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DCR-CTU Lecture

Using AI platforms to answer unanswered questions - How well do trials perform?

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Agenda

1. Clinical trial registries
2. Methods
3. Project 1: Delays in clinical trials
4. Project 2: Inclusiveness in clinical trials

Clinical trial register items[1]

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1. Primary trial identifying number
2. Date of registration
3. Secondary identifying number
4. Source of monetary of material support
5. Primary sponsor
6. Secondary sponsor(s)
7. Contact for public queries
8. Contact for scientific queries
9. Public title
10. Scientific title
11. Countries of recruitment
12. Health condition or problems studied
13. Intervention(s)
14. Key inclusion and exclusion criteria
15. Study type
16. Date of first enrollment
17. Sample size
18. Recruitment status
19. Primary outcome (s)
20. Key Secondary outcome(s)
21. Ethics review
22. Completion date
23. Summary results
24. Individual clinical trial participant-level data sharing statement

International clinical trial registry platform

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Primary registries:

- 17 registries[2] which meet the specific criteria[3] set by WHO

Partner registries

- Meet same criteria as primary registries but have some exceptions

Data providers

- Responsible for a database that is used by one or more registries

Depth of clinical trial registries

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Information to investigate different aspects of trials

- Condition
- Intervention
- Status of trials
- Termination cause
- Eligibility criteria
- ….

Pitfalls and Strengths

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- **Pitfalls**
  - Incomplete data
  - Data entry errors
  - Data standardization (among databases)
  - Incomplete reporting
  - Data maintenance
- **Strengths**
  - \+ Comprehensive data
  - \+ Transparency
  - \+ Research discovery
  - \+ Data accessibility
  - \+ Data standardization (within a database)

Methods: Collecting data

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Risklick AI tool RISKLICK

- Risklick AG, Spin off from University of Bern[4]
- Developed an AI to mine all historical data from clinical trials[5,6]
  - 18 Clinical trial registries
  - 11 publication sources
  - 4 regulatory agencies

  → Weekly updated
- Natural language processing technology to extract and structure data

Project 1: Delay in clinical trials

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7-11

Methods: Search Project 1
Breast cancer (BC)

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Search with 101 keyterms to cover three subtypes of breast cancer:

- Hormone receptor positive (HR+)
- Triple negative (TNBC)
- HER2 positive (HER2+)

Period of 2000 - till day of search (15. March 2023)

Breast cancer trials dataset

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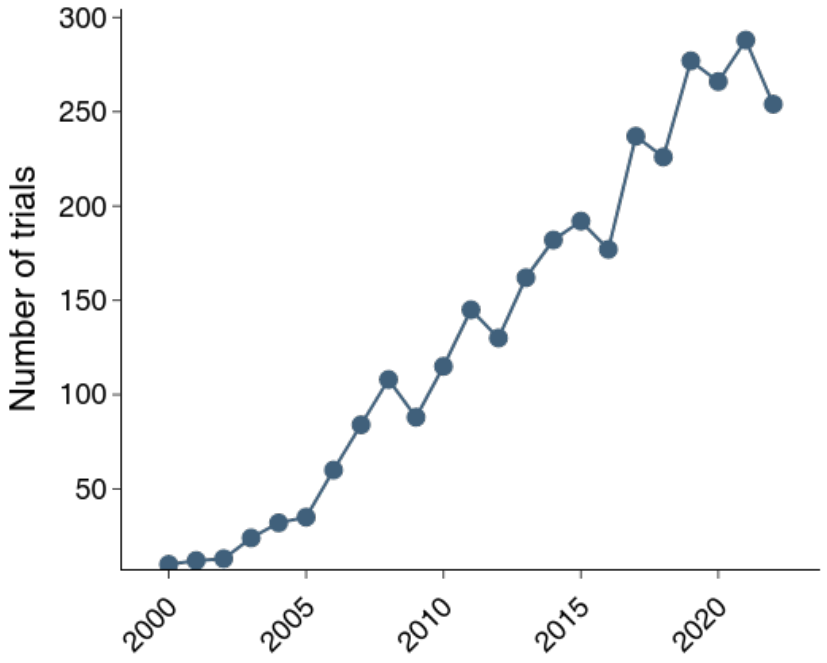
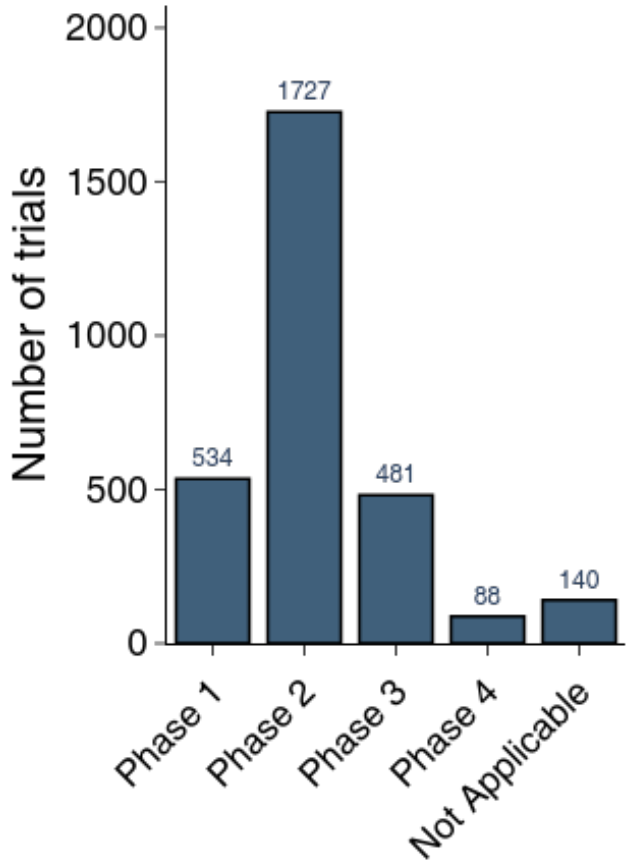
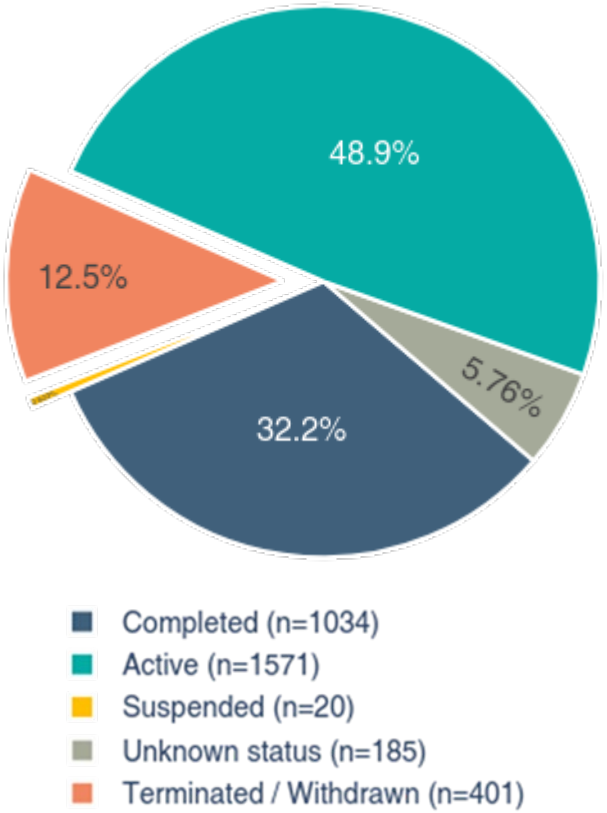
Time limit: 2000



Phase limit: 1-3



Status: Only completed



Excluded (n=452, missing data)

→ **Our dataset n=582**

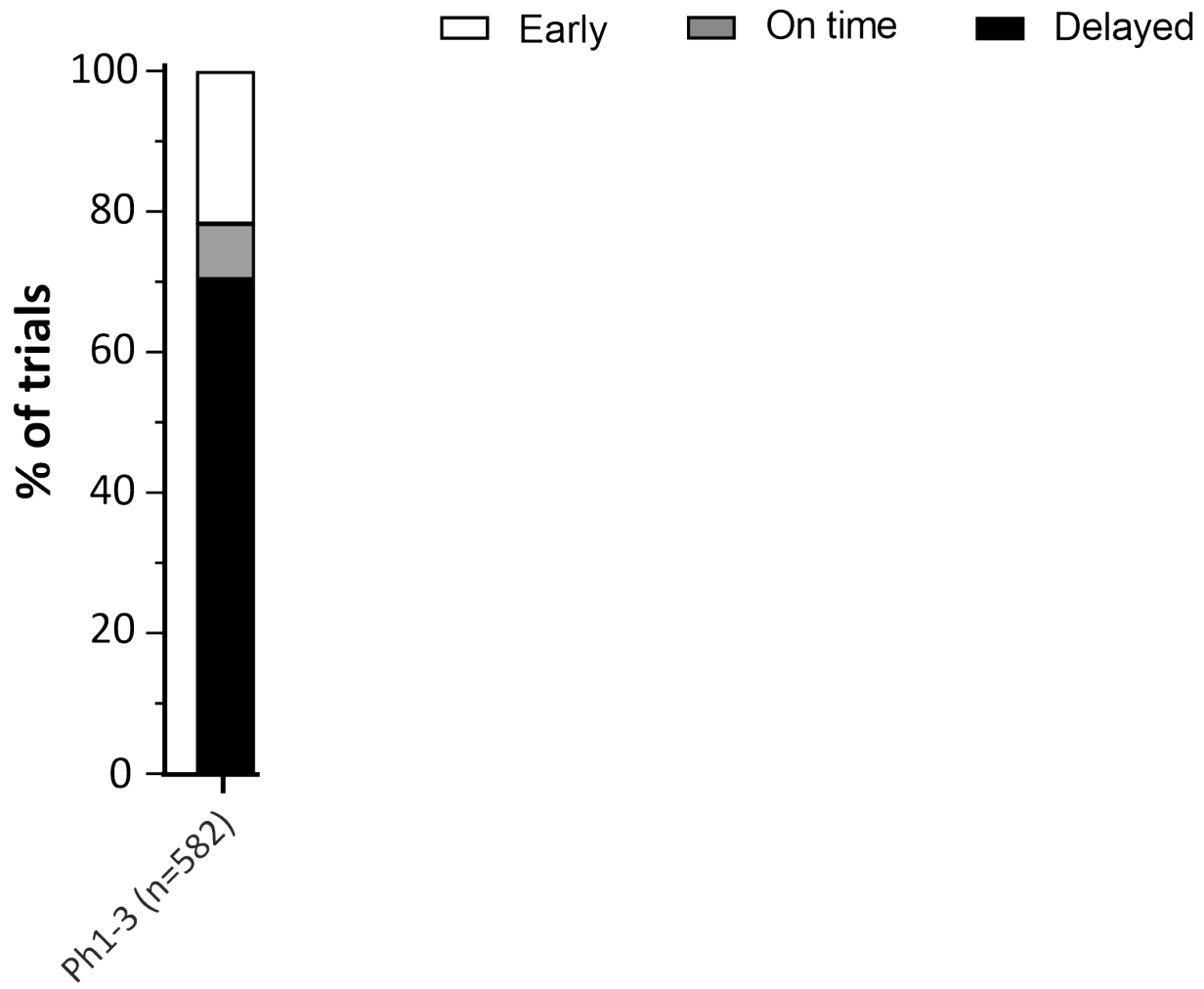
Methods: Duration

- Duration: '*the length of time that something lasts*'
- Calculated as: the time between starting date and planned OR final completion date

Early, on time and delay

- **Early:** Trial completed more than 1 month before planned completion date
- **On time:** Trial completed within 1 month of planned completion date
- **Delay**: Trial completed more than 1 month after planned completion date
- **Amount of delay:** The amount of additional time required to complete the trial compared to the planned duration

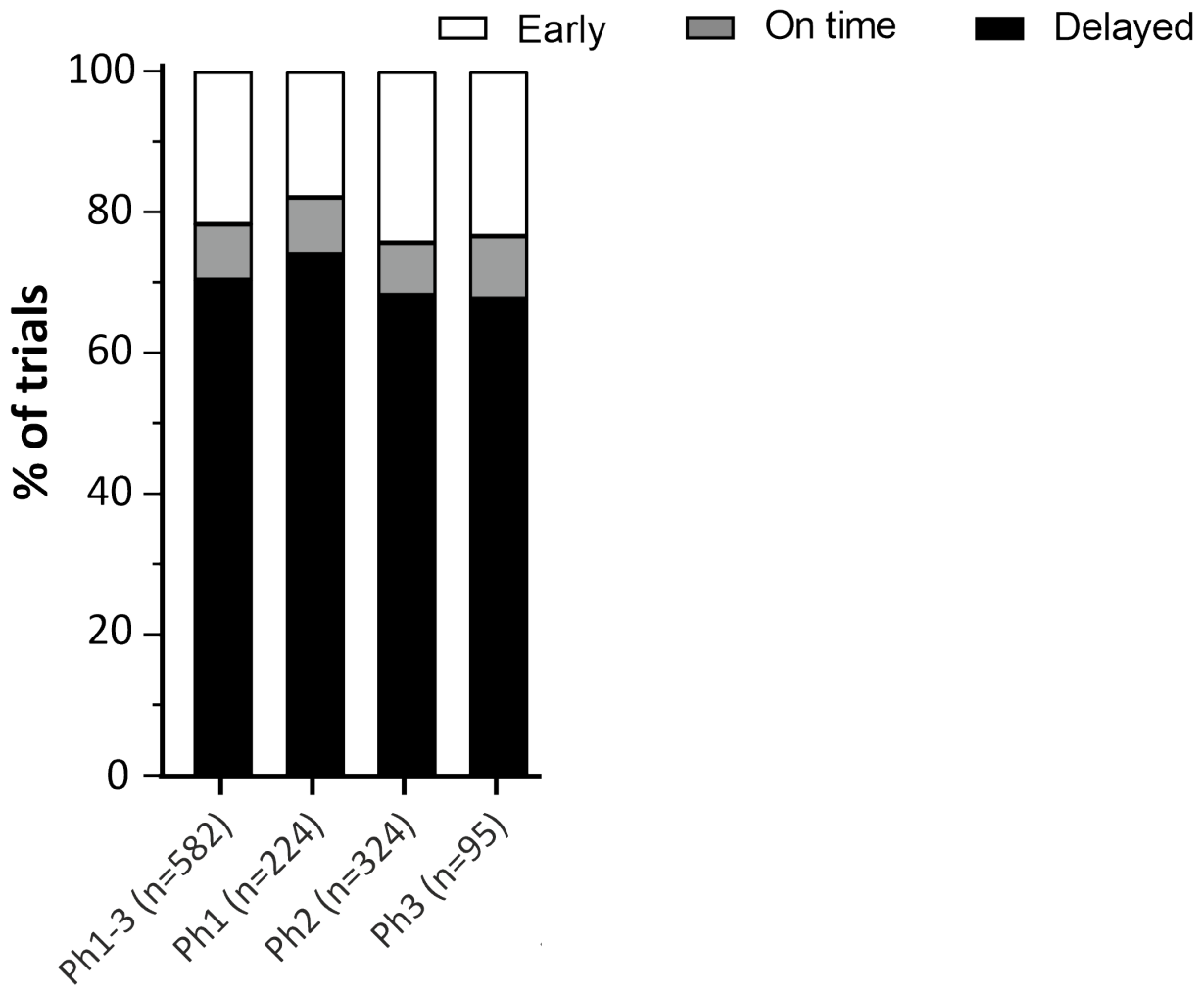
70.4% of BC trials face a delay



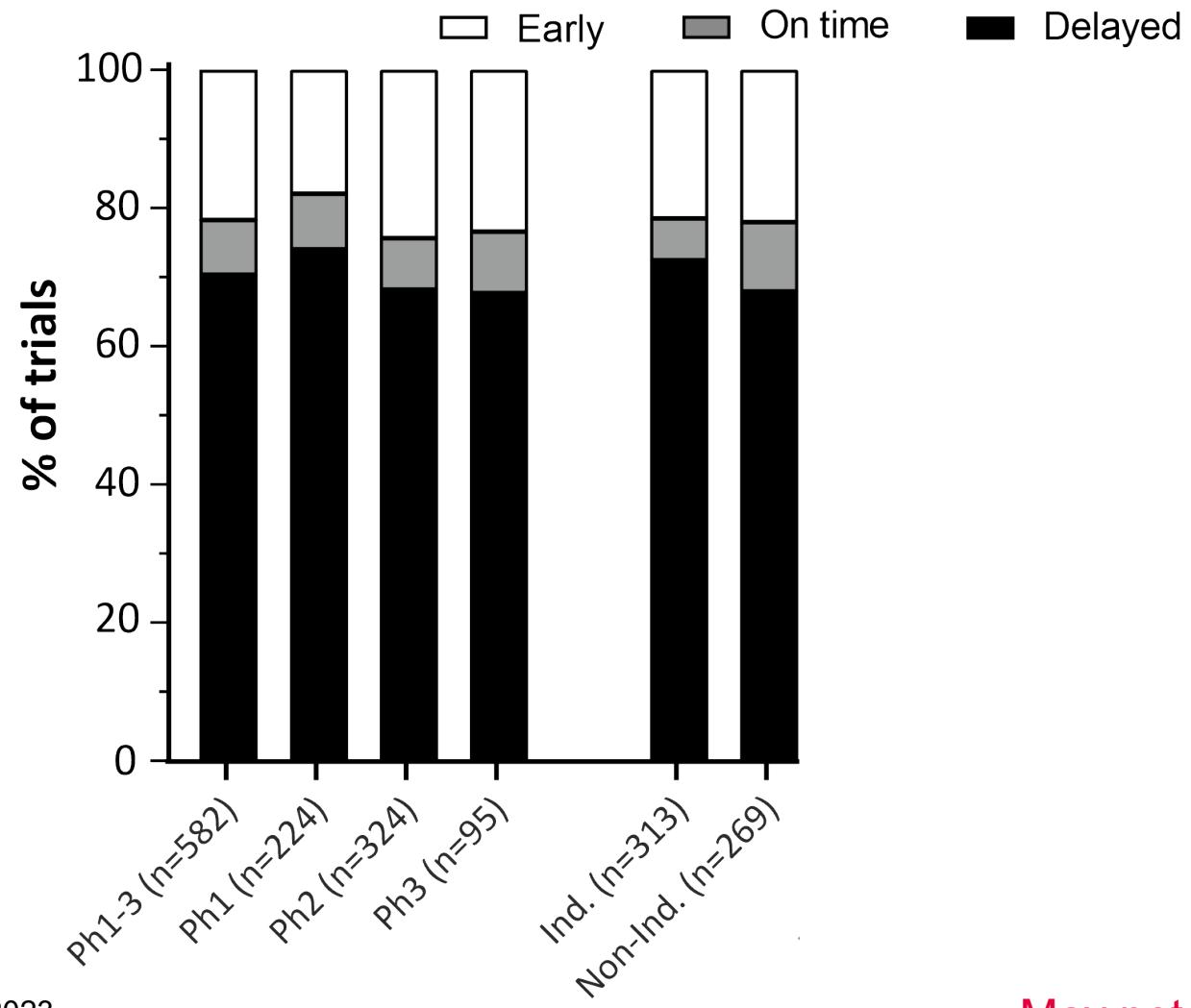
Delay analyzed by

- Phase
- Sponsor
- Disease extent
- Subtype
- Eligibility criteria
- Sample size

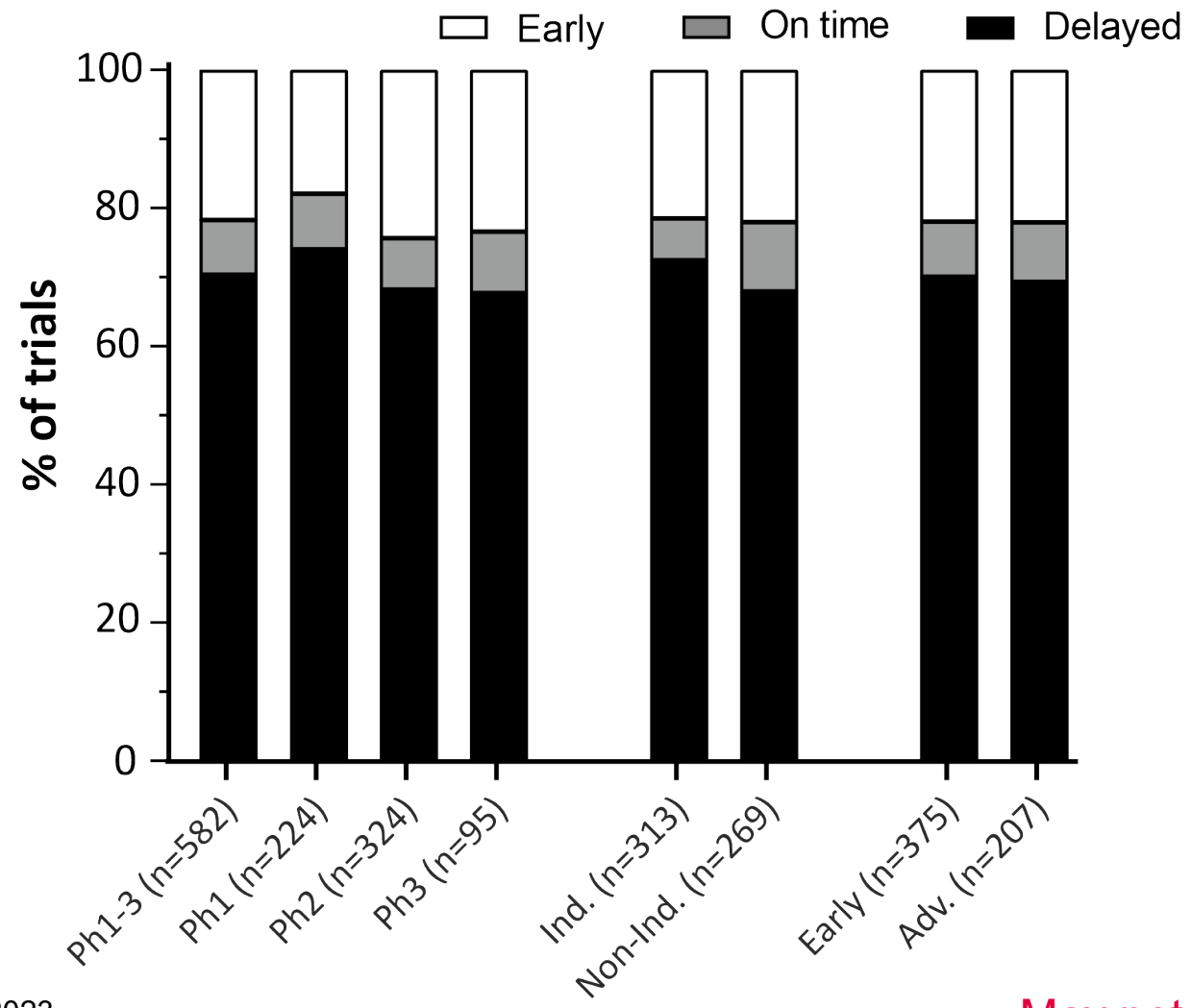
Trials facing a delay by phase



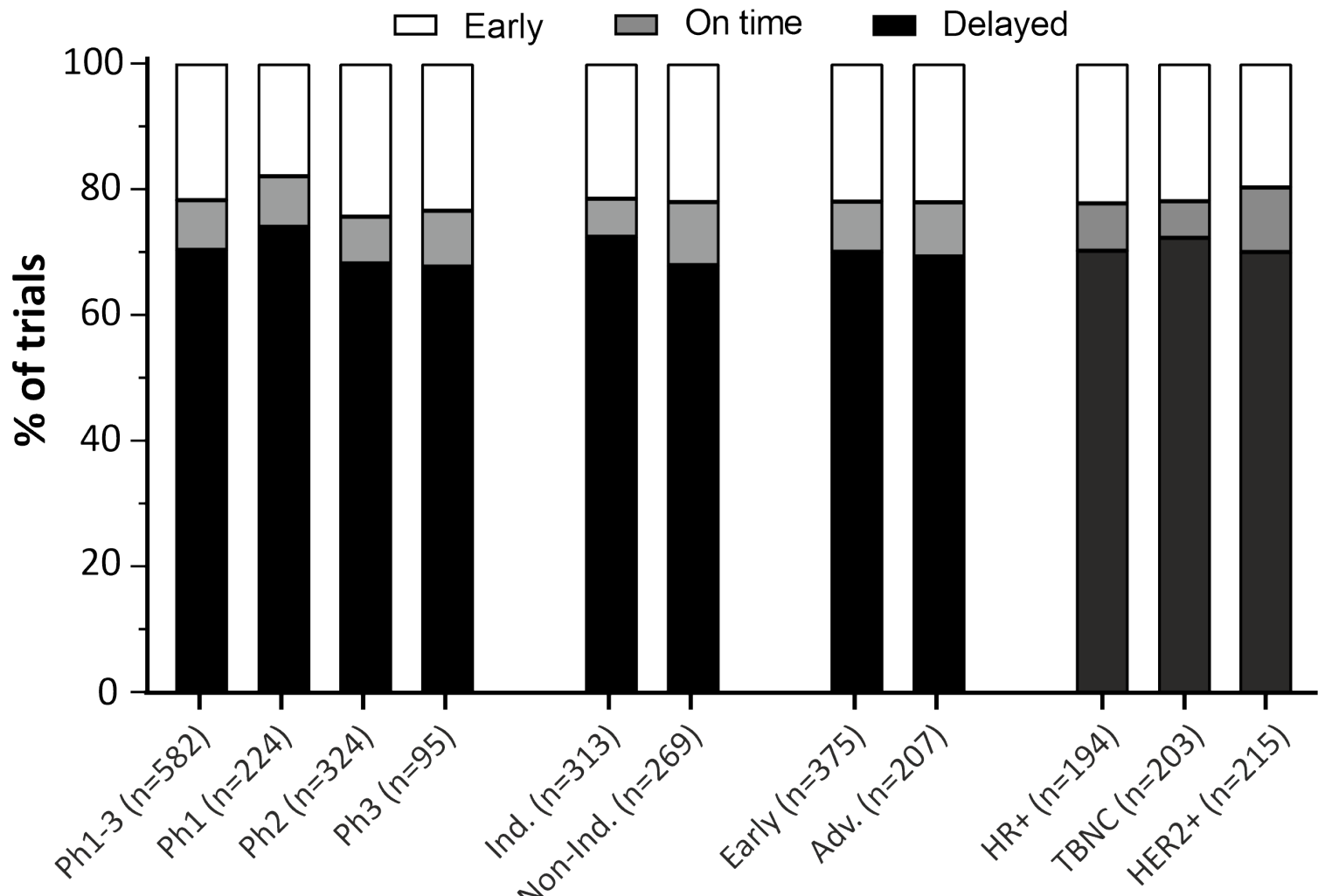
Trials facing a delay by sponsor



Trials facing a delay by disease extent



Trials facing a delay by suptype of BC



The average delay is 28.9 months

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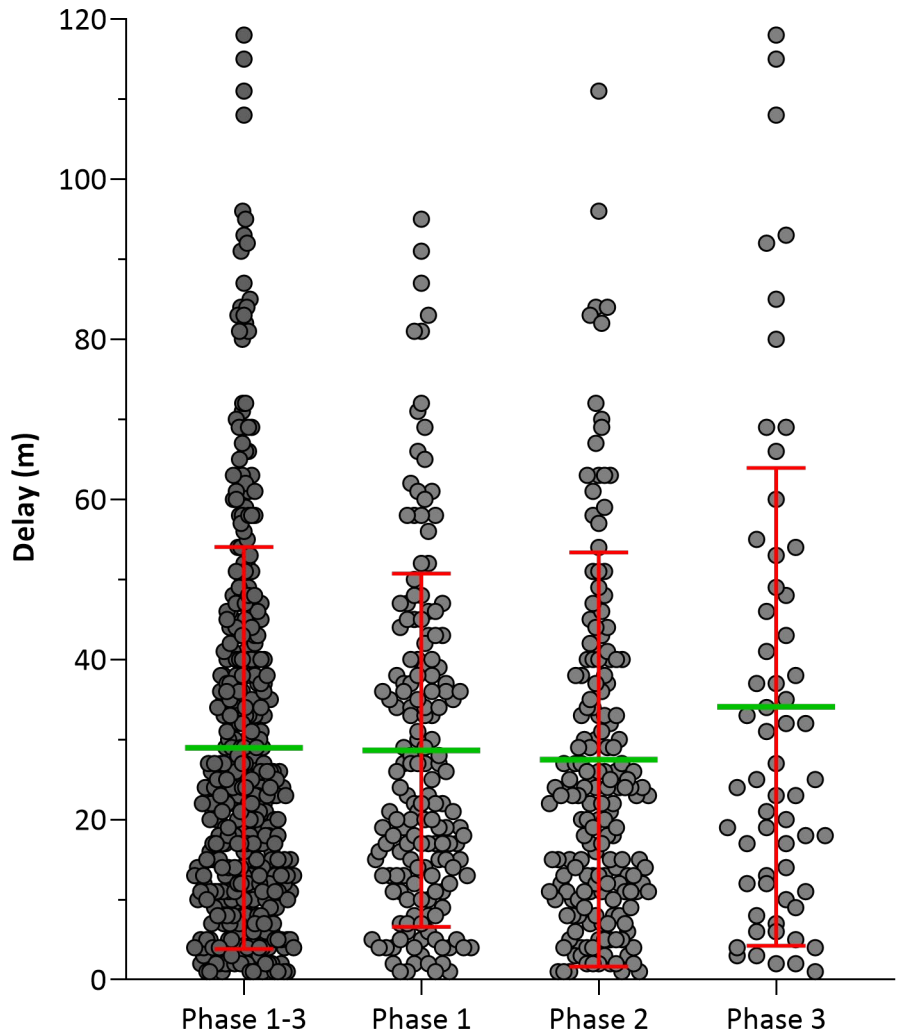
Average might be elevated due to extremes

→ median



The median delay is 23 months

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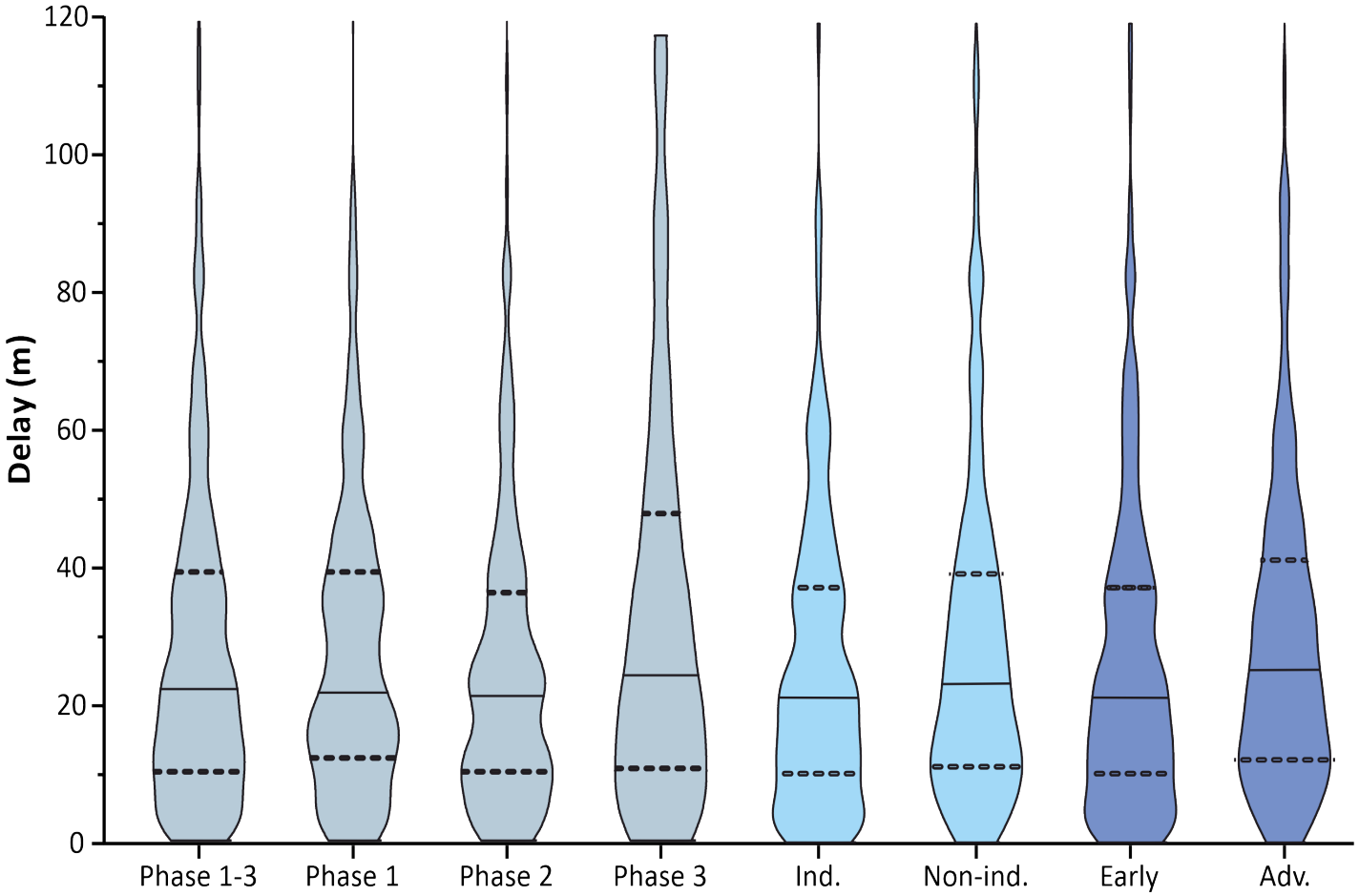
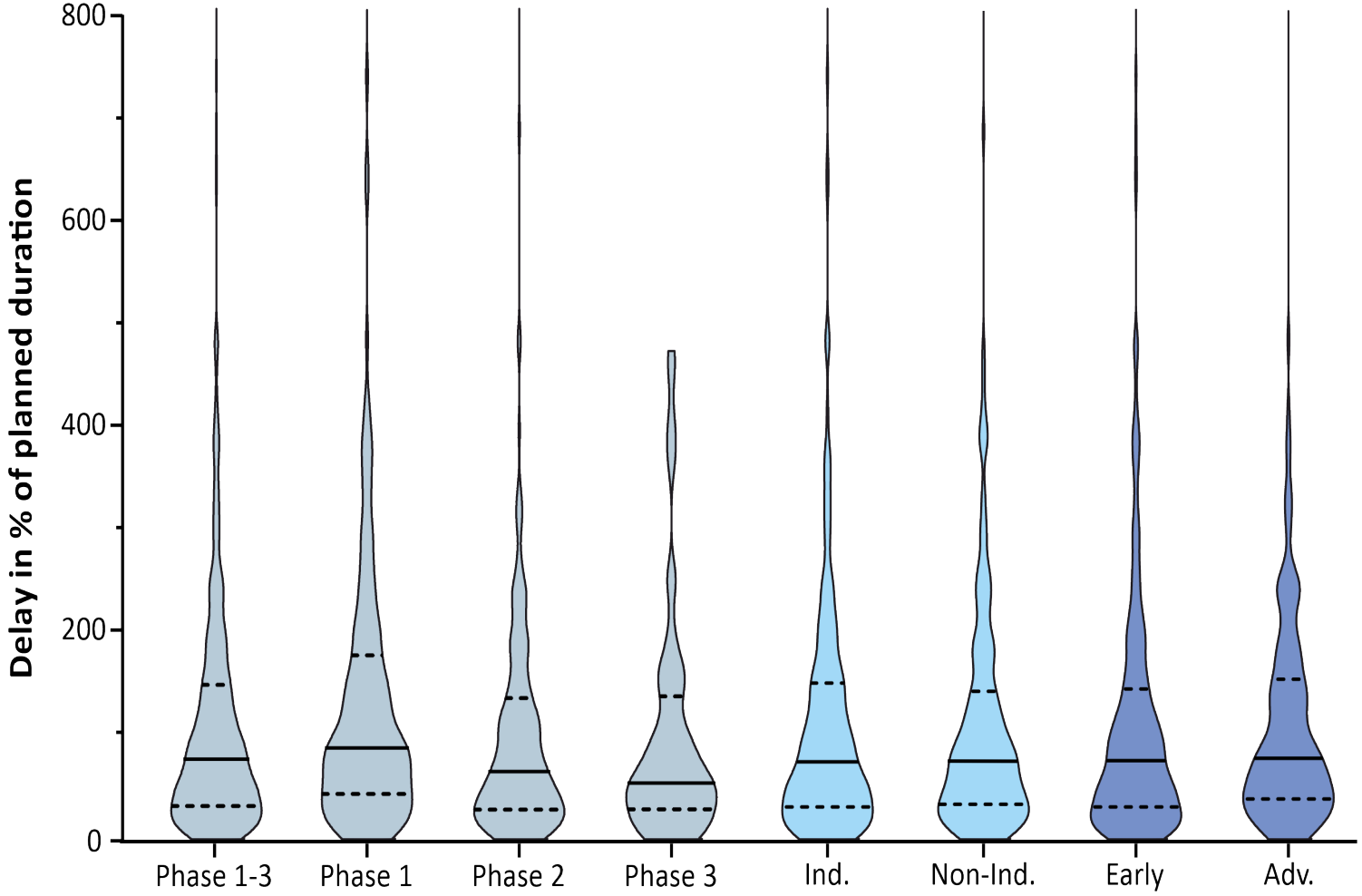
Delay in months might underestimate the seriousness of the delay

→ Delay as % of planned duration



78.4% more time needed to complete the trial



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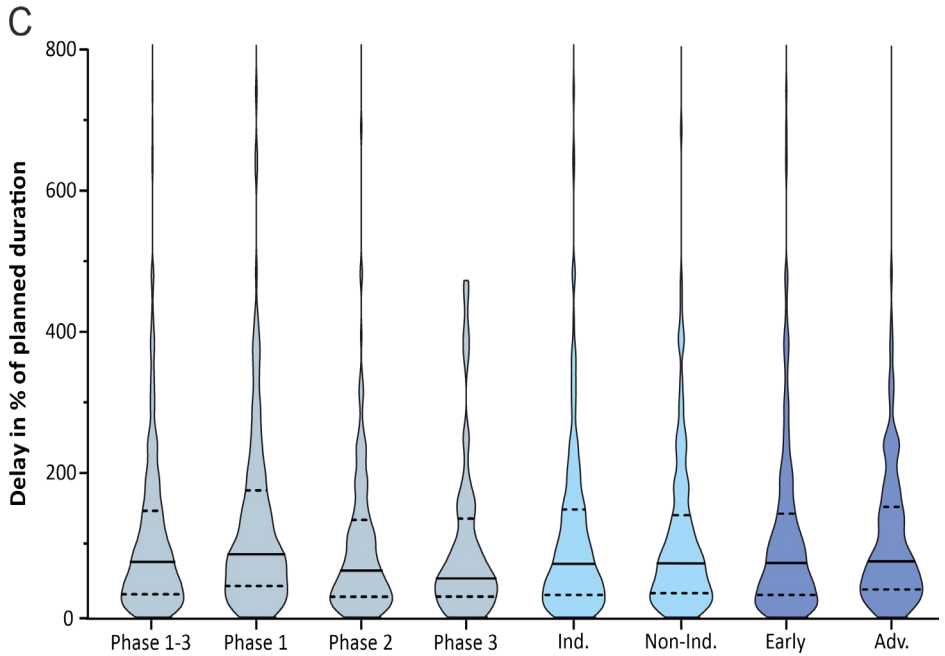
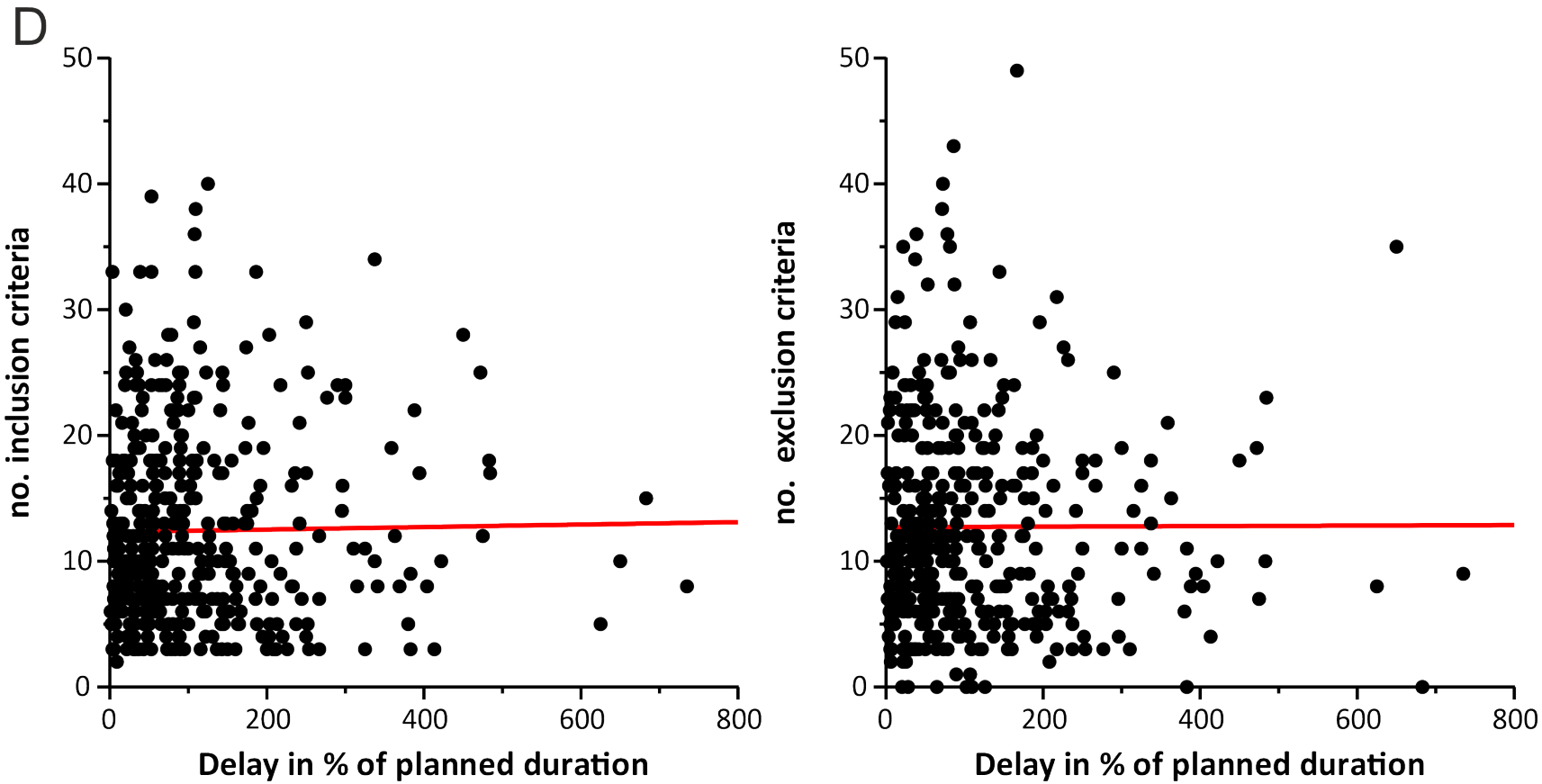


	Average (%)	Median	1. Quartile	3. Quartile
Phase 1-3	122.13	78.38	34.06	176.44
Phase 1	143.27	90.24	46.36	176.44
Phase 2	109.77	66.67	30.22	131.68
Phase 3	102.06	56.35	31.47	131.61
Industry	121.08	76.07	33.09	150.54
Non-industry	123.43	78.57	37.05	144.95
Metastatic	125.40	81.48	43.75	155.96
Non-metastatic	120.83	77.14	33.33	145.16

Delay does not correlate with number of eligibility criteria



Delay does not correlate with sample size

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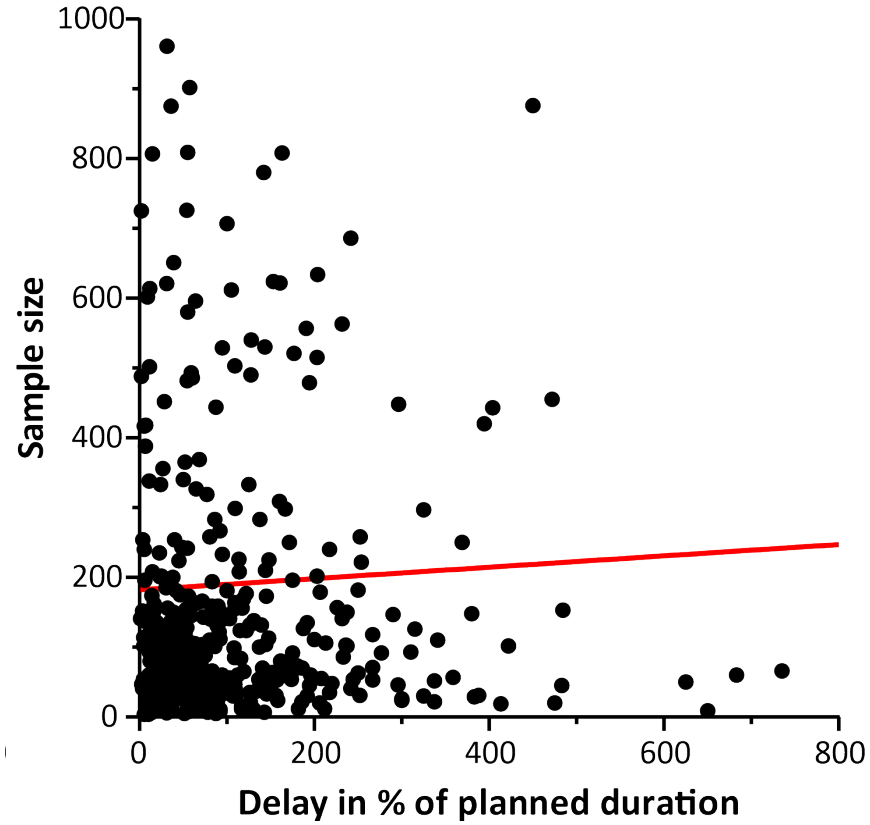

Future steps

- Other oncology fields
- Other medical fields
- Other influencing factors

Project 2: Inclusiveness

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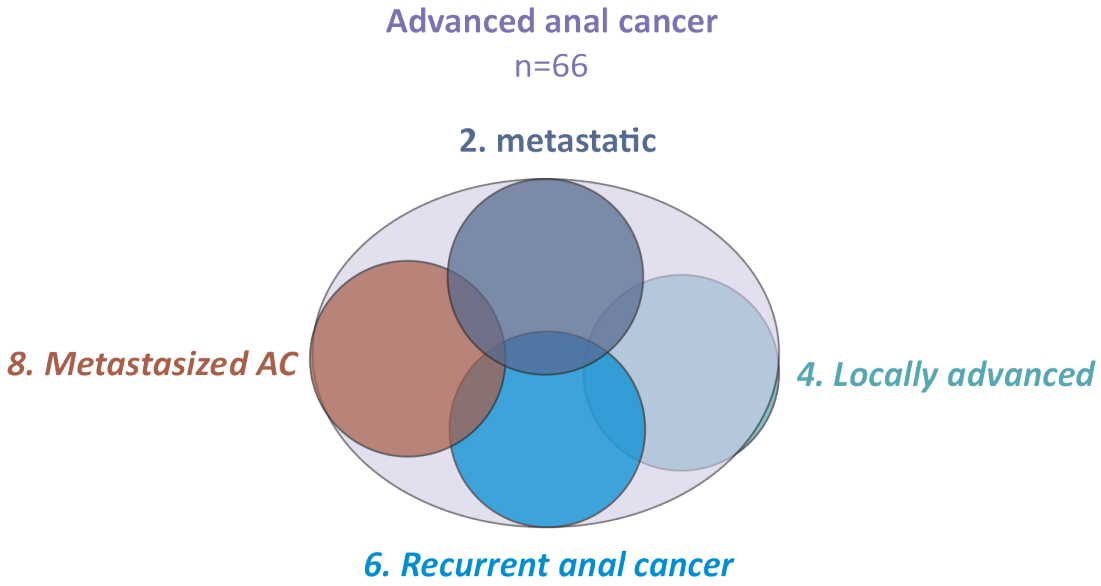
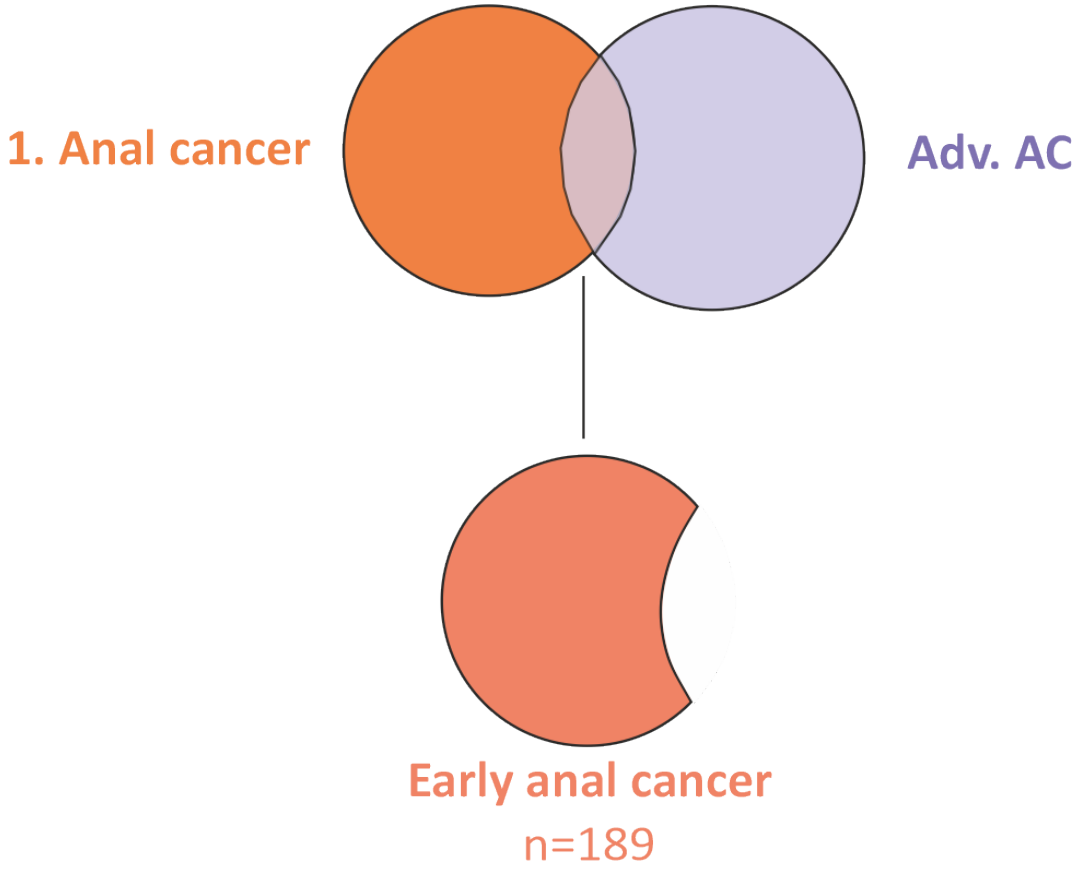
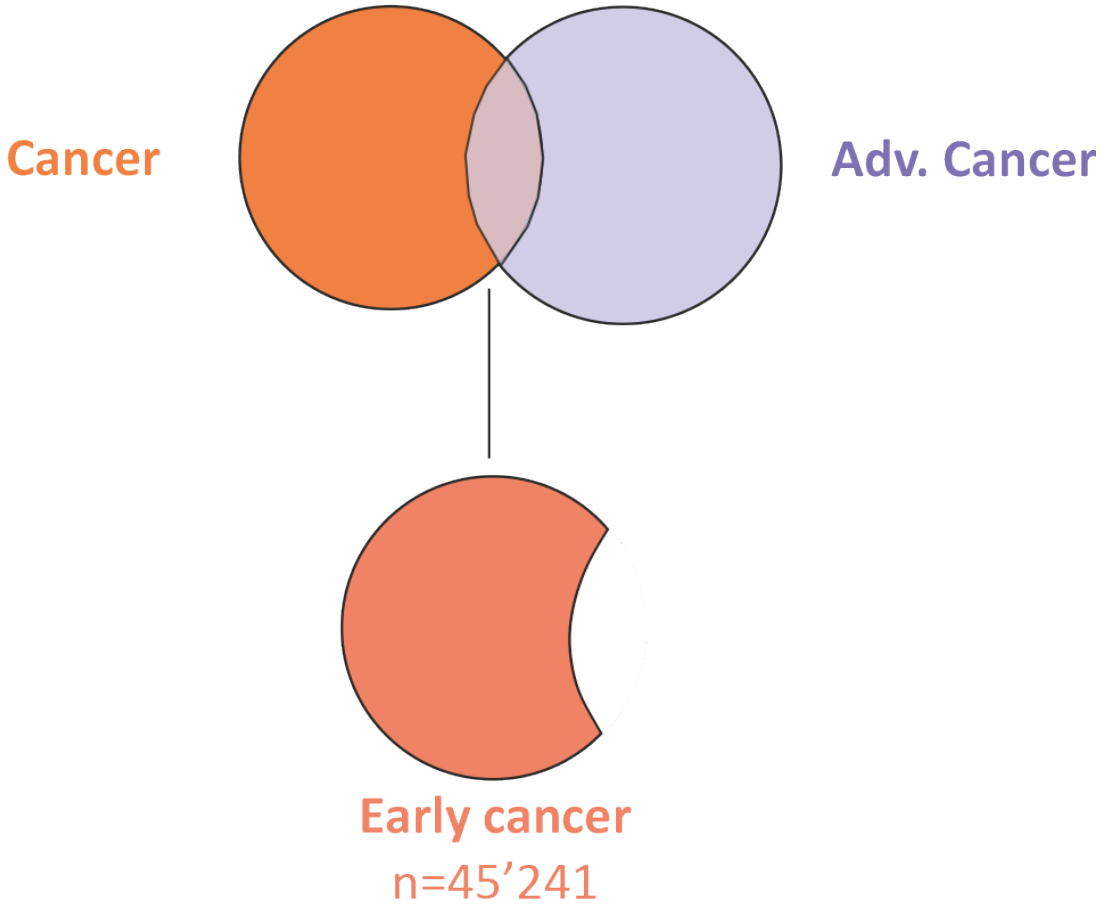
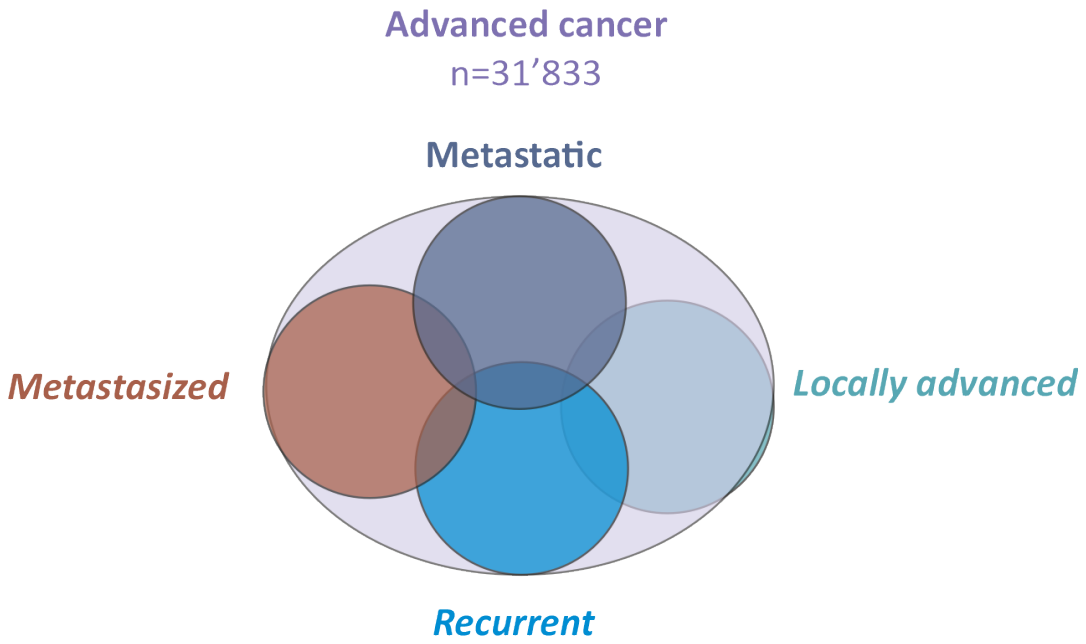
Methods: Search Project 2
Anal Cancer (AC)





Methods: Search Project 2
Oncology trials





Methods: Inclusion of HIV

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Screen eligibility criteria for

1. Mentioning HIV in eligibility criteria
2. No mention: automatically labeled as not specified
3. When mentioned are individuals with HIV
   - Included
   - Included under specific conditions
   - Excluded

Inclusion of individuals with HIV
Oncology trials

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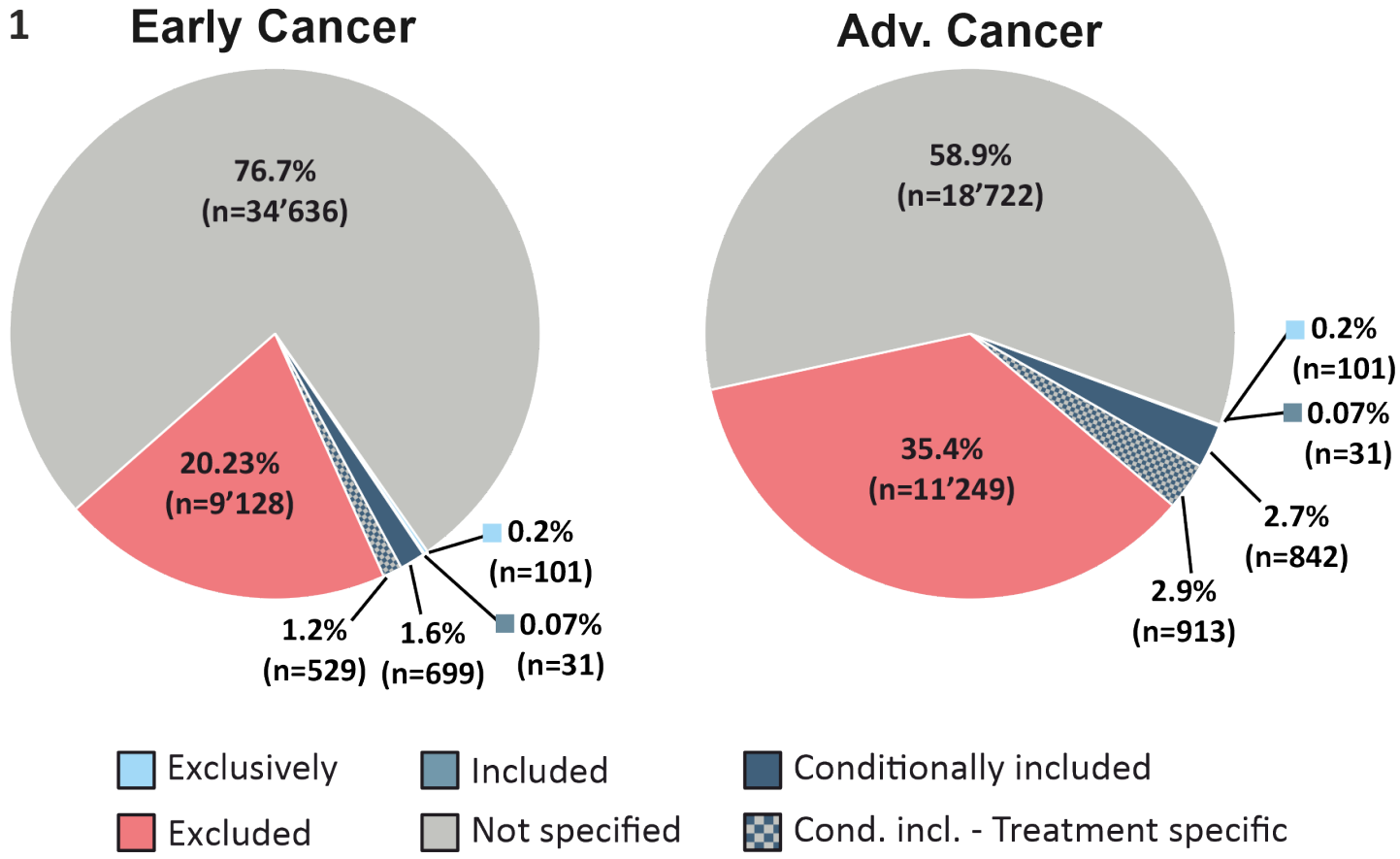
HIV status of participants is often not specified in eligibility criteria.

When specified, its often excluded.

Only 3.07% and 5.87% include individuals with HIV.



Inclusion of individuals with HIV
Anal cancer

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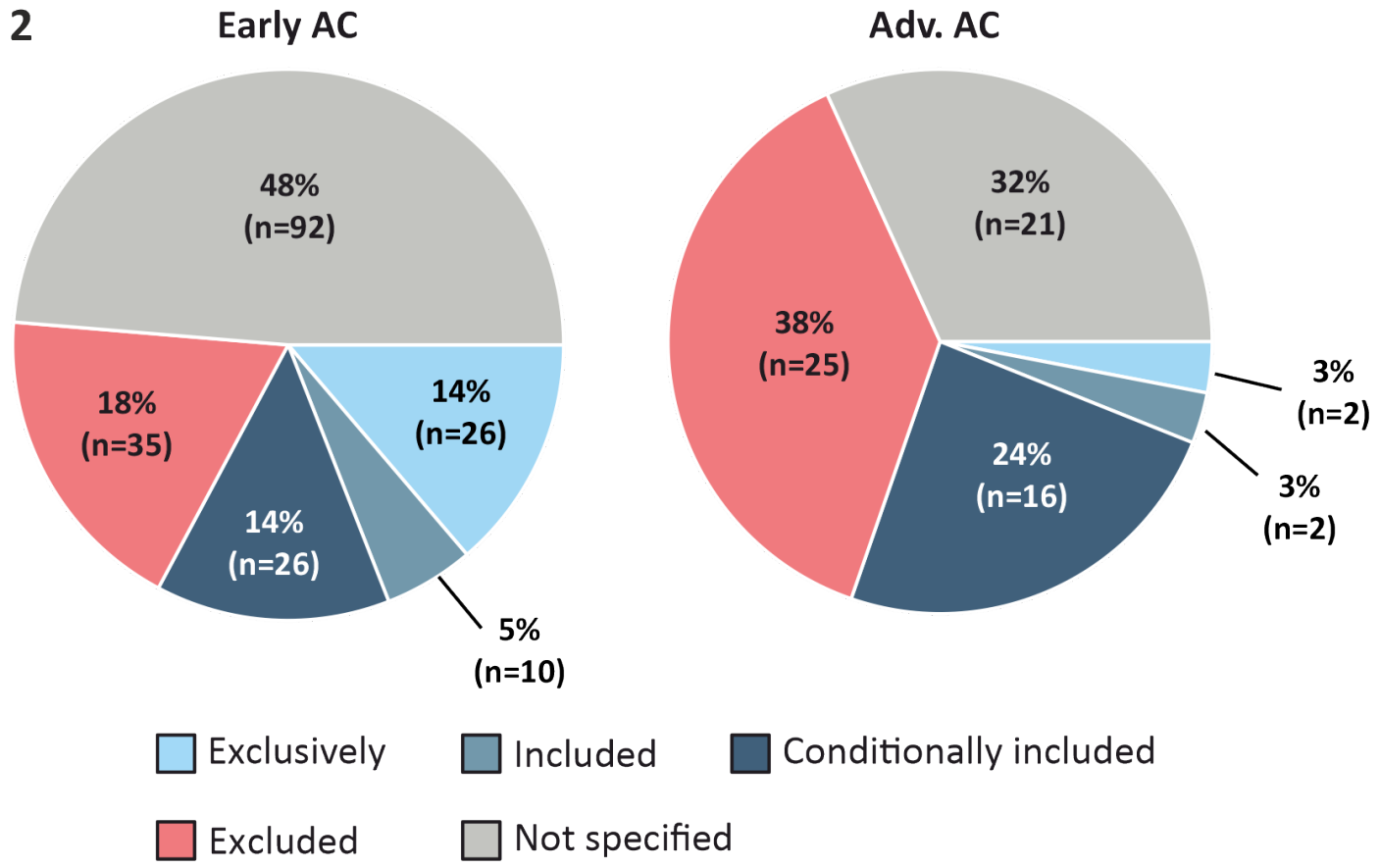
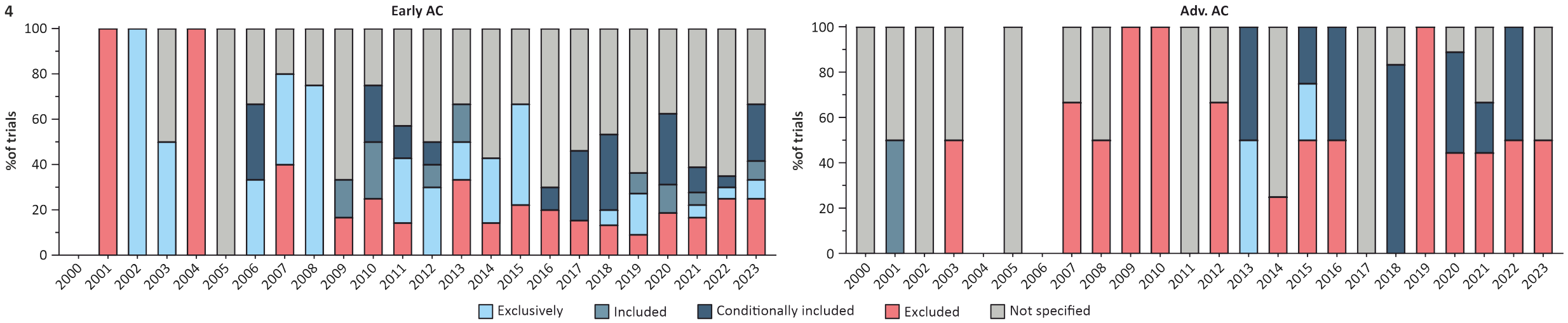
The majority of trials specify the HIV status of participants.

AC trials are more inclusive when individuals are HIV positive.



Inclusion over time
Anal cancer



Inclusion over time
Oncology trials

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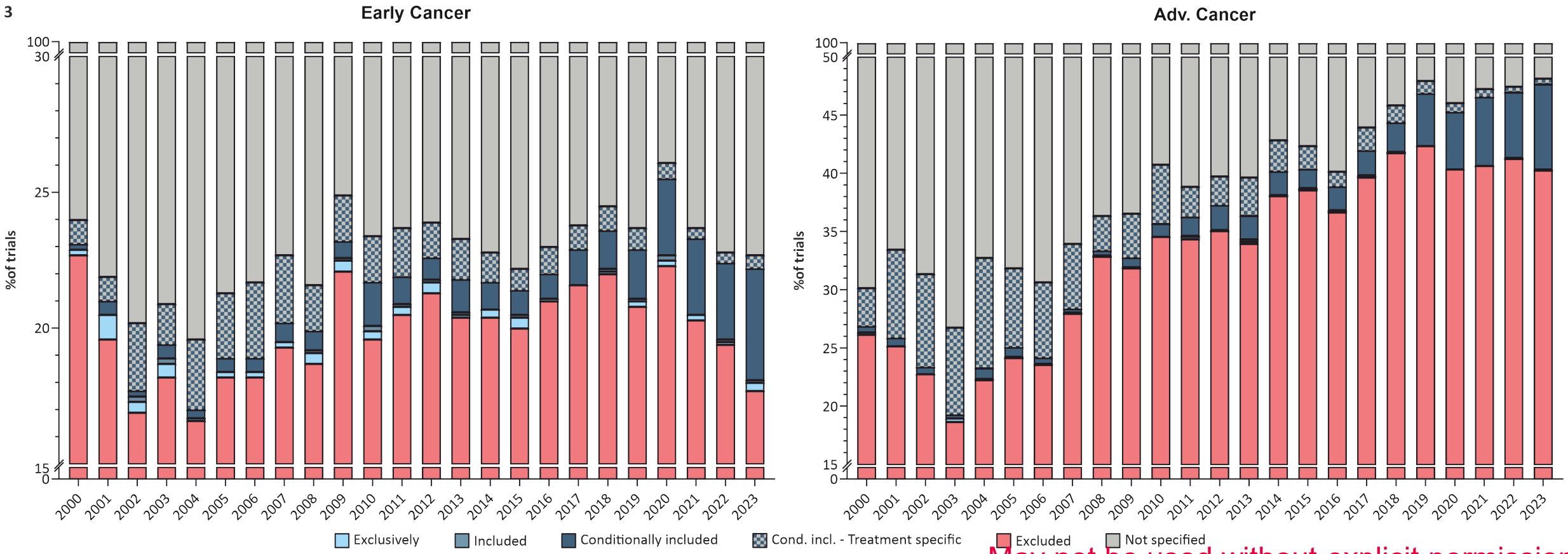

Take home message
How well do trials perform?

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Duration (and delays):

- Breast cancer clinical trials are doing poorly in estimating the duration of the trial

Inclusiveness

- Oncology trials showed increased exclusivity of individuals with HIV. Anal cancer trials are more inclusive for individuals with HIV.

Acknowledgements

- Department of Clinical Research
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Contact info

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