Assessment of Prevention, Diagnosis, and Treatment Options

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Session Objectives

- Describe the APDTO Program and available opportunities
- Discuss the LOI and application process
- Provide examples of what we are looking for
- Answer questions!

CER Funded by APDTO

- Generates and synthesizes evidence comparing benefits and harms of at least two different methods to prevent, diagnose, treat, and monitor a clinical condition or improve care delivery

Adapted from *Initial National Priorities for Comparative Effectiveness Research*, Institute of Medicine of the National Academies

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- Performed in real-world populations
- Informs a specific clinical or policy decision
- Describes results in subgroups of people
- Applies appropriate methods and data sources

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- Addresses a current gap in knowledge
- Addresses consequential choices faced by patients, clinicians, and other stakeholders
- Allows patients and caregivers to compare benefits and harms of options and provide relevant information about outcomes

"Broad" Studies

Seeks to produce information that can be directly adopted by providers.

- Compares two of more options for prevention, diagnosis, treatment, or management
- Often conducted in routine clinical settings
- Less complex than traditional trials

Overview

- Two Funding cycles per year
- Funds Available per Cycle: $20-30M
- Maximum Project Duration: 3 years
- Maximum Direct Costs per Project: $2M

Trends in APDTO Studies

- Clinical trials with larger sample sizes
  - Leveraging existing research collaborations
  - Partnering with clinical delivery sites
- Well designed observational studies
  - Built on registries and other high quality data sources
- Good response to PCORI's priority for research on rare conditions

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Pragmatic Clinical Studies

Seeks to produce information that can be directly adopted by providers.

- Compares two of more options for prevention, diagnosis, treatment, or management
- Often conducted in routine clinical settings
- Less complex than traditional trials
- *Large and able to focus on subgroups*
- *Focused on high priority topics designated by PCORI*

Overview

- Two Funding cycles per year
- Funds Available per Cycle: *$90M*
- Maximum Project Duration: *5 years*
- Maximum Direct Costs per Project: *$10M*

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Steps in the Review of Proposals

1. Investigators submit Letter of Intent (LOI)
2. PCORI staff reviews LOIs for adherence to programmatic goals and approves those for full application invitations
3. All applications are reviewed by merit review panels comprised of scientists, patients, and clinical stakeholders
4. Program selects the most meritorious applications for funding
5. Board of Governors approves

Strong LOIs

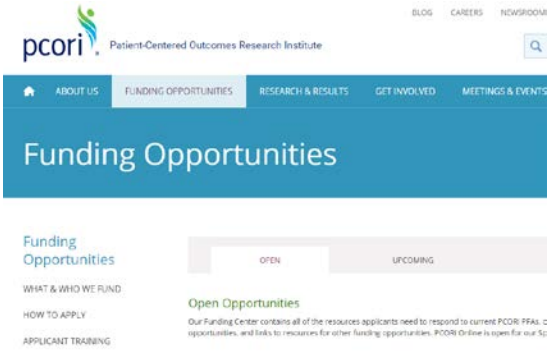
- Clear decisional dilemma
- Well-documented evidence gap
- Viable comparators
- Scientifically solid
- Plan for stakeholder involvement
- Doesn't duplicate current PCORI efforts

Most Serious Deficiencies in LOIs

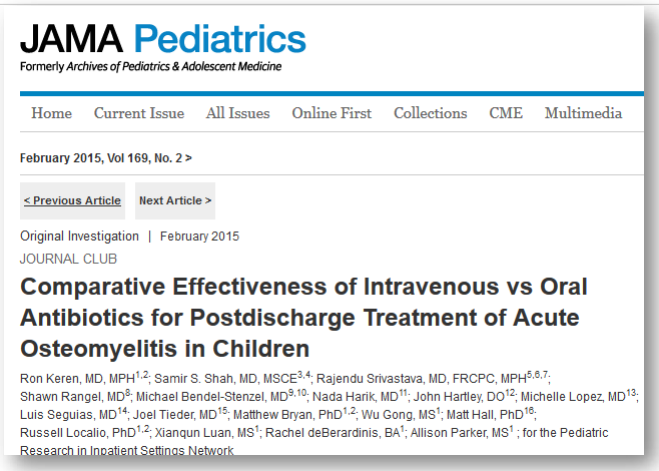
- Study appears to seek to establish efficacy
- Gap is not well documented
- Sample size is not well-justified
  - Number is too low to be robust and convincing
  - Effect size is not based in evidence
- Engagement is weak

Applications

- Review the PFA carefully
- Follow instructions for completion



Example of a Successful Project



JAMA Pediatrics

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Original Investigation | February 2015

JOURNAL CLUB

Comparative Effectiveness of Intravenous vs Oral Antibiotics for Postdischarge Treatment of Acute Osteomyelitis in Children

Ron Keren, MD, MPH[1,2]; Samir S. Shah, MD, MSCE[3,4]; Rajendu Srivastava, MD, FRCPC, MPH[5,6,7]; Shawn Rangel, MD[8]; Michael Bendel-Stenzel, MD[9,10]; Nada Harik, MD[11]; John Hartley, DO[12]; Michelle Lopez, MD[13]; Luis Seguias, MD[14]; Joel Tieder, MD[15]; Matthew Bryan, PhD[1,2]; Wu Gong, MS[1]; Matt Hall, PhD[16]; Russell Localio, PhD[1,2]; Xianqun Luan, MS[1]; Rachel deBerardinis, BA[1]; Allison Parker, MS[1] ; for the Pediatric Research in Inpatient Settings Network

Keren R, et al. JAMA Pediatr. 2015;169(2):120-128.

Comparative Effectiveness of Intravenous vs. Oral Antibiotic Therapy for Serious Bacterial Infections

PI: Ron Keren, MD, MPH

Children's Hospital of Philadelphia

Study Objective

- To compare oral antibiotics vs. intravenous antibiotics delivered via a central venous catheter in children who require prolonged home antibiotic therapy after hospitalization for three different serious bacterial infections: perforated appendicitis, complicated pneumonia, and osteomyelitis

Documenting the evidence gap

IDSA GUIDELINES

Clinical Practice Guidelines by the I… Diseases Society of Ame… Methicillin-R…

37. The optimal route of administration of antibiotic therapy has not been established. Parenteral, oral, or initial parenteral therapy followed by oral therapy may be used depending on individual patient circumstances (**A-III**).

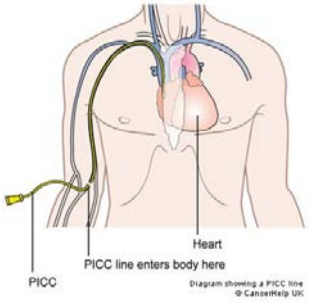
…Rachel J. Gorwitz,[9] …E. Murray,[12] Michael J. Rybak,[12,13] David …

…Diseases, University of California-San Francisco, San Francisco, California; [2]Division of Infectious Diseases, …Francisco, CA; [3]Division of Infectious Diseases, Harbor-UCLA Medical Center, Torrance, CA; [4]Divisions of Emergency …Diseases, Olive View-UCLA Medical Center, Sylmar, CA; [5]Department of Medicine, David Geffen School of Medicine at University …fornia Los Angeles; [6]Division of Infectious Diseases, Johns Hopkins Medical Institutions, Baltimore, Maryland; [7]Department of Pediatrics, Section of Infectious Diseases, University of Chicago, Chicago, Illinois; [8-9]Division of Healthcare Quality Promotion, Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; [10]Department of Pediatrics, Section of Infectious Diseases, Baylor College of Medicine, Houston, Texas; [11]Division of Infectious Diseases, Beth Israel Deaconess Medicine Center, Harvard Medical School, Boston, Massachusetts; [12] Department of Medicine, Division of Infectious Diseases, Wayne State University, Detroit Receiving Hospital and University Health Center, Detroit, Michigan; [13]Deparment of Pharmacy Practice, Wayne State University, Detroit Michigan; and [14]Division of Infectious Diseases and Center for the Study of Emerging and Re-emerging Pathogens, University of Texas Medical School, Houston, Texas

Liu, et al. Clinical Infectious Diseases 2011;52(3):285–292.

Intravenous vs. Oral Antibiotic Therapy - Rationale

- Peripherally inserted central catheters (PICCs) are effective for delivering high concentrations of antibiotic but are fraught with infectious, thrombotic, and mechanical complications.
- Oral antibiotics with high bioavailability make oral step-down therapy an appealing alternative.
- Only small case series and no clinical trials document the effectiveness of oral antibiotics in this setting.



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Comparative Effectiveness of Intravenous vs. Oral Antibiotic Therapy for Serious Bacterial Infections

- Study Conclusions:
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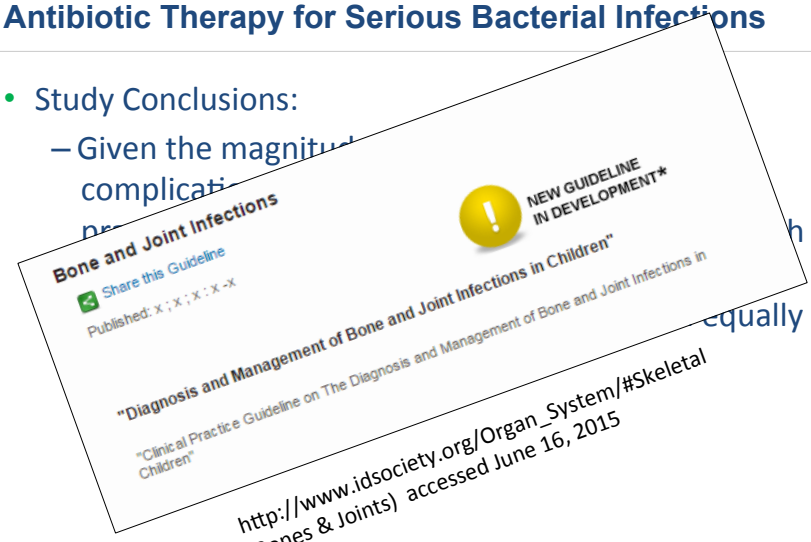

http://www.idsociety.org/Organ_System/#Skeletal (Bones & Joints) accessed June 16, 2015

Questions?

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