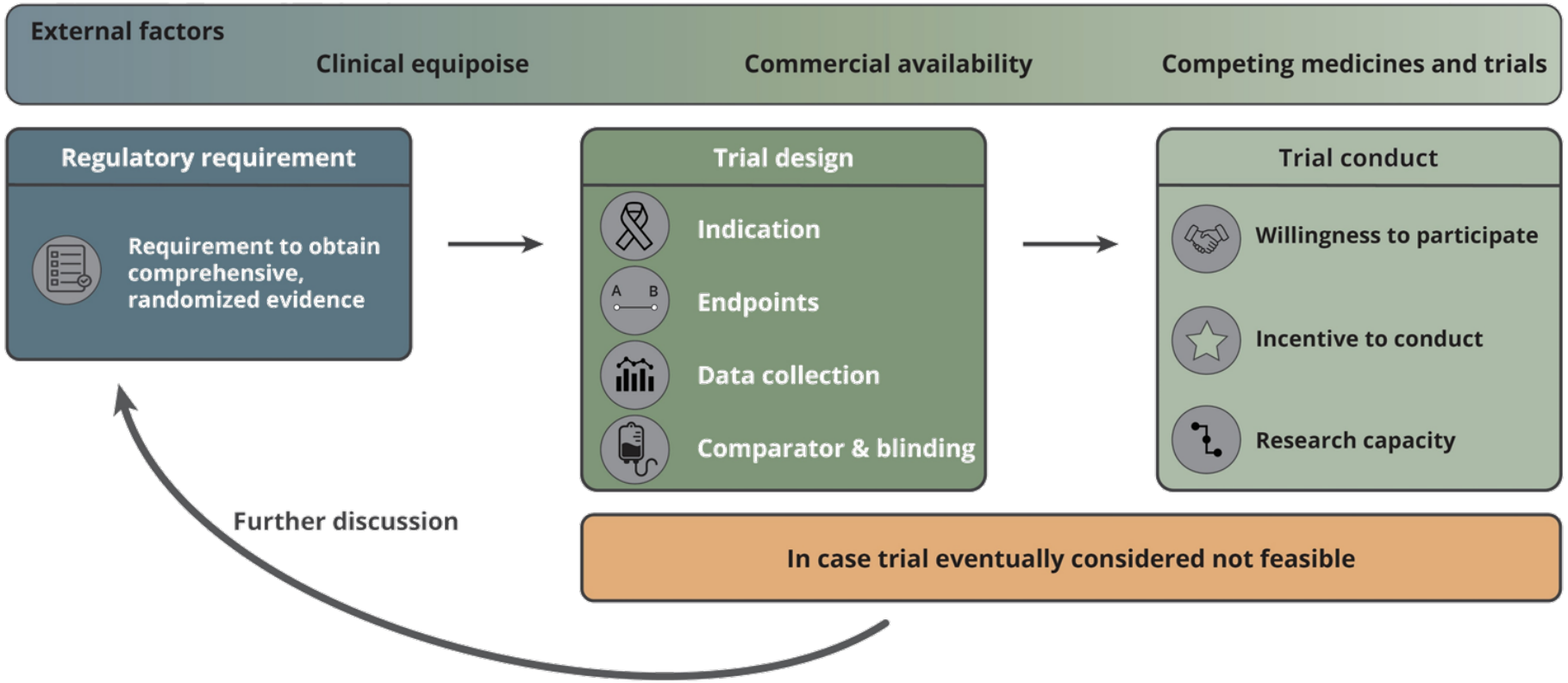
"The extent to which it is feasible, depends, I think, on the **enthusiasm in the field** about the new product. Because if it is a very promising product and the comparator is, well, in the eyes of a lot of people, inferior, then it will be very difficult to find people for such a trial."
- *Physician*





Discussion

Feasibility of post-authorization RCTs: a process visualization



Key takeaways

- Clinical equipoise perception varies between stakeholders
  - We recommend sponsors and regulators to better inform patients and physicians about remaining uncertainties
  - Empower to make well-informed decisions

- Tailor trial design to post-authorization setting
  - Pragmatism
  - Clinically relevant endpoints
  - Fair comparator

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