Considerations for Common Exclusion Criteria in Real-World (RW) Retrospective Observational Studies in Oncology

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Background and Rationale

- A key strength of well-designed real-world (RW) research studies is the potential to include larger and more representative populations than randomized-controlled trials.
- Two commonly applied exclusion criteria across RW oncology studies involve:
  - Patients from **clinical trials**
  - Patients with **other primary cancers**
- These two criteria are often specified to *maximize a study's internal validity (minimize bias)*, which is prioritized against *external validity (generalizability and transportability)*.
- However, they are heterogeneously defined across studies.
- There may be opportunities to examine their necessity and operational definitions when designing fit-for-purpose research.

Methodology

- We examined a series of RW studies conducted within the period from January 2020 to July 2022 based on oncology-specific electronic medical records (**Figure 1**).

Figure 1. Summary of Studies and DQ Rates

41 Studies across 12 Tumor Types	
15,240 Patients Examined, 3,963 Patients Excluded[1]	
38 Studies with Clinical Trial Exclusion	40 Studies with Other Cancer Exclusion
299 patients (~2%) Excluded	604 Patients (~4%) Excluded
Median DQ Rate: 1.3% [2]	Median DQ Rate: 2.7%[2]

1 Each study had unique inclusion and exclusion criteria, and this accounts for DQs for any reason.
2 DQ rate was attributable to the specific exclusion. Not mutually exclusive with the other exclusion criteria.

- Disqualification (DQ) rates were defined as # disqualified / # of reviewed patients.
- Based on the patterns observed in the DQ rates and differences in the verbiage applied, we identified key dimensions across which these two exclusion criteria have been differently defined and examined their impact on patient disqualification.
- We outline a set of key decisions for researchers to ensure that the implemented criteria are fit-for-purpose to address a study's research questions, based on a trade-off between:
  1. Sample size
  2. Bias reduction
  3. Operational efficiency

Figure 2. Dimensions for Clinical Trial Exclusion Criteria

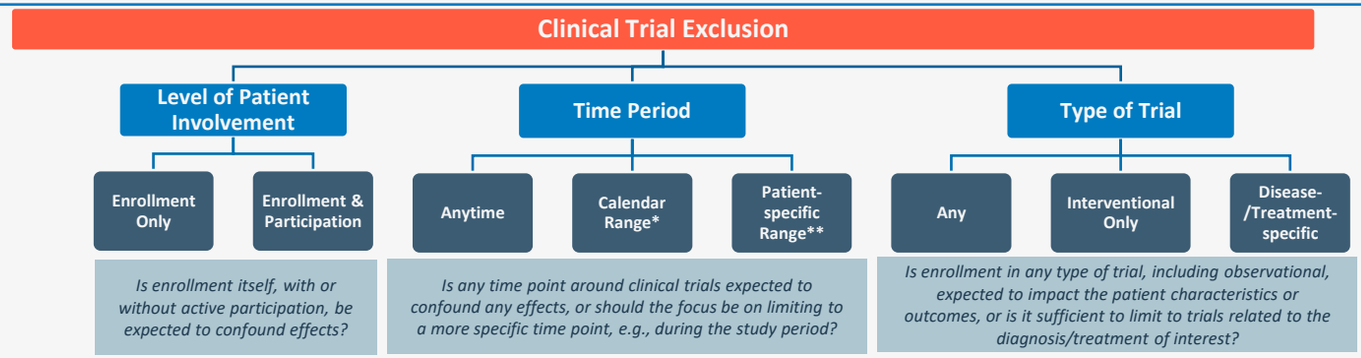
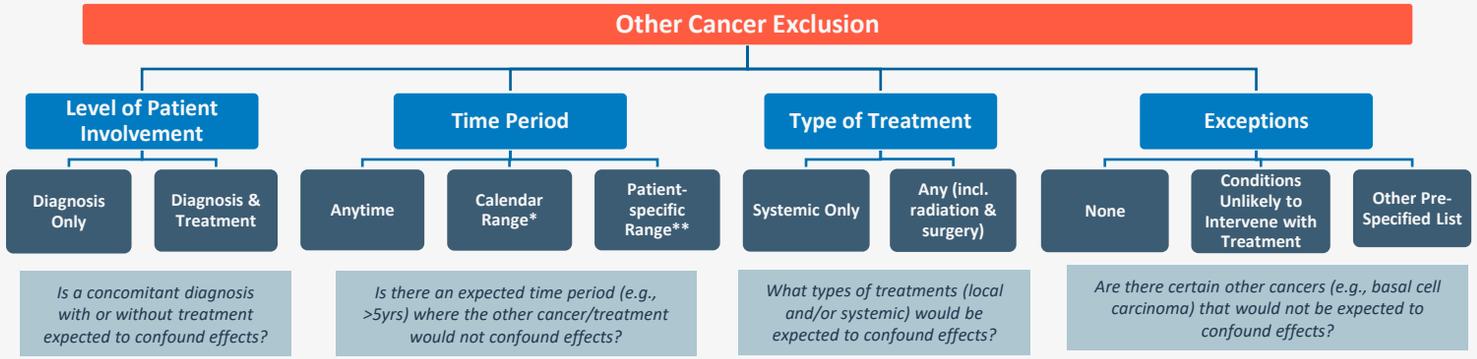


Figure 3. Dimensions for Other Cancer Exclusion Criteria



*Such as study identification period, observation period
**Such as index treatment, follow-up, prior medical history

Conclusions

- Exclusion of patients from clinical trials and/or patients with other primary cancers was common, and the application of these criteria may have a substantial impact on internal and external validity.
- Customization of criteria to reduce bias while maximizing sample size and representativeness is crucially important for RW study design. Not all criteria may be equally justifiable in the context of all research questions.
- Considerations should be made based on the research question as well as the dynamics of the specific treatment/disease and the etiologic time period of interest.
- We encourage investigators to standardize their decision process rather than defaulting to these prevalent, but sometimes restrictive, criteria.