CODA

Comparing Outcomes of Drugs & Appendectomy

Appendectomy vs. Antibiotics

The CODA Randomized Trial

Presenter Name x, for the CODA Collaborative

Maine Medical

Maine Medical Center

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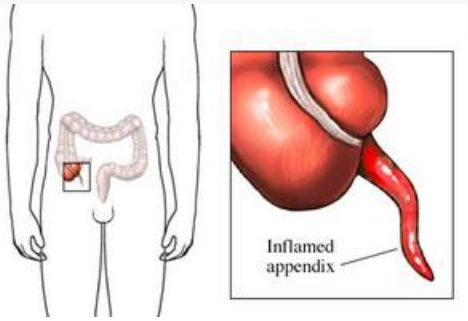
Appendicitis: Significance and Background

- 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)



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Appendicitis: Significance and Background

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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

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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?

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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.

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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.

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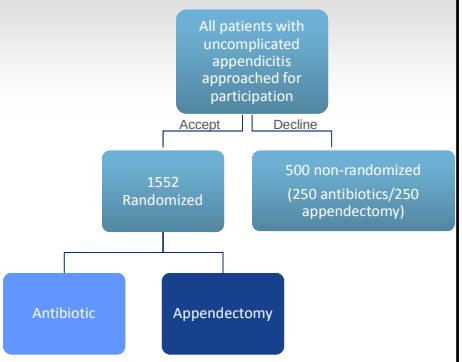
CODA Study Design

- 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)



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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

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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

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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)

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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[20] and 10-PROMIS[21] (3, 6, 9, 12,18, 24 months);
  - GIQLI[22] (3,12,18, 24 months); and
  - Decision Regret Scale[23] (3,12 months).

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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

West:
- University of Colorado Denver*

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**

Bolded sites have already launched
*Potential sites

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Site launches

- UT Health, LBJ & Maine Medical expected launch April/May
- Cornell expected launch this summer

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CODA Current Study Sites

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

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Standardized Information & Informed Consent Tool

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

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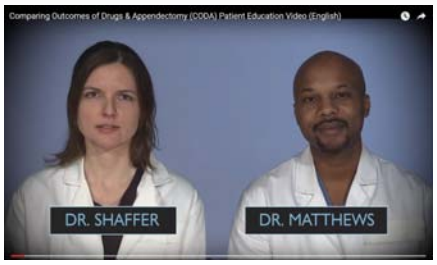
Standardizing Patient Information

- **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)



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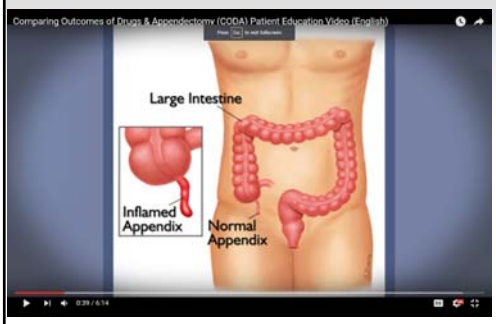
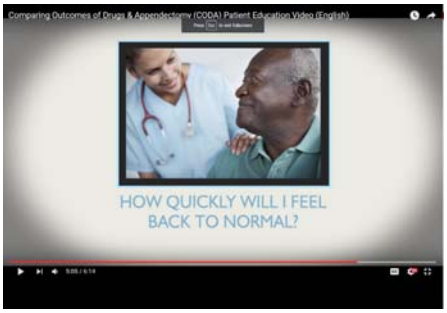
Standardizing Patient Information



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



- English and Spanish
- Collaborative development: surgeons, ED docs, media team and patient advisors

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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

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Questions and Information

codastudy.org

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