Treatment of Appendicitis & Implications from Recent Clinical Trials

Giana Davidson, MD MPH
Sara DePaoli, Research Manager

Center For Stewardship in Medicine (CSiM)
Tele-Microbial Stewardship Program (TASP) Meeting
November 2023

UNIVERSITY of WASHINGTON

CODA
Comparing Outcomes of Drugs & Appendectomy

SURGICAL OUTCOMES RESEARCH CENTER
SORCE

TRIAD
Treatment Individualized Appendicitis Decision Making Implementation Program

At the conclusion of this module, you will be able to:

1. Understand the evolution of the treatment of antibiotics

2. Describe the use of antibiotics for appendicitis and the evolution in treatment paradigms

Prior to the U.S. Trial:

CODA

Comparing Outcomes of Drugs & Appendectomy

N=1,724

Established Safety of Antibiotics

25-40% of those randomized to antibiotics had appendectomy by 1 yr

- 27% by 1 year
- 39% by 5 years

Evidence Gaps

- "Selected" patients
  - Surgeons determined who was approached
  - None with CT perforation or appendicolith
- Not typical U.S. practice
  - Inconsistent use of diagnostic imaging
  - Mandatory hospitalizations ~ 2 day
  - Mostly open surgery

BMJ Open

Comparison of Outcomes of antibiotic Drugs and Appendectomy (CODA) trial: a protocol for the pragmatic randomised study of appendicitis treatment

Giana H Davidson,[1] David R Flum,[1] David A Talan,[2] Larry G Kessler,[3] Danielle C Lavallee,[1] Bonnie J Bizzell,[4] Farhood Farjah,[1] Skye D Stewart,[1] Anusha Krishnadasan,[2] Erin E Carney,[1] Erika M Wolff,[1] Bryan A Comstock,[5] Sarah E Monsell,[5] Patrick J Heagerty,[5] Annie P Ehlers,[1] Daniel A DeUgarte,[6] Amy H Kaji,[7] Heather L Evans,[8] Julianna T Yu,[9] Katherine A Mandell,[10] Ian C Doten,[11] Kevin S Clive,[12] Karen M McGrane,[13] Brandon C Tudor,[14] Careen S Foster,[15] Darin J Saltzman,[16] Richard C Thirlby,[17] Erin O Lange,[1] Amber K Sabbatini,[18] Gregory J Moran[2]

Are antibiotics as effective as appendectomy for appendicitis?

- General health status
- Clinical outcomes
- Safety
- Time in healthcare

Which patients are most likely to have a successful outcome with antibiotics?

- What about the appendicolith…

Population

- Adults with imaging confirmed appendicitis
- Excluded: *those that are not eligible for 1 trial arm*
  - Abscess → needs drain and abx
  - Free air, diffuse peritonitis, septic shock→ to the OR
  - Pregnancy → we operate… mostly
  - Allergic to all trial drugs → to the OR
  - Immunocompromised → to the OR, outcomes are not generalizable
  - Recent surgery
- What about unhoused, international travel, elderly, rural, non-English speaking?

Intervention & Comparator

Antibiotics

- IV for at least 24 hours, then pills-total 10 days
  - Guidelines for intra-abdominal infections
- Either hospitalized or discharged from the ED after receiving IV antibiotics
- Standard discharge criteria
- Appendectomy recommended for development of diffuse peritonitis/septic shock at any time or for worsening signs and symptoms after 48 hours

Appendectomy

- Usual care

“Am I going to feel better?” EuroQol-5D

- What is the EQ5D?
- Why EQ5D?
- Why 30 days?

- Self report of fever, right sided pain and tenderness by 7, 14, and 30 days

Attribute	Level	Description
Mobility	1	No problems in walking about
	2	Some problems in walking about
	3	Confined to bed
Self-care	1	No problems with self-care
	2	Some problems with washing or dressing self
	3	Unable to wash or dress self
Usual activities	1	No problems with performing usual activities (ie, work, study, housework)
	2	Some problems with performing usual activities
	3	Unable to perform usual activities
Pain or discomfort	1	No pain or discomfort
	2	Moderate pain or discomfort
	3	Extreme pain or discomfort
Anxiety or depression	1	Not anxious or depressed
	2	Moderately anxious or depressed
	3	Extremely anxious or depressed

Secondary Outcomes

- Appendectomy (any indication) in the antibiotics group
- NSQIP-defined morbidity events
  - A subset were Serious Adverse Events (for DSMB reporting)
- Perforation (described by surgeon or pathology report)
- ED and urgent care visits
- Hospitalization days
- Days of missed work for patient and/or caregiver

CODA Collaborative

CERTAIN™

West:

University of Washington Medical Center
Harborview Medical Center
Virginia Mason Medical Center
Swedish Medical Center- First Hill
Providence Regional Medical Center- Everett
Madigan Army Medical Center
Harbor-University of California Los Angeles Medical Center
Olive View-University of California Los Angeles Medical Center
University of Colorado Denver

Midwest:

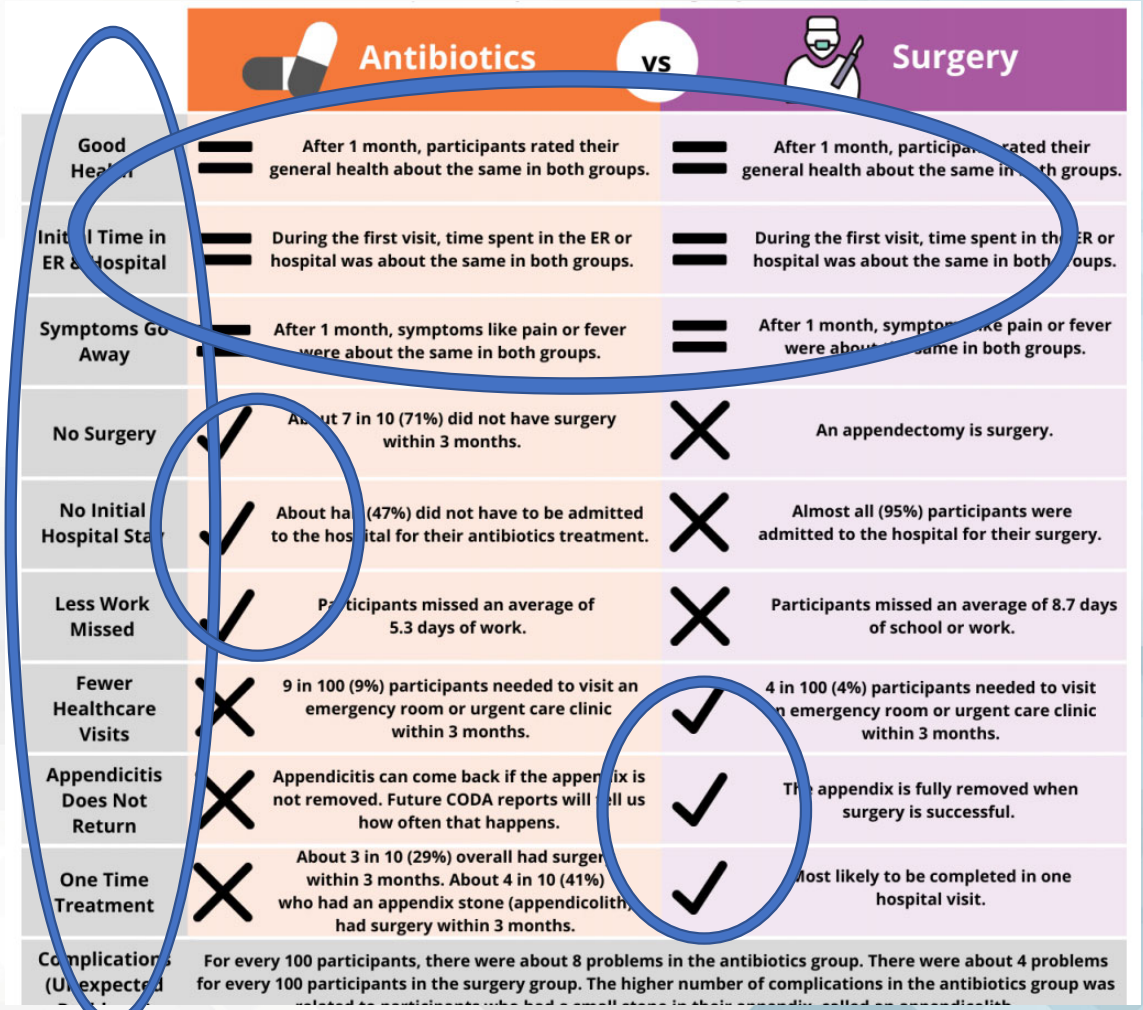
University of Michigan
The Ohio State University Wexner Medical Center
Henry Ford Health Systems
University of Iowa
Rush University Medical Center

South:

University of Mississippi
Vanderbilt Medical Center
University of Texas Lyndon B. Johnson General Hospital
University of Texas Health Science Center at Houston

East Coast:

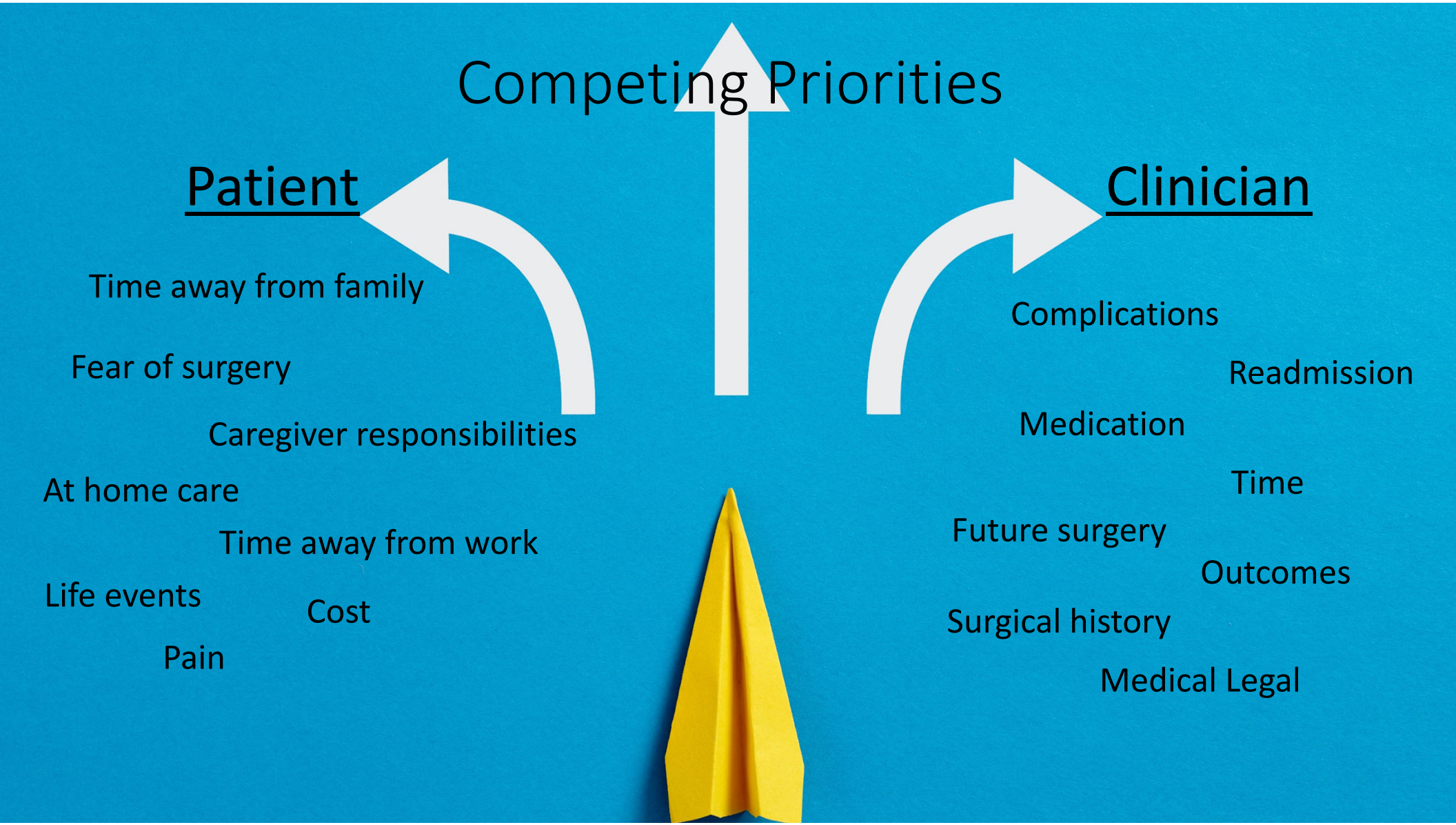
Bellevue Hospital Center New York University School of Medicine
Tisch Hospital New York University Langone Medical Center
Beth Israel Deaconess Medical Center
Boston University Medical Center
Columbia University Medical Center
Weill Cornell Medicine
Maine Medical Center


Antibiotics
vs
Surgery
Good Health
After 1 month, participants rated their general health about the same in both groups.
After 1 month, participants rated their general health about the same in both groups.
Initial Time in ER & Hospital
During the first visit, time spent in the ER or hospital was about the same in both groups.
During the first visit, time spent in the ER or hospital was about the same in both groups.
Symptoms Go Away
After 1 month, symptoms like pain or fever were about the same in both groups.
After 1 month, symptoms like pain or fever were about the same in both groups.
No Surgery
About 7 in 10 (71%) did not have surgery within 3 months.
An appendectomy is surgery.
No Initial Hospital Stay
About half (47%) did not have to be admitted to the hospital for their antibiotics treatment.
Almost all (95%) participants were admitted to the hospital for their surgery.
Less Work Missed
Participants missed an average of 5.3 days of work.
Participants missed an average of 8.7 days of school or work.
Fewer Healthcare Visits
9 in 100 (9%) participants needed to visit an emergency room or urgent care clinic within 3 months.
4 in 100 (4%) participants needed to visit an emergency room or urgent care clinic within 3 months.
Appendicitis Does Not Return
Appendicitis can come back if the appendix is not removed. Future CODA reports will tell us how often that happens.
The appendix is fully removed when surgery is successful.
One Time Treatment
About 3 in 10 (29%) overall had surgery within 3 months. About 4 in 10 (41%) who had an appendix stone (appendicolith) had surgery within 3 months.
Most likely to be completed in one hospital visit.
Complications (Unexpected
For every 100 participants, there were about 8 problems in the antibiotics group. There were about 4 problems for every 100 participants in the surgery group. The higher number of complications in the antibiotics group was

What we know after CODA….

- Antibiotics can be used in appendicitis
  - Definitions of effectiveness are “eye of the beholder”
- ~3-in-10 undergo appendectomy (higher in the appendicolith group)
  - Multiple outcomes favor one treatment or the other
- Recurrence after 30 days ~3-in-10 (95% pathology confirmed)
  - Appendicolith not associated
- Belief in antibiotics working is as important as appendicolith
- Antibiotics for appendicitis: a good choice for some, probably not all

Jama Surg 2022

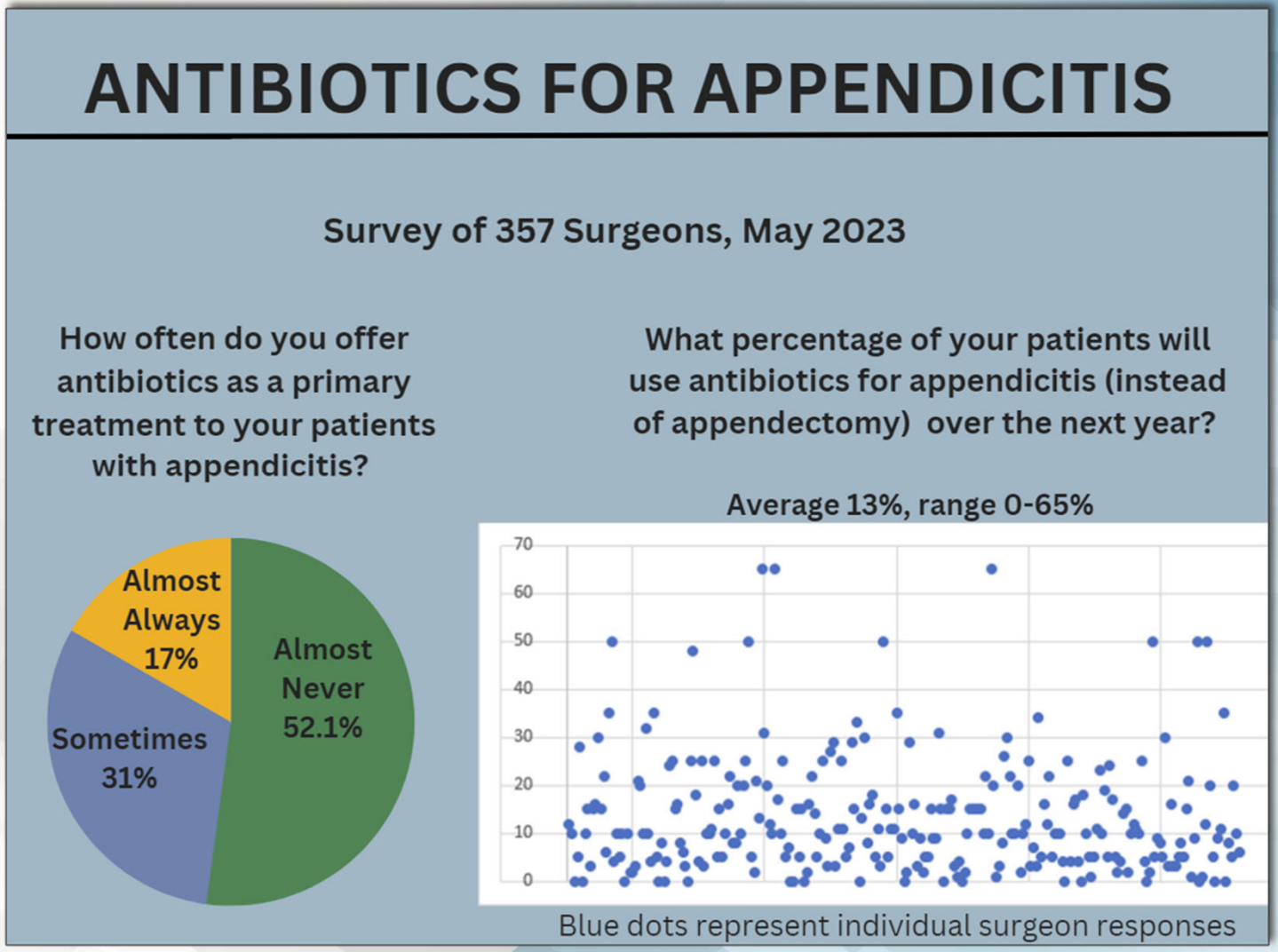

Competing Priorities
Patient
Time away from family
Fear of surgery
Caregiver responsibilities
At home care
Time away from work
Life events
Cost
Pain
Clinician
Complications
Readmission
Medication
Time
Future surgery
Outcomes
Surgical history
Medical Legal

What antibiotics can be used for appendicitis?

- Recommend SIS/IDSA guidelines.
- The first dose of antibiotics is given IV in ED at time of appendicitis diagnosis
- Oral x XX days
  - Very little data supports time for IV to PO
  - Any brilliant folks interested in antibiotic stewardship to do this study?!

https://doi.org/10.1086/649554
https://doi.org/10.1089/sur.2016.261

Now what?!


ANTIBIOTICS FOR APPENDICITIS
Survey of 357 Surgeons, May 2023
How often do you offer antibiotics as a primary treatment to your patients with appendicitis?
Almost Always 17%
Almost Never 52.1%
Sometimes 31%
What percentage of your patients will use antibiotics for appendicitis (instead of appendectomy) over the next year?
Average 13%, range 0-65%
70
60
50
40
30
20
10
0
Blue dots represent individual surgeon responses

TRIAD

Treatment Individualized Appendicitis Decision Making Implementation Program


Decision Support Tool
TRIAD
Treatment Individualized Appendicitis Decision Making Implementation Program
Clinician & Allied-health Professional Training
EHR-based protocol

Research reported in this presentation was funded through a Patient-Centered Outcomes Research Institute® (PCORI®) Award (PCS-1409-24099)

AHRQ grant to fund CERTAIN: R01HS22959

Thank you!

Giana Davidson, MD

ghd@uw.edu

Sara DePaoli

sdepaoli@uw.edu

UNIVERSITY of WASHINGTON

CODA
Comparing Outcomes of Drugs & Appendectomy

SURGICAL OUTCOMES RESEARCH CENTER
SORCE

TRIAD
Treatment Individualized Appendicitis Decision Making Implementation Program