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Innovative Data Strategies

Tried and True & New and Promising

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Disclosure

- No relevant disclosures

Objective

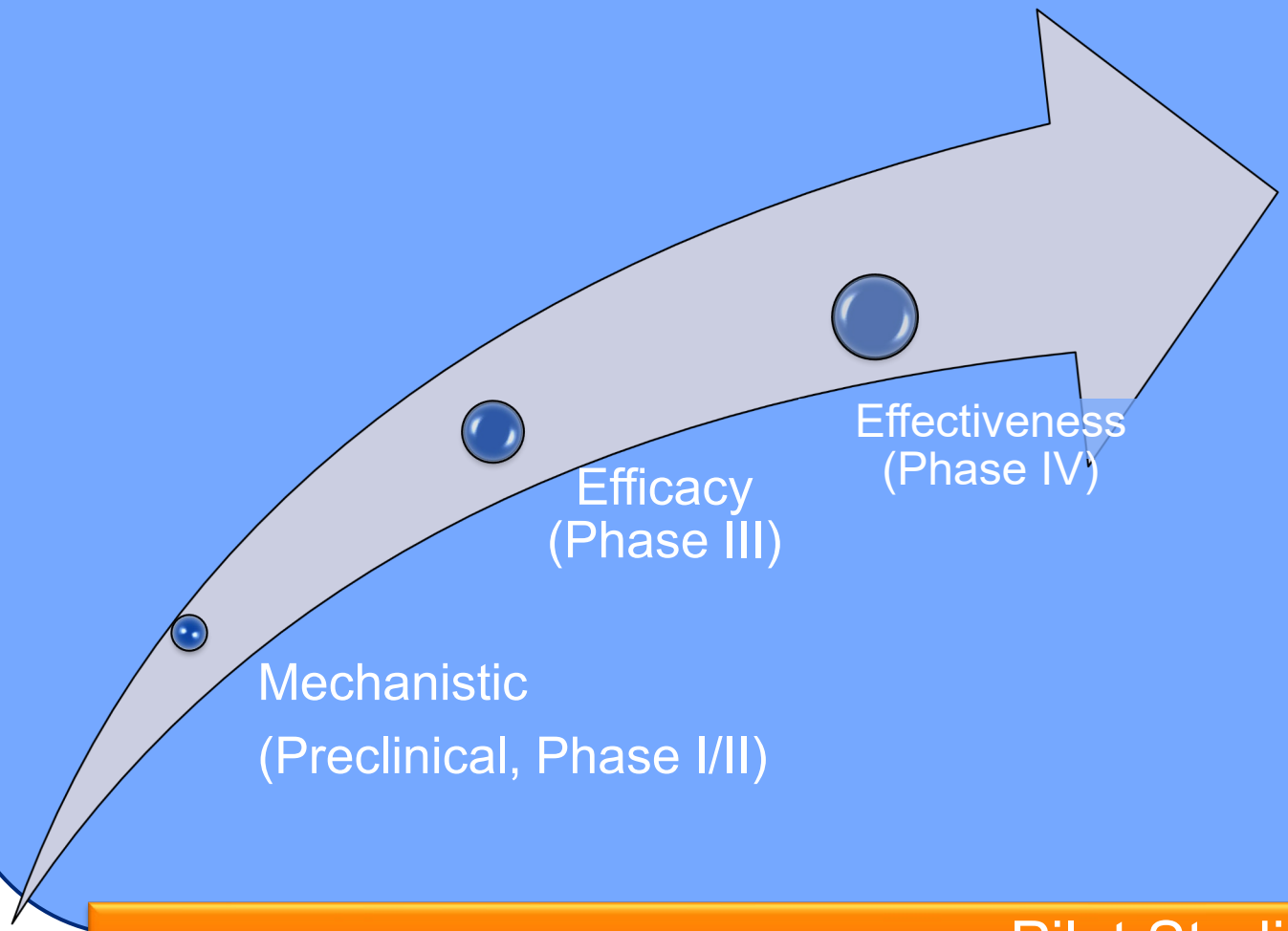
- Describe how implementing pragmatic elements to the study design may increase generalizability of the findings

Clinical Trials as a Spectrum

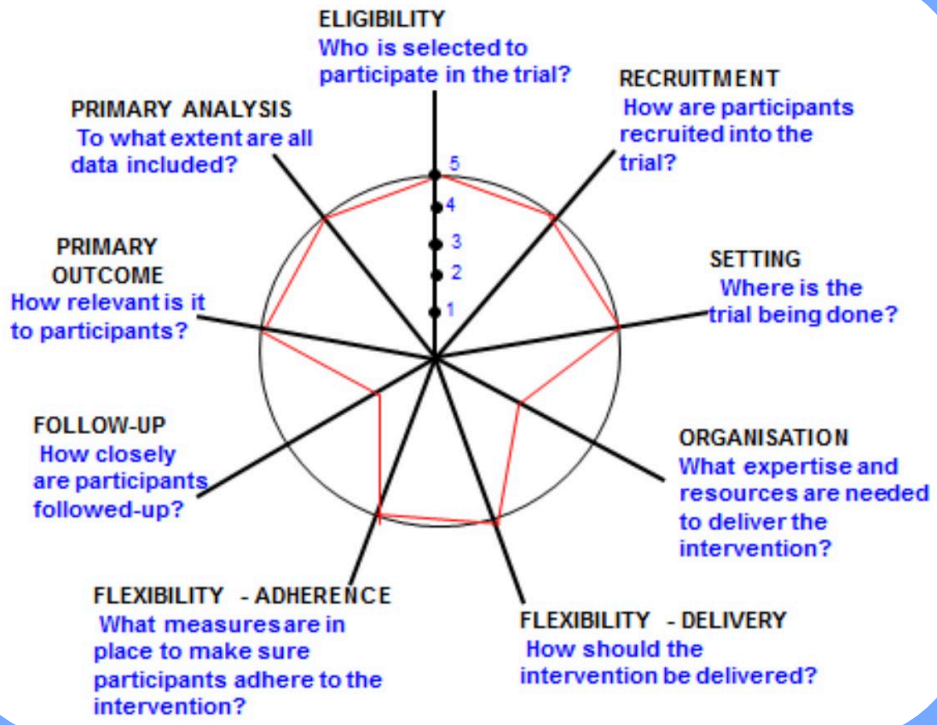
- No single trial provides “definitive” evidence
  - Rather, it’s the compilation of knowledge
- What is ”Real World”?

Clinical Trials as a Spectrum

Traditional Clinical Trial Phases



Pragmatic Clinical Trials



PRECIS-2, BMJ publication BMJ 2015;350:h2147

Pilot Studies

Pilot Studies

Recommendations for Planning Pilot Studies in Clinical and Translational Research

Charity G. Moore, Ph.D.[1], Rickey E. Carter, Ph.D.[2], Paul J. Nietert[3], and Paul W. Stewart, Ph.D.[4]

Abstract

Advances in clinical and translation science are facilitated by building on prior knowledge gained through expe
In the context of drug development, preclinical studies are followed by a progression of phase I through phase
the study design and statistical strategies are framed around research questions that are prerequisites for the
biomedical research, pilot studies are used for gathering preliminary support for the next research step. Howe
liberally applied to projects with little or no funding, characteristic of studies with poorly developed research pro
with no detailed thought of the subsequent study. In this article, we present a rigorous definition of a pilot stuc
the design, analysis and sample size justification of pilot studies in clinical and translational research, and emp
well-designed pilot studies play in the advancement of science and scientific careers. Clin Trans Sci 2011; Volu

Keywords: pilot studies, pilot study design, sample size, power calculations, confidence intervals

Clinical and Translational Science
https://ascpt.onlinelibrary.wiley.com/doi/full/10.1111/j.1752-8062.2011.00347.x

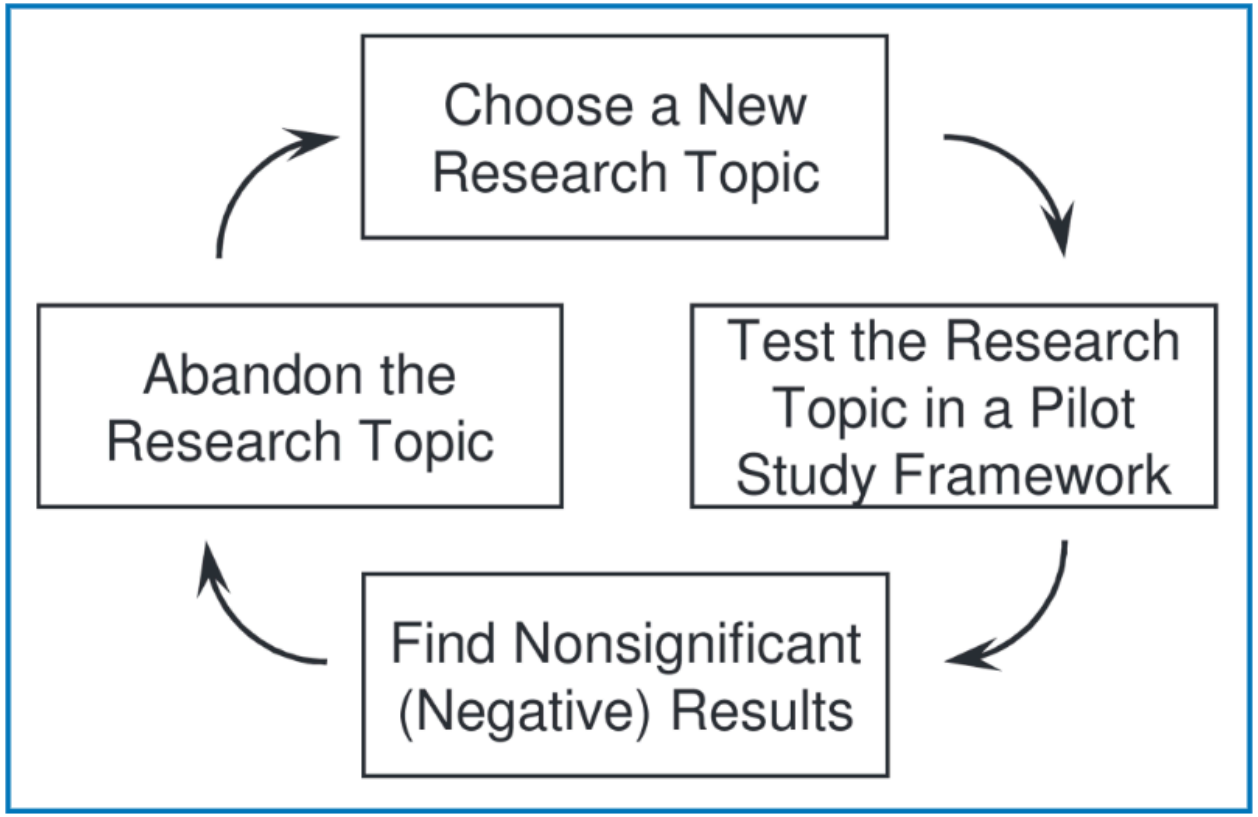


Figure 1. Nonproductive scientific strategy involving the use of pilot studies.

4 Strategies to Improve Pilot Studies

1. Keep the next study in mind

- What is it that we really need to learn with this study?
- Do we know if patients will accept randomization?
- Can we supply and administer the investigational product in time?
- Can we generate preliminary data to support further study?

4 Strategies to Improve Pilot Studies

2. Design with carefully specified aims

- (False) Aim – To conduct an under-powered, under-resourced clinical trial that will produce challenging to interpret data that will only result in a pay-for-publication article in an obscure open-access medical journal for a bargain price of $4,500.
- (Pilot) Aim – To quantify the rate of accrual by ascertaining the percentage of eligible patients that are successfully randomized into the clinical trial.

4 Strategies to Improve Pilot Studies

3. Justify the Sample Size

- All studies require adequate sample size justification
- This is an “art”; no single right answer
- There are wrong answers -
  - We think the clinically relevant difference is a reduction in mortality of 3 percentage points (RR = 0.9). However, our budget is limited so we will let the sample size calculations be based on a 25 percentage point difference (RR= 0.001) because that is all the subjects the budget allows.

4 Strategies to Improve Pilot Studies

4. Career Trajectories Matter

- Well designed pilot studies are quick to run
- Defined questions convincingly answered are publishable

Pilot Studies for Pragmatic Clinical Trials

- Assess logistics
  - Randomization workflow, particularly if individual patient randomization
  - Establish data collection procedures (i.e., EHR integration, electronic vs. “paper” collection)
  - Evaluate protocol compliance
  - Evaluate patient flow:
    - Patients => Screening Rate => Randomization Rate

Go / No Go Decisions

- Based on the believed study viability and funding
- “Gut check” – Is this really what you want to do for the next 3 – 7 years?
- Do you have the team assembled and ready?
- Could it be done? vs. Should it be done?

Case Study – Mayo Expert Advisor Study

CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

Computerized Advisory Decision Support for Cardiovascular Diseases in Primary Care: A Cluster Randomized Trial

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CLINICAL SIGNIFICANCE

- The studied clinical decision support tool improved adherence to guideline-recommended therapy for heart failure but not atrial fibrillation or hyperlipidemia.
- Complex diseases may respond more favorably to decision support tools.
- The limited use of decision support tools in a real-world clinical practice highlights the need to address barriers to usage before widespread implementation.

Clinical Decision Support Tool

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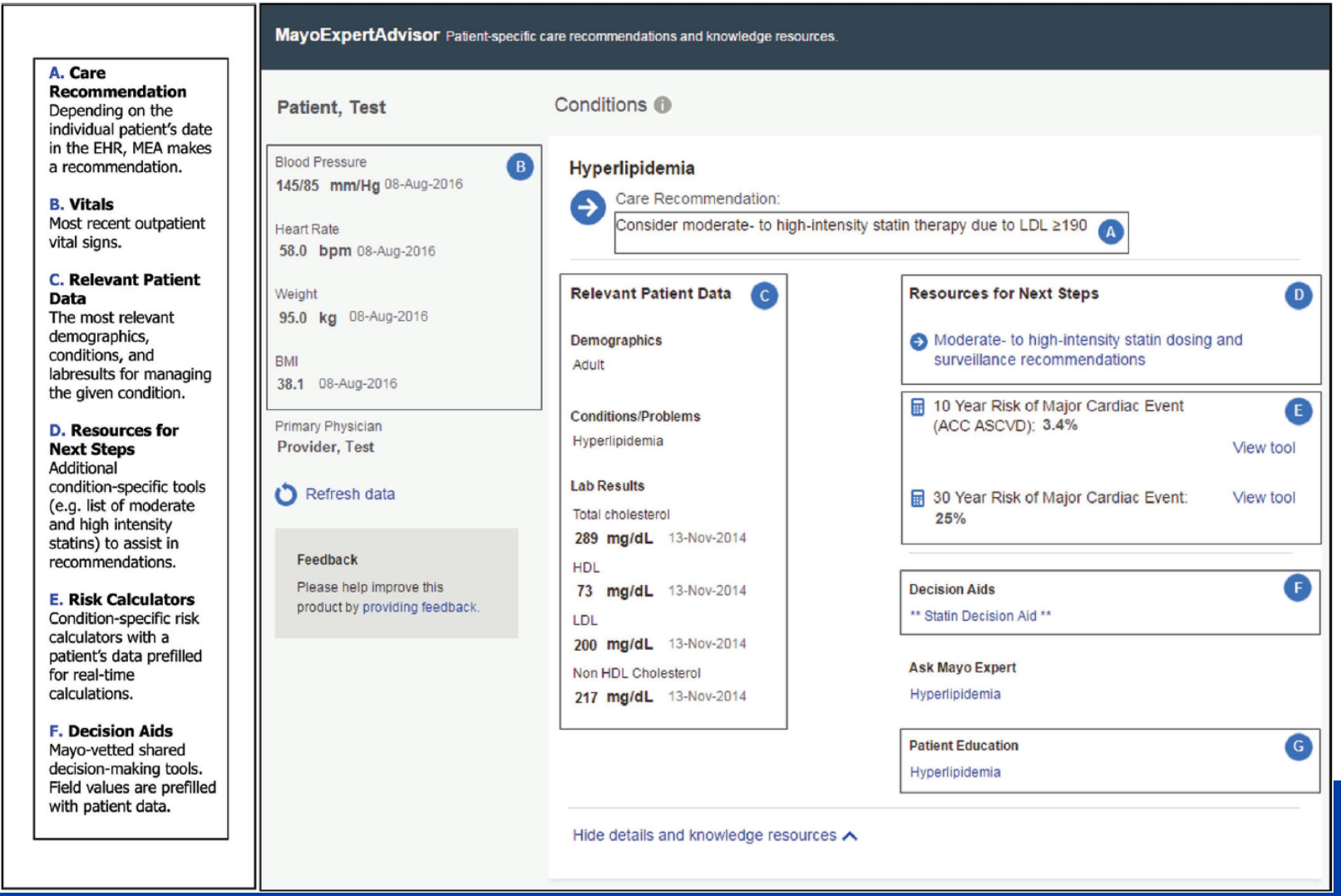

CDS Goal:

- Extract relevant history
- Cross reference with guidelines and best practice
- Provide actionable recommendation

Recipe for Success?

Actionable Encounters in Primary Care Setting

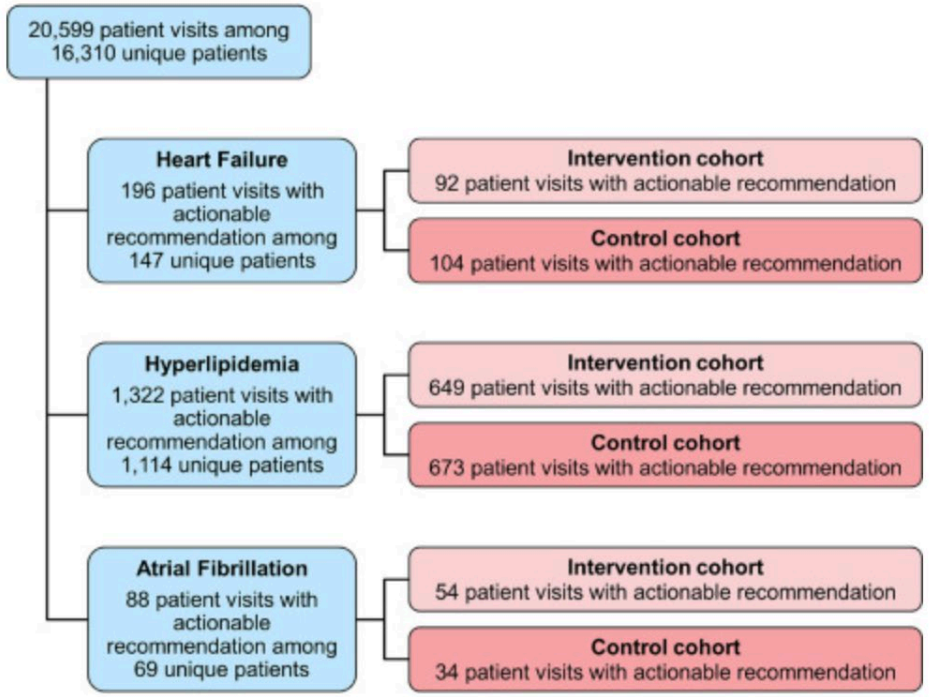

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Figure 1. Patient visits with a discrepancy between previsit treatment and guideline-recommended treatment for heart failure, hyperlipidemia, and atrial fibrillation.

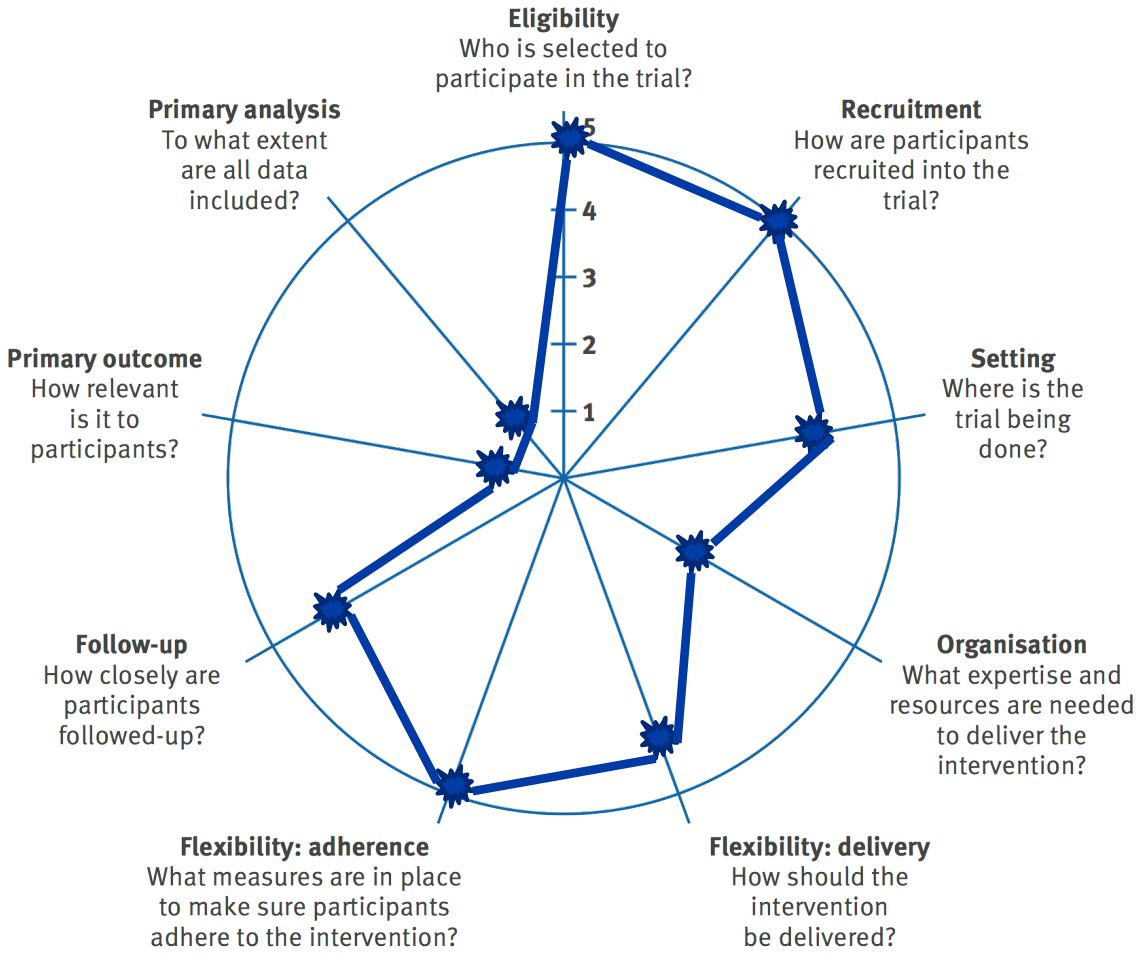
Relevant Pilot Questions

-What are the reasons for the primary care visits?

-Is chronic disease management actionable during these visits?

-"We will discuss at our next visit"

PRECIS Applied to Mayo Expert Advisor Study



Eligibility – 5 (Usual Care)

Recruitment – 5 (Cluster rand.)

Setting – 3 (MC Primary Care)

Organization – 2 (IT heavy)

Delivery – 4 (Just an extra ”click”)

Adherence – 5 (Ignorable)

Follow up – 4 (Mayo Care)

Outcome – 1 (Not patient focused)

Analysis – 1 (Heavy subsetting)

Where did all of the patients go? (“Lasagna’s Law”)

Incident Cases

Prevalent Cases

Randomized Cases

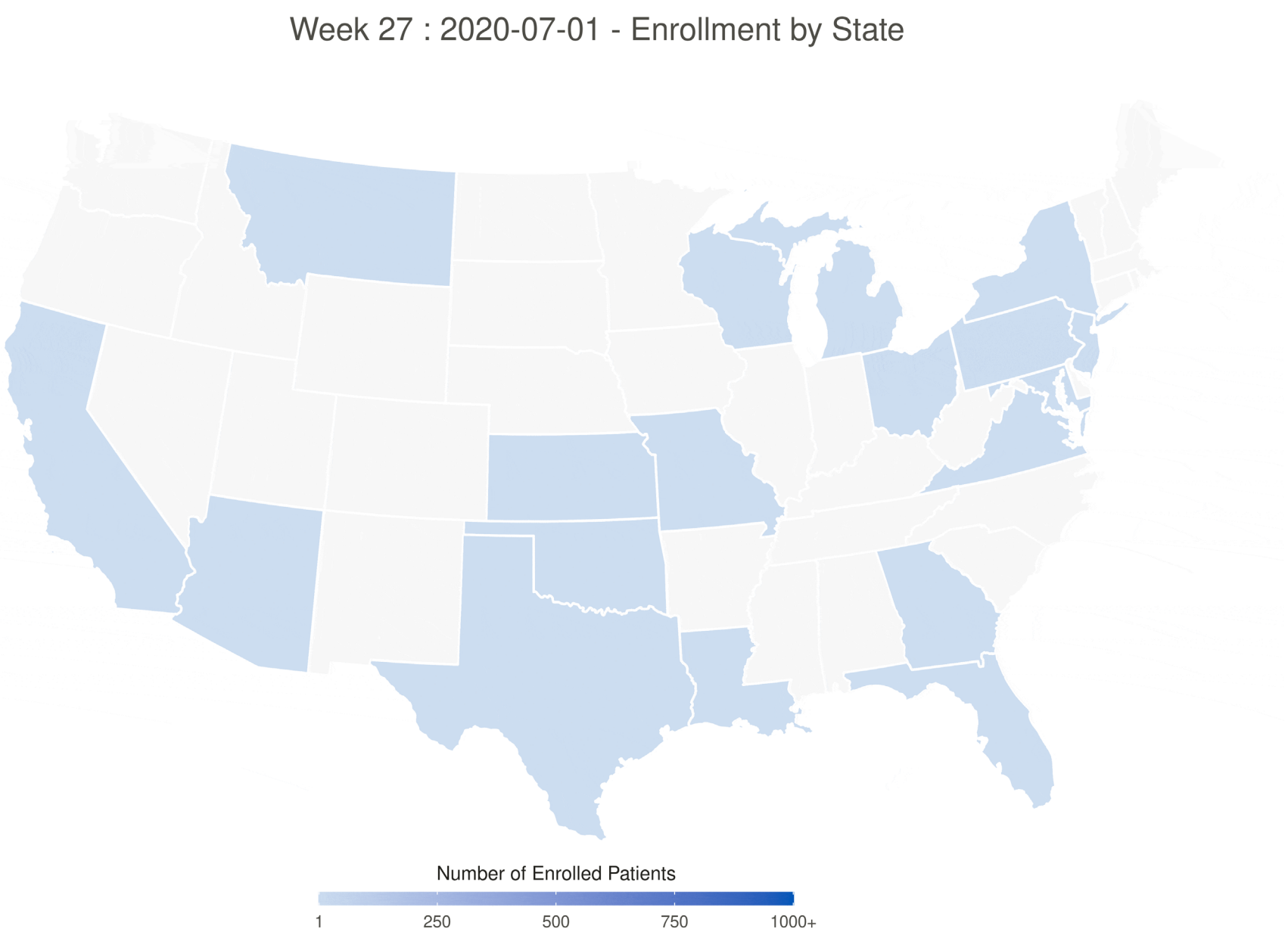
“We see these patients all the time”

Where did all of the patients go? (“Lasagna’s Law”)

Month 1

Months 1+

Randomization is based on incident cases



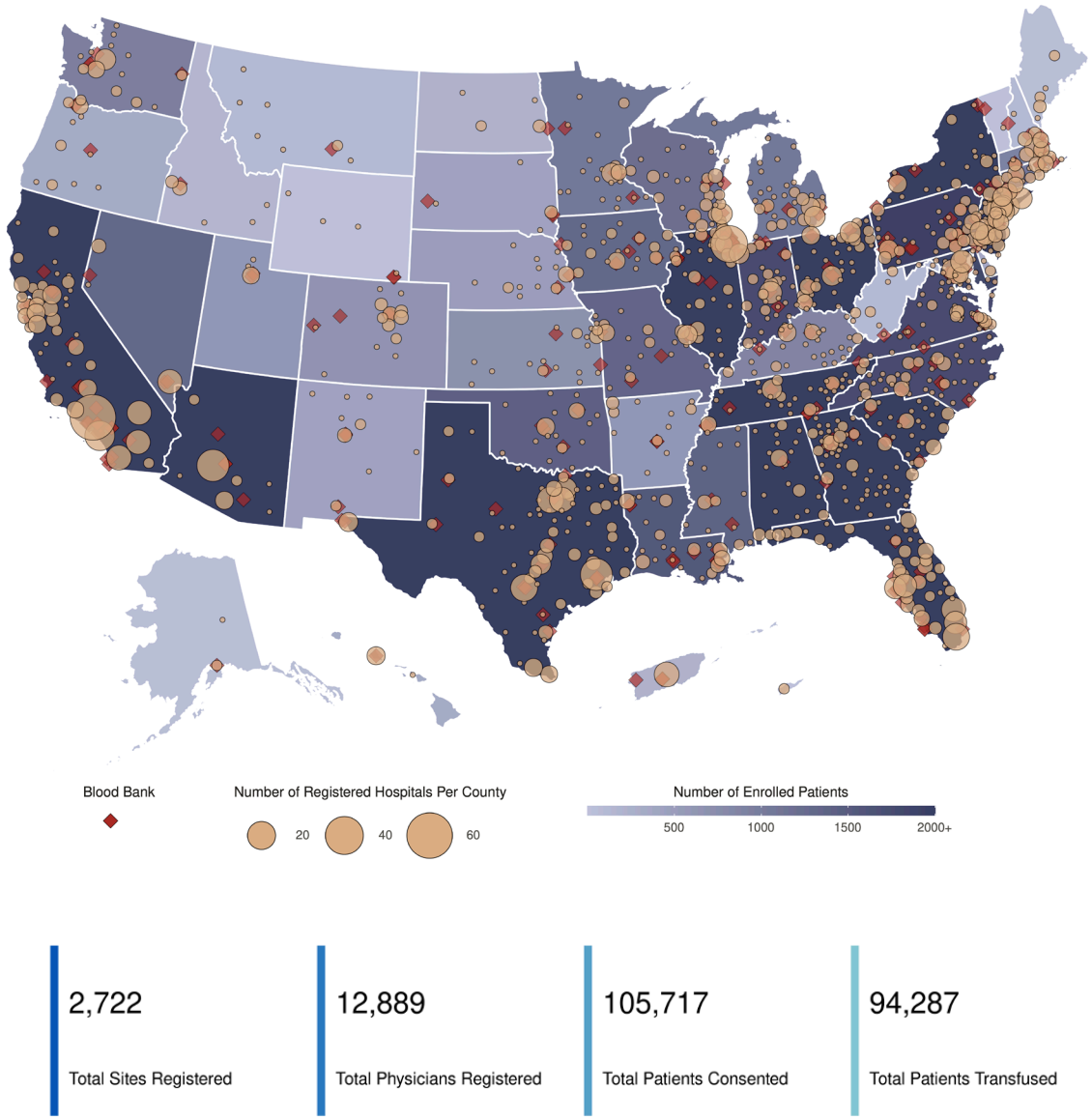
Pandemic Example Convalescent Plasma Trial Enrollment

Emphasizes need for adaptive enrollment strategies

The “global” pandemic required local attention

Opportunities for the Future

- Ready and waiting site network
  - Rapid activation/deactivation
- “Warm” infrastructure beneficial
- Focus on diversity
  - Rural vs. Urban, Academic vs Community, Private vs. Government Insurance



2,722	12,889	105,717	94,287
Total Sites Registered	Total Physicians Registered	Total Patients Consented	Total Patients Transfused

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THANK YOU

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