Appendectomy vs. Antibiotics
The CODA Randomized Trial
Presenter Name x, for the CODA Collaborative
Maine Medical

Appendicitis: Significance and Background

• Lifetime risk is 7-12%
• Appendectomy is most common urgent general surgical procedure
  – Performed in nearly 300,000 Americans each year (97.5% of appendicitis patients)
Appendicitis: Significance and Background

A Look at the Evidence

• N=1,724

• Common outcomes
  – Complications higher for surgery
  – Less pain for antibiotics
  – Fewer days away from work for antibiotics
  – Length of stay is similar

• Outcomes unique to one arm
  – All surgical patients undergo appendectomy
  – By 1 year, 25-40% of those randomized to antibiotics had an appendectomy
  – No higher rate of perforation
Evidence Gaps

• Selection bias
• Inconsistent or unstandardized diagnostic criteria
• Inadequate antibiotic coverage
• High rates of open surgery (44-95%)
• Outcome dependent on treatment strategy
• No standardized use of PROs

Stakeholder Perspective: Why Rock the Boat?

• Patients
• Hospital
• Surgeon
• Payer
CODA Research Proposal Development

- Engaged patients, clinicians, healthcare administrators, funders and researchers across WA State
- Used multi-modal approach to engagement
- Planning took place over 7 months
- Non-funded work

What Matters to Patients

Are the benefits of avoiding surgery outweighed by the potential burdens?
- Recurrence of appendicitis and eventual surgical intervention
- Lingering symptoms
- Anxiety and uncertainty impacting quality of life and return to work/school
- Long-term antibiotics
CODA: Research Questions

1. Are antibiotics as effective as appendectomy for uncomplicated appendicitis?

2. Which patients are most likely to have a successful outcome with antibiotics-first?

CODA: Study Aim 1

- **Aim 1.** Compare patient reported outcomes (PROs) in patients randomized to the antibiotics or appendectomy strategy.
  - **Sub Aim 1.** Compare PROs in patients without appendicolith randomized to the antibiotics or appendectomy strategy.
- **Exploratory Aim A.** Assess the rate of eventual appendectomy after starting the antibiotics treatment regimens in the first week, early (1-4 weeks) and late (2-24 months) periods and identify patient clinical characteristics (e.g., appendicolith) as well as clinician and practice site characteristics associated with eventual appendectomy in the antibiotic therapy group.
CODA: Study Aim 2

- **Aim 2.** Compare clinical outcomes in patients randomized to antibiotics versus appendectomy.
  - **Sub Aim 2.** Compare clinical outcomes in patients without appendicolith randomized to the antibiotics or appendectomy strategy.
- **Exploratory Aim B.** Compare randomized patients to those in a concurrent observational cohort to identify selection characteristics and outcome differences between the two groups.

CODA Study Design

- **Randomized-controlled trial**
  - Large-scale (n=1,552)
  - Non-inferiority based
    - Antibiotics “just as good as” appendectomy
  - Pragmatic
    - Routine clinical practice settings, heterogeneous population
- **Parallel observational cohort** (n=500)
How is this study pragmatic?

• “Real world” setting and practice
  – Routine practice
    • European vs. American
  – Open vs. laparoscopic surgery
  – Outpatient vs. inpatient management
  – Antibiotics adherence
    • Antibiotics-first approach requires 7 days of treatment at home
  – Antibiotics regimen
    • Flexibility in antibiotics choice

• Heterogeneity of treatment effect
  – Large sample/site size
  – Patients
  – Clinicians and healthcare settings

CODA: Study Population

• Consecutive patients recruited across 8 sites in 2 states

• Diverse demographics – CERTAIN Network
  – Urban and rural
  – Includes non-English speakers (Spanish)
  – Populations not typically engaged in research
  – Varying socioeconomic status
Inclusion & Exclusion Criteria

- A≥18 years; speaks English or Spanish
- Presenting with a diagnosis of uncomplicated appendicitis, imaging confirmed (CT, ultrasound, or MRI)
- Without contraindication to either:
  - Antibiotics (Known severe allergy or reaction to all of the proposed antibiotics, septic shock or diffuse peritonitis)
  - Appendectomy (Advanced disease related to appendicitis such that patient is ineligible for surgery, e.g., severe phlegmon, abscess)

Patient Measures at Follow-Up

At regular quarterly intervals through 12 months, then at 18 months and 24 months, phone, mail, or web-based surveys will be used to assess:

- Complications, signs and symptoms related to appendicitis and related healthcare utilization, time spent in healthcare, time away from work/school, out of pocket expenses (3, 6, 9, 12, 18, 24 months);
  - Work Productivity Index (3 months);
  - EQ-5D\textsuperscript{20} and 10-PROMIS\textsuperscript{21} (3, 6, 9, 12, 18, 24 months);
  - GIQLI\textsuperscript{22} (3, 12, 18, 24 months); and
  - Decision Regret Scale\textsuperscript{23} (3, 12 months).
Site Expansion

East Coast:
- NYU-Tisch And Bellevue Hospital Centers
- Beth Israel Deaconess Medical Center (BIDMC)
- Boston University Medical Center (BMC)
- Columbia University Medical Center
- Weill Cornell Medicine
- Maine Medical Center

South:
- University of Mississippi
- Vanderbilt Medical Center
- UT Health & LBJ Medical Center (TX)

Midwest:
- University of Michigan
- The Ohio State University
- Henry Ford Health Systems

West:
- University of Colorado Denver*

Bolded sites have already launched
*Potential sites

Site launches

- UT Health, LBJ & Maine Medical expected launch April/May
- Cornell expected launch this summer
### CODA Current Study Sites

<table>
<thead>
<tr>
<th>Medical Center</th>
</tr>
</thead>
<tbody>
<tr>
<td>UW Medical Center</td>
</tr>
<tr>
<td>Harborview Medical Center</td>
</tr>
<tr>
<td>Madigan Army Medical Center</td>
</tr>
<tr>
<td>UCLA Medical Center – Olive View</td>
</tr>
<tr>
<td>UCLA Medical Center – Harbor</td>
</tr>
<tr>
<td>University of Mississippi Medical Center</td>
</tr>
<tr>
<td>Beth Israel Deaconess Medical Center</td>
</tr>
<tr>
<td>Columbia University Irving Medical Center</td>
</tr>
<tr>
<td>Vanderbilt University Medical Center</td>
</tr>
<tr>
<td>Boston Medical Center (Boston University)</td>
</tr>
<tr>
<td>Virginia Mason Medical Center</td>
</tr>
<tr>
<td>Providence Regional Medical Center – Everett</td>
</tr>
<tr>
<td>Swedish Medical Center – First Hill</td>
</tr>
<tr>
<td>University of Michigan Medical Center</td>
</tr>
<tr>
<td>Tisch Hospital NYU Langone Medical Center</td>
</tr>
<tr>
<td>Bellevue Hospital Center NYU School of Medicine</td>
</tr>
<tr>
<td>Henry Ford Health System</td>
</tr>
<tr>
<td>The Ohio State Wexner Medical Center</td>
</tr>
</tbody>
</table>

### Standardized Information & Informed Consent Tool

- Improves communication to patients
  - Clear message regarding treatment
- Need to normalize options
- Improve patient expectations
- Decrease crossover
Standardizing Patient Information

• **Challenge**: deliver standardized patient information across all sites
  - Urban and rural
  - Academic and private
  - Variation in information
    • Doctors (residents, ED, surgeons); nurses (ED, triage); radiology (imaging techs, radiologists)

• **Solution**: 6-minute video given to all patients diagnosed with appendicitis

• English and Spanish
• Collaborative development: surgeons, ED docs, media team and patient advisors
Our Progress to Date

• $12.9 million funded last year
• Protocol development and IRB complete
• May 2016: Enrollment began in English at UW Medical Center and Harborview Medical Center
• June-October 2016: Enrollment began in English and Spanish at all remaining sites

Questions and Information

codastudy.org