Sponsored by the National Institutes of Health Common Fund

Design & Analysis of Embedded

Pragmatic Clinical Trials

Panel 2:
To Cluster or Not to Cluster?

NIH Collaboratory *Rethinking Clinical Trials®*

Health Care Systems Research Collaboratory

Improving Chronic Disease Management with Pieces: ICD-Pieces

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Intervention and Outcomes

PIECES
(Information Technology)

Practice Facilitators

Primary Care Practices

Improved Outcomes
for Patients with CKD, Diabetes, and HTN

Reduced:

1. Hospitalizations
2. ED Visits
3. Readmissions
4. CV Events / Deaths

Trial Specific Problem:
Diverse Systems: Diverse Clusters

Parkland

Public Safety Net
Few Large Clinics

Texas Health Resources®

Private Nonprofit
Many Small Clinics

ProHealth PHYSICIANS

Private ACO
Many Small Clinics

U.S. Department of Veterans Affairs

Government Hospital
Few Large Clinics

Difficulties/ considerations

- Complex intervention delivered over time
- Risk of cross-contamination
- Cluster heterogeneity –
  - Impact on ICC
  - Sample size

Resolution : Practices

- Each Health System-> unique workflows
- Separate teams→ **practices**
- Unique patient panel cared for by team-no overlap
- Minimal risk of cross-contamination
- Practice facilitator can alert/ activate intervention
- Similar cluster size across all sites

PPACT:
Collaborative Care for Chronic Pain in Primary Care

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PPACT Overview

AIM: Integrate interdisciplinary services into primary care to help patients adopt self-management skills to:

- Manage chronic pain (decrease pain severity / improve functioning)
  - Limit use of opioid medication
  - Identify exacerbating factors amenable to treatment

Focus on feasibility and sustainability

DESIGN: Cluster (PCP)-randomized pragmatic clinical trial *(106 clusters, 273 PCPs, 850 patients)*

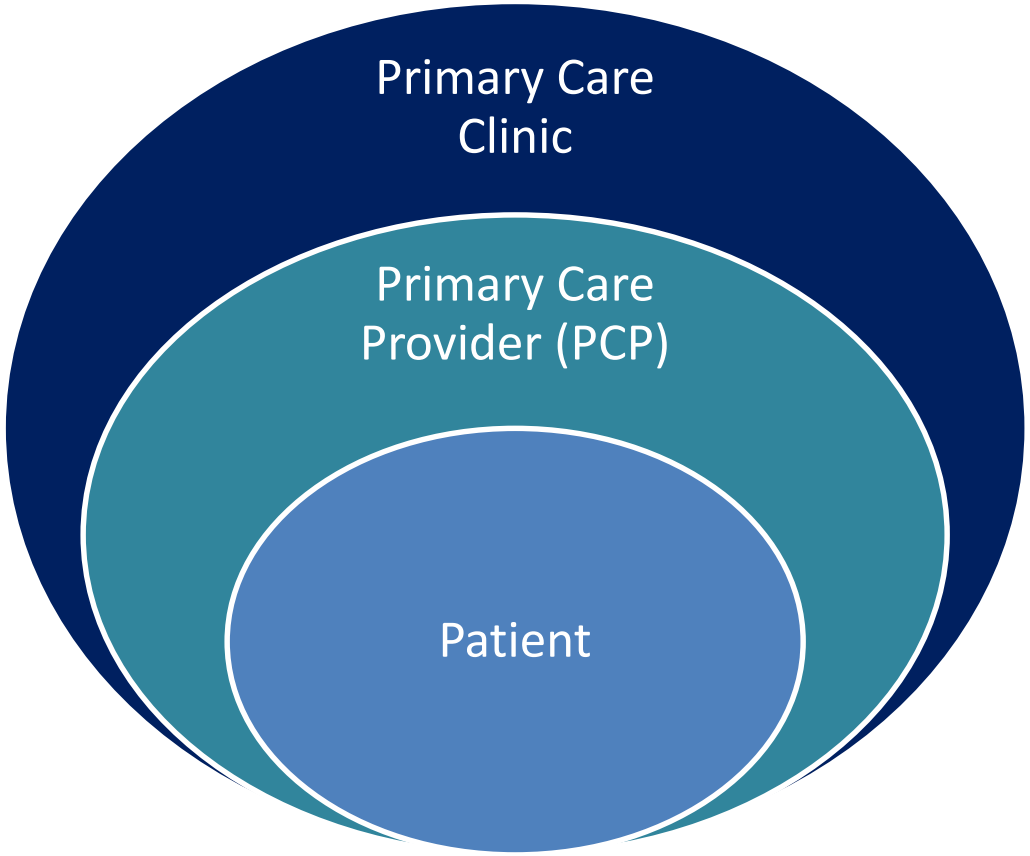
ELIGIBILITY: Chronic pain, long-term opioid tx (prioritizing ≥ 120 MED, benzodiazepine co-use, high utilizers [≥ 12 visits in 3 months])

INTERVENTION: Behavioral specialist, nurse case manager, PT, and pharmacist team; 12-week core CBT + adapted movement groups

OUTCOMES: Pain (4-item PEGS), opioid MED, pain-related health services, and cost

PPACT's Clustering Dilemma

Clustering? Not clustering? Level of clustering?



Difficulties / Considerations from Each Perspective

Statistical	Clinical / Logistical
Clinic vs. PCP Clusters: Originally planned for clinic-level randomization but…	
• Clinics heterogenous and difficult to balance • More power with PCP-level clustering	• Clinic-level staffing not as expected – PCMH (nursing) and integrated behavioral health models not fully adopted
Patient-level randomization…	
• Concerns with contamination if PCP had patients in active intervention and usual care	• Would have been great but not seen as consistent with study design considerations / priorities of Collaboratory at that time

Resolution and Future Considerations

- Clustered at PCP-level with some negative consequences
  - Logistics of EHR-based PCP panel identification complex and very time consuming
  - Prevented organic clinical adoption (research as usual / poor partnership)

- Individual randomization might have been better approach
  - Studies* suggest contamination very unlikely

* Lin et al. *Medical Care*, 1997; 35: 831-842; Pedersen et al. *Implementation Science, 2018; 13:99*.

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Health Care Systems Research Collaboratory

Suicide Prevention Outreach Trial: Where to randomize?

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Susan Shortreed PhD

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Question:

Can population-based outreach programs reduce risk of suicide attempt (compared to usual care) among outpatients reporting frequent thoughts of death or self-harm on routinely administered depression questionnaires?

Trial overview:

- Participants automatically identified from EHRs – based on responses to routine depression questionnaires
- Everyone eligible randomly assigned to usual care (no contact) or either of two outreach interventions
- Those offered interventions are free to decline or discontinue
- Outcomes (suicide attempts and suicide deaths) ascertained from health system records and state vital statistics
- 18,887 randomized, intervention and follow-up ongoing

Interventions:

- Outreach, risk assessment and care management to maintain appropriate engagement in outpatient mental health care
- Online training in Dialectical Behavior Therapy skills, supported by online coaching
- Common to both interventions:
  - Supplements to (not replacements for) usual care
  - Delivered by centralized coach or care manager
  - Feedback to and coordination with outpatient providers
  - Delivered primarily by online messaging (with telephone as backup)

Where do the interventions act?

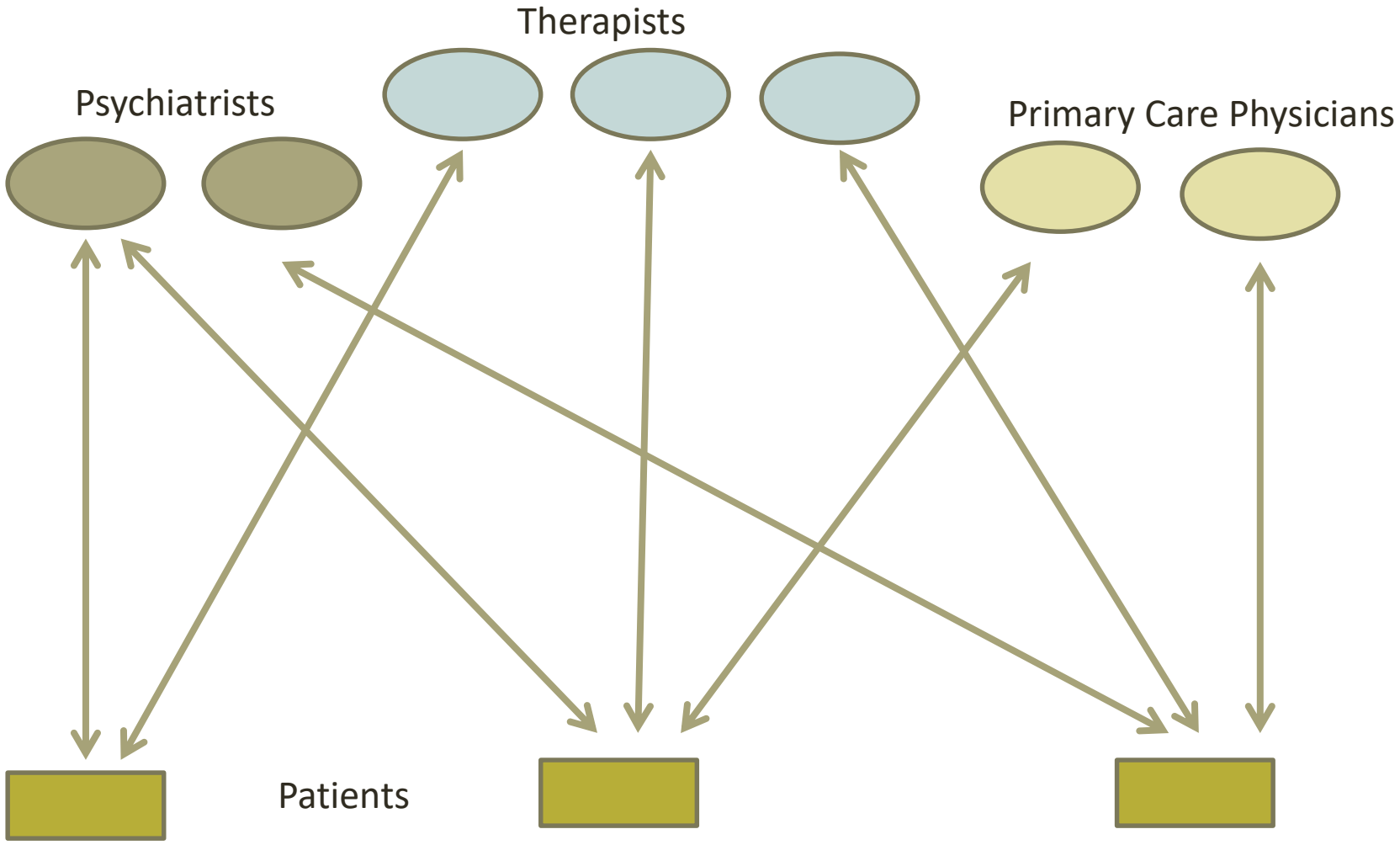
- Care management
  - Patient-level: Outreach, risk assessment, care facilitation, non-specific support
  - Provider-level: Patient-specific messages to facilitate/coordinate follow-up care. No training or practice support/facilitation
  - Clinic-level: None
- Skills training
  - Patient-level – Online skills training, online coaching, non-specific support
  - Provider-level: FYI messages to providers. No training or practice support/facilitation
  - Clinic-level: None

What we learned from collaborative care trials

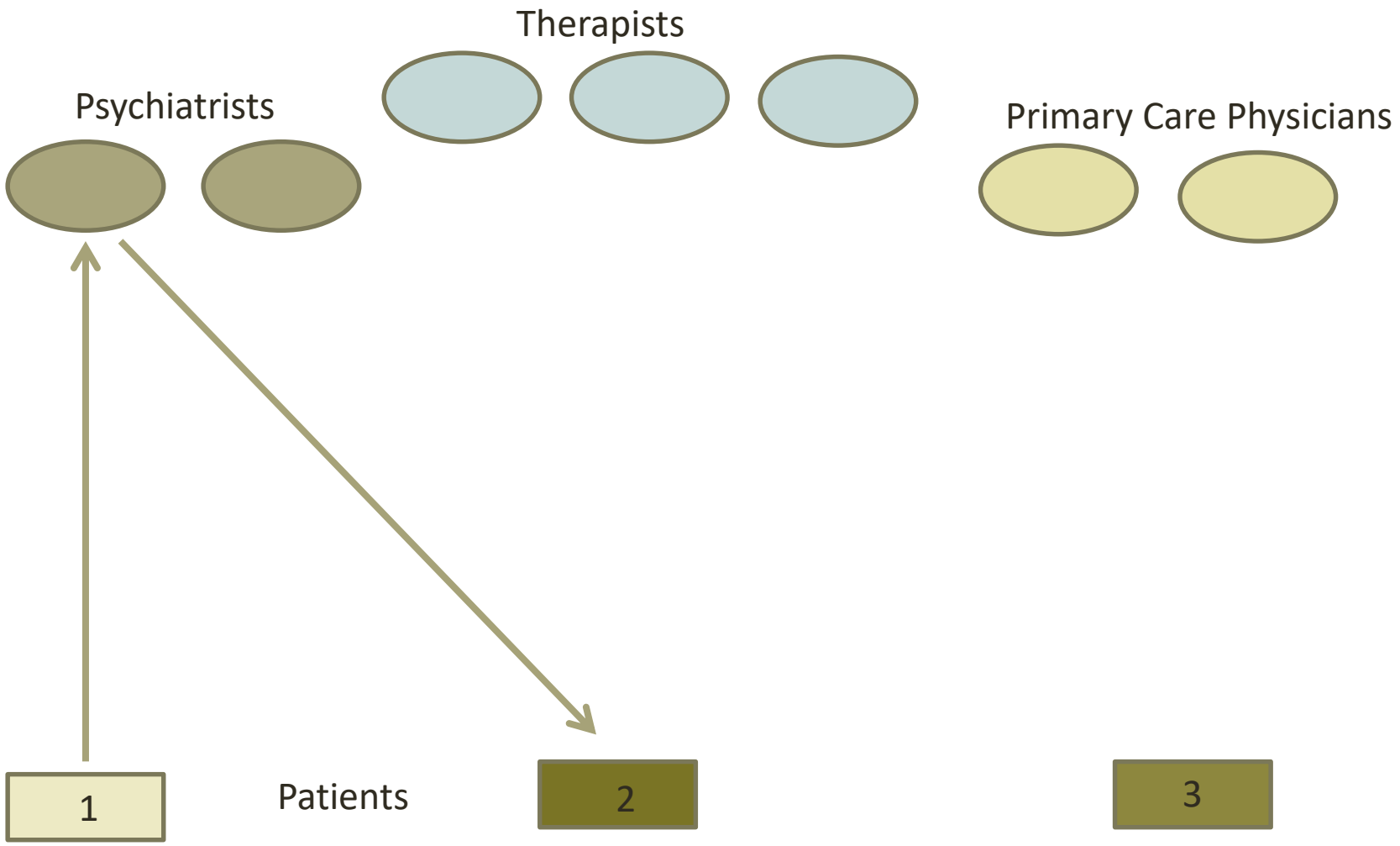
- Trivial level of provider clustering of depression treatment adherence and outcomes (1)
- No evidence of “spillover” effect of CC interventions (2)
- No evidence of before-after effects on treatment quality (2)

1. Katon W, Rutter C, Lin E, Simon G, VonKorff M, Bush T, et al. Are there detectable differences in quality of care or outcome of depression across primary care providers? Med Care. 2000;38:552-61.
2. Lin E, Katon W, Simon G, VonKorff M, Bush T, Rutter C, et al. Achieving guidelines for treatment of depression in primary care: Is physician education enough? Med Care. 1997;35:831-42.

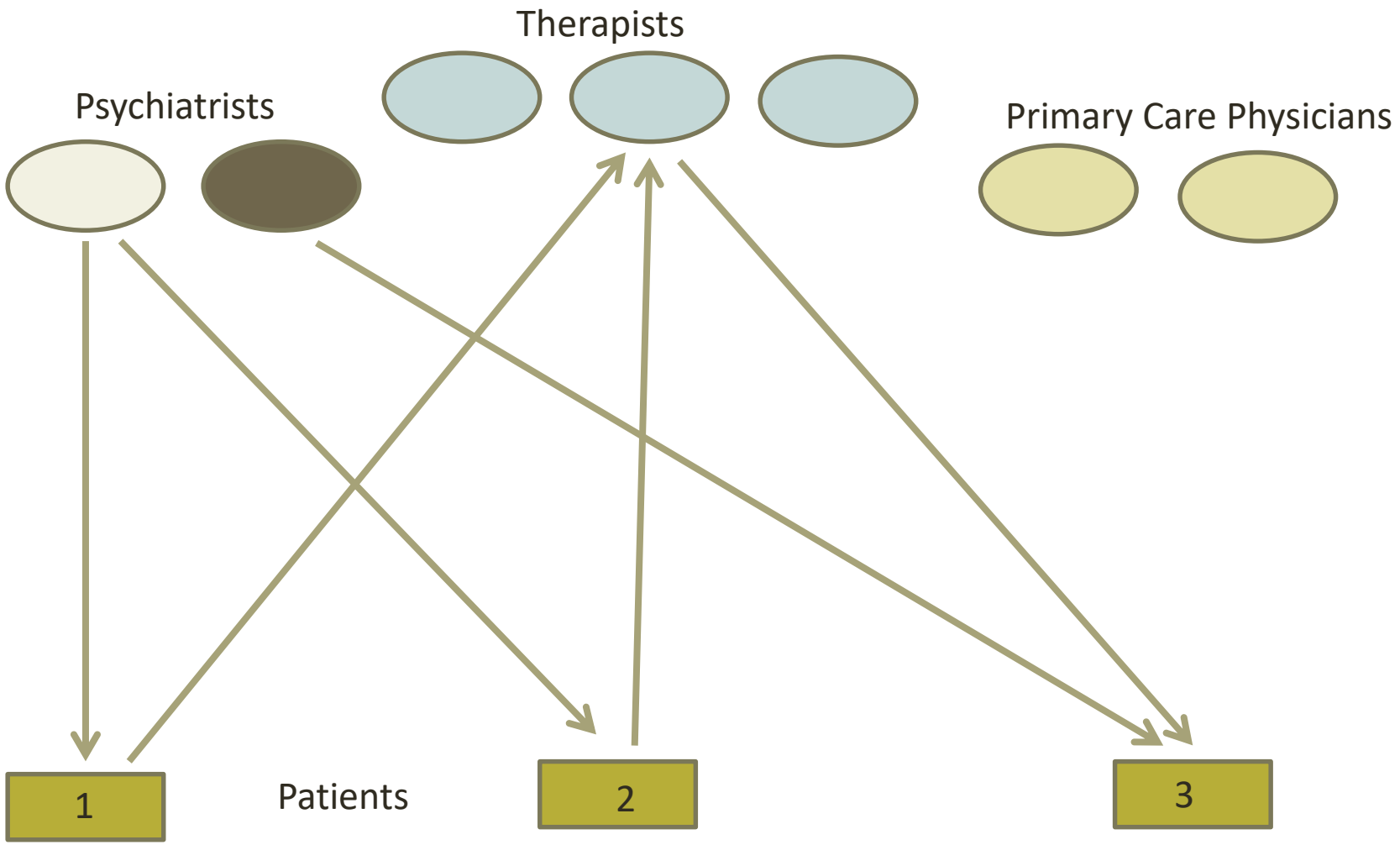
How would we define clusters?



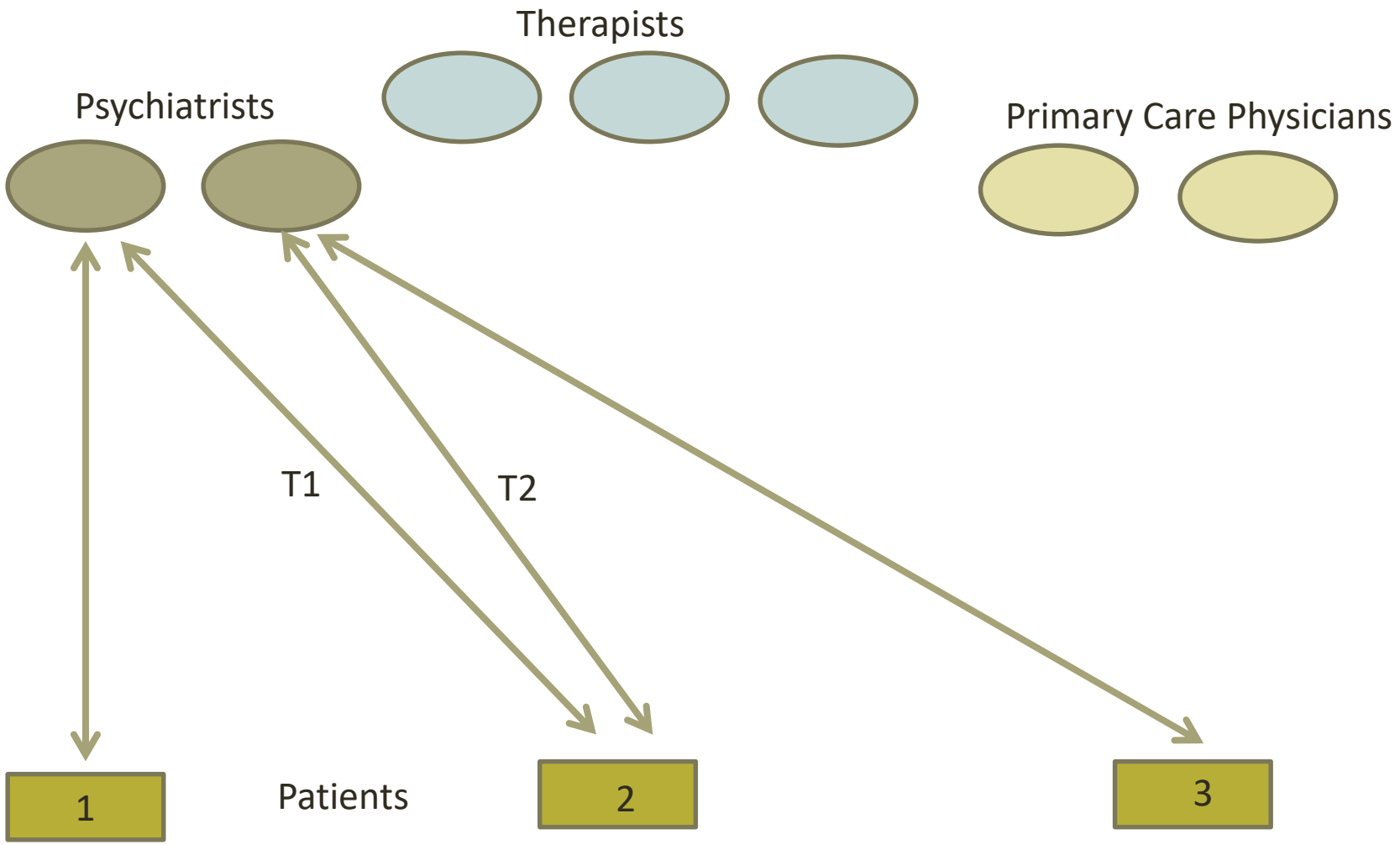
Contamination under individual-level randomization



Contamination under provider-level randomization: Multiple provider types



Contamination under provider-level randomization
Changes over time



Where we ended up

- Individual-level randomization
- Stratified by:
  - Study site (health system)
  - Level of self-reported suicidal ideation on eligibility questionnaire

Questions and Answers

Please submit questions for the panelists to:

PragClinTrialsWkshp@mail.nih.gov