ePCT Design

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Learning goals

- Identify common experimental designs and randomization schemes in ePCTs
- Understand the importance of monitoring adherence and fidelity
- Discuss design considerations to ensure delivery of actionable evidence, including why ePCTs are well-suited to evaluating implications of innovative technologies for clinical care delivery
- Provide an overview of effectiveness-implementation hybrid trial designs

Design Considerations

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Three kinds of randomized trials

- Traditional randomized controlled trials (RCTs)
- Individual randomized group treatment (IRGT) trials
- Cluster randomized trial (CRTs)
  - Parallel CRT
  - Stepped-wedge CRT

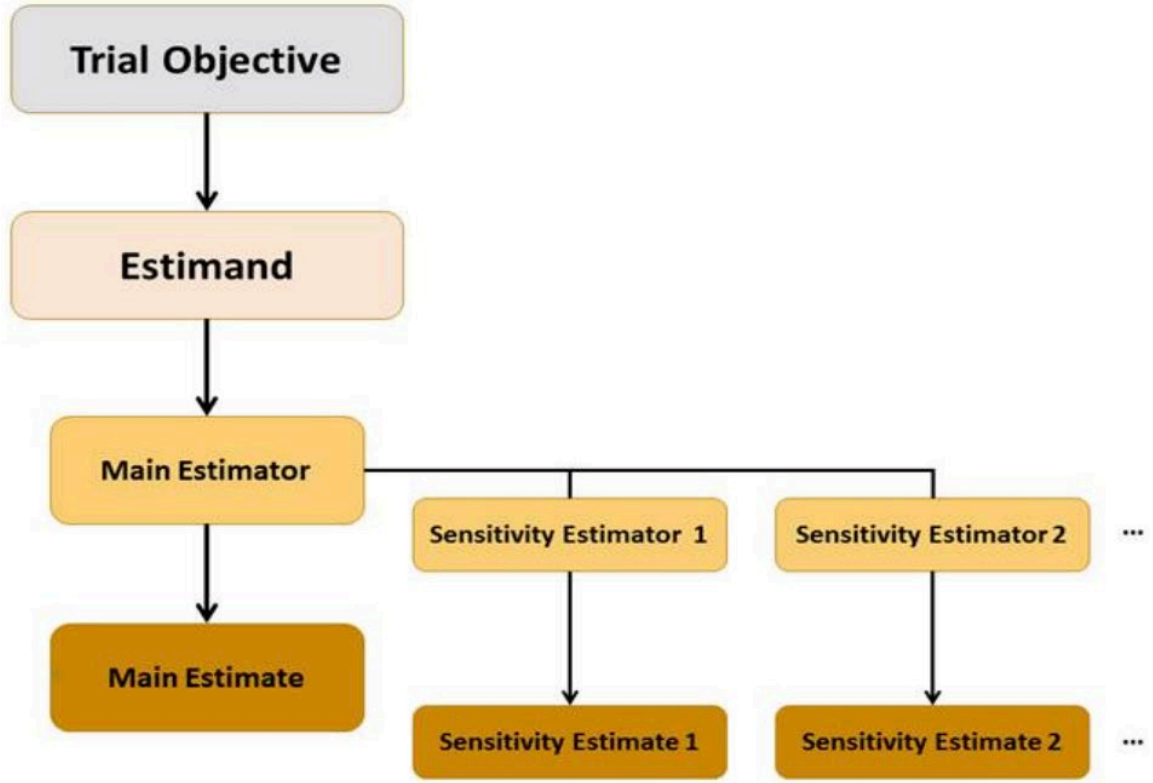
Methods for pragmatic trials

- As with traditional RCTs:
  - State a hypotheses
  - Prespecify the analyses
  - Calculate the sample size needed for desired power
  - Consider restricted randomization (such as stratified randomization)
  - Determine what data on participant characteristics will be collected
  - Anticipate sources of heterogeneity
- The trial design you choose will depend on the research question and how the intervention will be delivered

Start with a clear research question

Elements of a research question:

- **P**opulation
- **I**ntervention
- **C**omparisons
- **O**utcomes
- **T**iming
- **S**etting



Source: European Medicines Agency, ICH E9 (R1): Aligning target of estimation, method of estimation, and sensitivity analysis, for a given trial objective

Important things to know

Studies that randomize groups, or deliver interventions to groups, face special design and analytic challenges

Failure to address challenges of outcome clustering in design and analysis will result in an underpowered study and/or invalid inferences

Appropriate designs and analytic methods are the only way to advance the science

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OPTIMUM, an NIH Collaboratory Trial

Optimum
Optimizing Pain Treatment
in Medical Settings
Using Mindfulness

Optimizing Pain Treatment In Medical Settings Using Mindfulness (OPTIMUM)

- Intervention: Group-based, mindfulness-based stress reduction to reduce pain and opioid use
- Population: 450 adults with chronic low back pain
- Unit of randomization: individual
- Group-based online intervention; groups must be formed by study team; postrandomization interactions between participants
- **Individually randomized group treatment (IRGT) trial**, because post-randomization groupings potentially induce correlated outcomes

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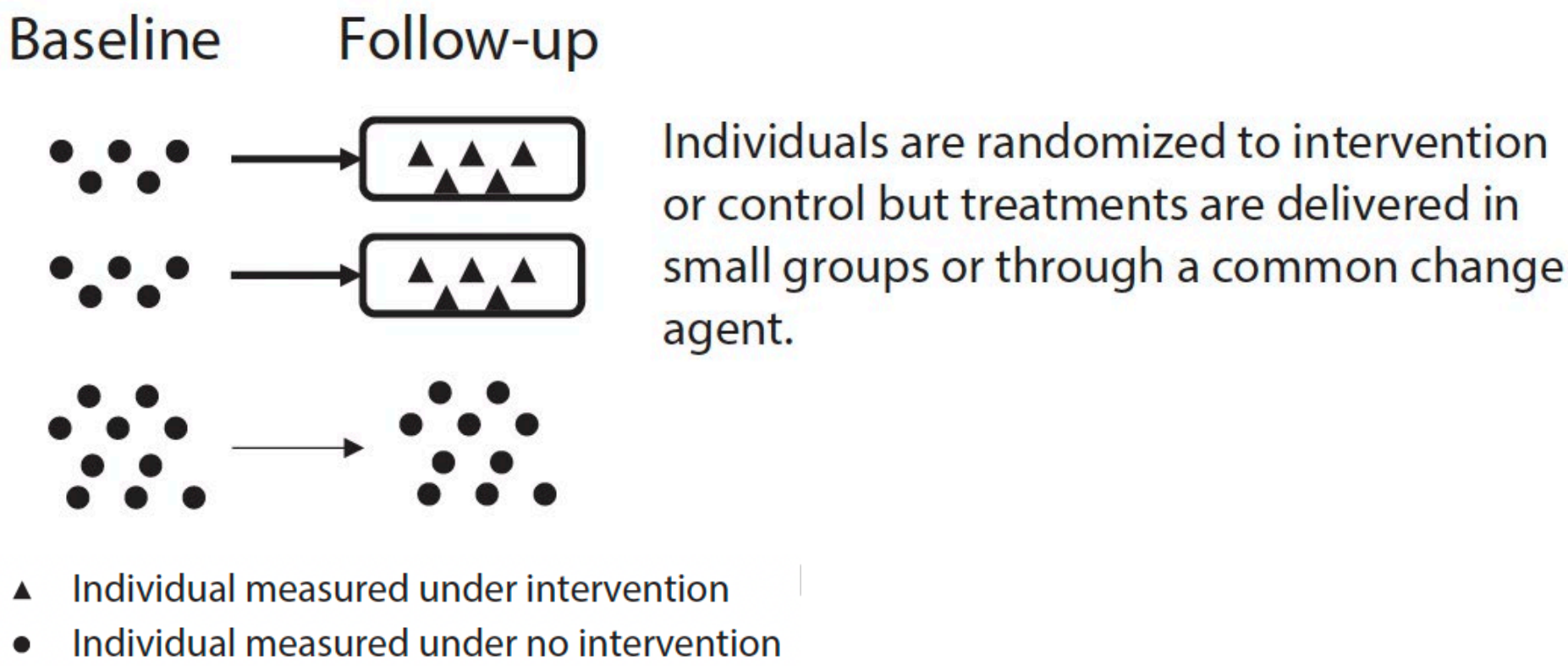
IRGT trial design in OPTIMUM



From Turner et al. *Am J Public Health*. 2017;107(6).

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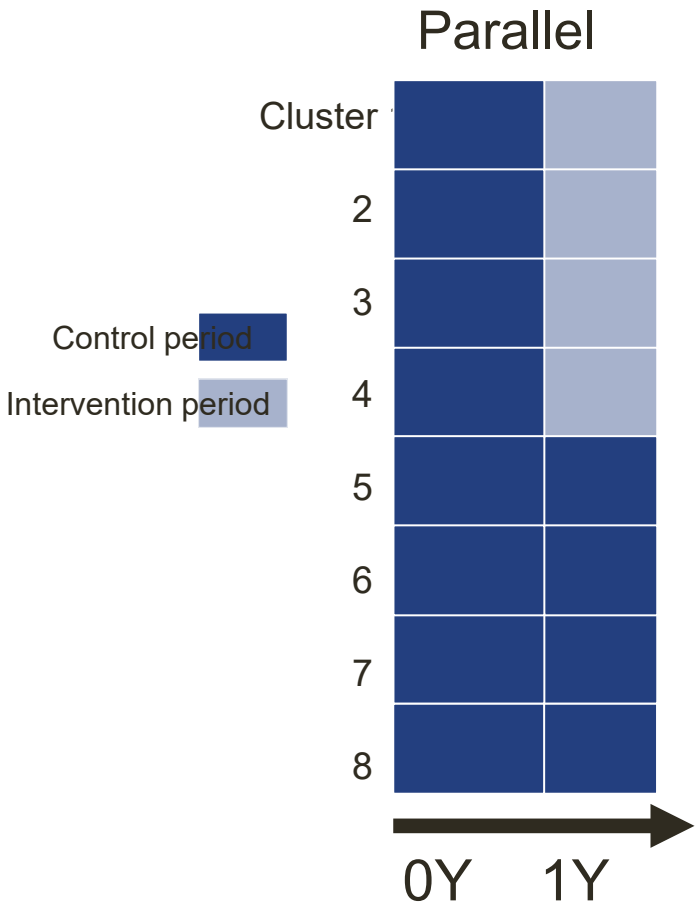
In this example:
- 8 clusters
- 1-year intervention



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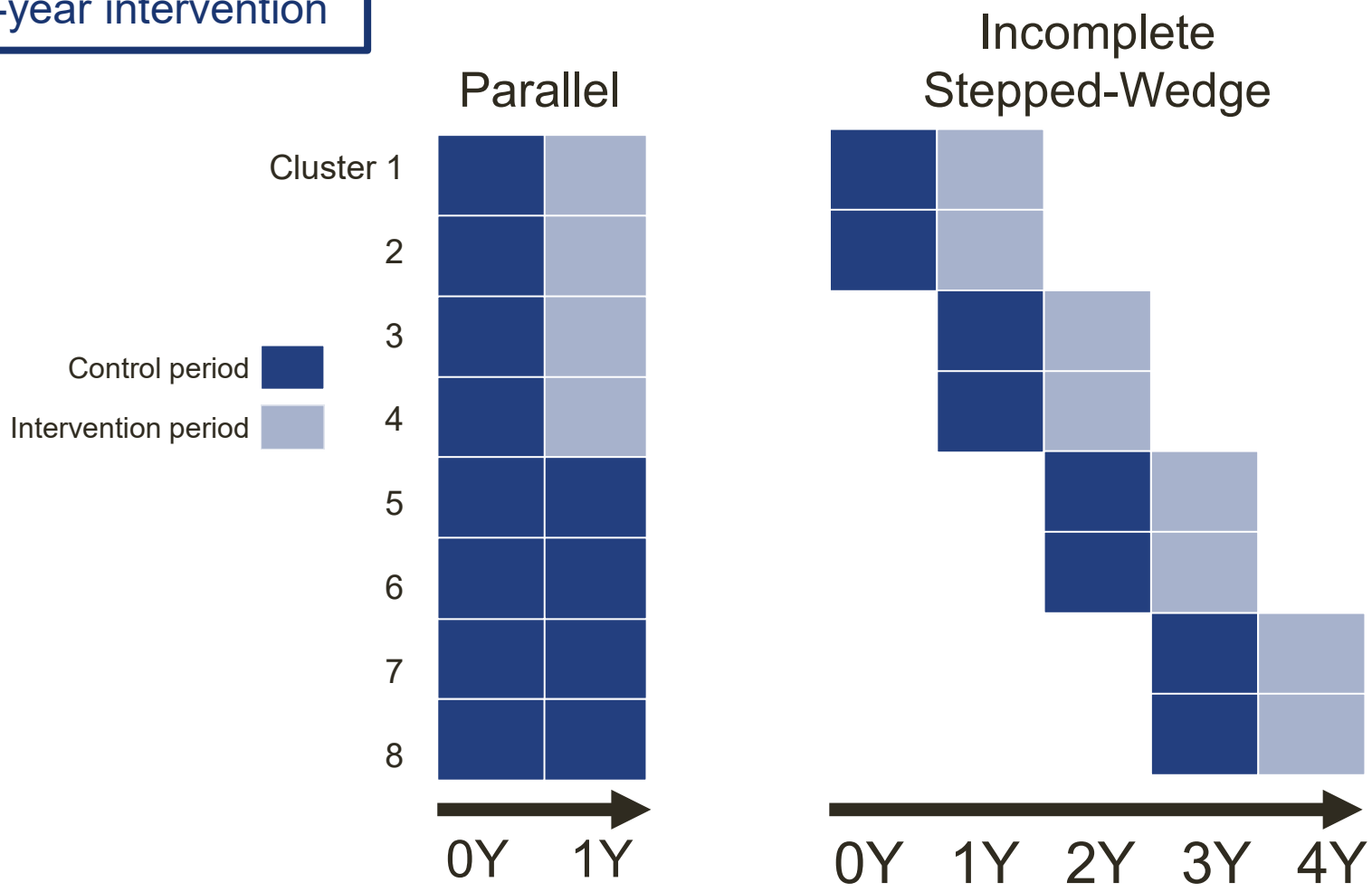

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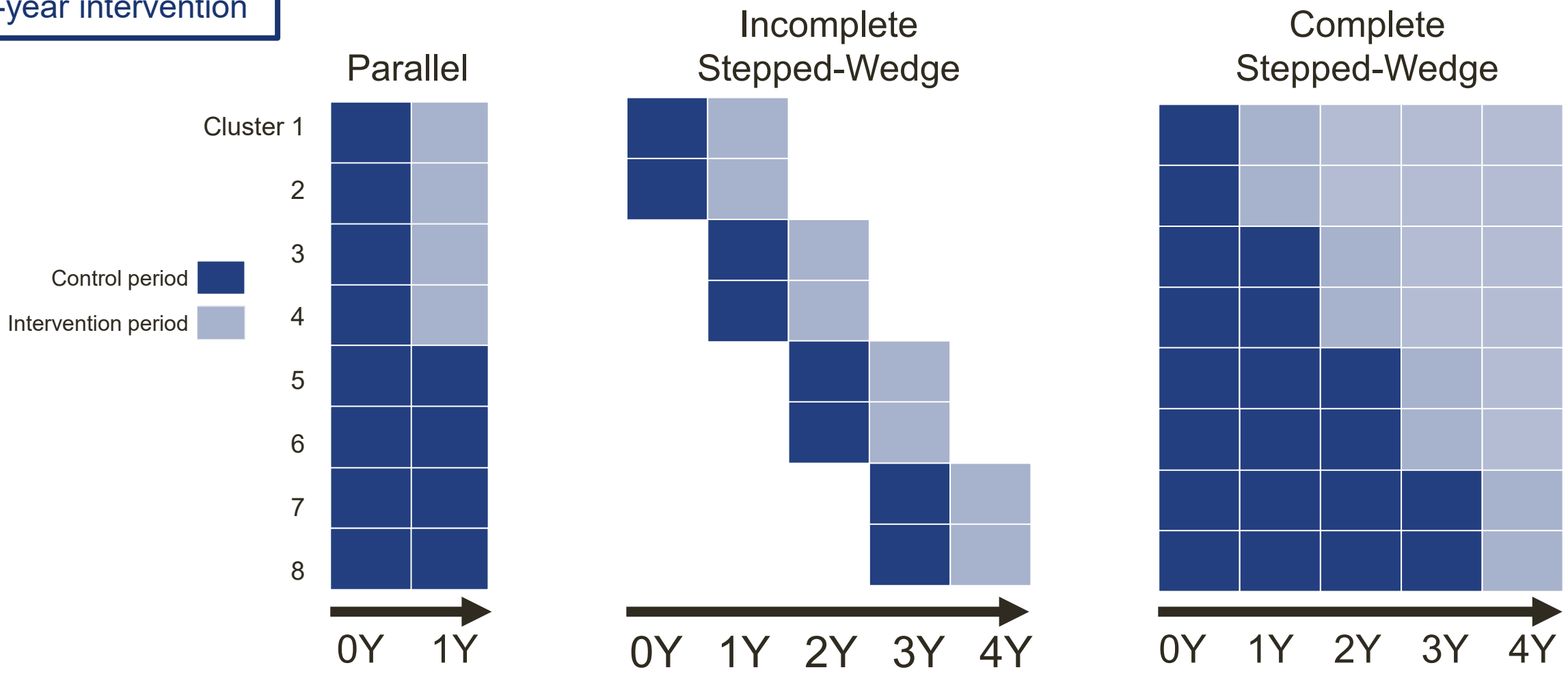

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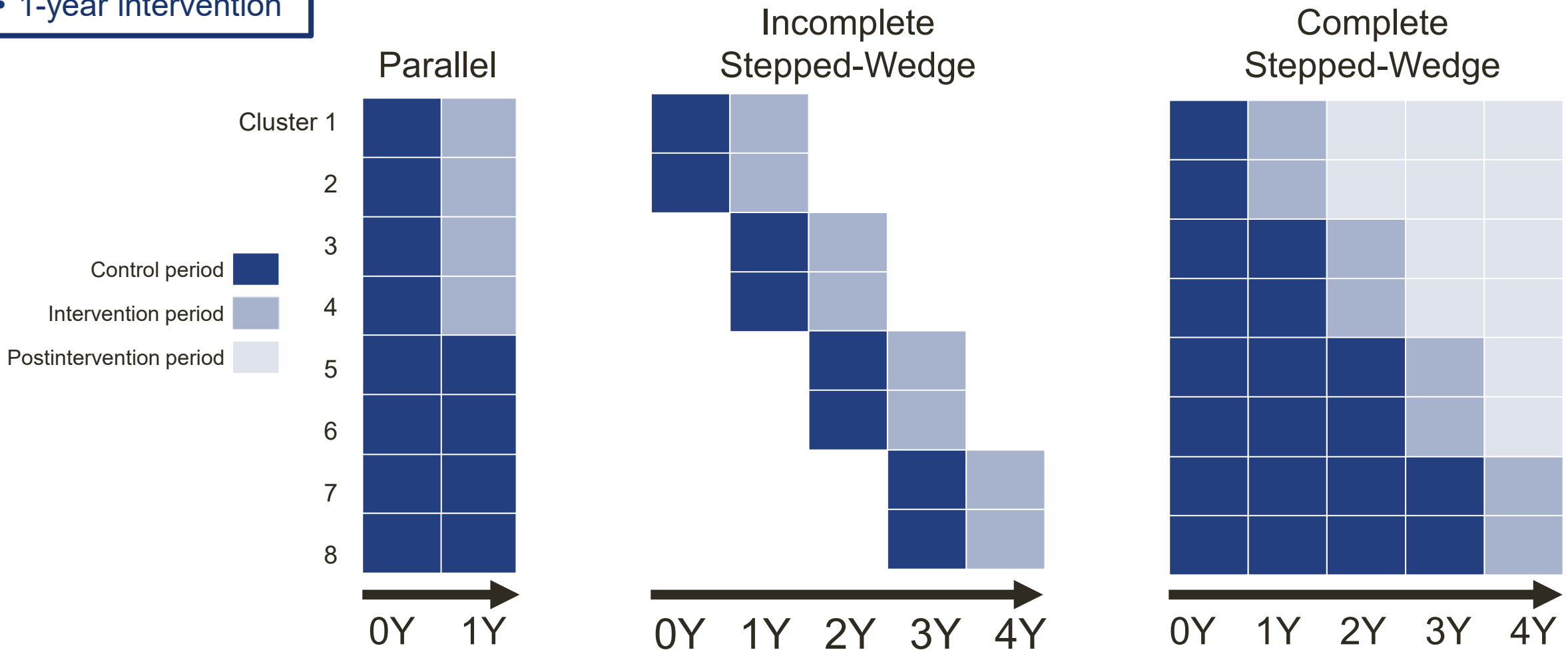

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STOP CRC, an NIH Collaboratory Trial

stop screen to prevent colon cancer

Strategies and Opportunities to Stop Colorectal Cancer in Priority Populations (STOP CRC)

- Population: More than 40,000 patients at 26 clinical sites
- Intervention: Healthcare system–based program to improve rates of colorectal cancer screening
- Unit of randomization: clinic
- Two-arm **cluster randomized trial (CRT)**

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Reasons to randomize clusters instead of individuals

- The intervention targets healthcare units rather than individuals

Healthcare Units

Individuals

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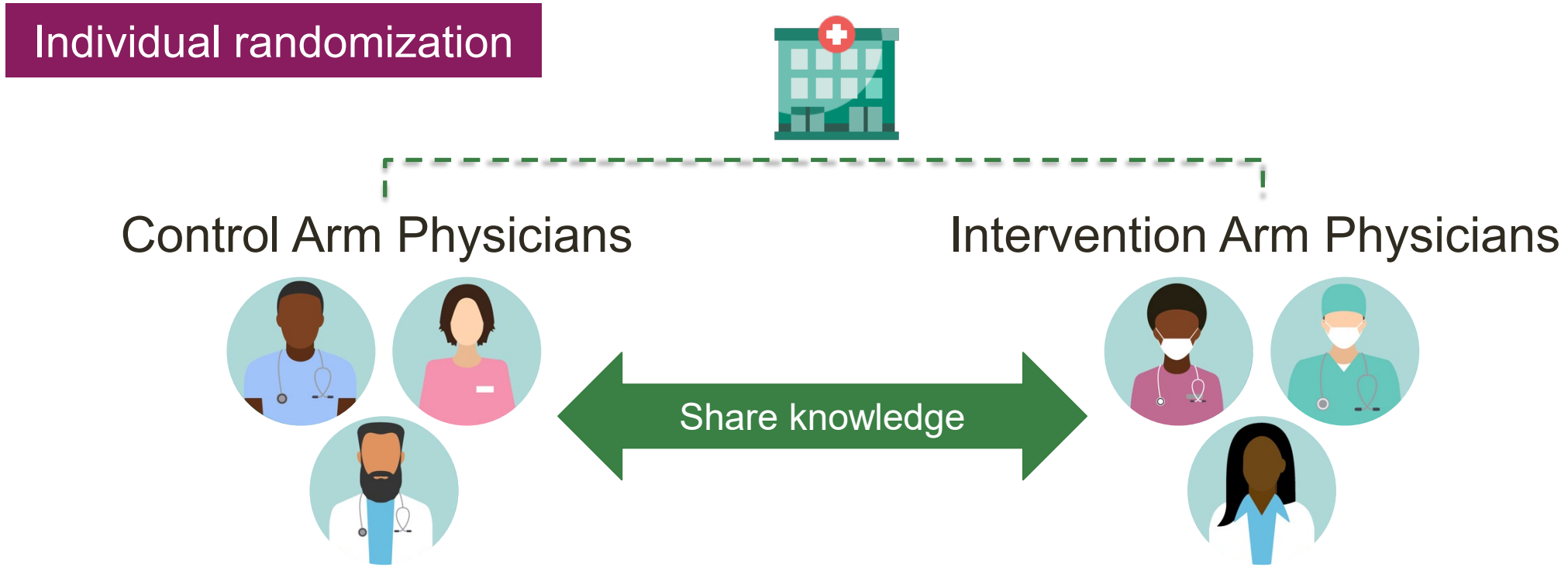
Reasons to randomize clusters instead of individuals

- The intervention targets individuals, but there is risk of contamination



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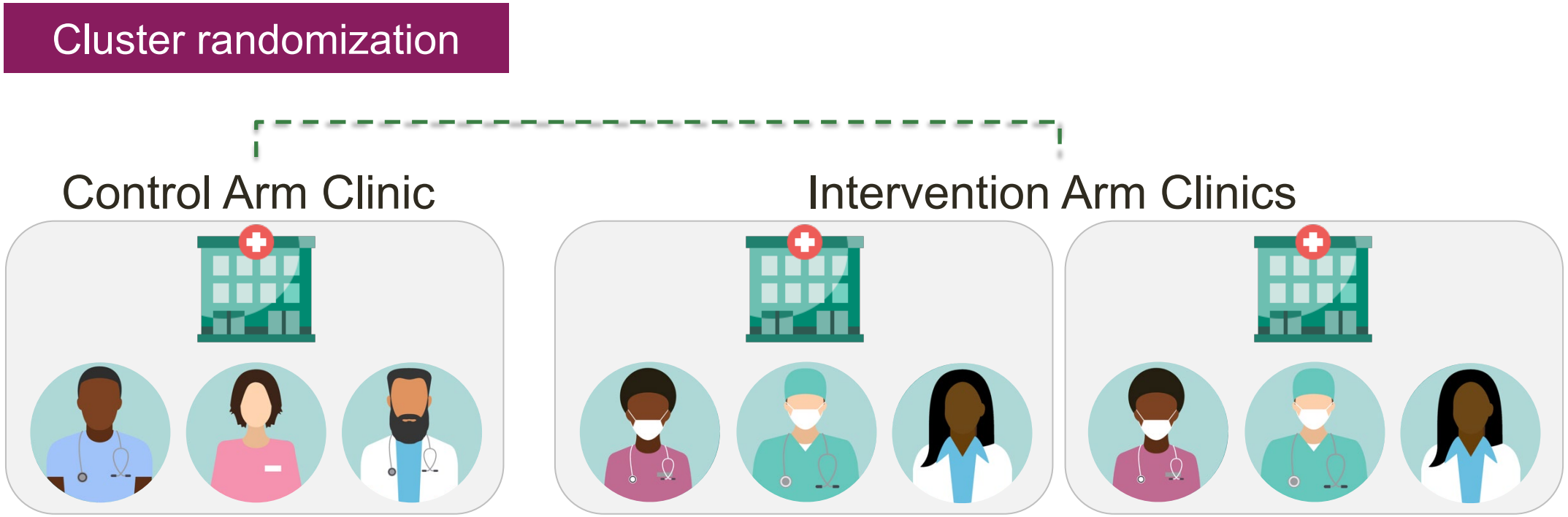

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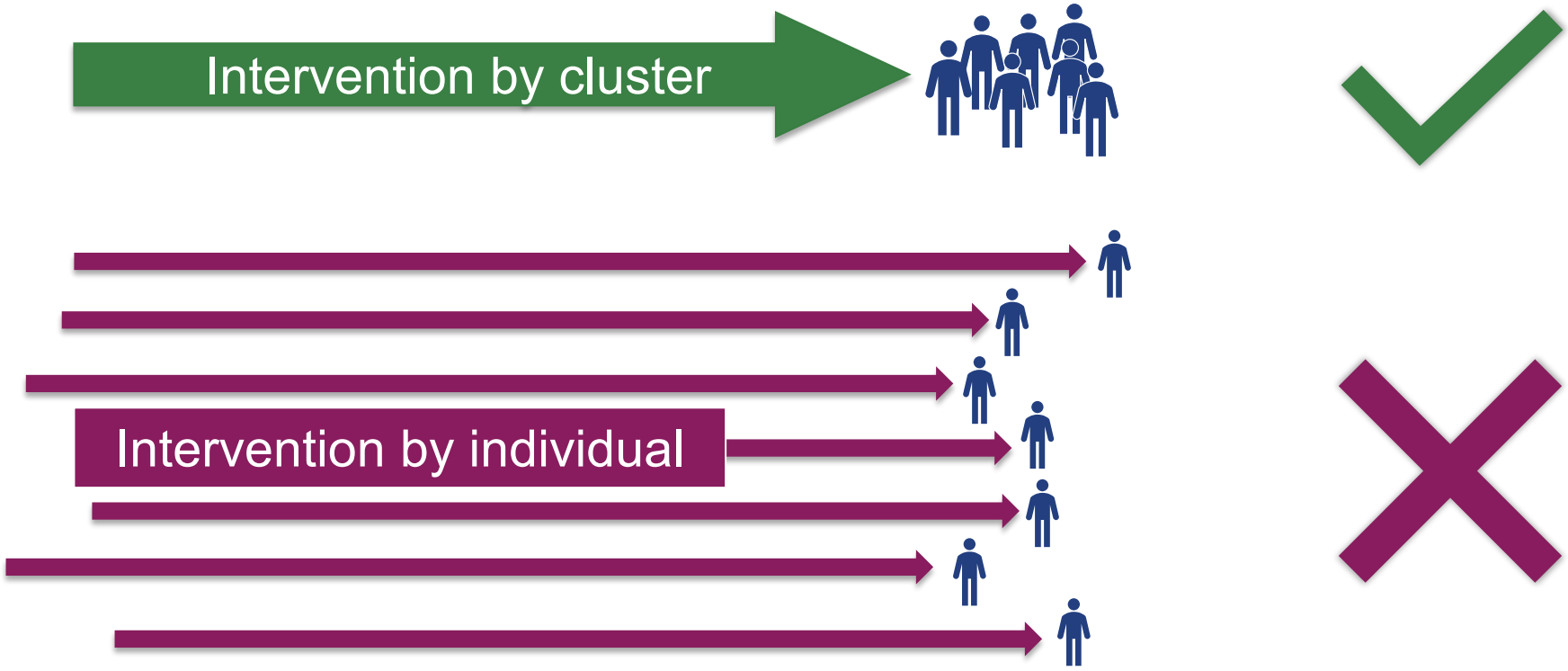
Reasons to randomize clusters instead of individuals

- Logistically easier to implement the intervention by cluster



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Cluster randomization in the STOP CRC trial

stop screen to prevent colon cancer

Target population	40,000 patients across 26 clinical sites
Intervention	Health system–based program to improve colorectal cancer screening rates

Cluster

Cluster

Cluster

Level 2

Randomize at the level of the clinic

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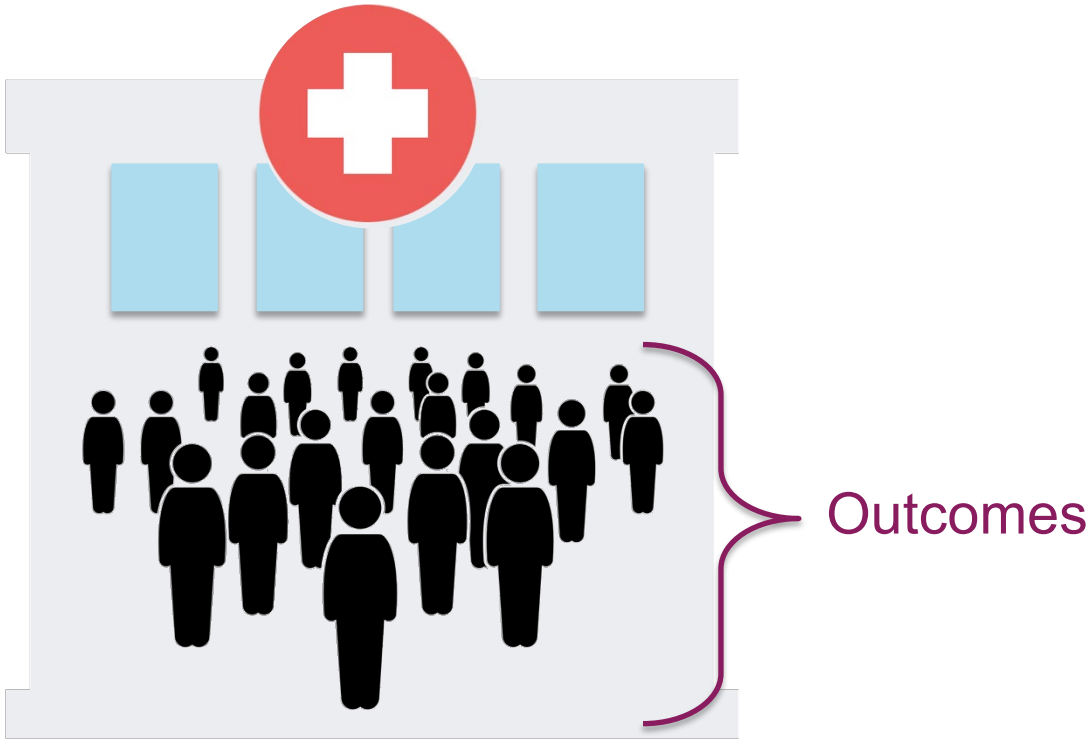

Level 1

Patient-level outcomes are nested within the clinic

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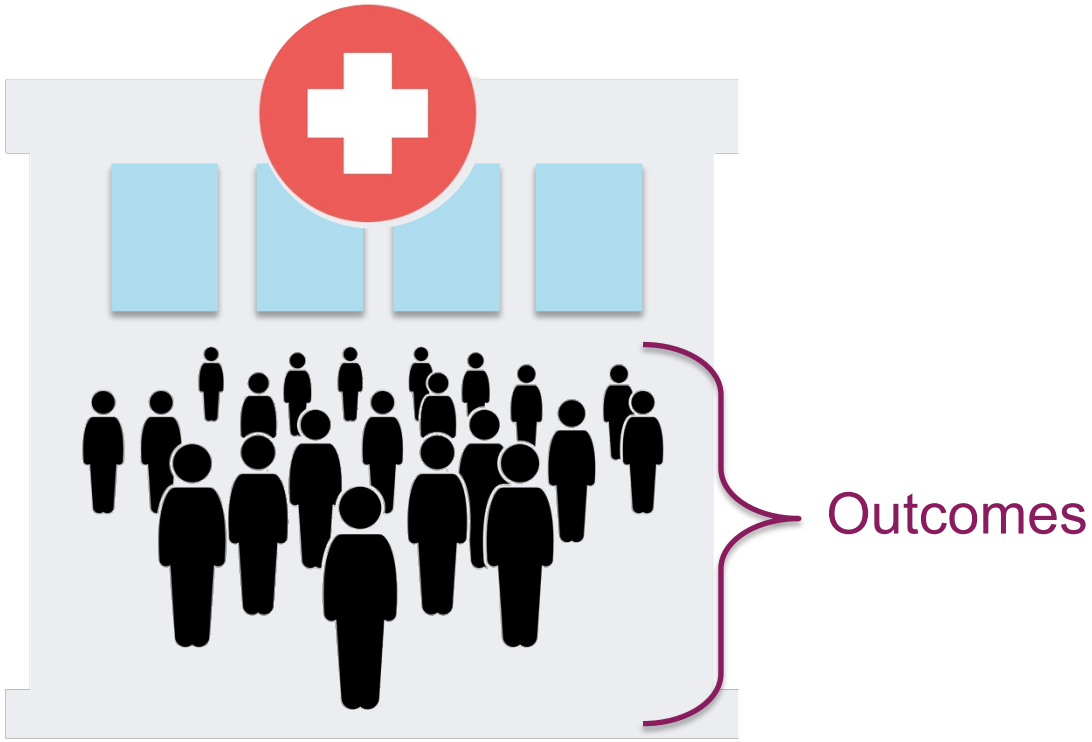

STOP CRC outcomes

Did the patients agree to be screened for colorectal cancer?

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stop
screen to prevent
colon cancer

Individual outcomes within the same clinic are expected to be correlated

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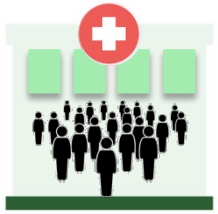
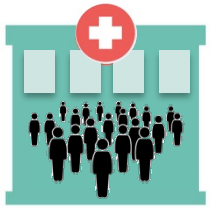
Clustering = Outcome Clustering



Outcomes

Outcomes



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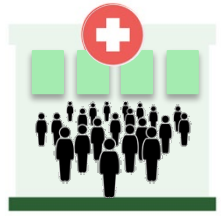

Outcomes

Outcomes

stop
screen to prevent
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STOP CRC outcomes

Did the patient agree to be screened for colorectal cancer?

Binary outcome

Yes

No

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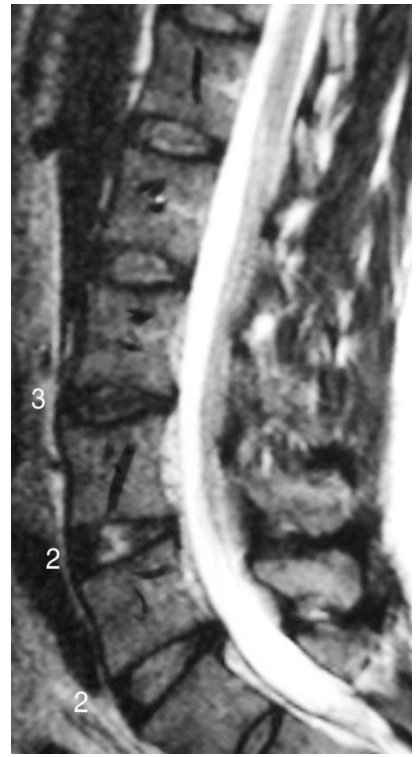
LIRE, an NIH Collaboratory Trial

Lumbar Imaging With Reporting of Epidemiology (LIRE)

- Population: 250,401 patients in 98 primary care clinics in 4 large healthcare systems
- Intervention: Insert benchmark information about common imaging findings in lumbar spine imaging reports to reduce spine-related healthcare utilization
- Unit of randomization: clinic
- All clinics will eventually receive intervention
- **Stepped-wedge CRT**



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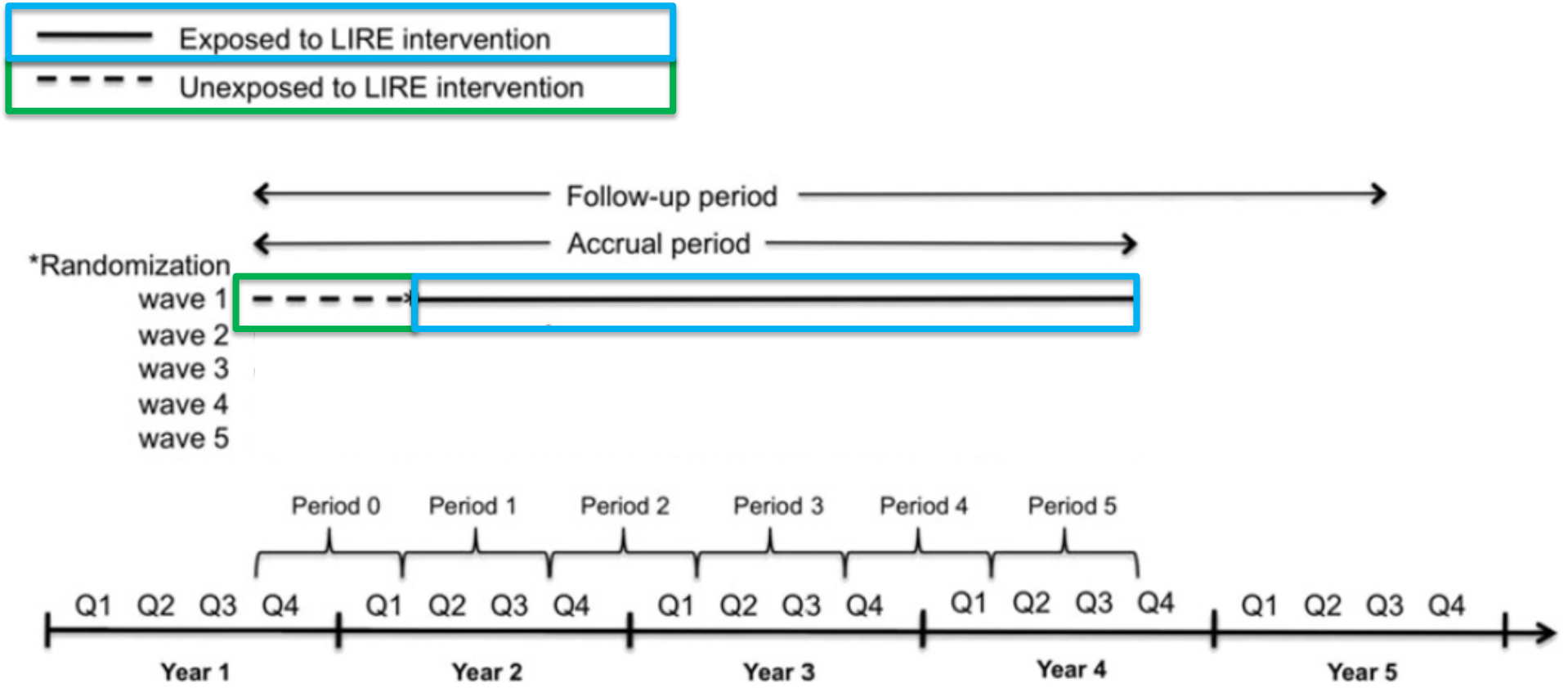
Design of LIRE trial



Source: Jarvik JG et al. *Contemp Clin Trials*. 2015;45(Pt B):157-163.

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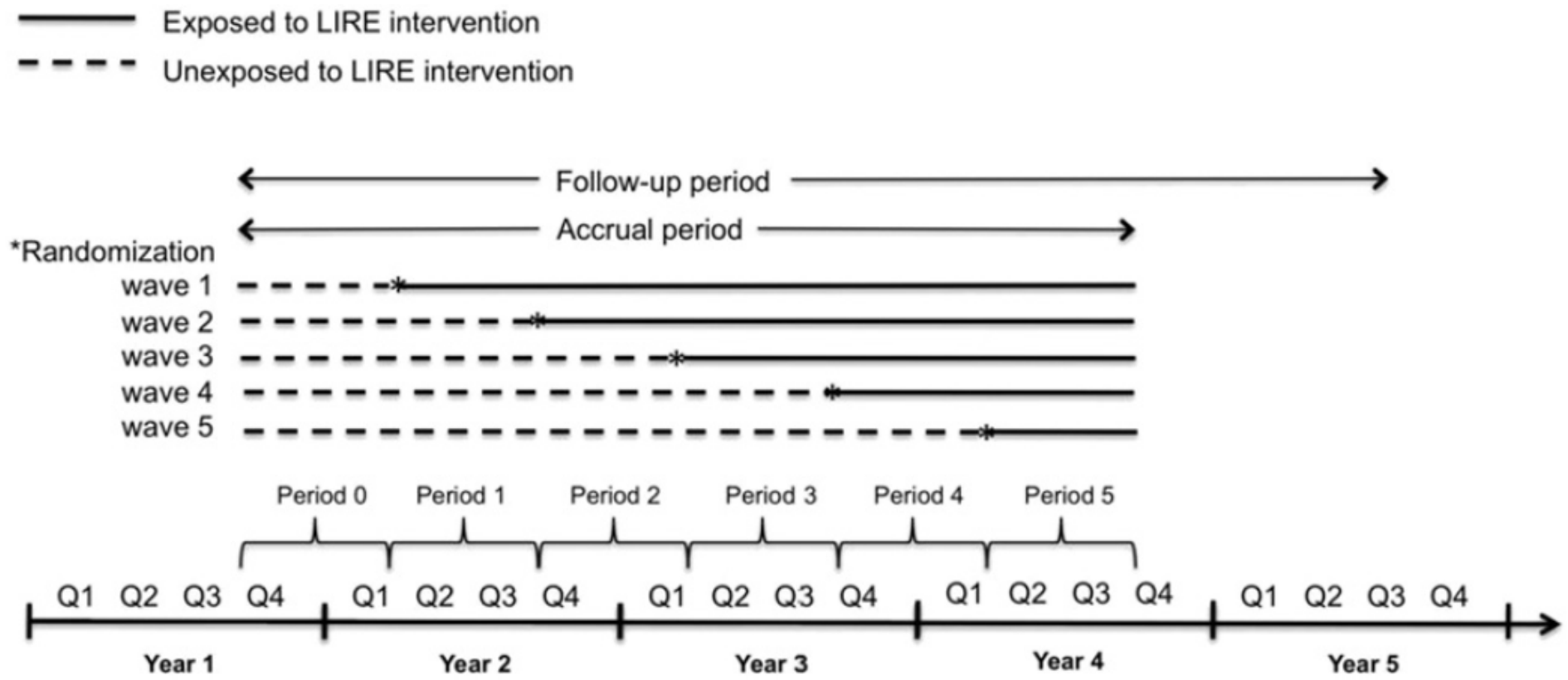

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Knowledge checkpoint

- Researchers are interested in the effect of participation in support groups vs usual care on weight loss. The intervention involves attending group meetings, while usual care involves no group meetings. Out of 20 enrolled participants, 10 are randomly assigned to the intervention and attend support groups. Two therapists each lead a support group that meets on different weekday nights. Participants' BMI will be measured at baseline (before randomization) and at 3 months.
  - What design is this trial?
  - Researchers powered this study assuming an randomized controlled trial with 20 participants. How is the power likely to change if the IRGT nature of the trial is properly accounted for?
  - What would be better approach to address correlated observations: Increase the caseloads of the 2 therapists, or increase the number of therapists leading support groups?

Q&A

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