

# Alternative endpoints for multi-cancer detection clinical trials

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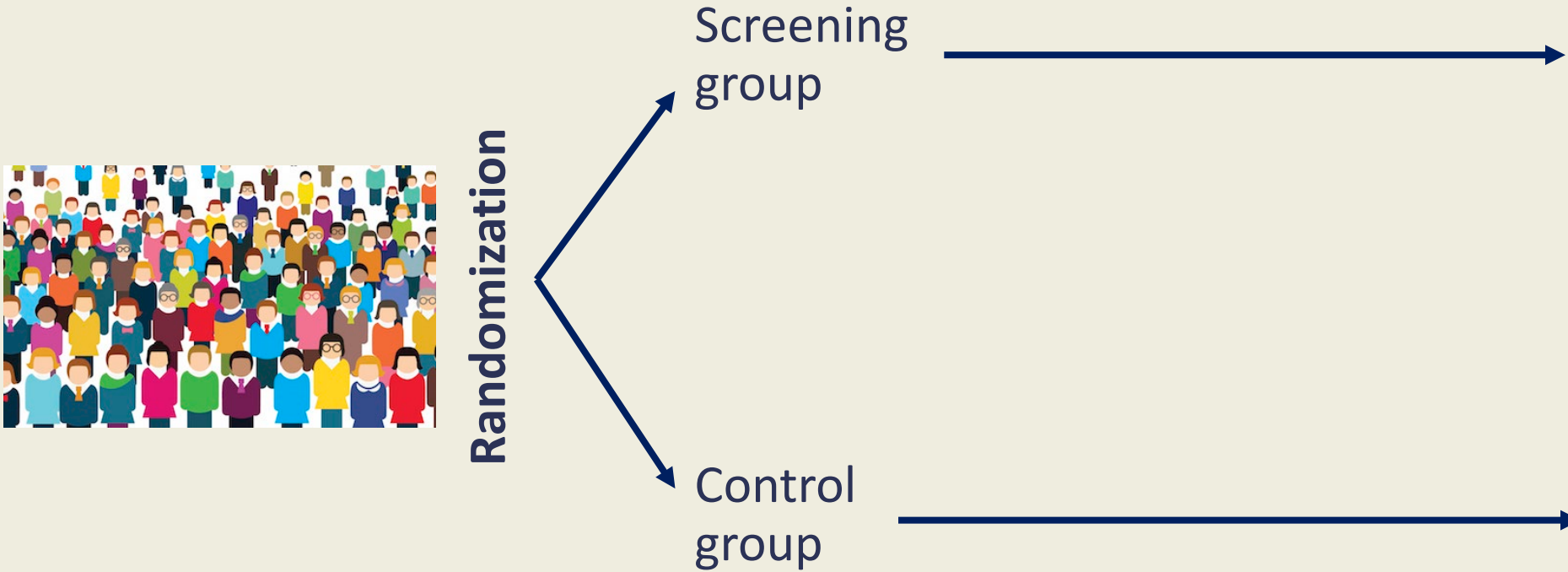




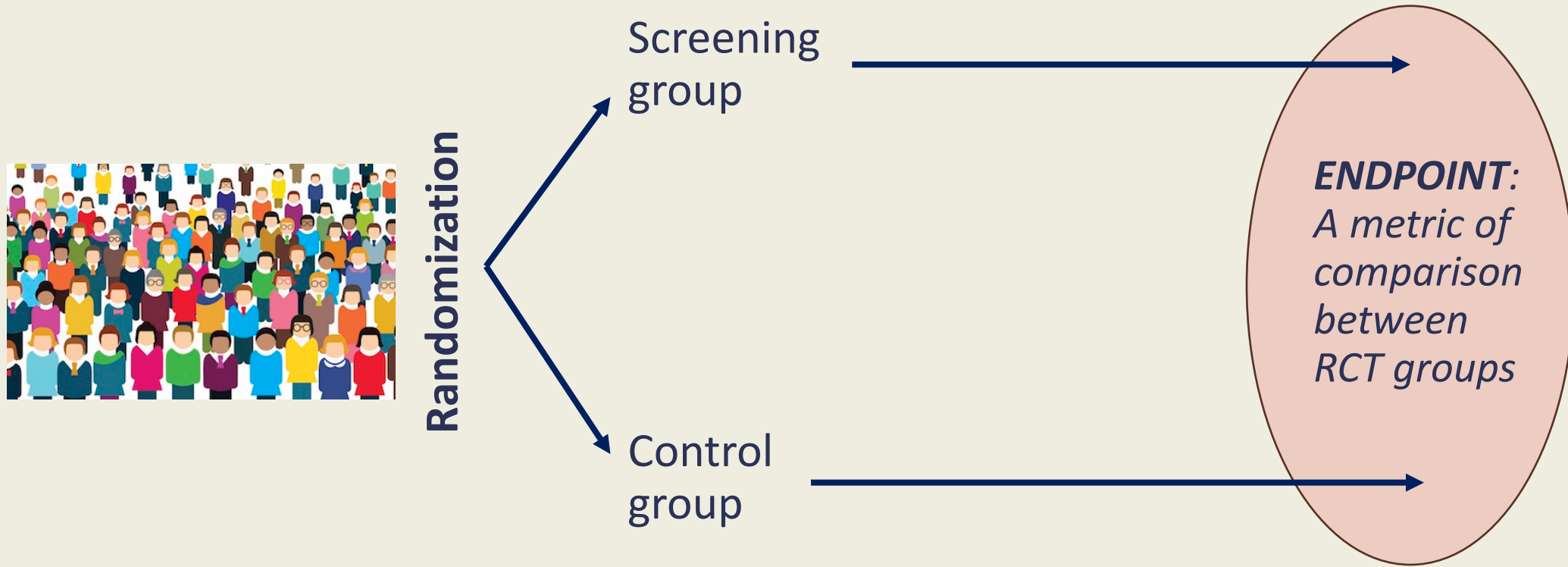
# Disclosures

I have no conflicts of interest.

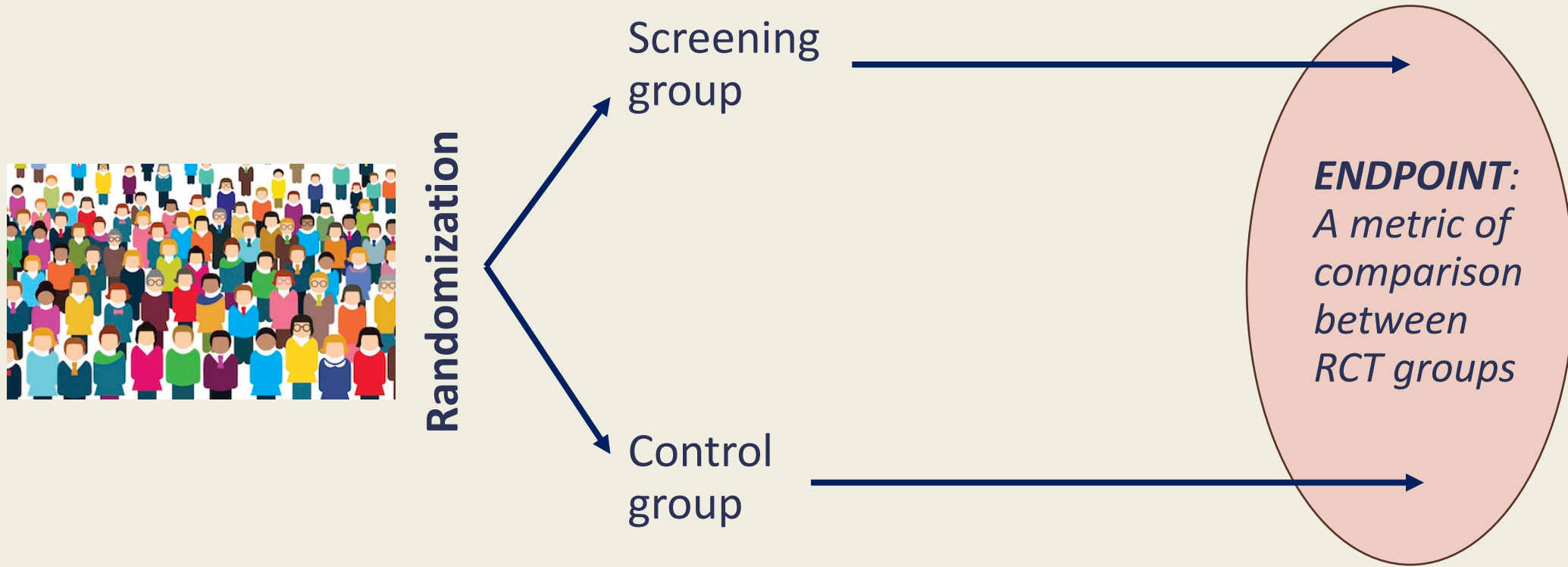
# Endpoints in randomized clinical trials of cancer screening



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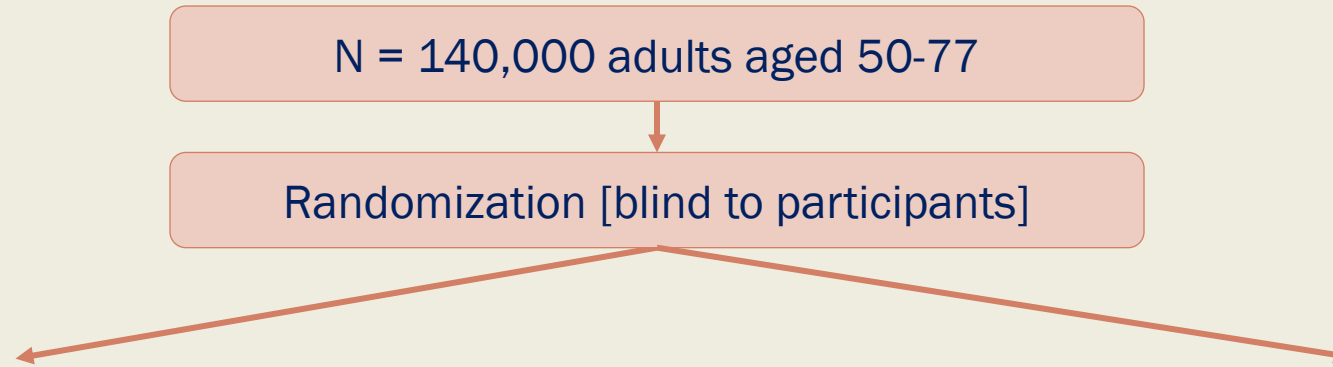


# Endpoints in randomized clinical trials of cancer screening

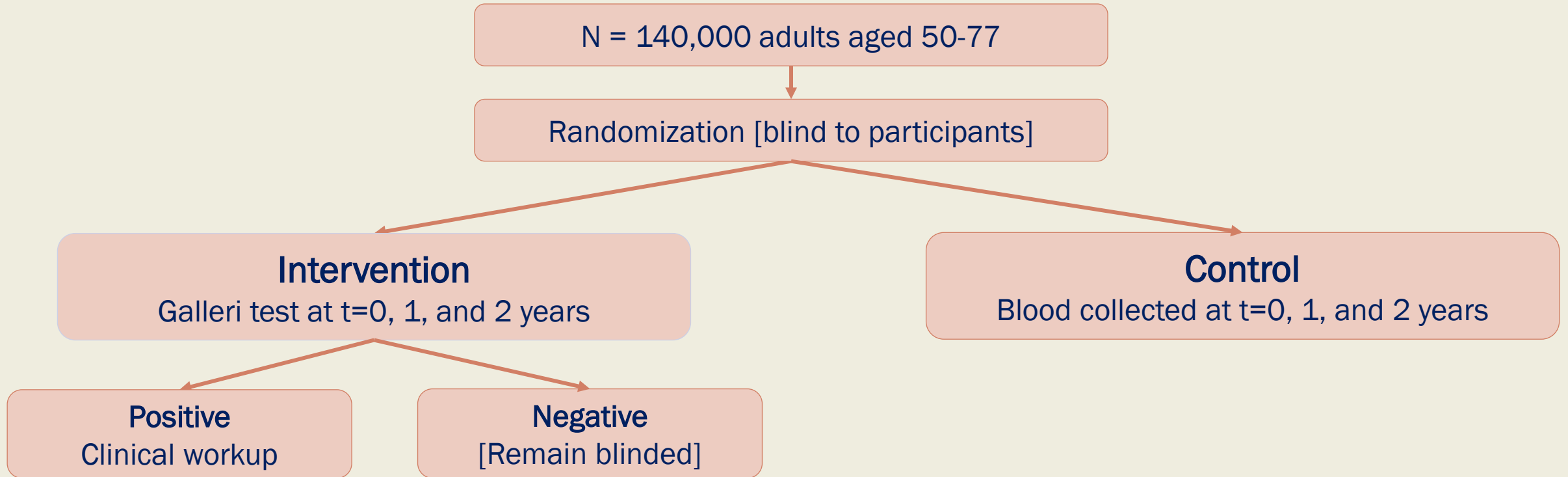


- **Gold standard endpoint:** Relative reduction in rate of cancer-specific mortality
- **Leading 'alternative' endpoint:** Relative reduction in rate of late-stage cancer
- Absolute reductions can also be considered – but vary strongly over follow-up time

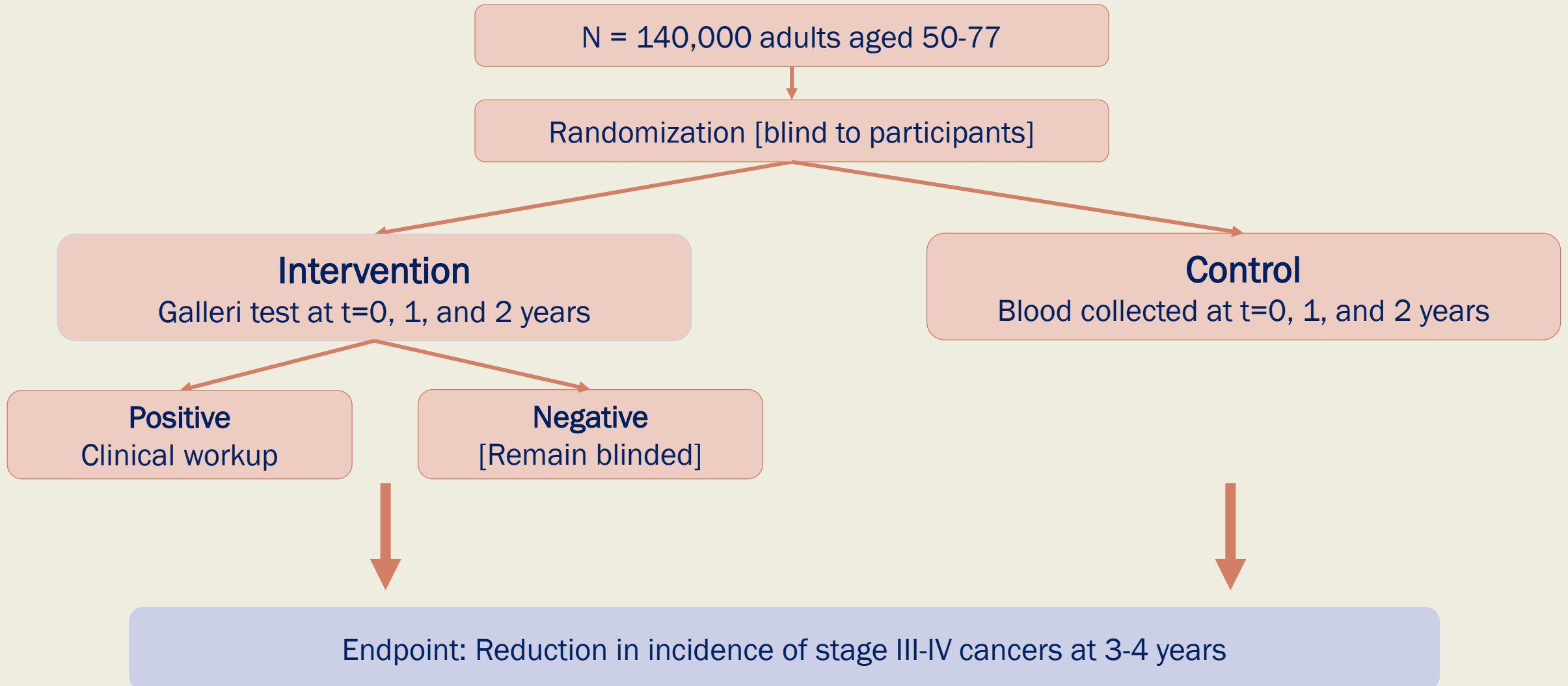
# Design of the NHS-Galleri Study (England)



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# Learning from prior screening trials:

## Comparison of stage and mortality endpoints

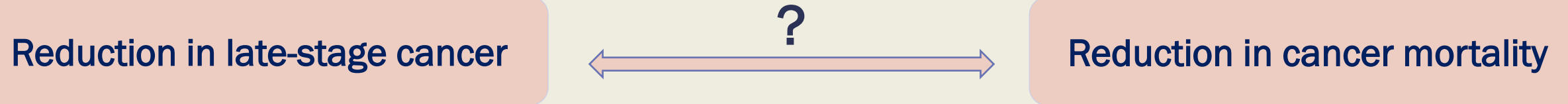
Reduction in late-stage cancer



Reduction in cancer mortality

# Learning from prior screening trials:

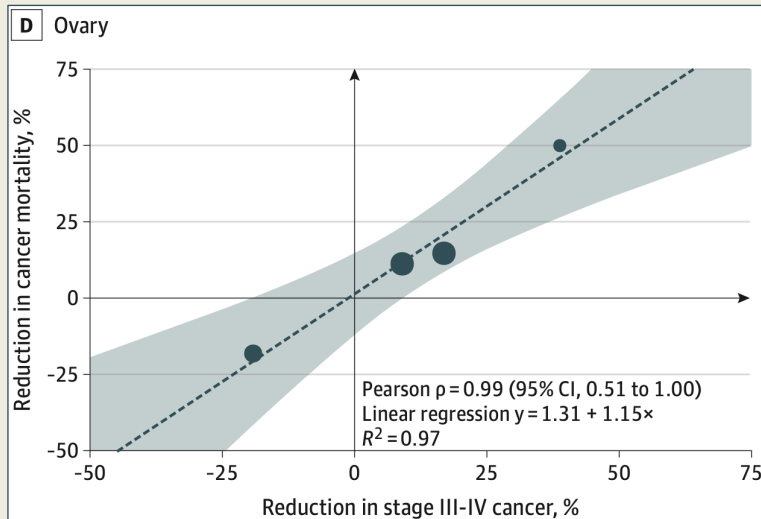
## Comparison of stage and mortality endpoints



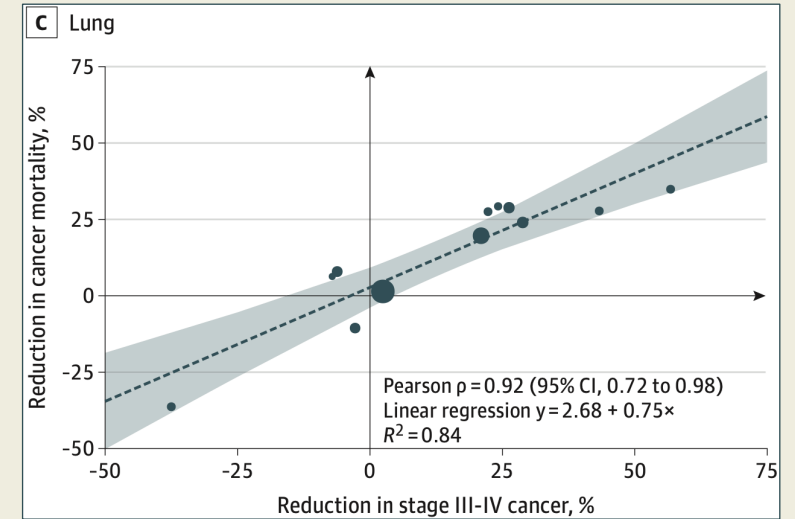
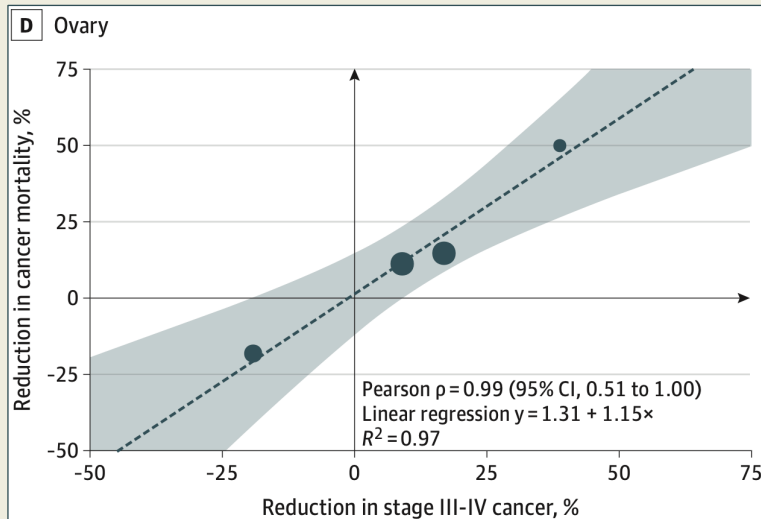
1. **Correlation:** does the reduction in late-stage cancer closely associate with the reduction in cancer mortality?
2. **Slope:** does reduced late-stage cancer imply a similar amount of reduced cancer mortality?

# Comparison of stage and mortality endpoints for screening: Reduction in stage III-IV cancer

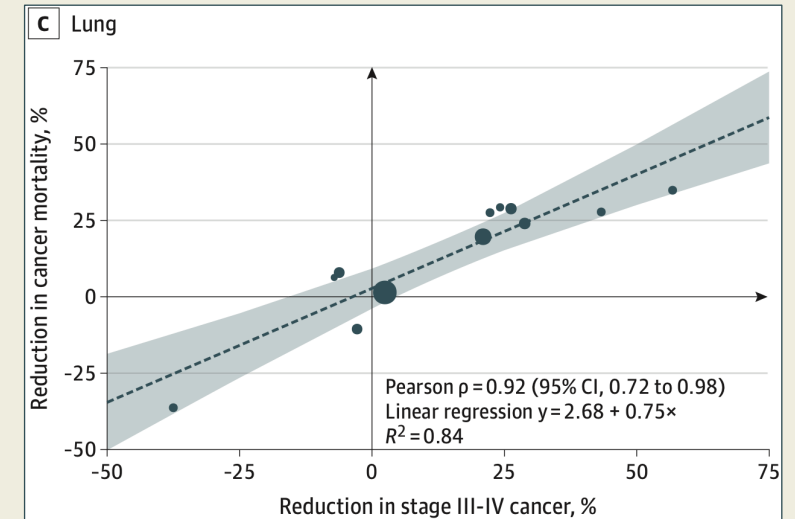
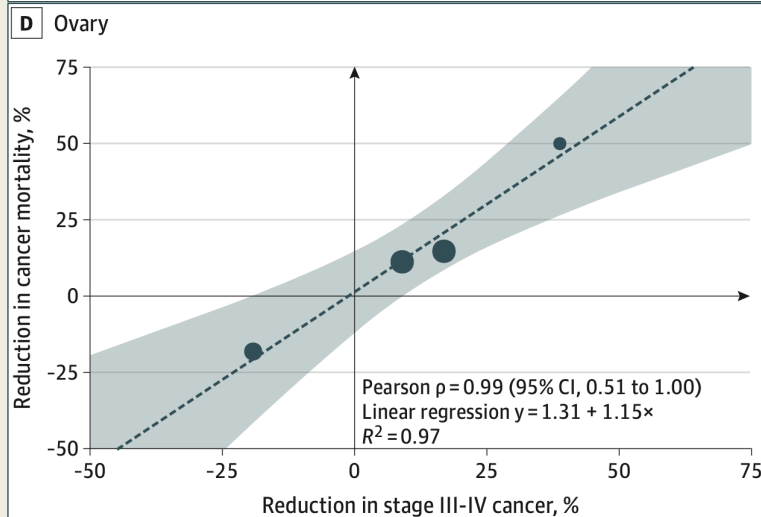
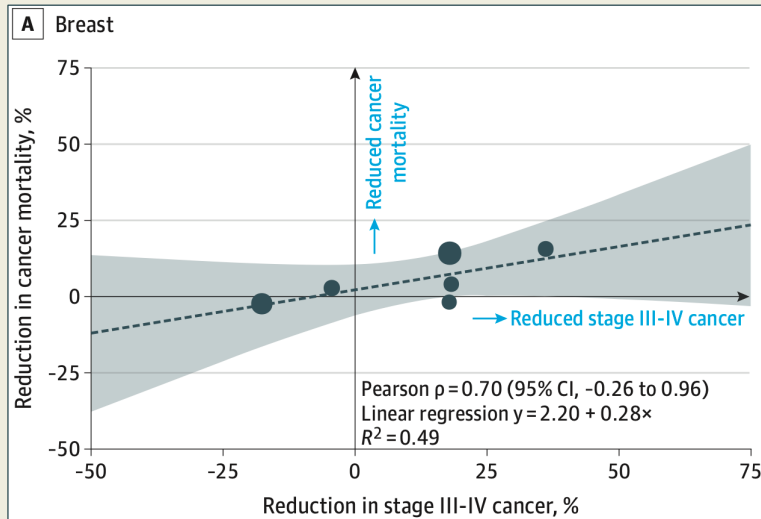
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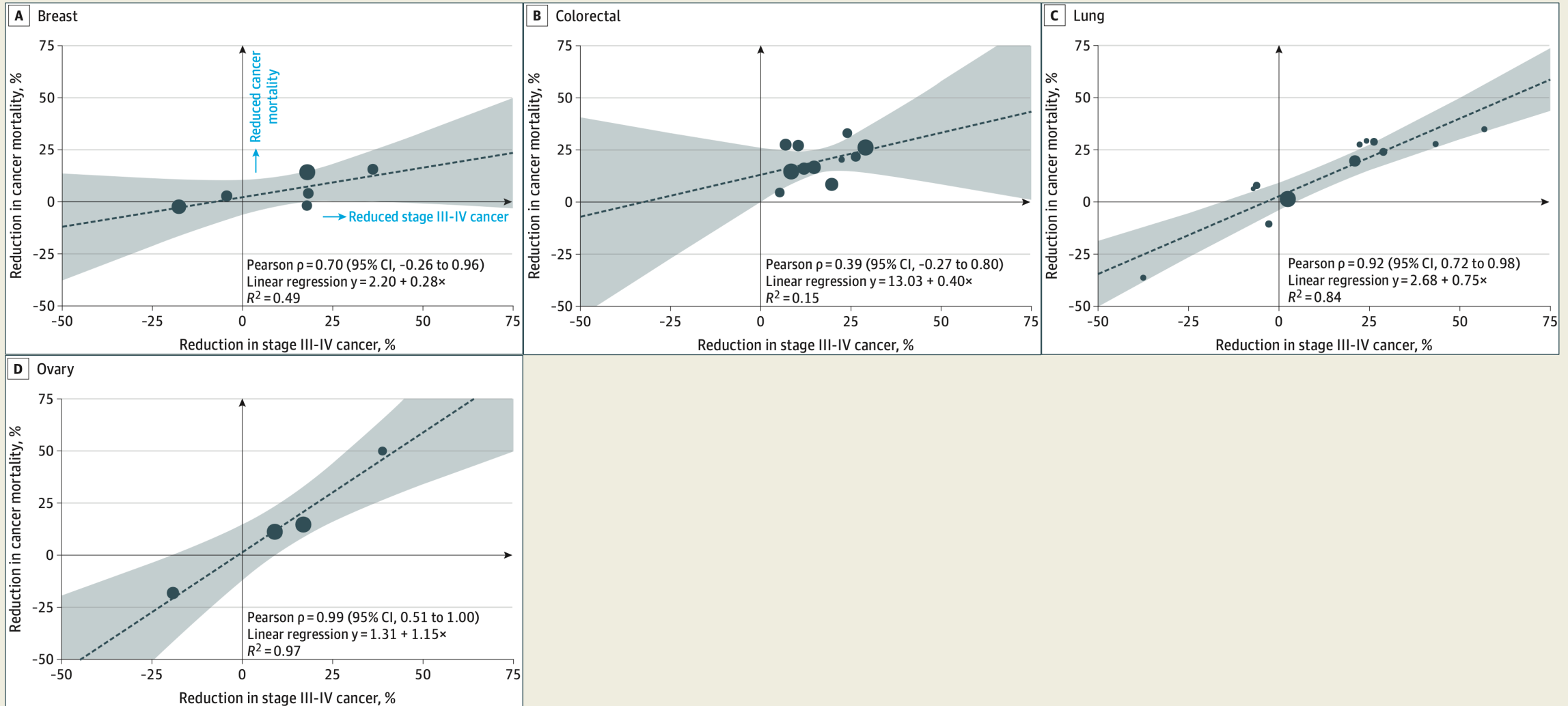
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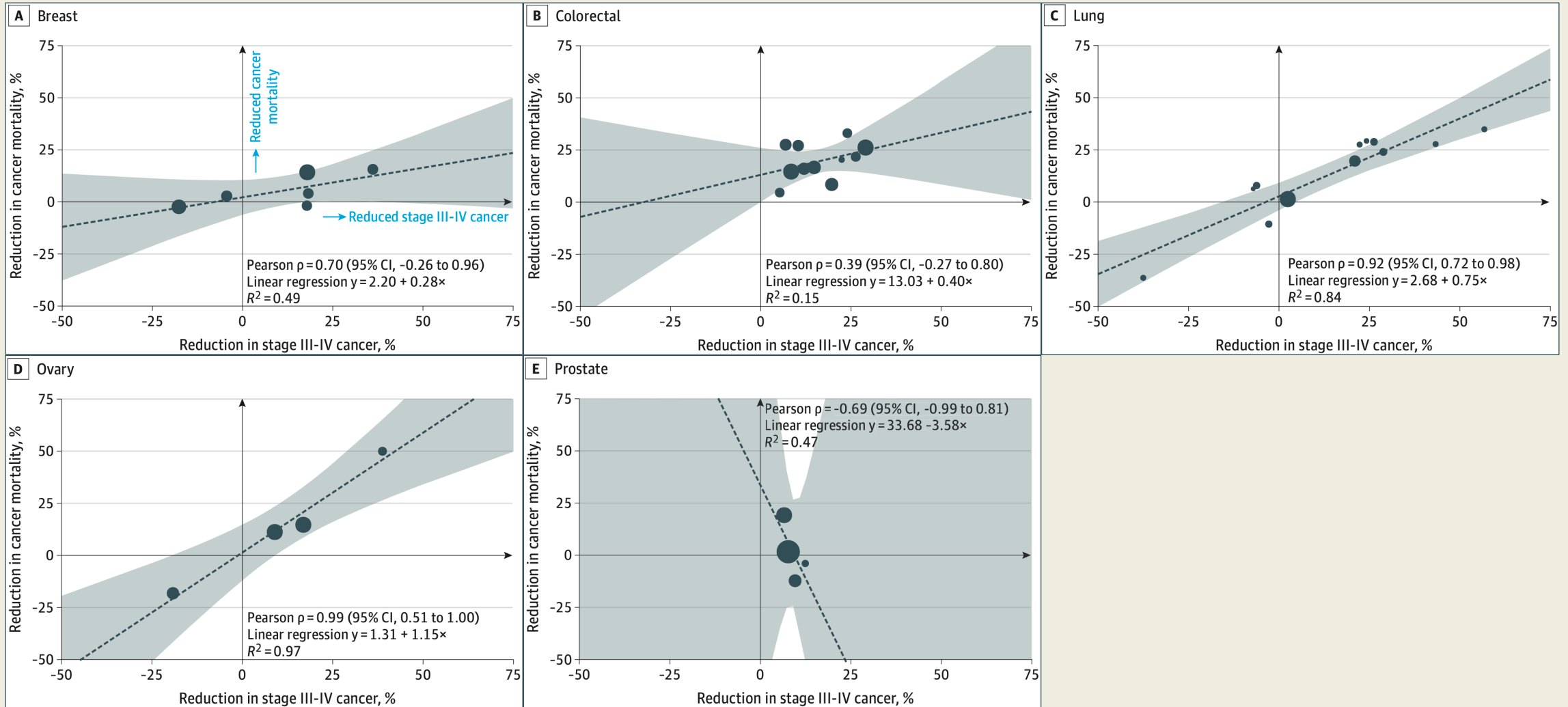
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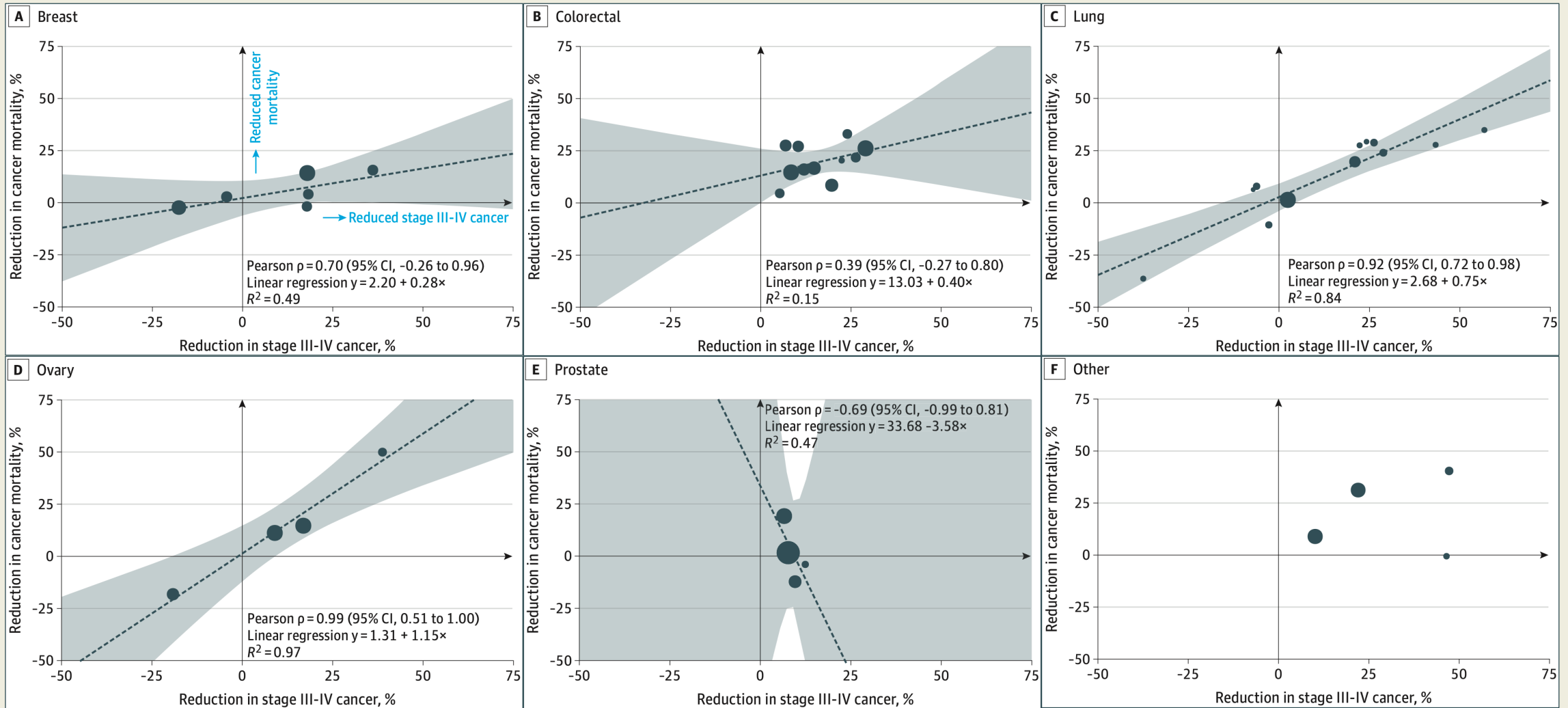


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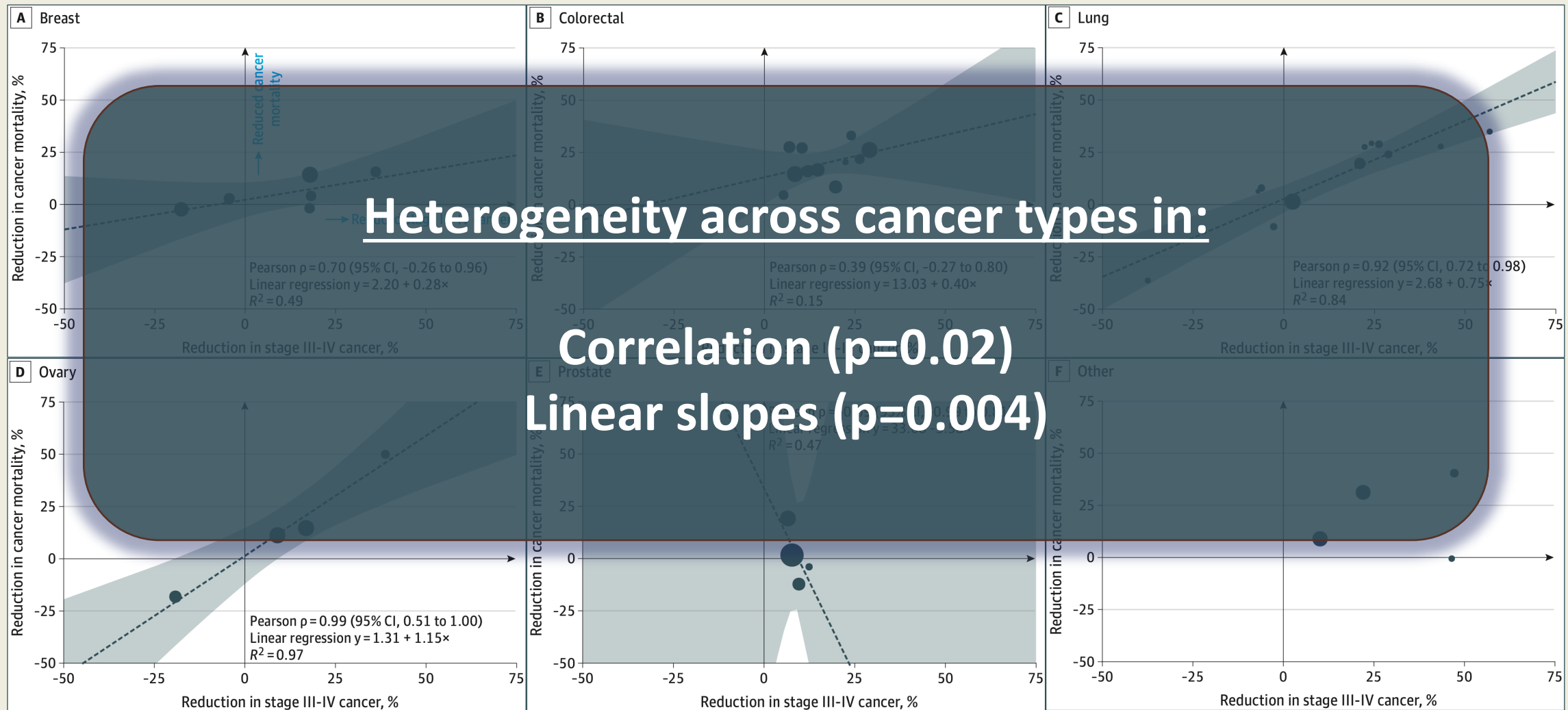




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# “Sticky” aspects for MCD trial endpoints

- Cancers detectable by cfDNA-based MCD tests have lower survival
- Some screening tests prevent cancer from occurring
- Improvements in cancer treatment over time produce changes in stage-specific survival
- False reassurance – only observable with return of negative results

# Caution is required when using alternative endpoints in place of cancer-specific mortality

Is late-stage cancer a suitable alternative endpoint to cancer mortality in screening RCTs?

→ *It depends on the cancer type*

→ *For many cancer types, we have no idea*

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If a multi-cancer detection test reduces late-stage cancer, can we draw a conclusion about its effect on cancer mortality?

→ *Probably not*



# It takes a village

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