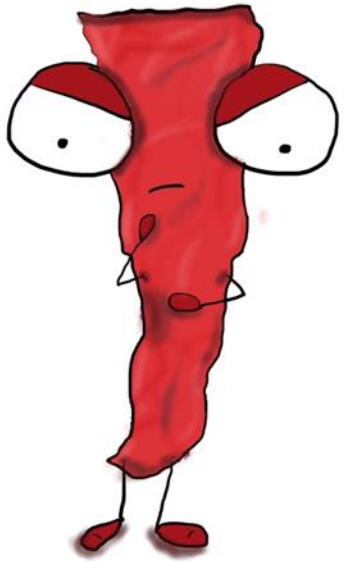
CODA

Comparing Outcomes of Drugs & Appendectomy

The CODA Collaborative

NIH Collaboratory Grand Rounds, November 6, 2020



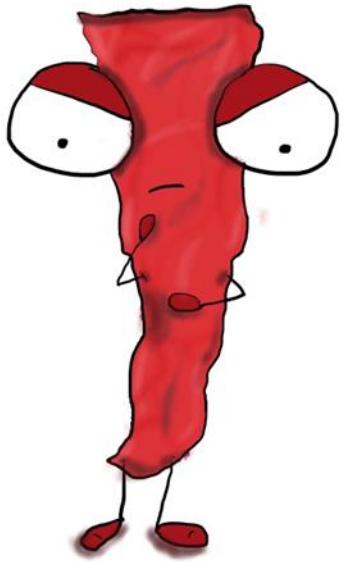
CODA

Comparing Outcomes of Drugs & Appendectomy

The CODA Collaborative

NIH Collaboratory Grand Rounds, November 6, 2020

Presented on behalf of the CODA Collaborative by;
David R. Flum, MD MPH
Department of Surgery
University of Washington
Seattle, WA



CODA Collaborative

Midwest:

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

West:

University of Washington Medical Center
Harborview Medical Center
Virginia Mason Medical Center
Swedish Medical Center- First Hill
Providence Regional Medical Center
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

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

South:

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

CERTAIN™

CODA: Site Investigators

Bellevue NYU School of Medicine
Onaona Gurney, MD
William Chiang, MD
Patricia Ayoung-Chee, MD, MPH

Beth Israel Deaconess Medical Center
Charles Parsons, MD
Nathan Shapiro, MD, MPH

Boston University Medical Center
Thurston Drake, MD, MPH
Sabrina Sanchez, MD, MPH

Columbia University Medical Center
Katherine Fischkoff, MD
Aleksandr Tichter, MD, MS

Harbor-UCLA Medical Center
Daniel A. DeUgarte, MD
Amy Kaji, MD, PhD

Harborview Medical Center
Joe Cuschieri, MD
Amber K Sabbatini, MD, MPH
Heather Evans, MD

Henry Ford Health Hospital
Jeffrey Johnson, MD
Joe Patton, MD

Madigan Army Medical Center
Vance Sohn, MD
Karen McGrane, MD

Maine Medical Center
Damien Carter, MD

The Ohio State University
Jon Wisler, MD
Amy Rushing, MD

Olive View-UCLA Medical Center
Darin Saltzman, MD, PhD
David Talan, MD
Gregory Moran, MD

Providence Regional Medical Center
Careen Foster, MD
Brandon Tudor, MD

Rush University Medical Center
Thea P Price, MD

Swedish Medical Center
Katherine Mandell, MD, MPH

Tisch NYU Langone Medical Center
Onaona Gurney, MD
William Chiang, MD

UCHealth University of Colorado
Lisa Ferrigno, MD, MPH
Matthew Salzberg, MD, MBA

University of Iowa Healthcare
Dionne Skeete, MD
Brett Faine, PharmD, MS

University of Michigan Medical Center
Pauline Park, MD
Hasan Alam, MD

University of Mississippi
Matthew Kutcher, MD, MS
Alan Jones, MD

University of Texas at Houston
Lillian Kao, MD, MS

University of Texas LBJ
Mike Liang, MD

University of Washington
Giana H. Davidson, MD, MPH
Amber K Sabbatini, MD, MPH
David R. Flum, MD MPH Co-PI

Vanderbilt University Medical Center
Wesley Self, MD, MPH
Callie Thompson, MD

Virginia Mason Medical Center
Abigal Wiebusch, MD
Juliana Yu, MD

Weill Cornell Medical Center
Robert Winchell, MD
Sunday Clark, ScD, MPH

CERTAIN™

CODA: Site Investigators

Bellevue NYU School of Medicine
Onaona Gurney, MD
William Chiang, MD
Patricia Ayoung-Chee, MD, MPH

Beth Israel Deaconess Medical Center
Charles Parsons, MD
Nathan Shapiro, MD, MPH

Boston University Medical Center
Thurston Drake, MD, MPH
Sabrina Sanchez, MD, MPH

Columbia University Medical Center
Katherine Fischkoff, MD
Aleksandr Tichter, MD, MS

Harbor-UCLA Medical Center
Daniel A. DeUgarte, MD
Amy Kaji, MD, PhD

Harborview Medical Center
Joe Cuschieri, MD
Amber K Sabbatini, MD, MPH
Heather Evans, MD

Henry Ford Health Hospital
Jeffrey Johnson, MD
Joe Patton, MD

Madigan Army Medical Center
Vance Sohn, MD
Karen McGrane, MD

Maine Medical Center
Damien Carter, MD

The Ohio State University
Jon Wisler, MD
Amy Rushing, MD

Olive View-UCLA Medical Center
Darin Saltzman, MD, PhD
David Talan, MD Co-PI
Gregory Moran, MD

Providence Regional Medical Center
Careen Foster, MD
Brandon Tudor, MD

Rush University Medical Center
Thea P Price, MD

Swedish Medical Center
Katherine Mandell, MD, MPH

Tisch NYU Langone Medical Center
Onaona Gurney, MD
William Chiang, MD

UCHealth University of Colorado
Lisa Ferrigno, MD, MPH
Matthew Salzberg, MD, MBA

University of Iowa Healthcare
Dionne Skeete, MD
Brett Faine, PharmD, MS

University of Michigan Medical Center
Pauline Park, MD
Hasan Alam, MD

University of Mississippi
Matthew Kutcher, MD, MS
Alan Jones, MD

University of Texas at Houston
Lillian Kao, MD, MS

University of Texas LBJ
Mike Liang, MD

University of Washington
Giana H. Davidson, MD, MPH
Amber K Sabbatini, MD, MPH
David R. Flum, MD MPH Co-PI

Vanderbilt University Medical Center
Wesley Self, MD, MPH
Callie Thompson, MD

Virginia Mason Medical Center
Abigal Wiebusch, MD
Juliana Yu, MD

Weill Cornell Medical Center
Robert Winchell, MD
Sunday Clark, ScD, MPH

CERTAIN™

No conflicts of interest reported

Appendectomy Research

Transvaginal Endoscopic Appendectomy

Rigid Instruments

J Am Assoc Gynecol Laparosc. 2001 Aug;8(3):438-41.

Operative culdolaparoscopy: a new approach combining operative culdoscopy and minilaparoscopy.

Tsin DA, Colombero LT, Mahmood D, Padouvas J, Manolas P.

Flexible Instruments

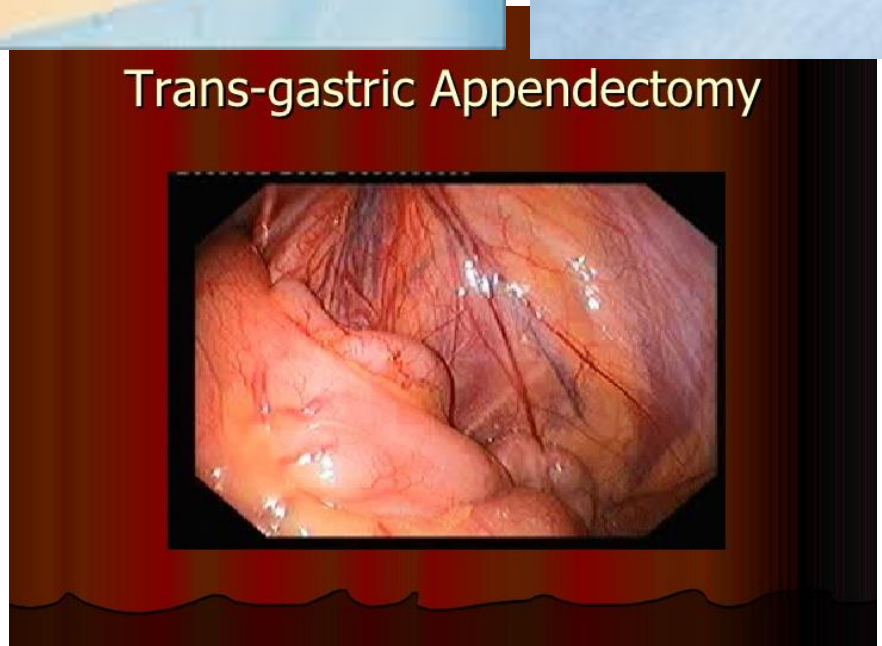
Surg Endosc. 2008 May;22(5):1343-7. Epub 2008 Mar 18.

Transvaginal endoscopic appendectomy in humans: a unique approach to NOTES--world's first report.

Palanivelu C, Rajan PS, Rangarajan M, Parthasarathi R, Senthilnathan P, Prasad M.

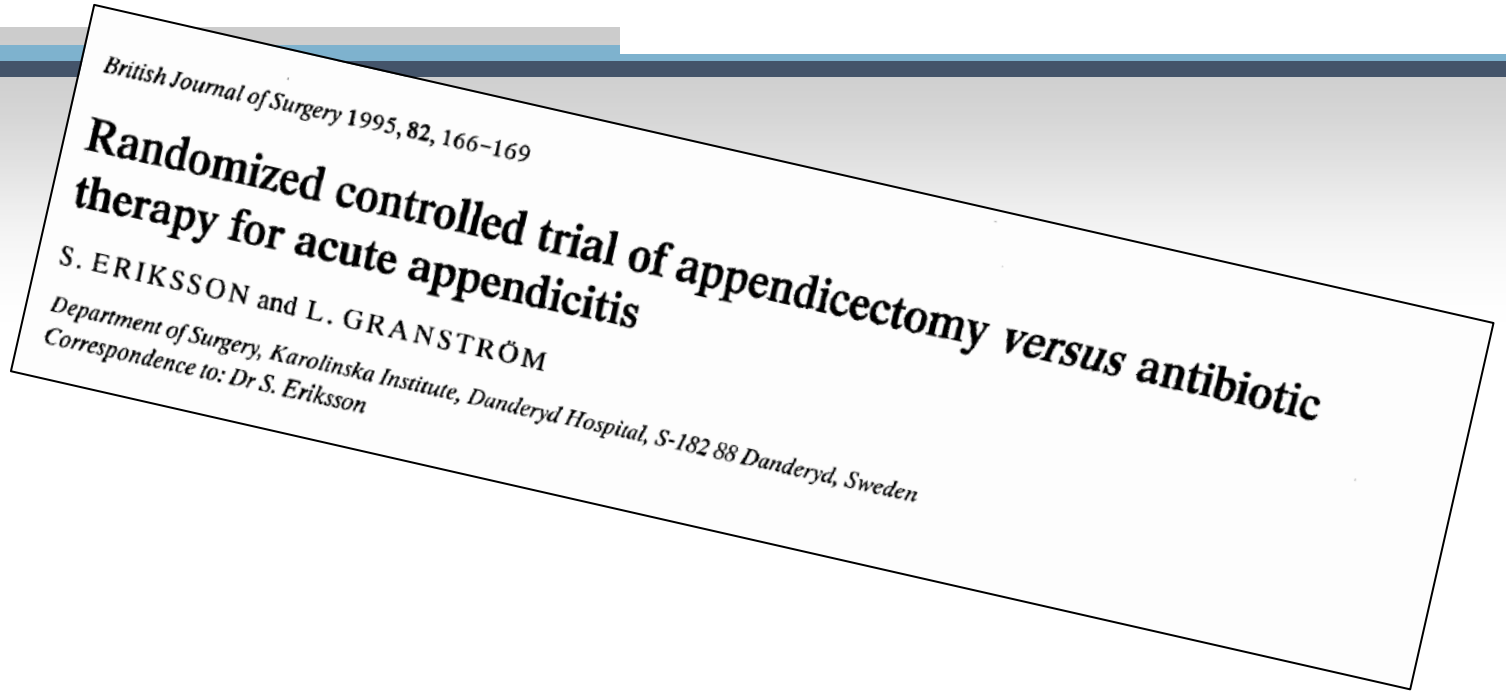
08/07/11

32



Appendicitis Research

Appendicitis Research



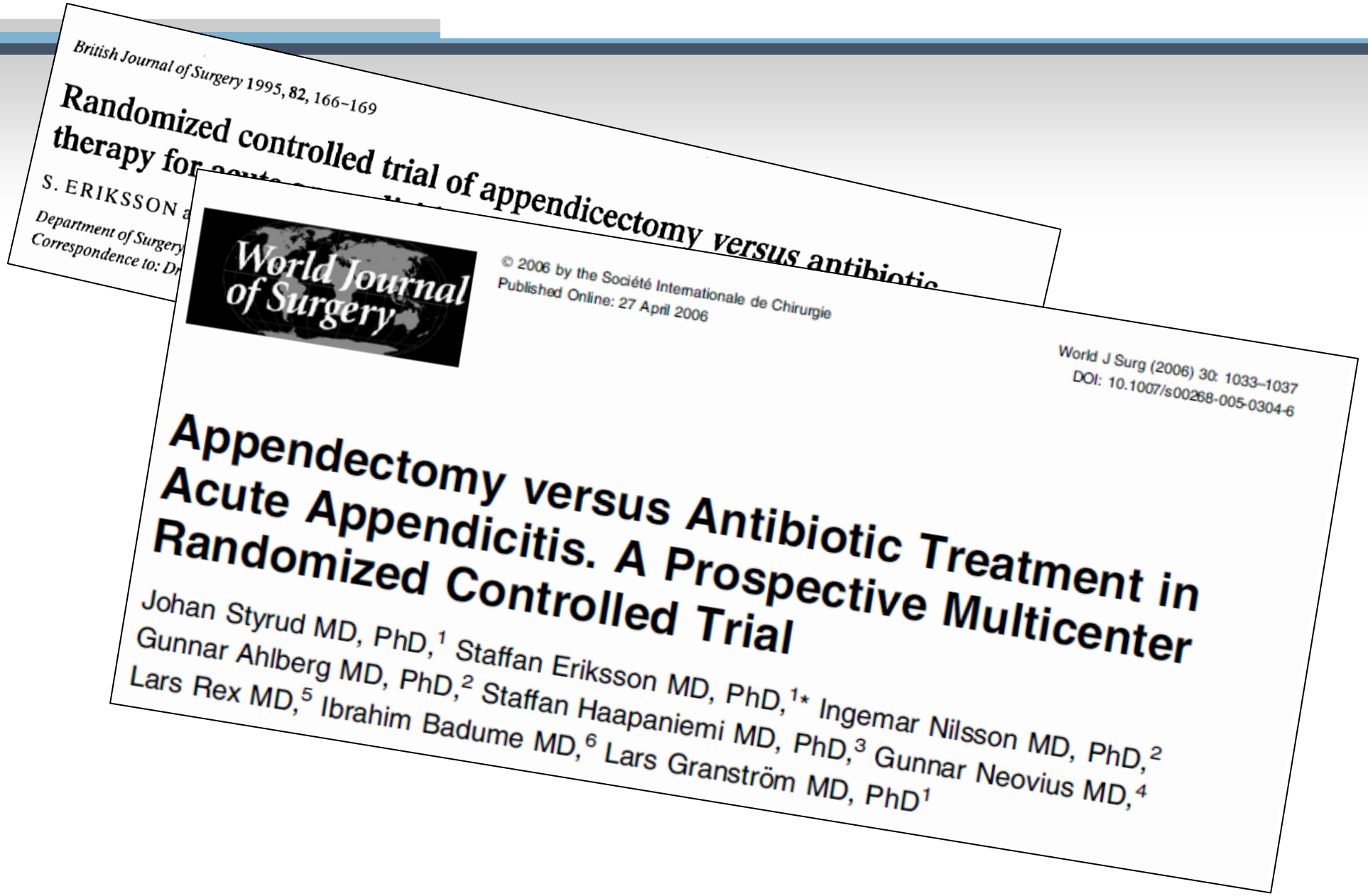
British Journal of Surgery 1995, 82, 166–169

Randomized controlled trial of appendicectomy *versus* antibiotic therapy for acute appendicitis

S. ERIKSSON and L. GRANSTRÖM

Department of Surgery, Karolinska Institute, Danderyd Hospital, S-182 88 Danderyd, Sweden
Correspondence to: Dr S. Eriksson

Appendicitis Research



British Journal of Surgery 1995, 82, 166–169

Randomized controlled trial of appendicectomy versus antibiotic therapy for

S. ERIKSSON a

Department of Surgery
Correspondence to: Dr

World Journal of Surgery

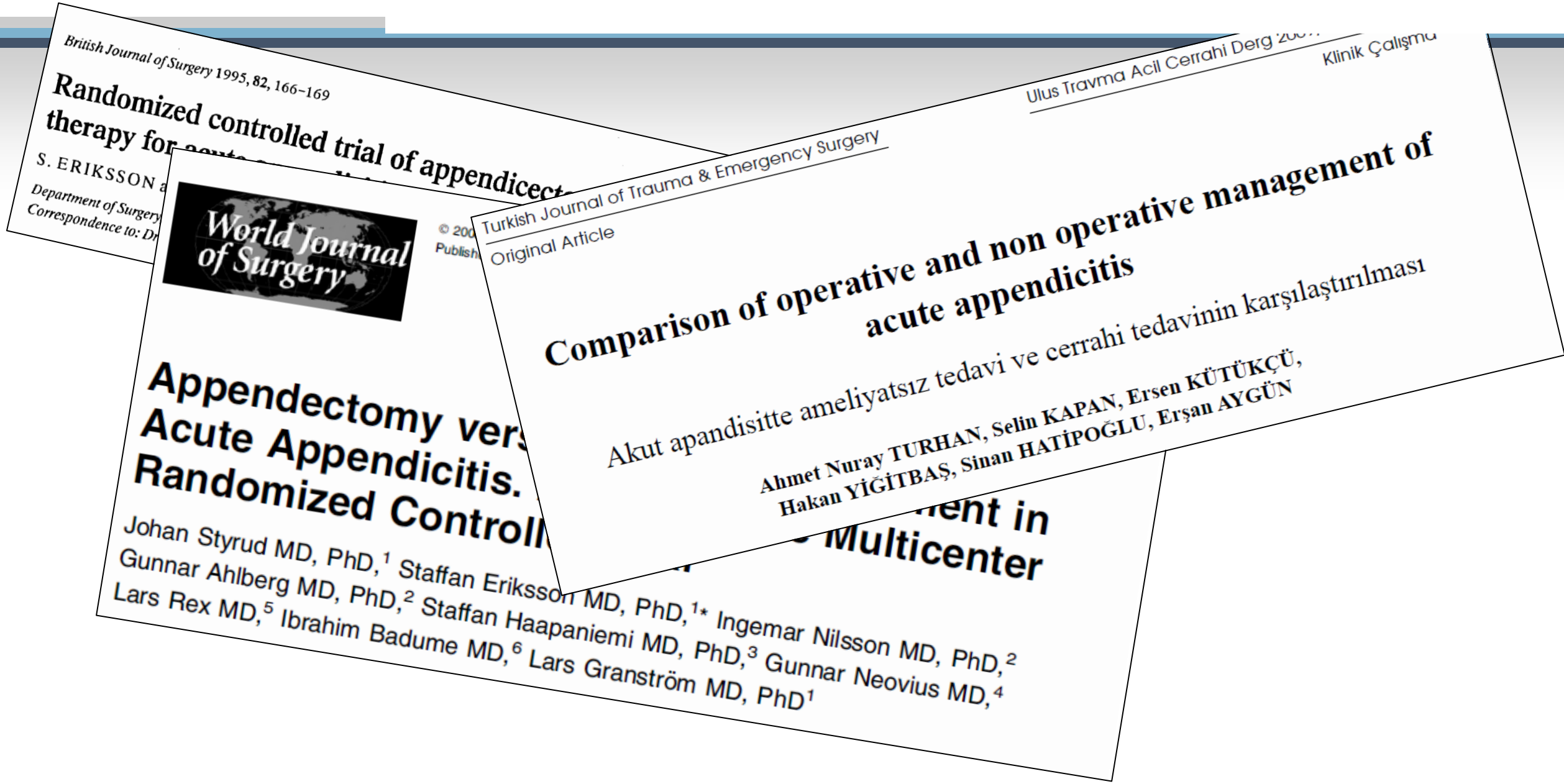
© 2006 by the Société Internationale de Chirurgie
Published Online: 27 April 2006

World J Surg (2006) 30: 1033–1037
DOI: 10.1007/s00268-005-0304-6

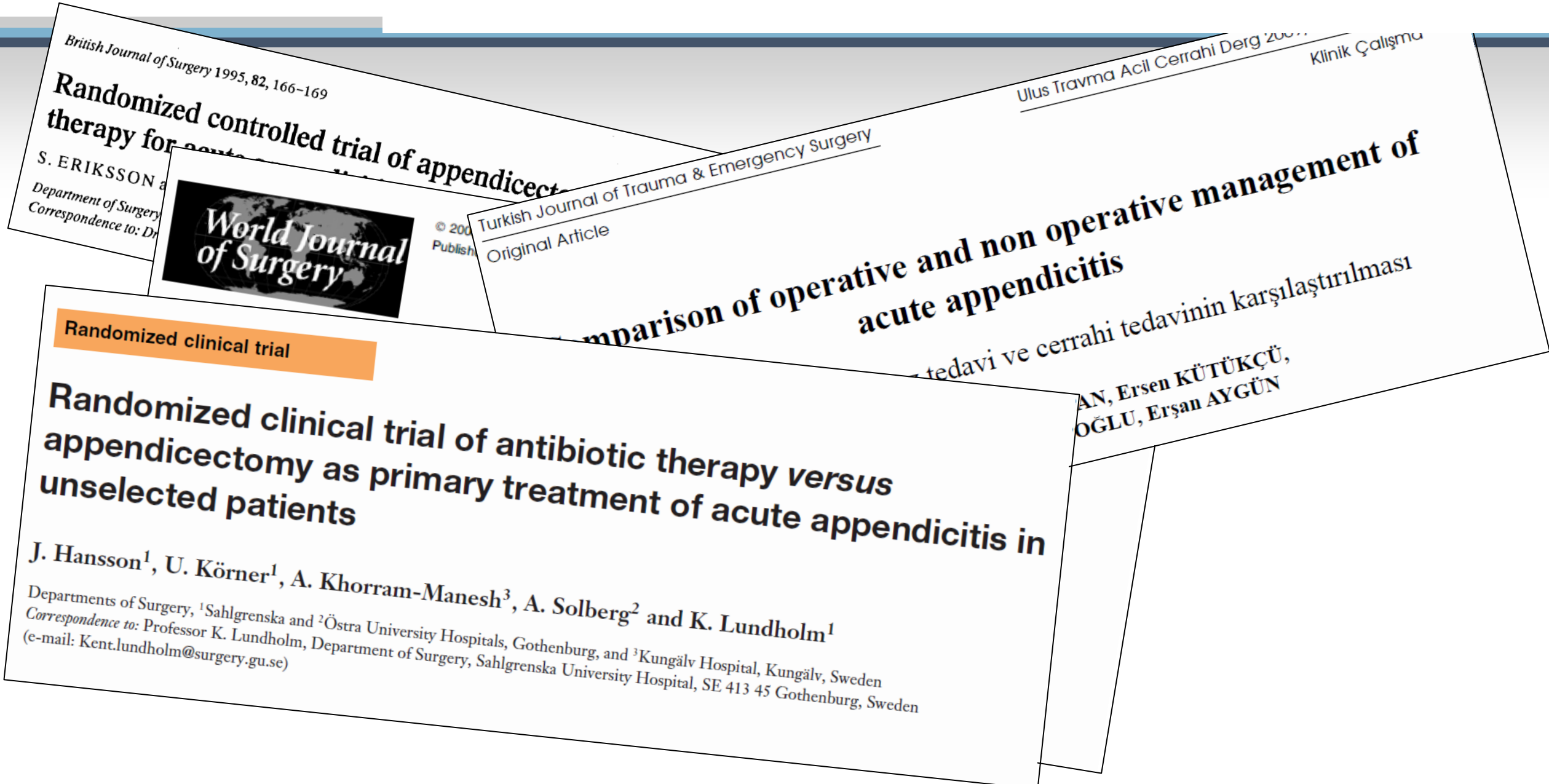
Appendectomy versus Antibiotic Treatment in Acute Appendicitis. A Prospective Multicenter Randomized Controlled Trial

Johan Styrud MD, PhD,[1] Staffan Eriksson MD, PhD,[1*] Ingemar Nilsson MD, PhD,[2] Gunnar Ahlberg MD, PhD,[2] Staffan Haapaniemi MD, PhD,[3] Gunnar Neovius MD,[4] Lars Rex MD,[5] Ibrahim Badume MD,[6] Lars Granström MD, PhD[1]

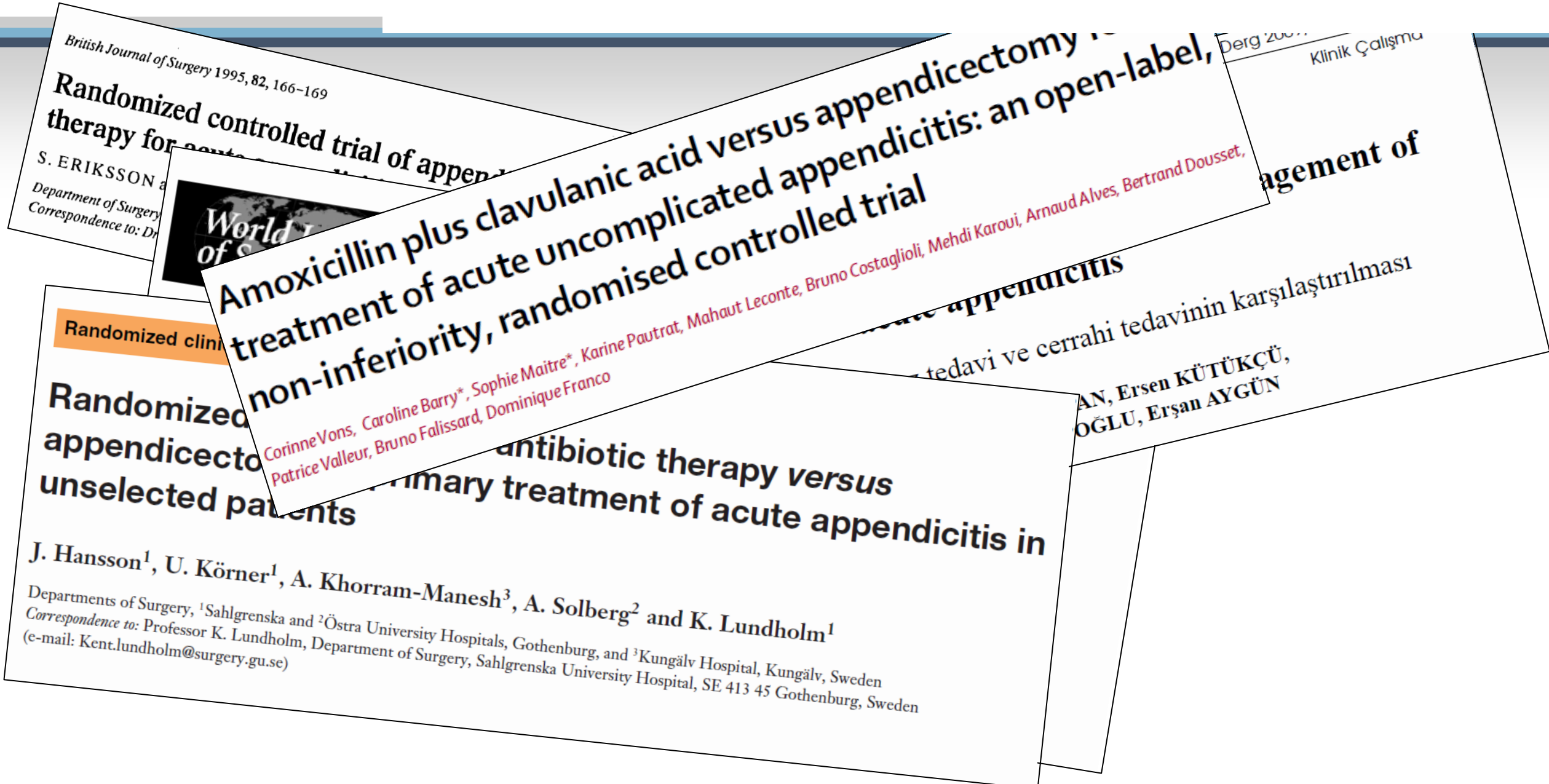
Appendicitis Research



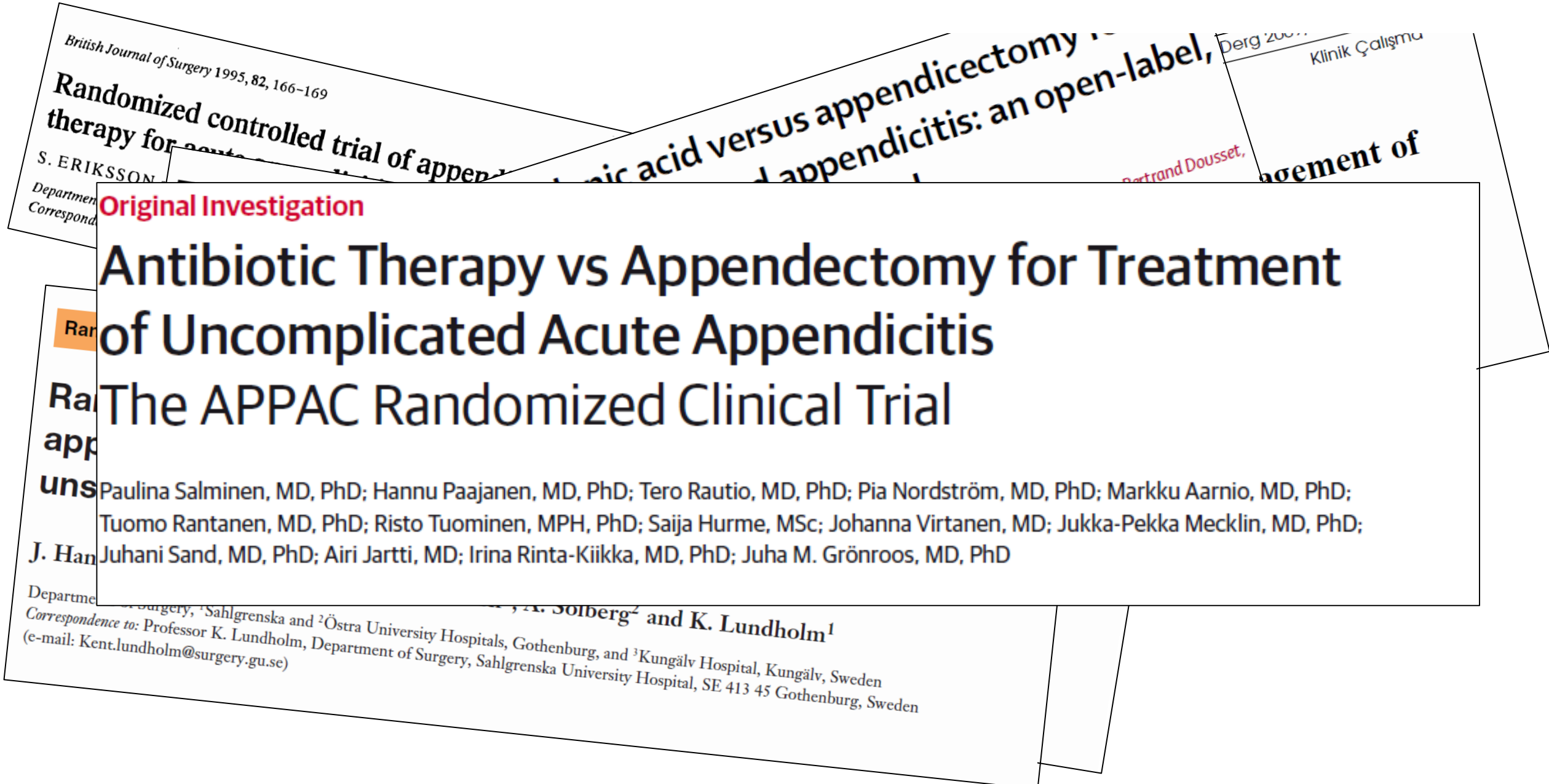
Appendicitis Research



Appendicitis Research



Appendicitis Research



The Evidence

The Evidence

- N=1,724

The Evidence

- N=1,724
- Outcomes common to both treatment arms
  - Complications, pain and days away from work-all more for surgery

The Evidence

- N=1,724
- Outcomes common to both treatment arms
  - Complications, pain and days away from work-all more for surgery
- Outcomes unique to antibiotics arm

The Evidence

- N=1,724
- Outcomes common to both treatment arms
  - Complications, pain and days away from work-all more for surgery
- Outcomes unique to antibiotics arm
  - 25-40% of those randomized to antibiotics had appendectomy by 1 yr

The Evidence

- N=1,724
- Outcomes common to both treatment arms
  - Complications, pain and days away from work-all more for surgery
- Outcomes unique to antibiotics arm
  - 25-40% of those randomized to antibiotics had appendectomy by 1 yr
  - Largest study (APPAC, n=257 antibiotics)
    - 27% by 1 year
    - 39% by 5 years

Evidence Gaps

Evidence Gaps

- “Selected” patients
  - Surgeons determined who was approached
  - None with CT perforation or appendicolith
  - Perforation rate in surgical arm of APPAC <2%

Evidence Gaps

- “Selected” patients
  - Surgeons determined who was approached
  - None with CT perforation or appendicolith
  - Perforation rate in surgical arm of APPAC <2%
- Not typical US practice
  - Inconsistent use of diagnostic imaging
  - Mandatory hospitalizations
  - Mostly open surgery

Evidence Gaps

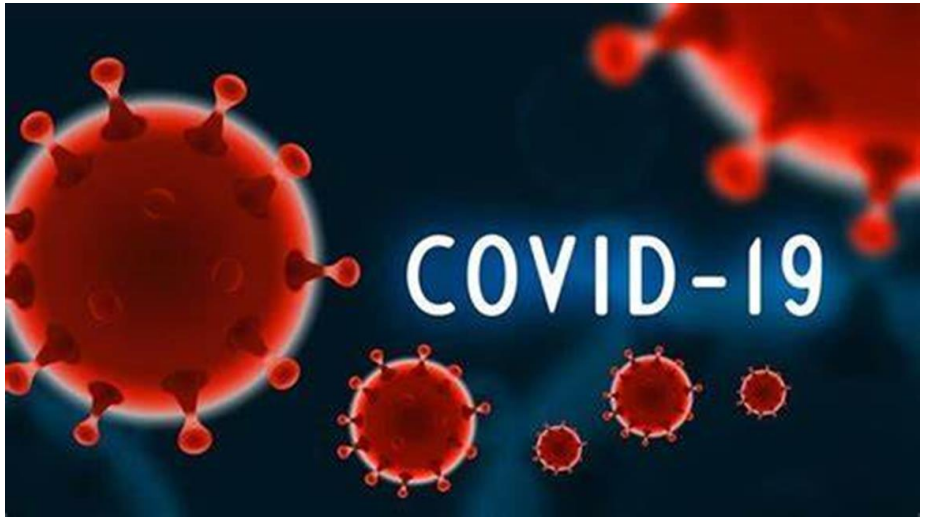
- "Selected" patients
  - Surgeons determined who was approached
  - None with CT perforation or appendicolith
  - Perforation rate in surgical arm of APPAC <2%
- Not typical US practice
  - Inconsistent use of diagnostic imaging
  - Mandatory hospitalizations
  - Mostly open surgery
- Little uptake of antibiotics in US

….So Why Rock the Boat?

….So Why Rock the Boat?

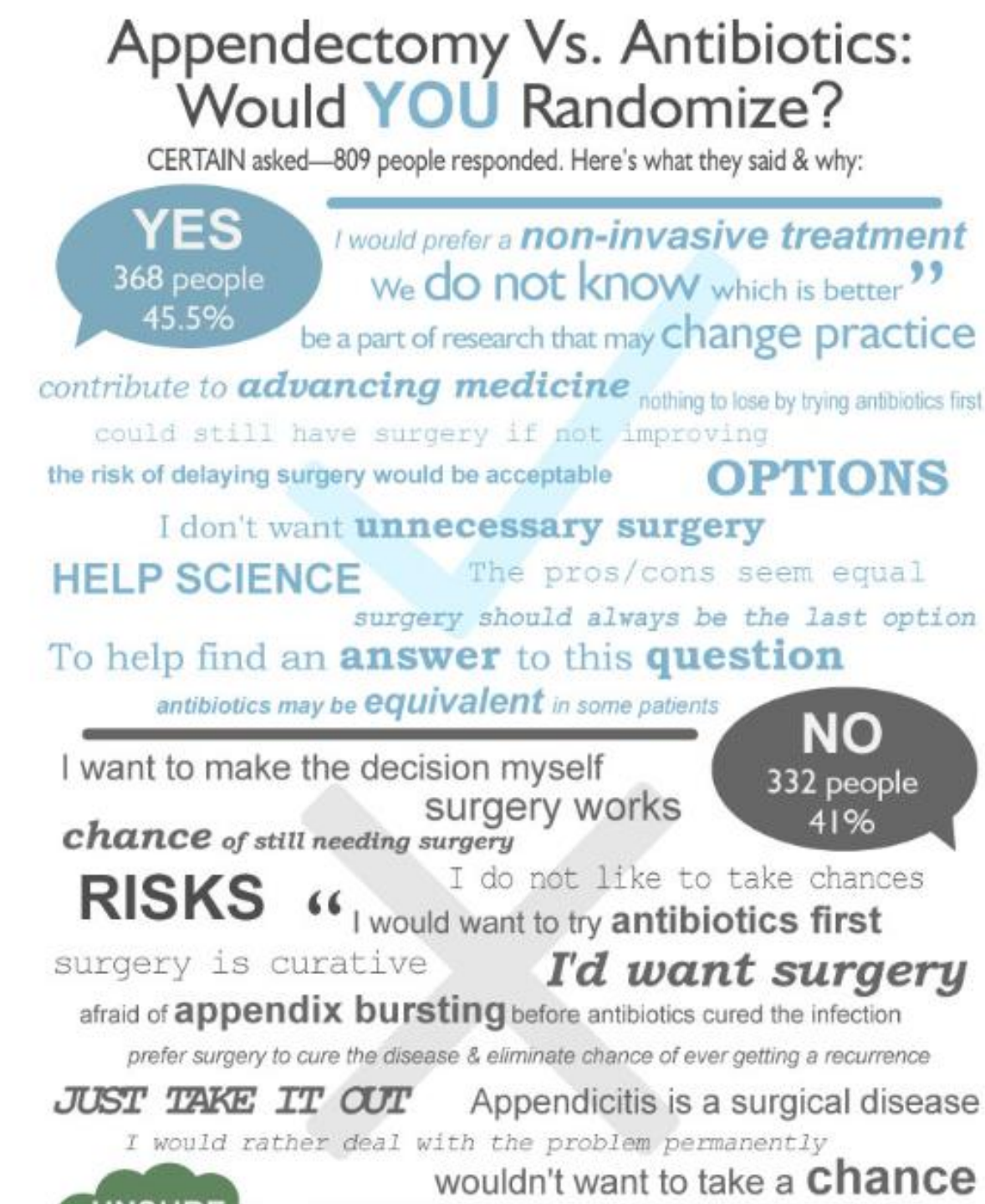
….So Why Rock the Boat?

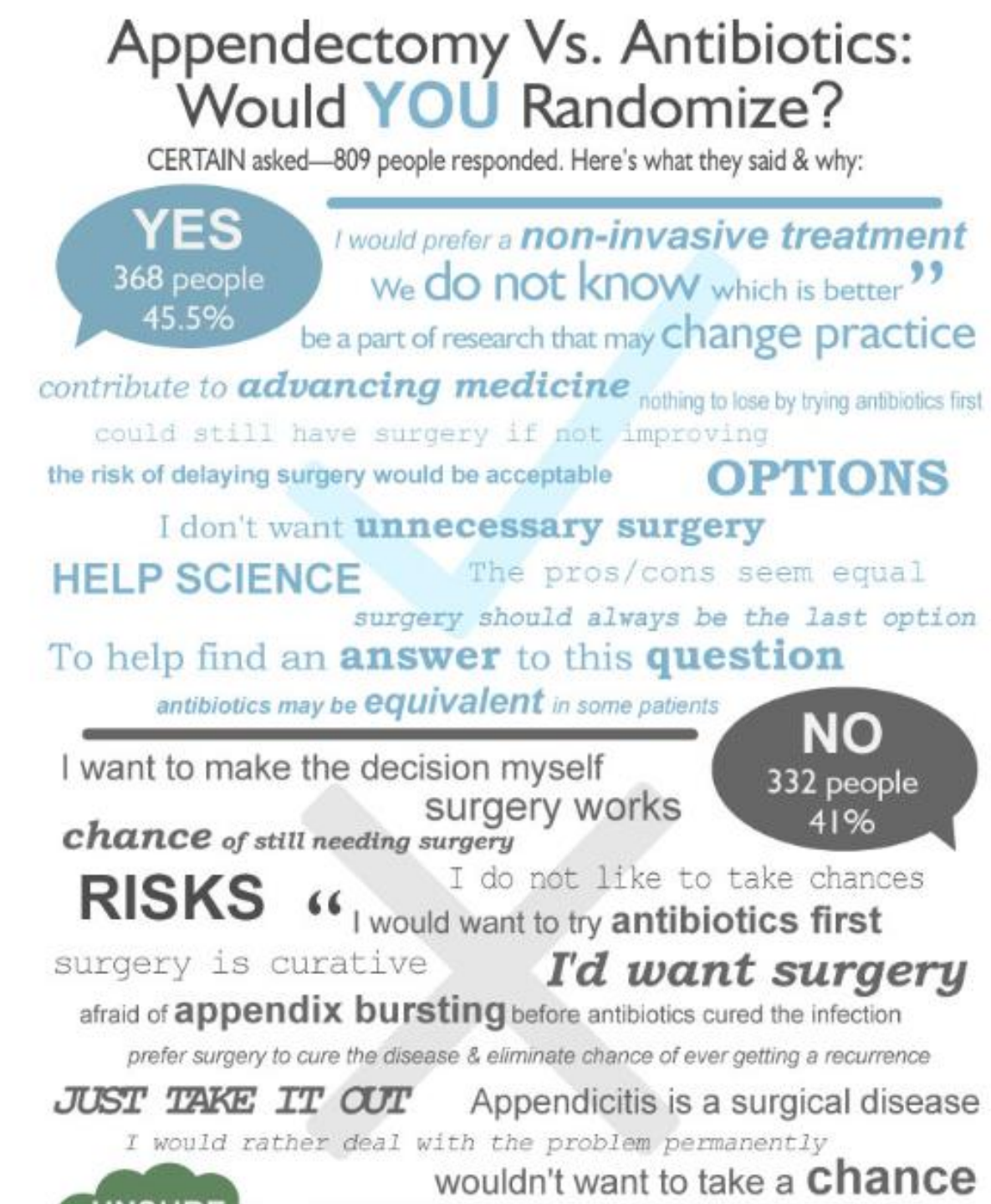
….So Why Rock the Boat?



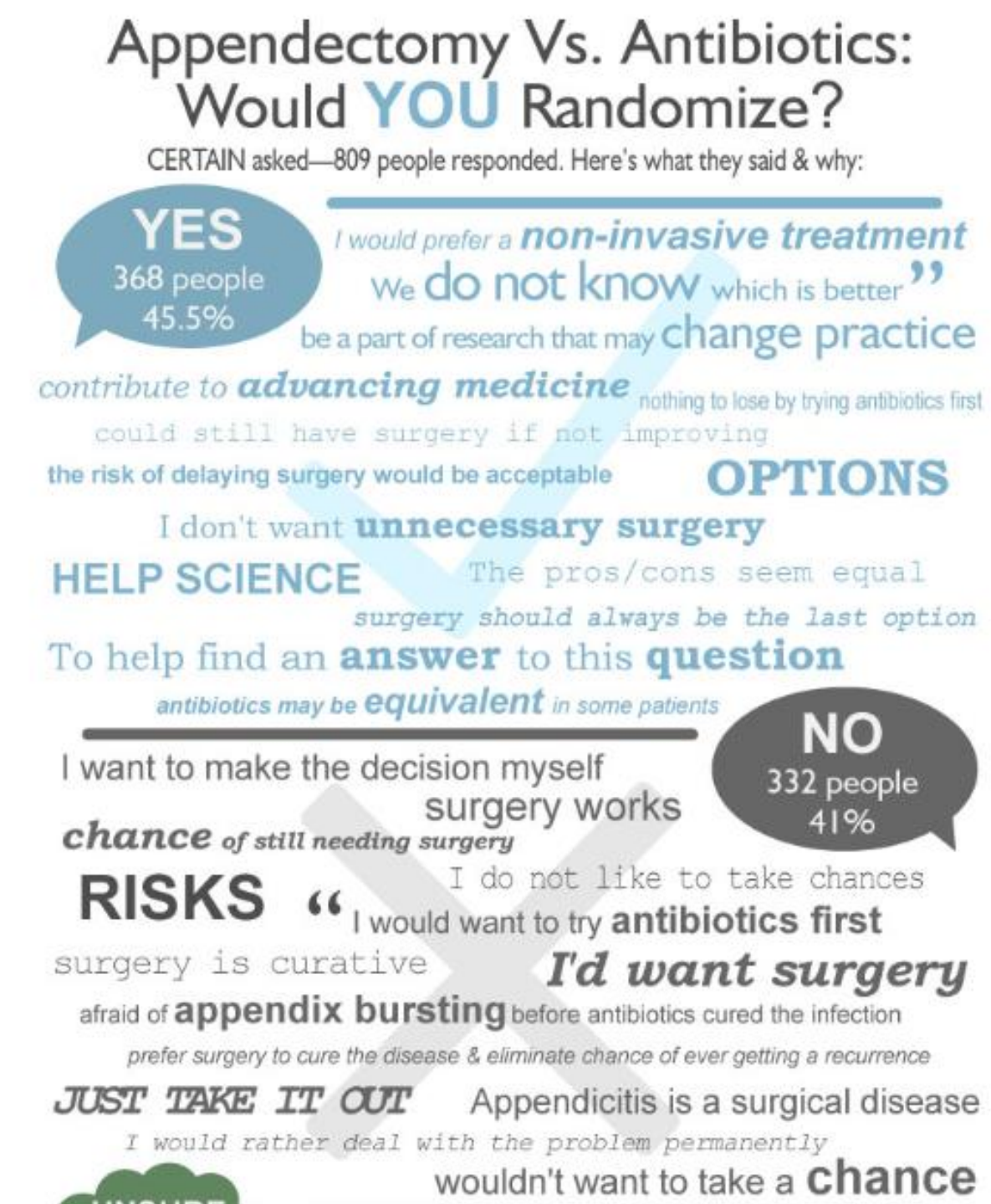
Appendectomy Vs. Antibiotics: Would YOU Randomize?

CERTAIN asked—809 people responded. Here's what they said & why:



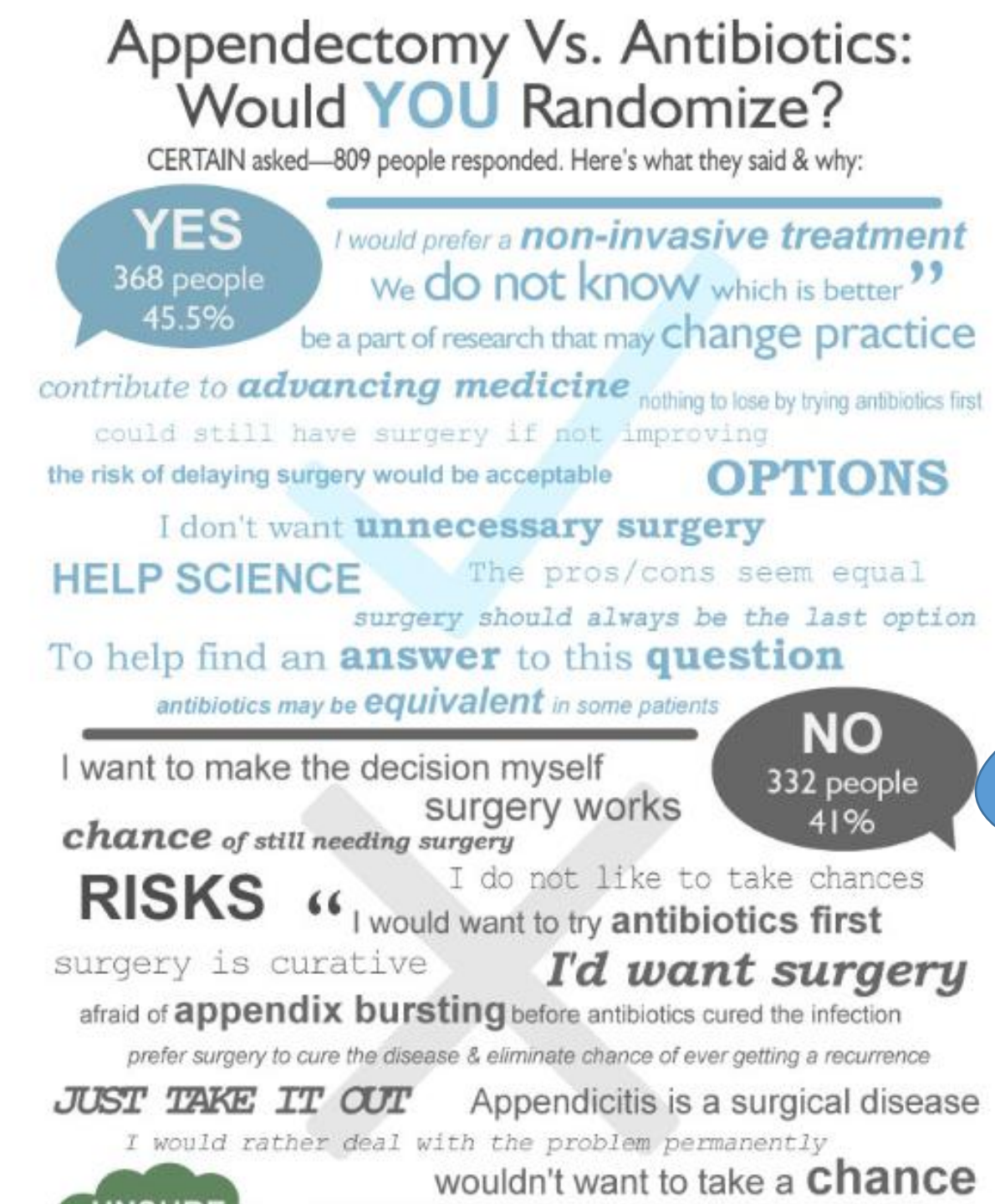


Am I going to feel better and when?



Am I going to feel better and when?

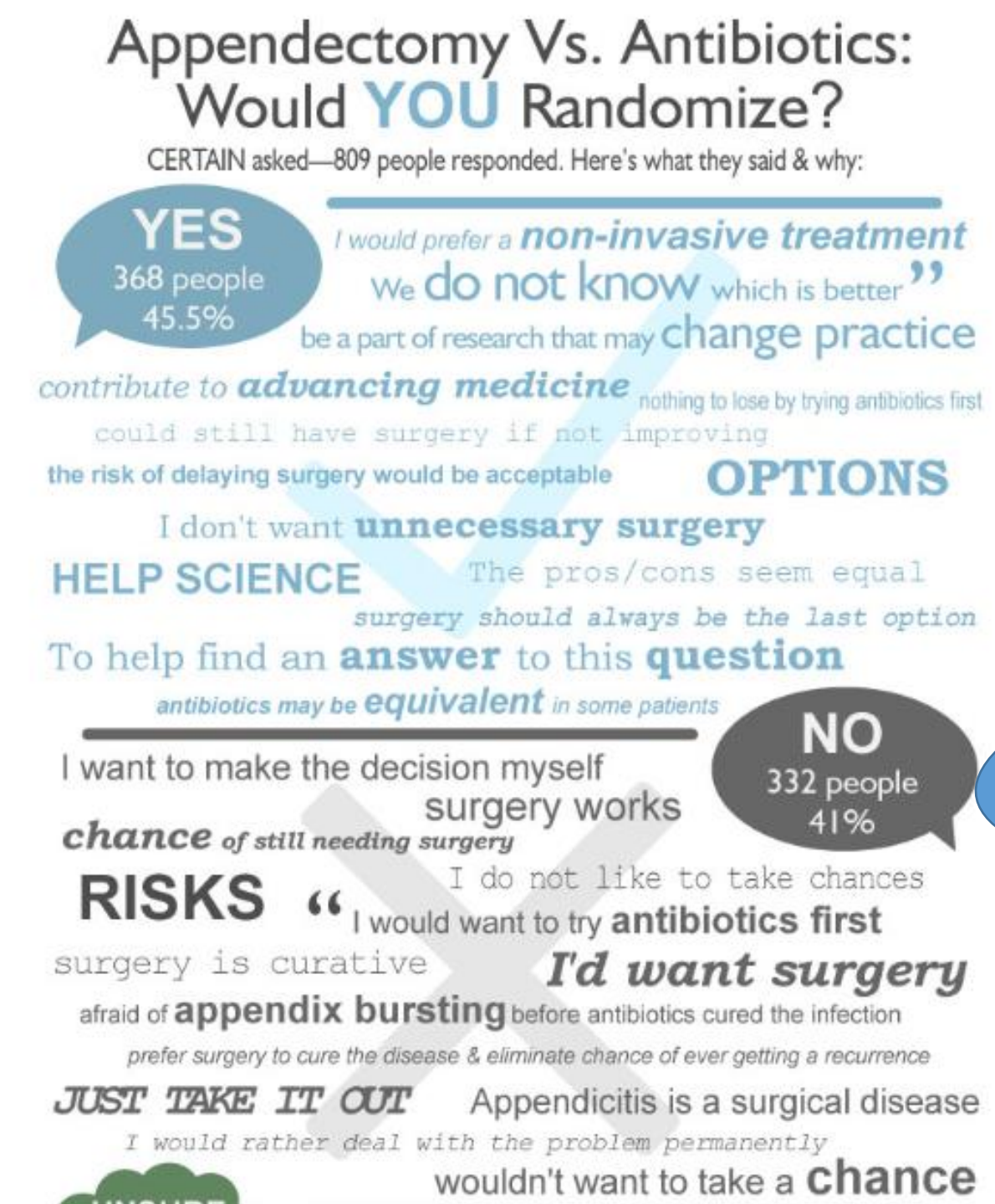
What's the chance I can avoid surgery?



Am I going to feel better and when?

What's the chance I can avoid surgery?

Are both treatments safe?



Am I going to feel better and when?

What's the chance I can avoid surgery?

Are both treatments safe?

Which treatment will get me back to work sooner and cost me less?


CODA
Comparing Outcomes of Drugs & Appendectomy

Are antibiotics as effective as appendectomy for appendicitis?

Are antibiotics as effective as appendectomy for appendicitis?

- General health status

Are antibiotics as effective as appendectomy for appendicitis?

- General health status
- Clinical outcomes

Are antibiotics as effective as appendectomy for appendicitis?

- General health status
- Clinical outcomes
- Safety

Are antibiotics as effective as appendectomy for appendicitis?

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

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?

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?

- Appendicolith subgroup

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?

- Appendicolith subgroup

A Pragmatic Trial

Population

Population

- Adults with imaging confirmed appendicitis
  - Perforation and appendicolith allowed

Population

- Adults with imaging confirmed appendicitis
  - Perforation and appendicolith allowed
- Excluded
  - Abscess, free air, diffuse peritonitis, septic shock
  - Ileocolectomy likely b/c of severe phlegmon
  - Pregnancy
  - Both treatments are not an option:
    - Contraindication
    - Allergies
    - Immunocompromised

Intervention and Comparator

Intervention and 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

- Laparoscopic and open-technique not standardized.

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

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

- What is the EQ5D?

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

- What is the EQ5D?

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

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

- What is the EQ5D?
- Why EQ5D?

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

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

- What is the EQ5D?
- Why EQ5D?
- Why 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

“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

Secondary outcomes

- Appendectomy (any indication) in the antibiotics group

Secondary outcomes

- Appendectomy (any indication) in the antibiotics group
- NSQIP-defined morbidity events

Secondary outcomes

- Appendectomy (any indication) in the antibiotics group
- NSQIP-defined morbidity events
  - A subset were Serious Adverse Events (for DSMB reporting)

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)

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

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

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

Methods: Analysis

- Intention-to-treat analysis, appendicolith subgroup pre-specified
- Non-inferiority
  - Rule out an EQ-5D difference as small as 0.05
  - Secondary “treated per protocol” analysis
- Binomial regression-relative risks, Poisson regression (rate ratio) for count data, linear regression for continuous outcomes.
- Kaplan Meier-based cumulative incidence curve for appendectomy through 90 days

We didn’t expect to be here today…

We didn’t expect to be here today…

- Main analytic outcome time point- 30 days

We didn’t expect to be here today…

- Main analytic outcome time point- 30 days
- Planned to focus on all outcomes at 1 year, finished recruitment in February

We didn’t expect to be here today…

- Main analytic outcome time point- 30 days
- Planned to focus on all outcomes at 1 year, finished recruitment in February

We didn’t expect to be here today…

- Main analytic outcome time point- 30 days
- Planned to focus on all outcomes at 1 year, finished recruitment in February

Coronavirus daily news updates, March 15: What to know today about COVID-19 in the Seattle area, Washington state, and the nation

March 15, 2020 at 6:45 am | *Updated June 11, 2020 at 5:15 pm*

COVID-19 Guidelines for Triage of Emergency General Surgery Patients

Updated March 25, 2020

Download a print-friendly version

These guidelines are meant to provide advice for surgeons and to serve the best interests of patients based on estimates of risk for *average* patients (in terms of clinical condition, patient health, hospital resource availability) and are meant to be considered for patients presenting with general surgical emergencies during this pandemic. For patients who are known to be COVID-19 positive or at high clinical suspicion for COVID infection, non-operative management is preferred, if feasible and safe for the patient. If operation is required in these patients then appropriate PPE should be utilized and precautions taken to protect the healthcare team.

- The American College of Surgeons has a tremendous amount of respect and trust in the judgment and commitment of our Fellows. The information provided should not be considered rigid guidelines, and are not intended to supplant clinical judgment. Nor is the information intended to impede the development of consensus regarding institutional and local approaches to treatment guidelines. There is a great deal of uncertainty around this evolving pandemic and a large amount of regional variability. In this fluid and variable environment, information changes rapidly.
- It is very likely that the strategies outlined in this document may change as our understanding of unique challenges that COVID-19 poses within each country, state, and healthcare environment evolves.

Elective Case Triage Guidelines for Surgical Care

COVID-19 Guidelines for Triage of Emergency General Surgery Patients

Updated March 25, 2020

Download a print-friendly version

These guidelines are meant to provide advice for surgeons and to serve the best interests of patients based on estimates of risk for *average* patients (in terms of clinical condition, patient health, hospital resource availability) and are meant to be

Appendicitis, Uncomplicated

There is some evidence that suggests that patients with uncomplicated appendicitis can be managed with IV antibiotics followed by transition to PO antibiotics. High failure rates of this approach (30-50%) have been noted with appendicolith and with CT evidence of disease extension outside of the RLQ. Based on the surgeon's judgment and the patient condition, a trial of antibiotics can be considered. Short stay or outpatient laparoscopic appendectomy is likely associated with a shorter length of stay. The duration of hospital stay should be weighed against the use of OR resources in this circumstance and should be based on surgeon judgment.

Elective Case Triage Guidelines for Surgical Care

COVID-19 Guidelines for Triage of Emergency General Surgery Patients

Updated March 25, 2020

Download a print-friendly version

These guidelines are meant to provide advice for surgeons and to serve the best interests of patients based on estimates of risk for *average* patients (in terms of clinical condition, patient health, hospital resource availability) and are meant to be

Appendicitis, Uncomplicated

There is some evidence that suggests that patients with uncomplicated appendicitis can be managed with IV antibiotics followed by transition to PO antibiotics. High failure rates of this approach (30-50%) have been noted with appendicolith and with CT evidence of disease extension outside of the RLQ. Based on the surgeon's judgment and the patient condition, a trial of antibiotics can be considered. Short stay or outpatient laparoscopic appendectomy is likely associated with a shorter length of stay. The duration of hospital stay should be weighed against the use of OR resources in this circumstance and should be based on surgeon judgment.

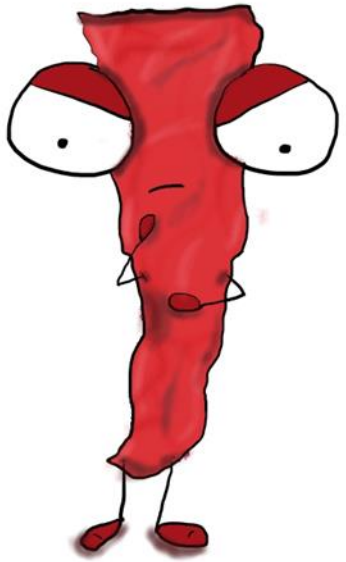
CODA

Comparing Outcomes of Drugs & Appendectomy

The CODA Collaborative

American College of Surgeons Clinical Congress October 5, 2020

Presented on behalf of the CODA Collaborative by;
David R. Flum, MD MPH and Giana H. Davidson, MD MPH
Department of Surgery
University of Washington
Seattle, WA



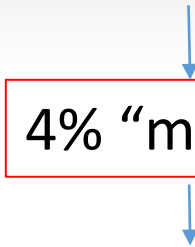
Recruitment and Retention

Recruitment and Retention

8168 Adults with imaging confirmed appendicitis

Recruitment and Retention

8168 Adults with imaging confirmed appendicitis



4% “missed”

Recruitment and Retention

8168 Adults with imaging confirmed appendicitis

4% “missed”

~10% excluded for appendix-related reasons

~10% excluded for other clinical reasons

Recruitment and Retention

8168 Adults with imaging confirmed appendicitis

↓

4% “missed”

↓

~10% excluded for appendix-related reasons

~10% excluded for other clinical reasons

↓

1.2% clinician deemed “ineligible” beyond these criteria

Recruitment and Retention

8168 Adults with imaging confirmed appendicitis

↓

4% “missed”

↓

~10% excluded for appendix-related reasons

~10% excluded for other clinical reasons

↓

1.2% clinician deemed “ineligible” beyond these criteria

31% of eligible randomized

Recruitment and Retention

8168 Adults with imaging confirmed appendicitis

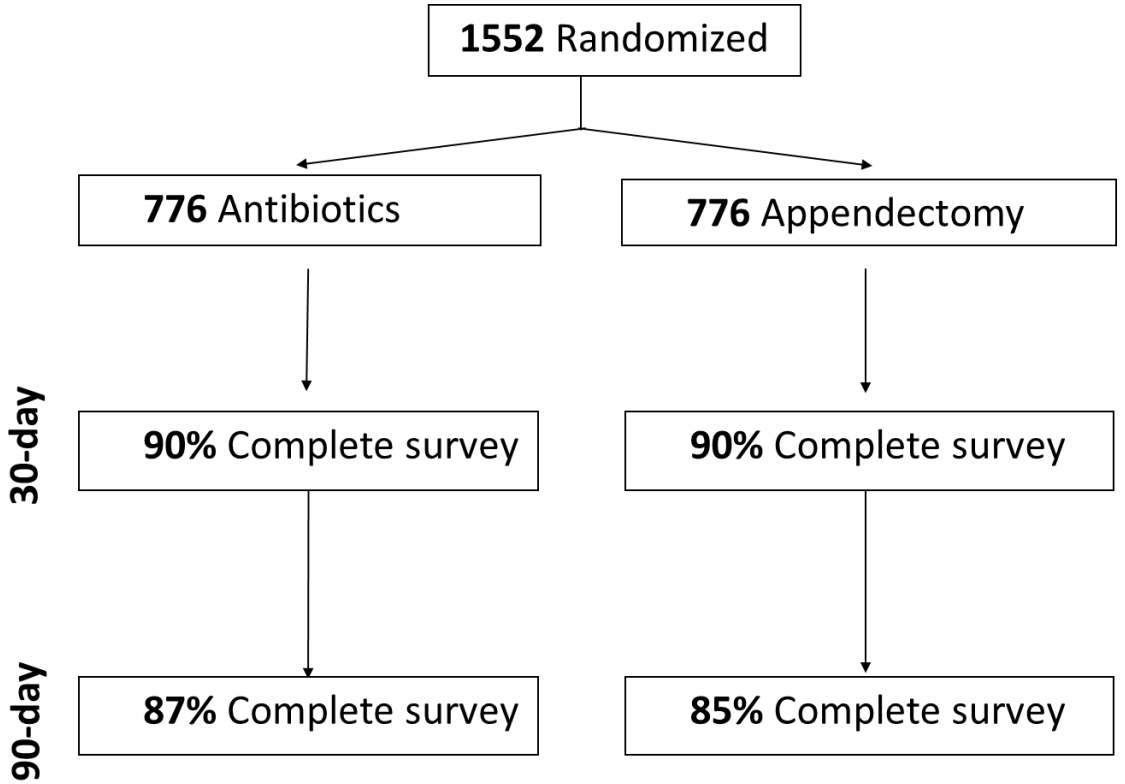
4% “missed”

~10% excluded for appendix-related reasons

~10% excluded for other clinical reasons

1.2% clinician deemed “ineligible” beyond these criteria

31% of eligible randomized



Demographics

Sex (male)	63%
Age	
Mean	38 years
18-29	31%
50+	19%
Race	
White	62%
Multiple/other	24%
Black/African American	9%
Asian	6%
American Indian/Alaska Native	1%
Native Hawaiian/Pacific Islander	0.5%
Language (Spanish)	34%
Insurance	
Commercial	42%
Medicaid	18%

Characteristics at ED presentation

	Overall (n=1552)
BMI mean(range)	29 (15.8-62)
Duration of symptoms (days) mean	1.7
Report of fever (%)	24%
Initial WBC mean	13.1K

Characteristics at ED presentation

	Overall (n=1552)
BMI mean(range)	29 (15.8-62)
Duration of symptoms (days) mean	1.7
Report of fever (%)	24%
Initial WBC mean	13.1K

CT scanning in 96% (n=1493)

Characteristics at ED presentation

	Overall (n=1552)
BMI mean(range)	29 (15.8-62)
Duration of symptoms (days) mean	1.7
Report of fever (%)	24%
Initial WBC mean	13.1K

CT scanning in 96% (n=1493)

Appendix maximum diameter (mm)	11.4
Appendicolith	27%
Peri-appendiceal fat stranding	75%
Perforation (or ambiguous)	3%
Periappendiceal or pelvic fluid	26%

Treatment

Treatment

- Antibiotics-assigned
  - 47% ED-to-home

    79% of these discharged w/i 24 hours
  - Outpatient approach varied from 0-81% across sites

Treatment

- Antibiotics-assigned
  - 47% ED-to-home

    79% of these discharged w/i 24 hours
  - Outpatient approach varied from 0-81% across sites
  - Time from randomization to d/c (overall)-1.3 days
  - Index LoS of >5 days-5%

Treatment

- Antibiotics-assigned
  - 47% ED-to-home

    79% of these discharged w/i 24 hours
  - Outpatient approach varied from 0-81% across sites
  - Time from randomization to d/c (overall)-1.3 days
  - Index LoS of >5 days-5%
  - 11% receive another course of antibiotics within 90 days

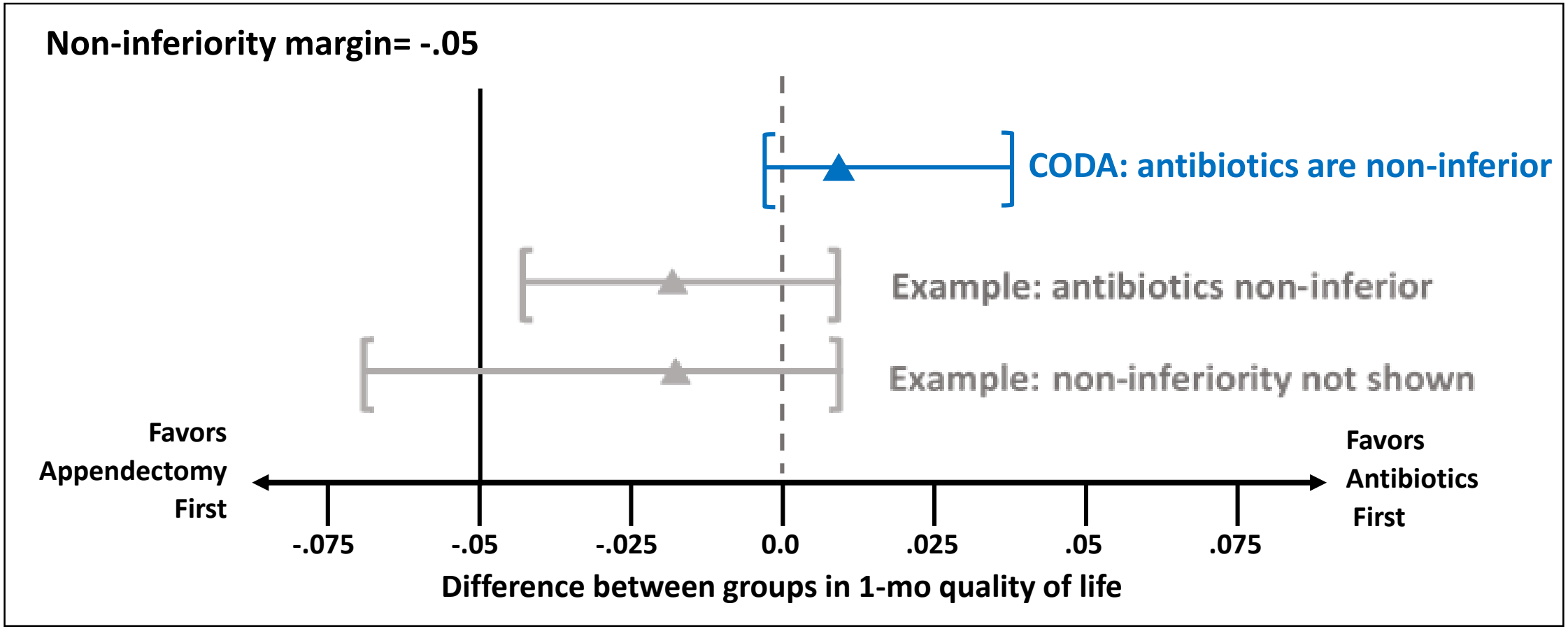
Treatment

- Antibiotics-assigned
  - 47% ED-to-home
    79% of these discharged w/i 24 hours
  - Outpatient approach varied from 0-81% across sites
  - Time from randomization to d/c (overall)-1.3 days
  - Index LoS of >5 days-5%
  - 11% receive another course of antibiotics within 90 days
- Appendectomy-assigned
  - 94% had surgery at index, 97% laparoscopic

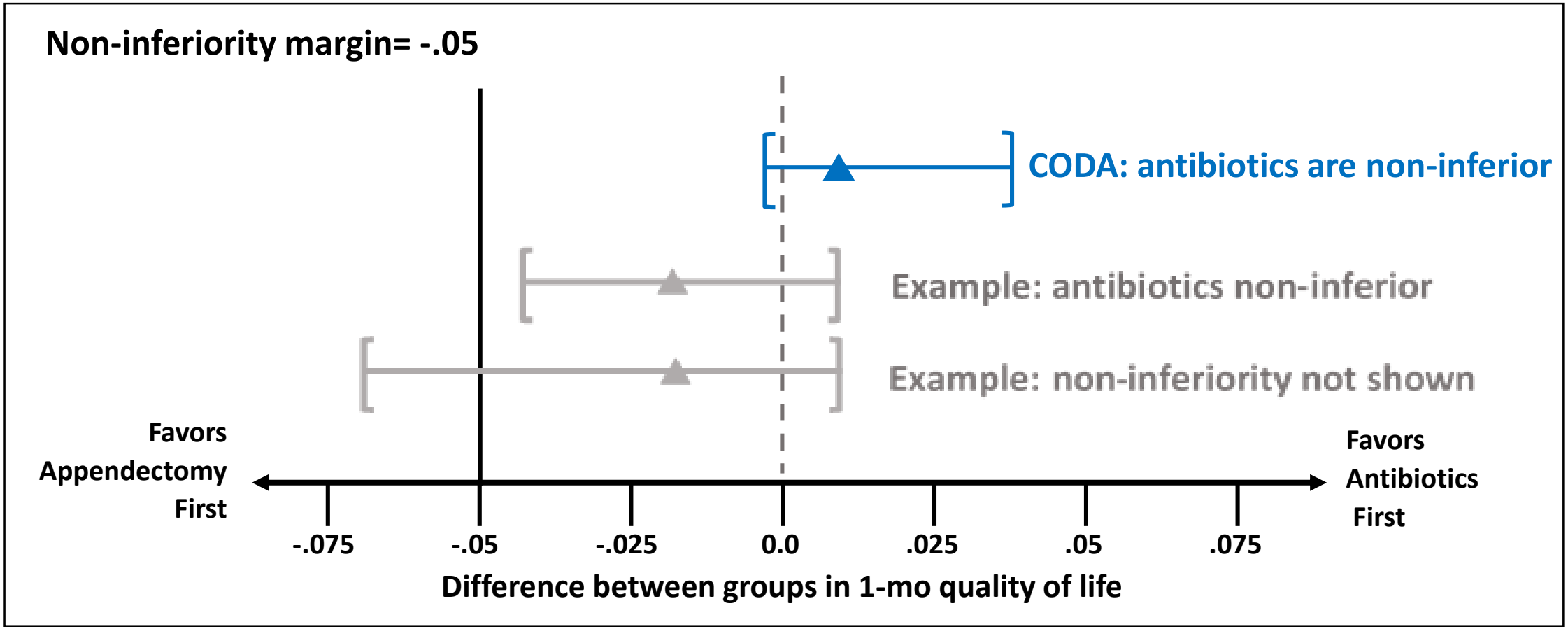
Treatment

- Antibiotics-assigned
  - 47% ED-to-home
    79% of these discharged w/i 24 hours
  - Outpatient approach varied from 0-81% across sites
  - Time from randomization to d/c (overall)-1.3 days
  - Index LoS of >5 days-5%
  - 11% receive another course of antibiotics within 90 days
- Appendectomy-assigned
  - 94% had surgery at index, 97% laparoscopic
  - Time from randomization to d/c (overall)-1.3 days
  - Index LoS of >5 days-2%

Non-inferiority of EQ-5D at 30 days



Non-inferiority of EQ-5D at 30 days



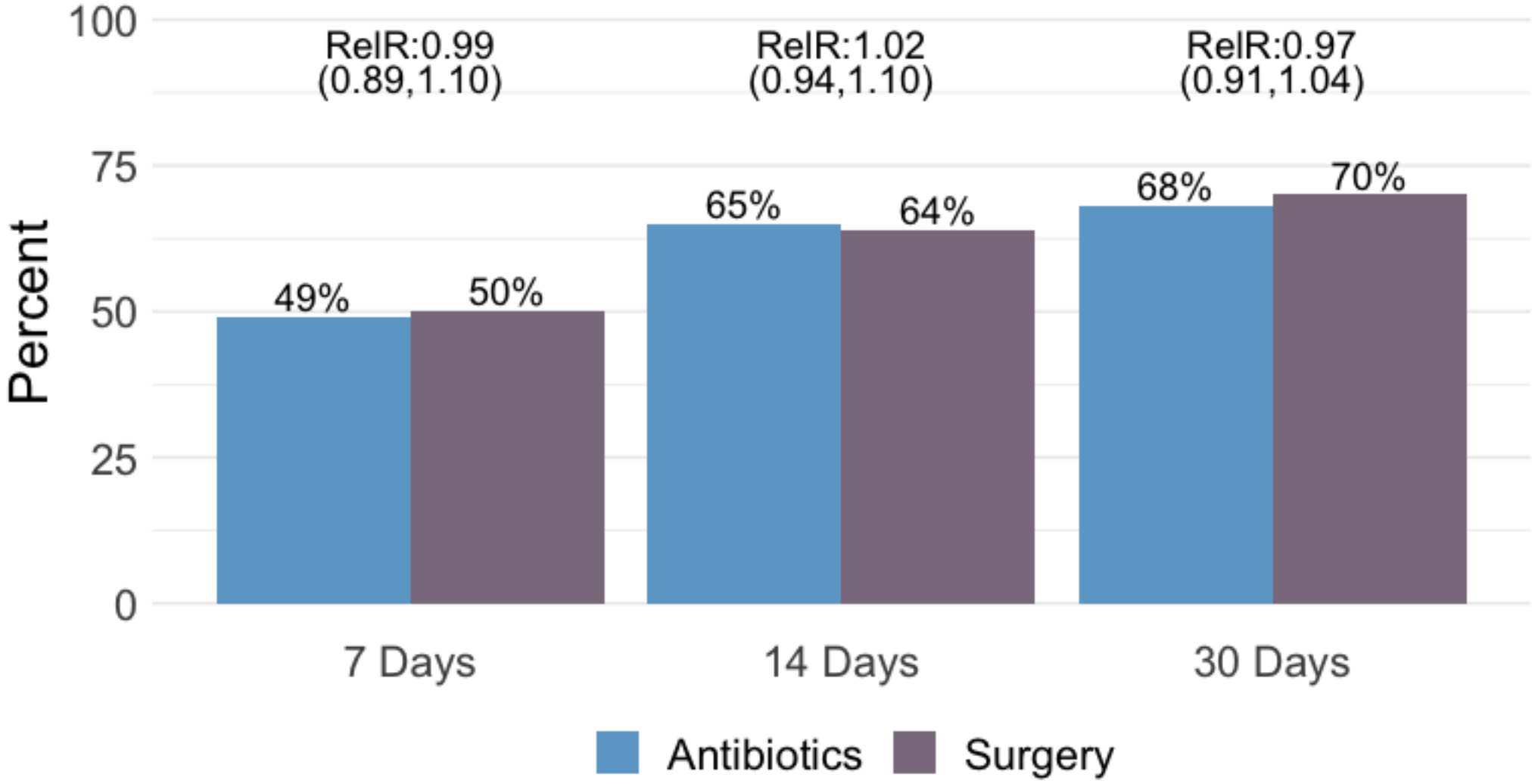
Mean difference overall: 0.01 (-0.001,0.03)

Appendicolith: -0.01 (-0.03,0.02)

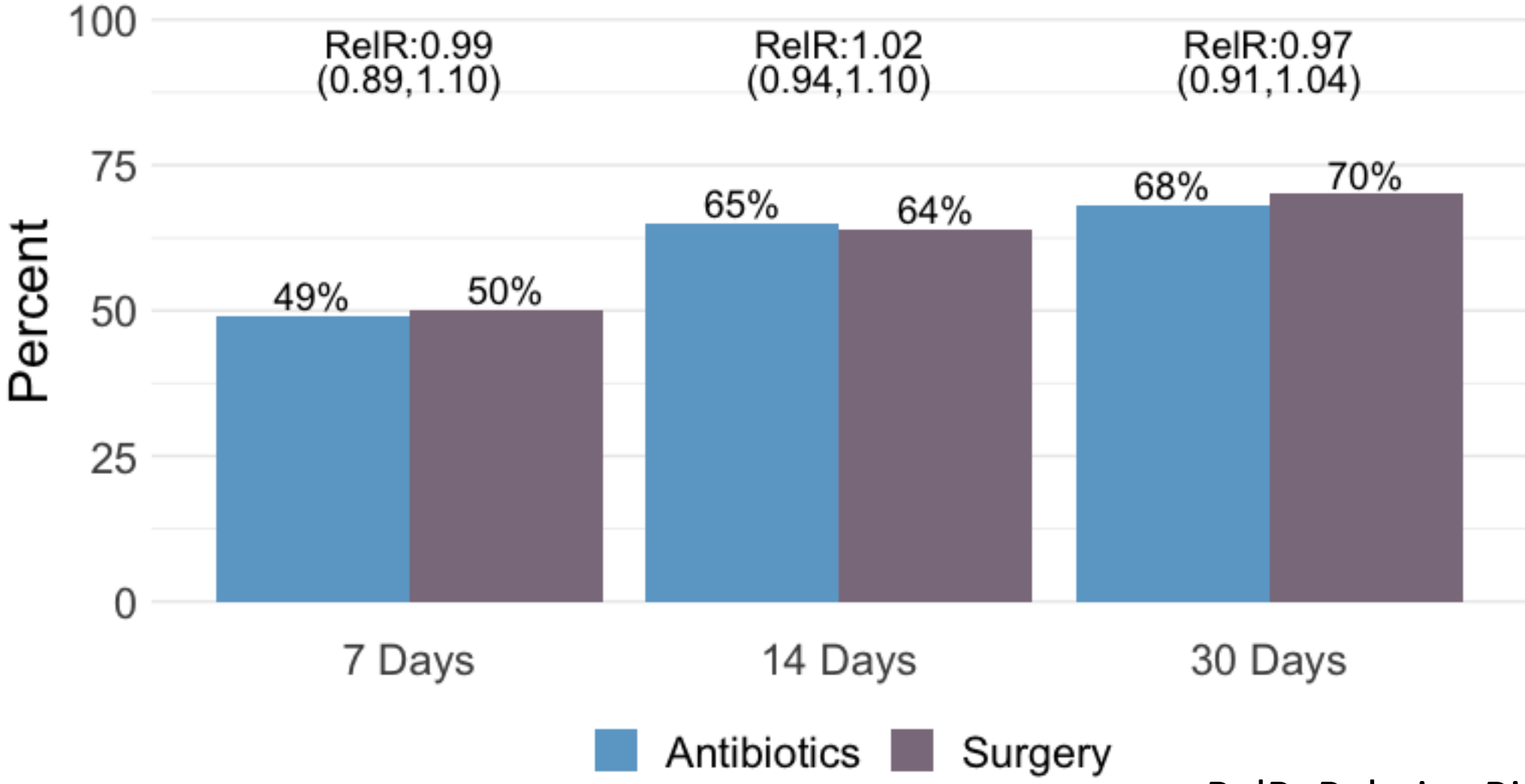
Not appendicolith: 0.02 (0.003,0.03)

Self-report of Fever, RLQ Pain and Tenderness

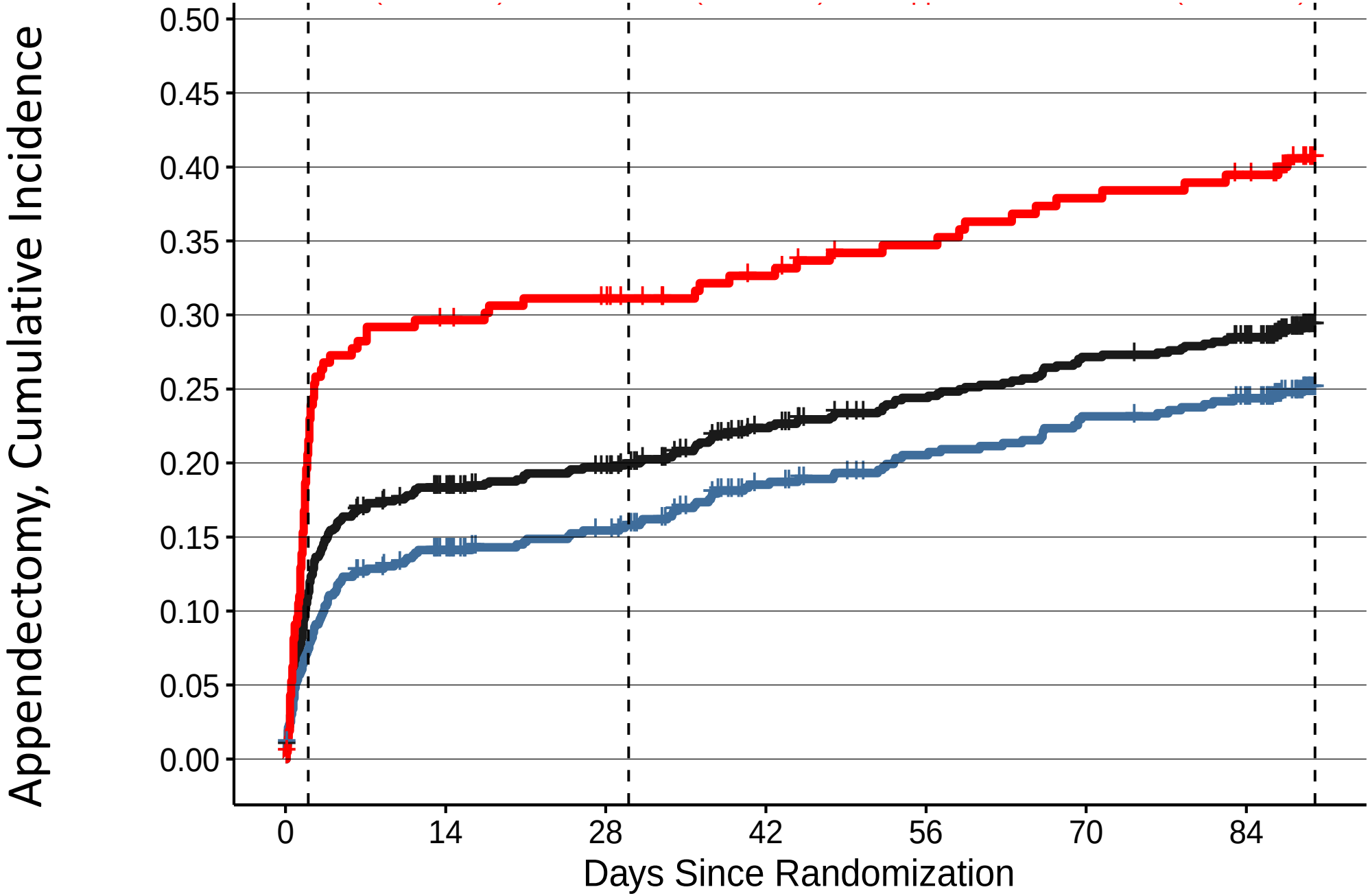
Self-report of Fever, RLQ Pain and Tenderness

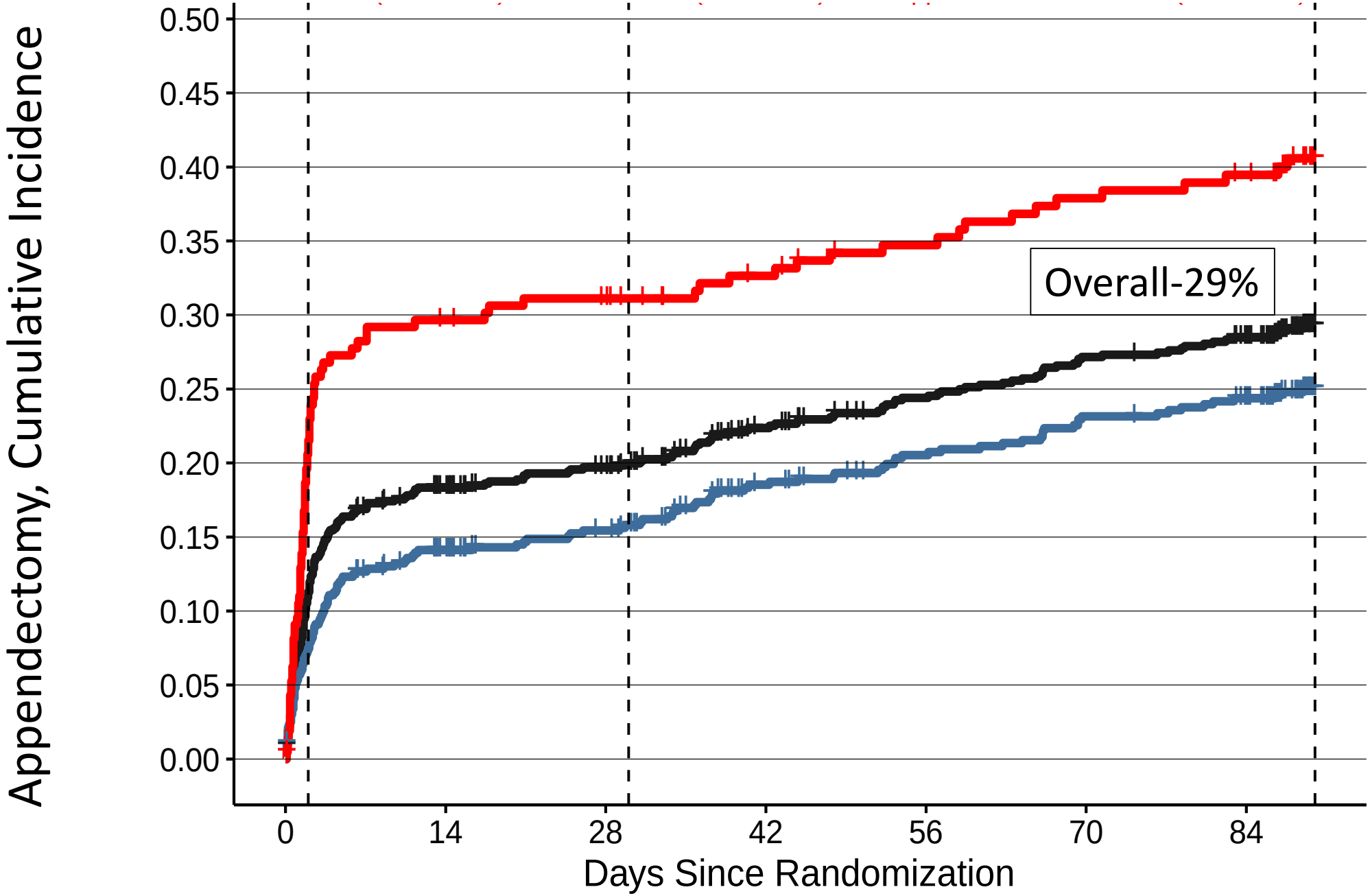


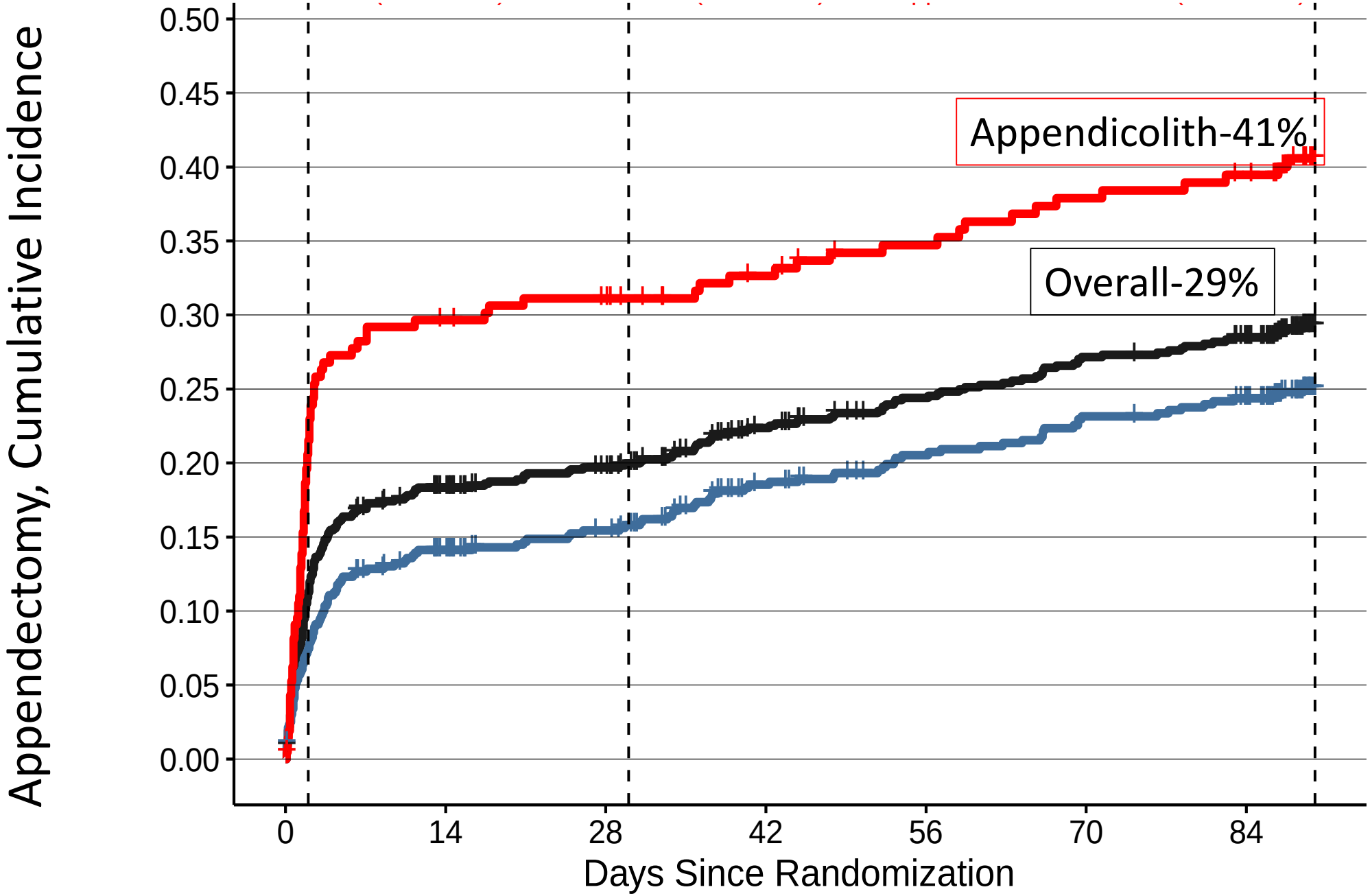
Self-report of Fever, RLQ Pain and Tenderness

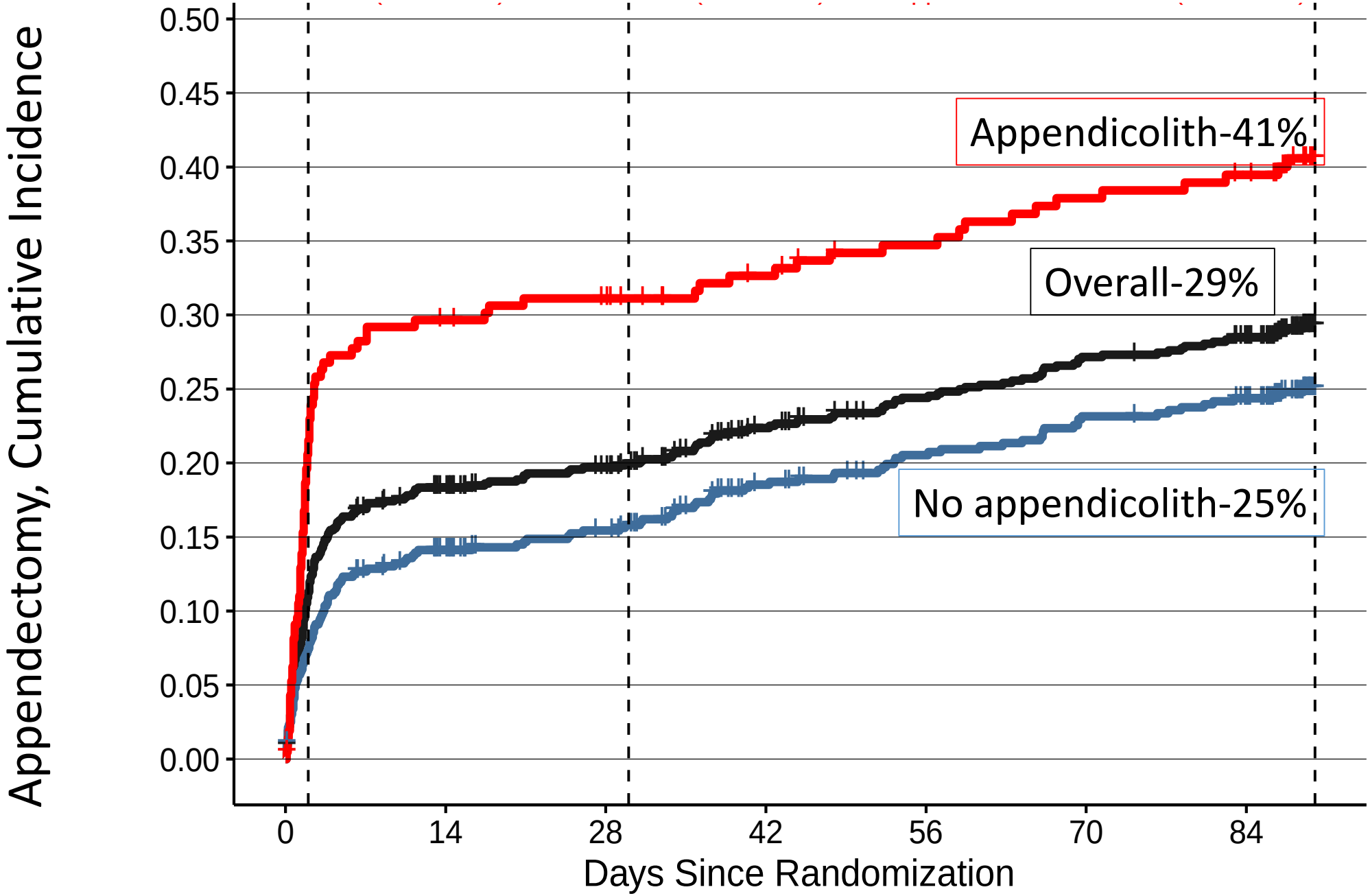


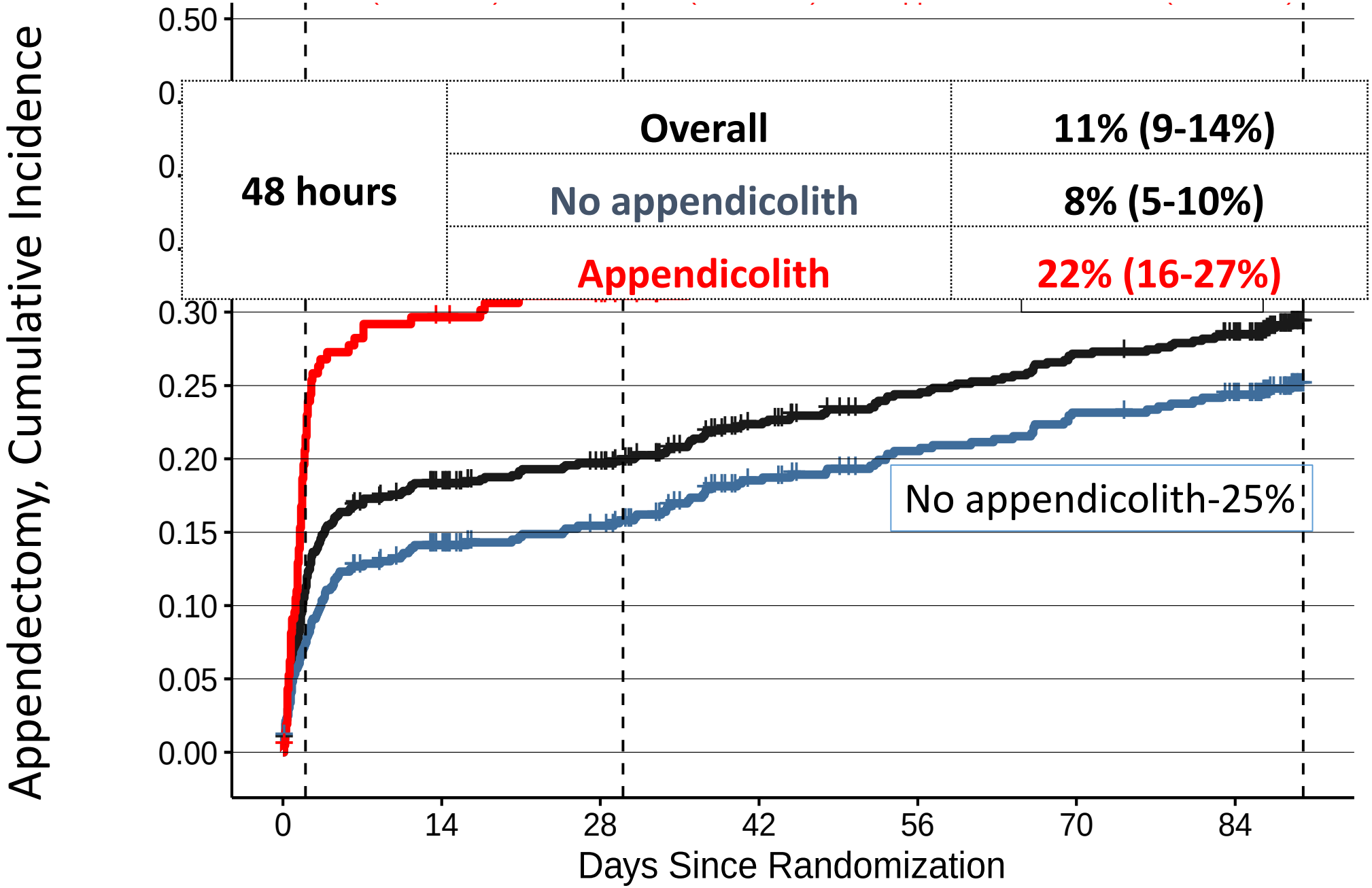
RelR=Relative Risk (95% CI)

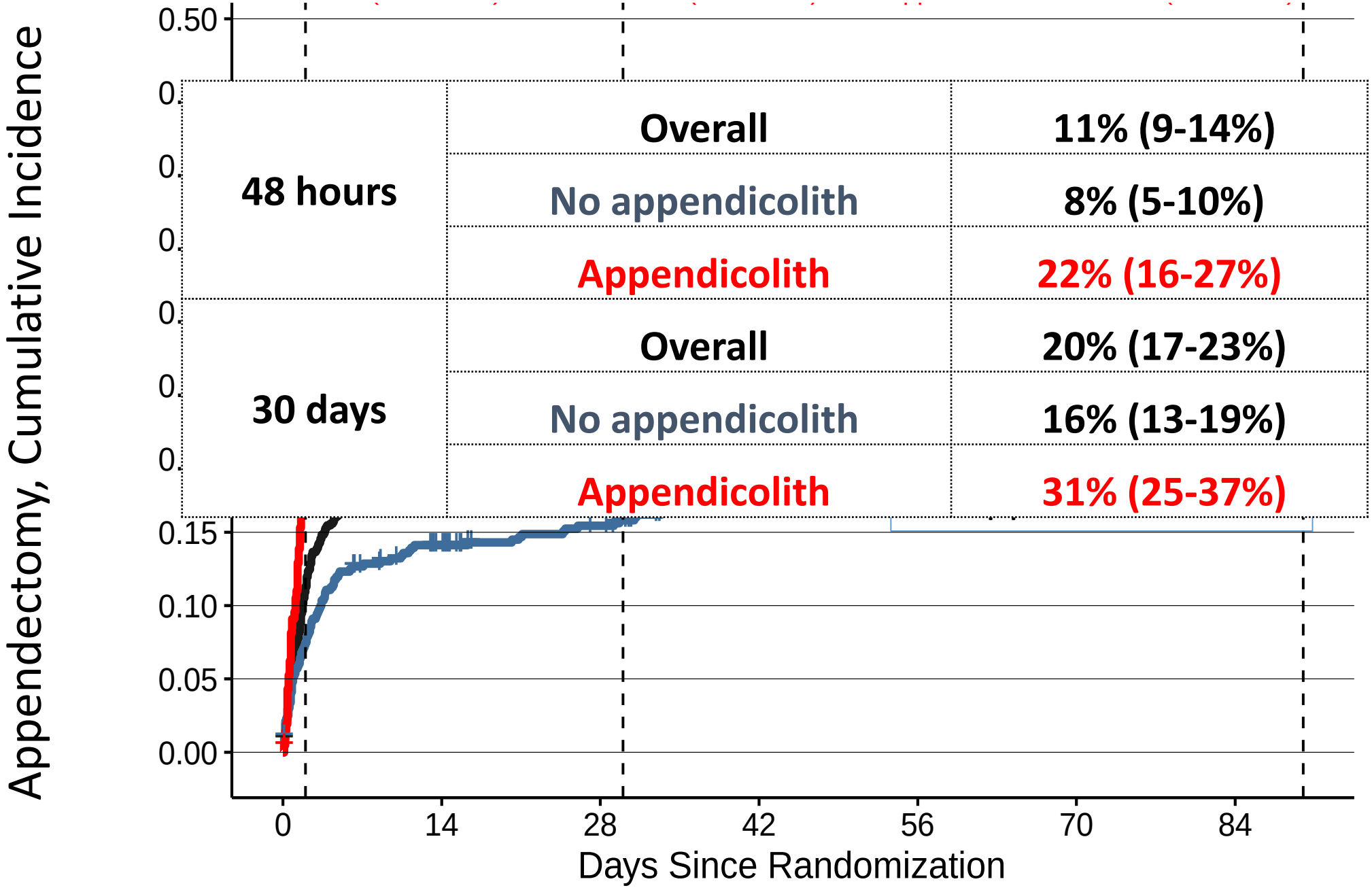

Appendectomy, Cumulative Incidence
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
0
14
28
42
56
70
84
Days Since Randomization

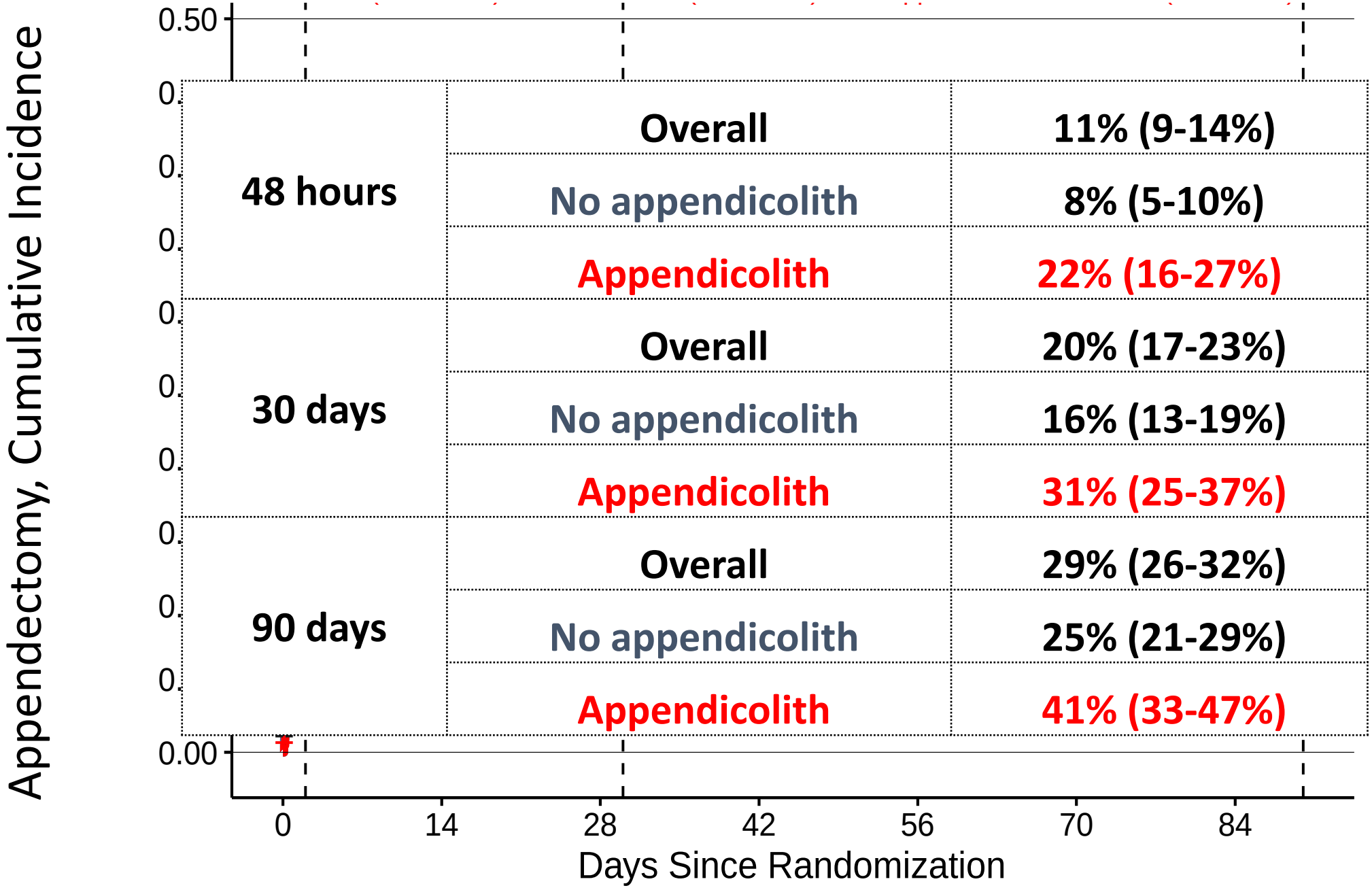

Appendectomy, Cumulative Incidence
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
Overall-29%
0
14
28
42
56
70
84
Days Since Randomization


Appendectomy, Cumulative Incidence
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
Appendicolith-41%
Overall-29%
0
14
28
42
56
70
84
Days Since Randomization


Appendectomy, Cumulative Incidence
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
Appendicolith-41%
Overall-29%
No appendicolith-25%
0
14
28
42
56
70
84
Days Since Randomization

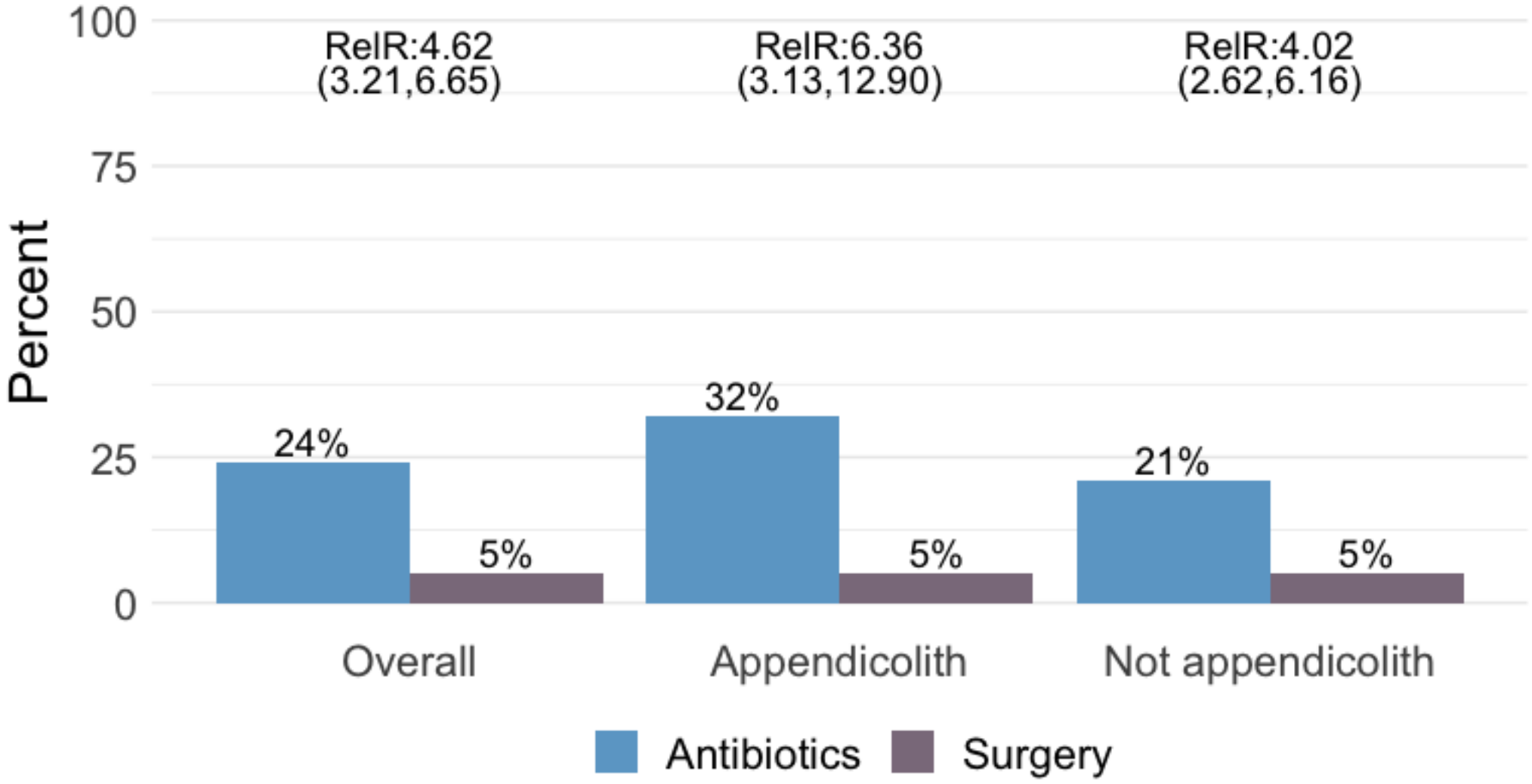

Appendectomy, Cumulative Incidence
0.50
0.
0.
0.
0.30
0.25
0.20
0.15
0.10
0.05
0.00
48 hours
Overall
11% (9-14%)
No appendicolith
8% (5-10%)
Appendicolith
22% (16-27%)
No appendicolith-25%
0
14
28
42
56
70
84
Days Since Randomization


Appendectomy, Cumulative Incidence
0.50
0.15
0.10
0.05
0.00
0
14
28
42
56
70
84
Days Since Randomization
48 hours
Overall
11% (9-14%)
No appendicolith
8% (5-10%)
Appendicolith
22% (16-27%)
30 days
Overall
20% (17-23%)
No appendicolith
16% (13-19%)
Appendicolith
31% (25-37%)

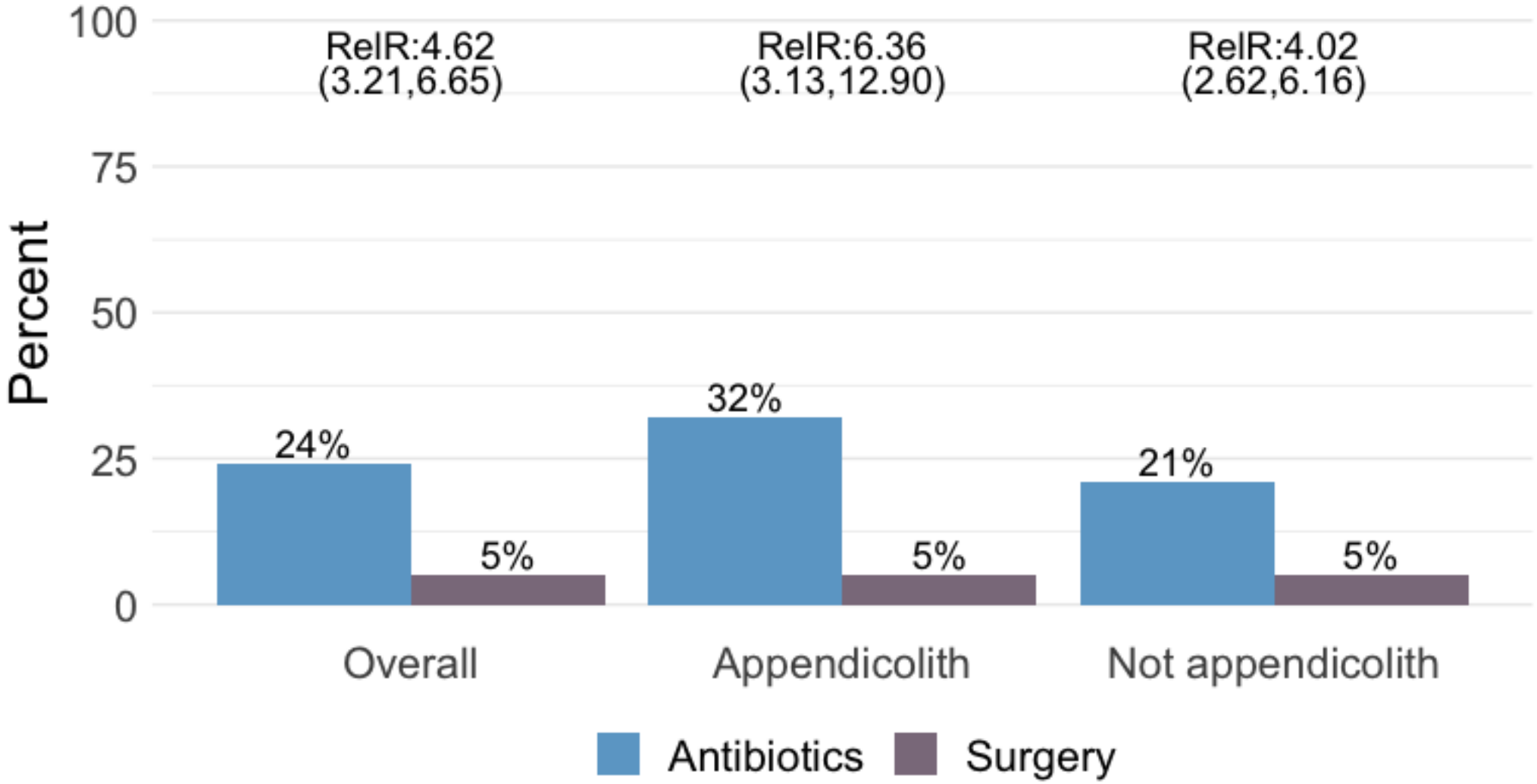

Appendectomy, Cumulative Incidence
0.50
0.
0.
0.
0.
0.
0.
0.
0.
0.00
0
14
28
42
56
70
84
Days Since Randomization
48 hours
Overall
11% (9-14%)
No appendicolith
8% (5-10%)
Appendicolith
22% (16-27%)
30 days
Overall
20% (17-23%)
No appendicolith
16% (13-19%)
Appendicolith
31% (25-37%)
90 days
Overall
29% (26-32%)
No appendicolith
25% (21-29%)
Appendicolith
41% (33-47%)

Any hospitalization (any reason) after index within 90 days

Any hospitalization (any reason) after index within 90 days



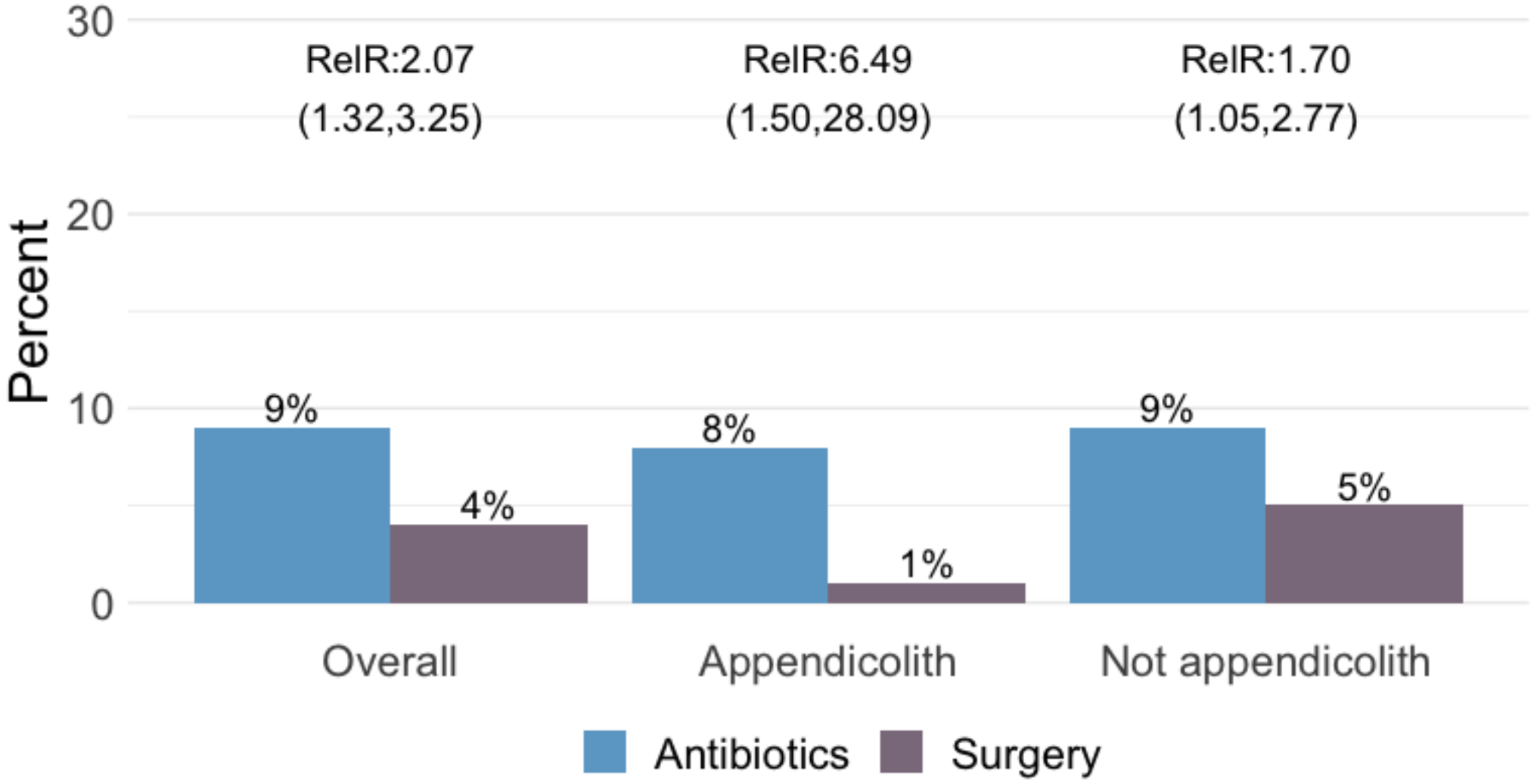
Any hospitalization (any reason) after index within 90 days



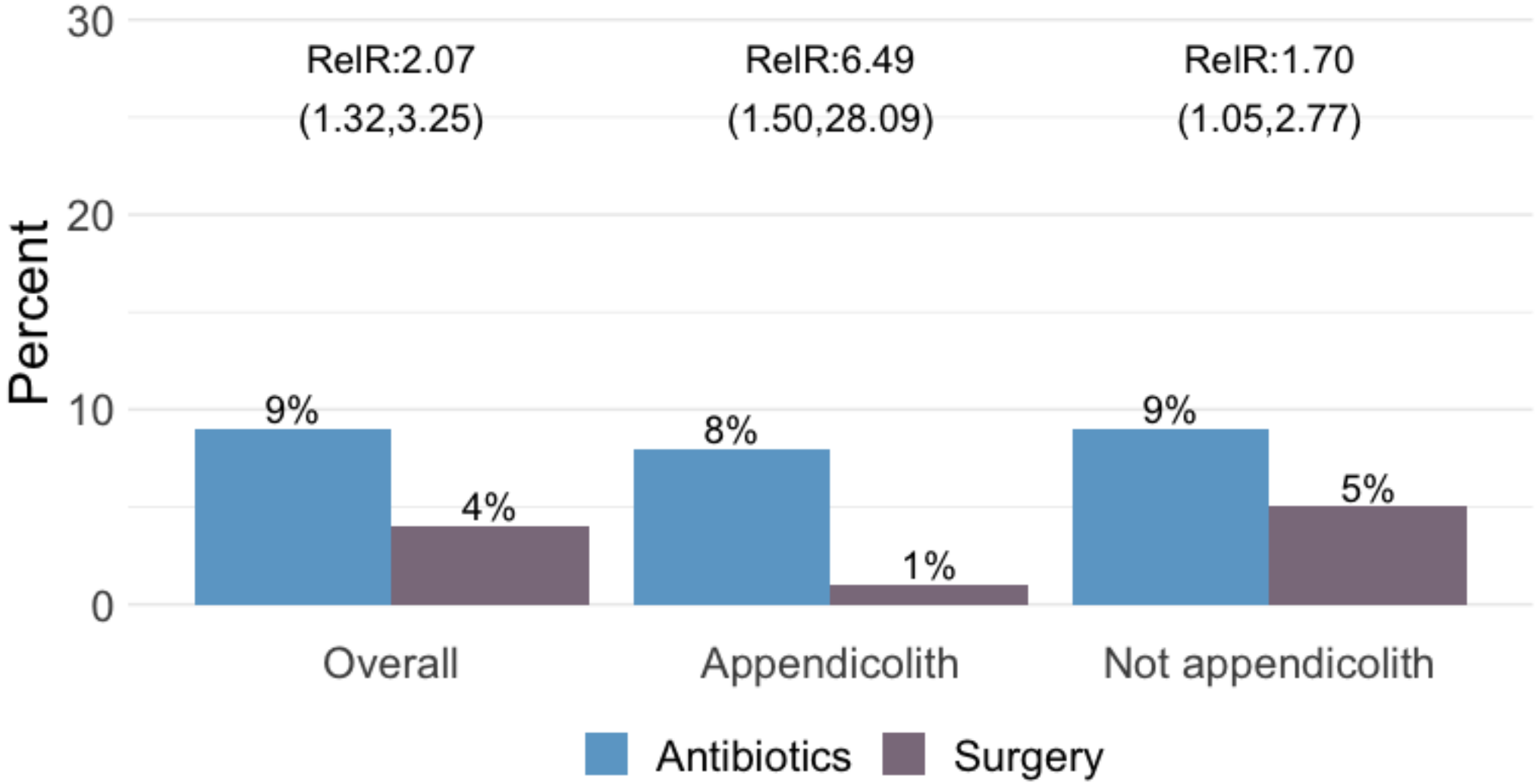
RelR=Relative Risk (95% CI)

Any ED/UC visits After Index within 90 days

Any ED/UC visits After Index within 90 days

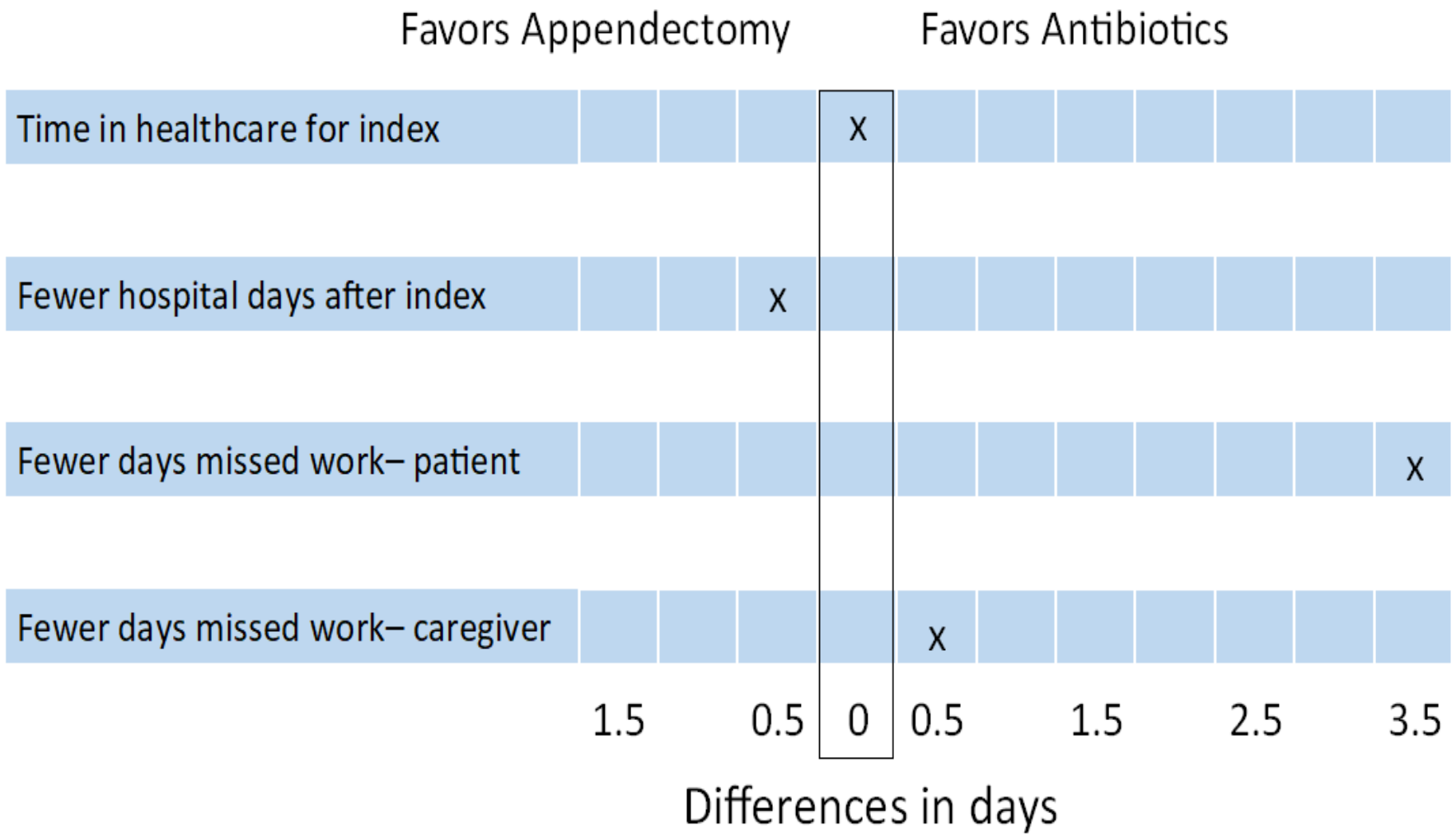


Any ED/UC visits After Index within 90 days



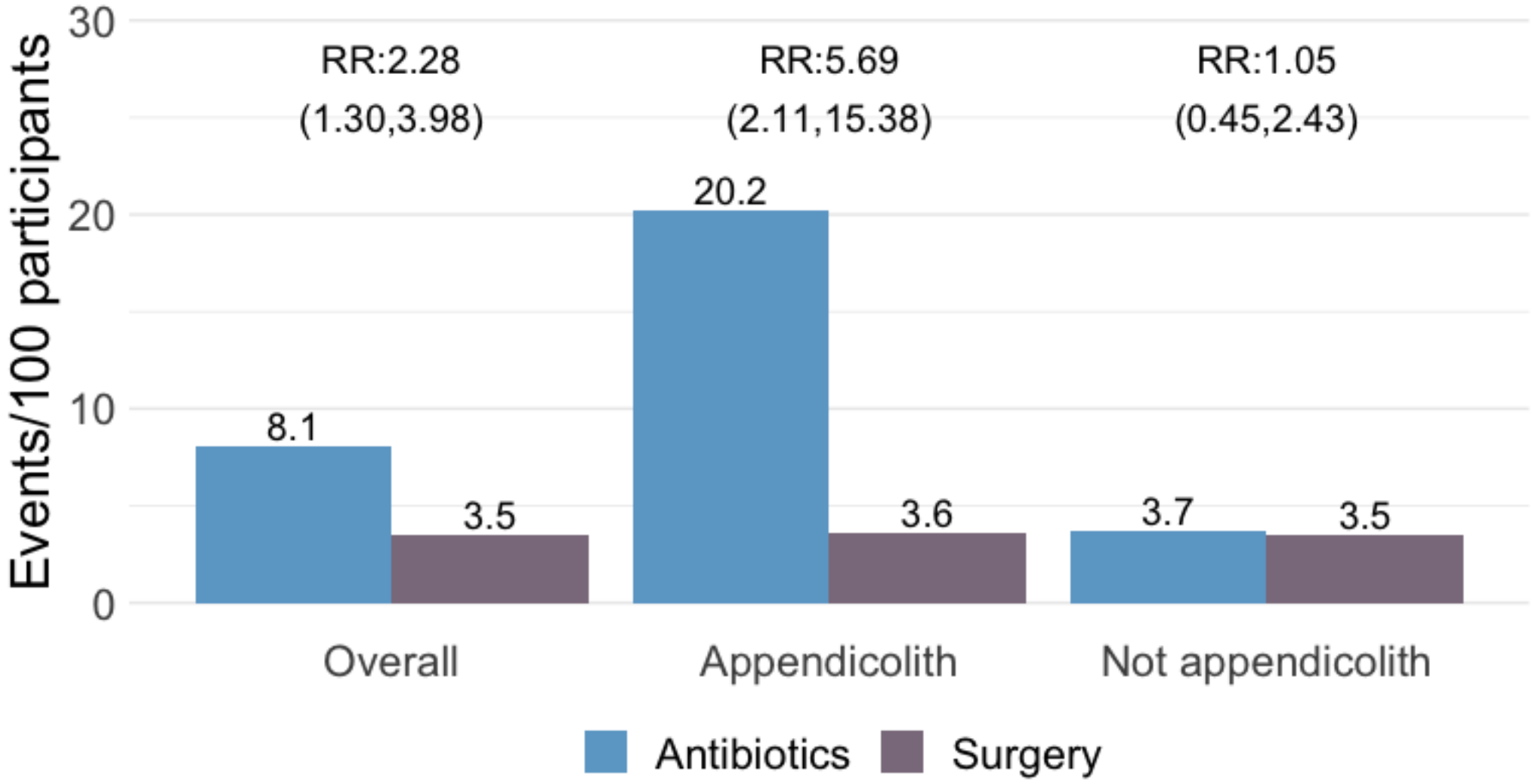
RelR=Relative Risk (95% CI)

Differences in Days in Healthcare/Away from Work

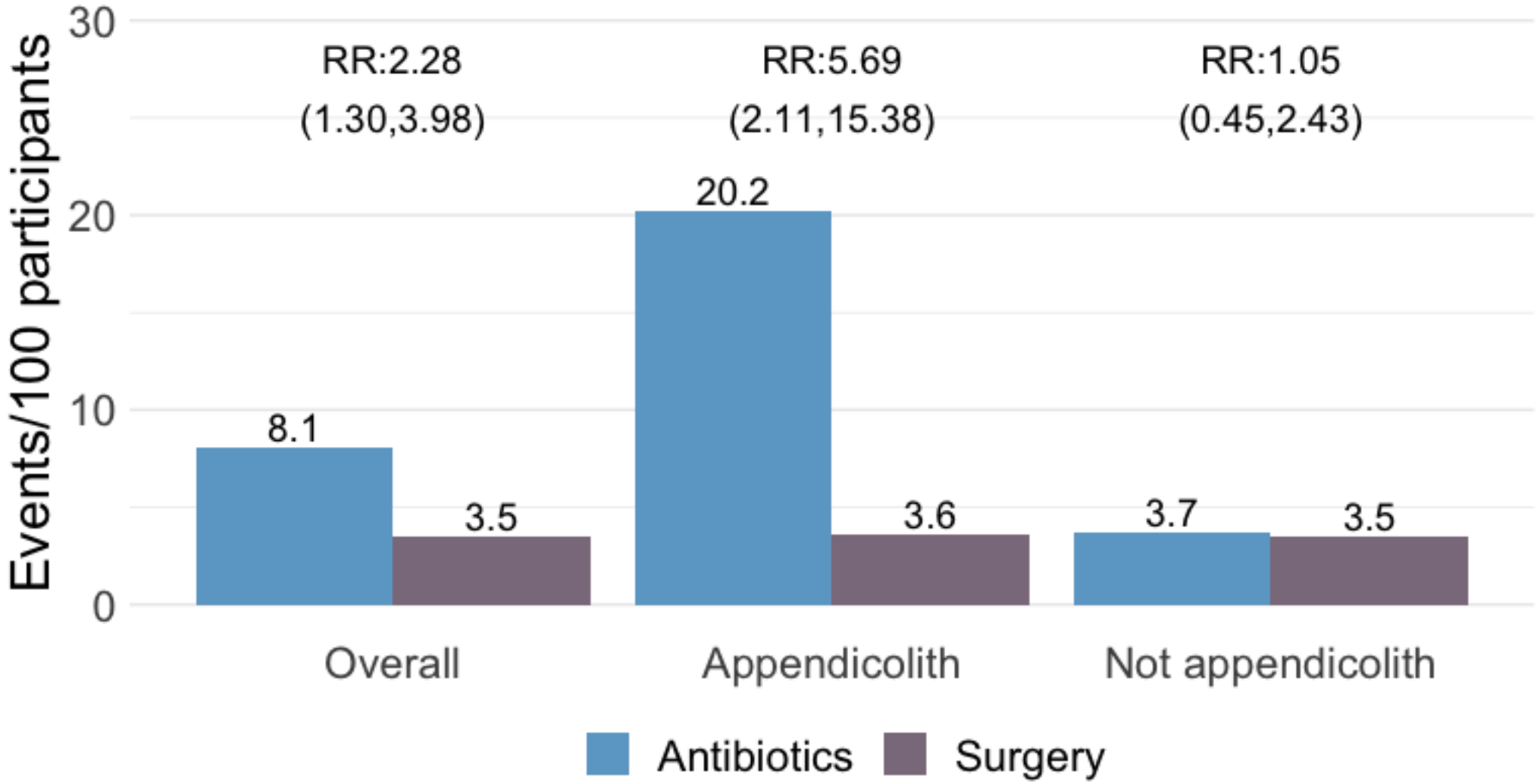


NSQIP morbidity events (per 100 patients) within 90 days

NSQIP morbidity events (per 100 patients) within 90 days



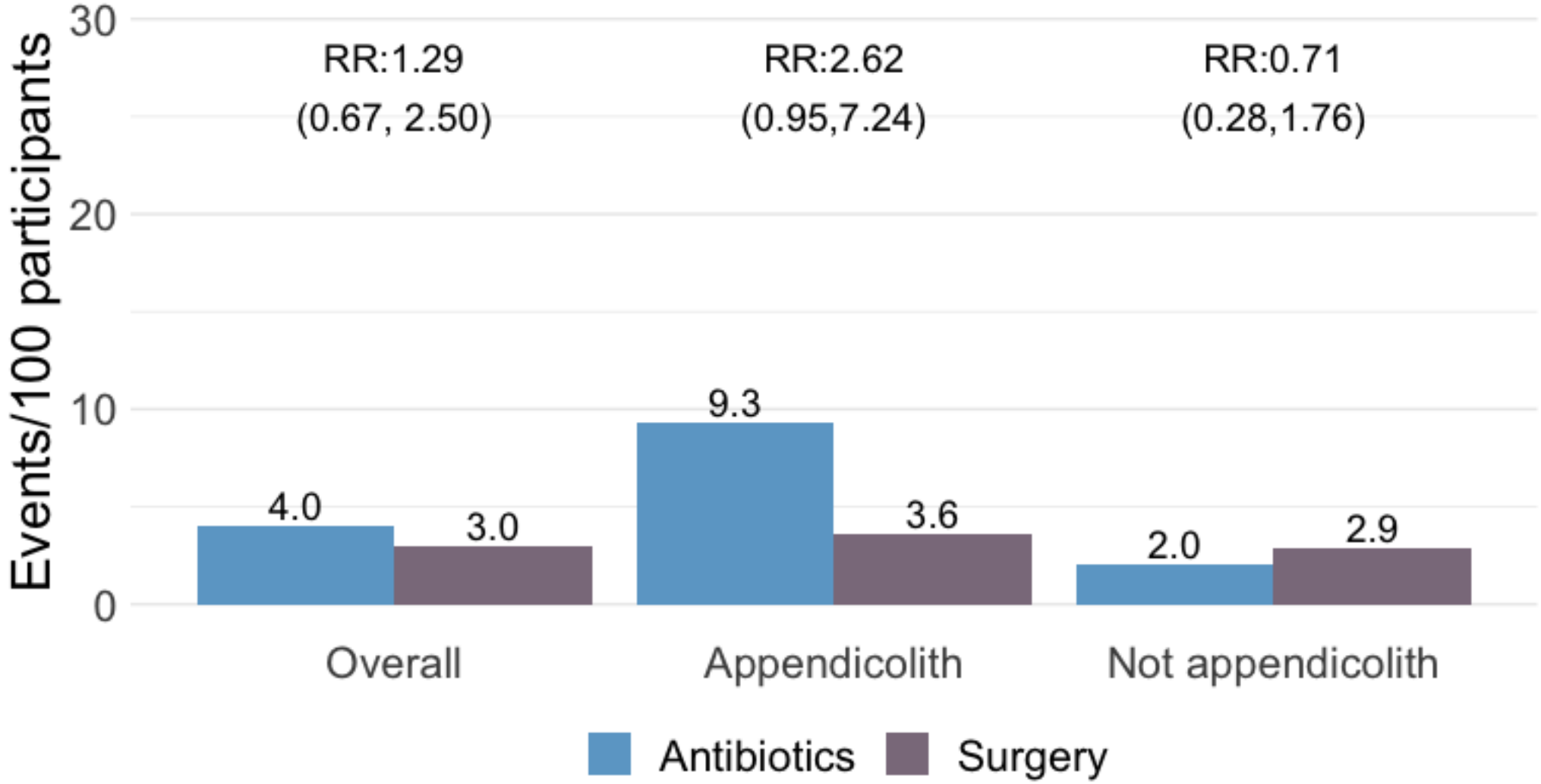
NSQIP morbidity events (per 100 patients) within 90 days



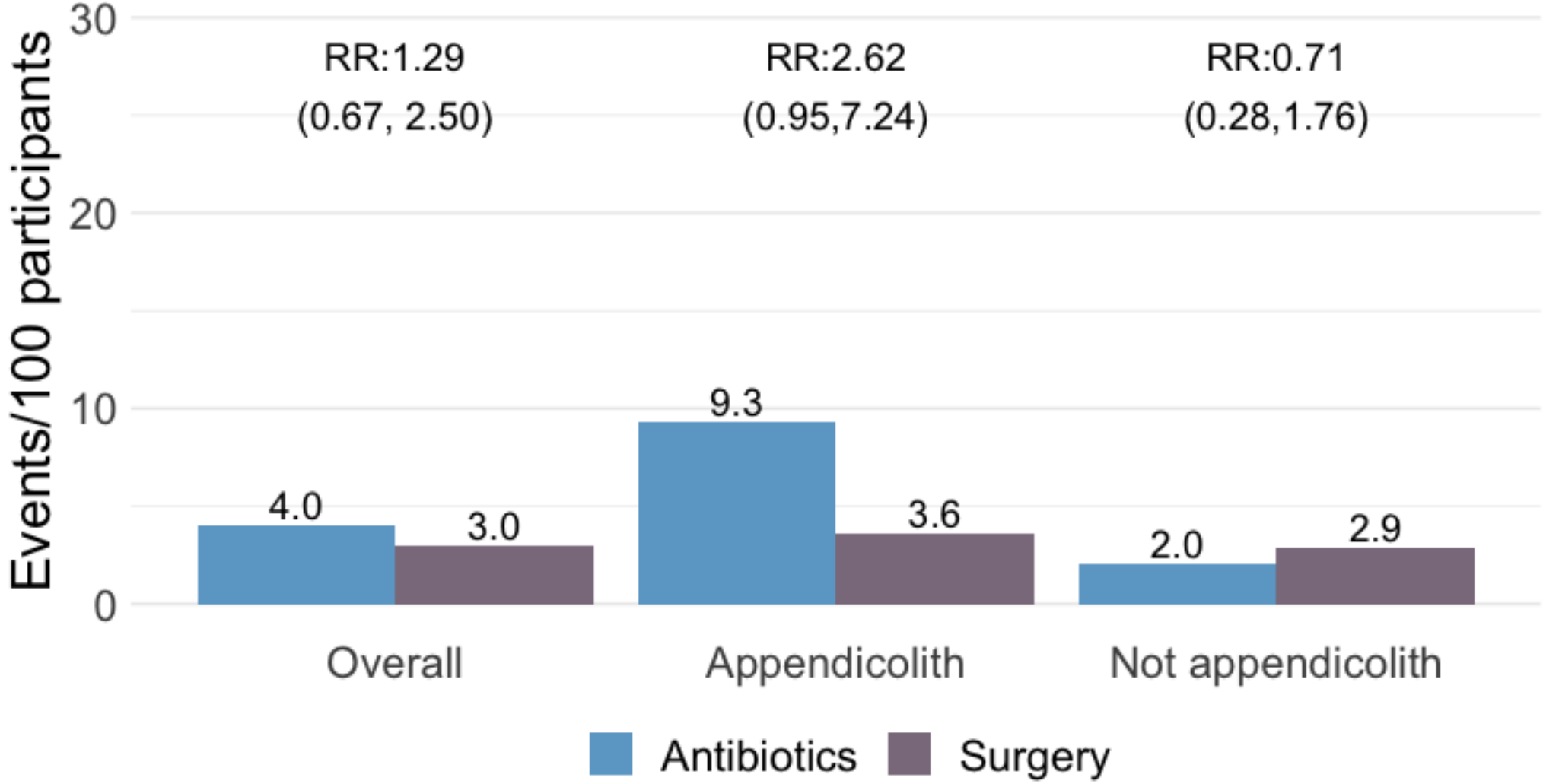
RR=Rate Ratio (95% CI)

Serious Adverse Events (at least one) within 90 Days

Serious Adverse Events (at least one) within 90 Days



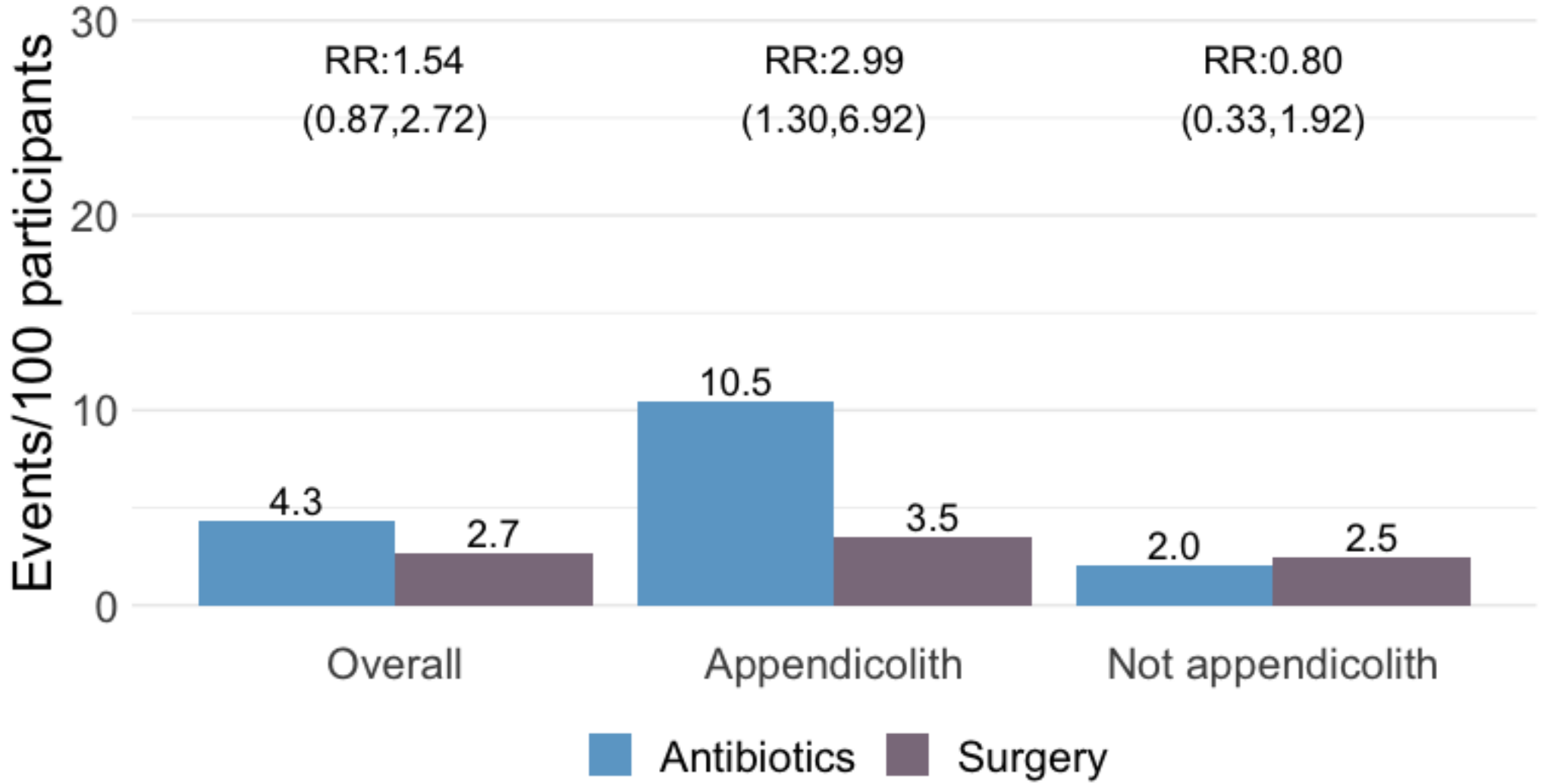
Serious Adverse Events (at least one) within 90 Days



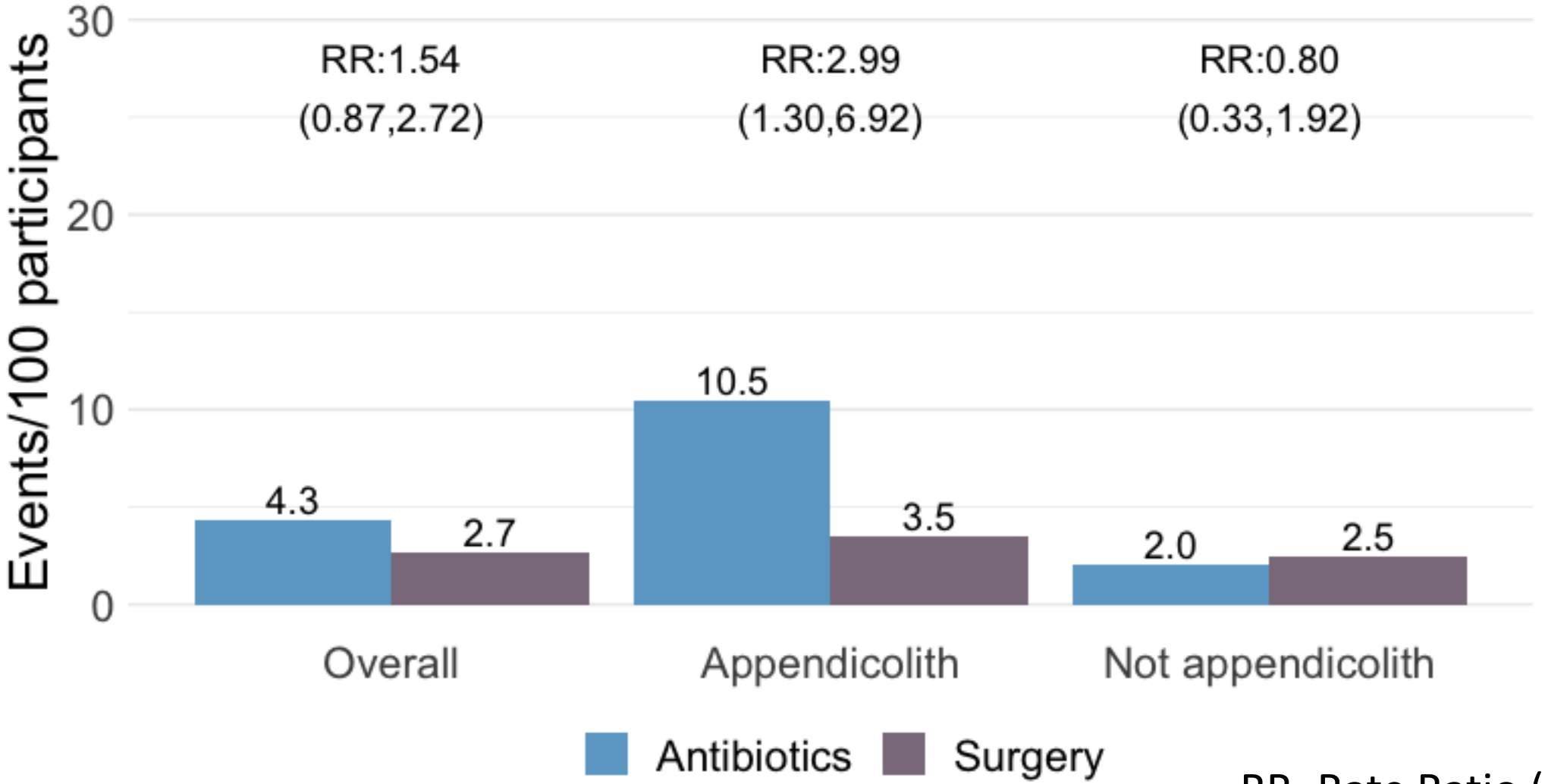
RR=Rate Ratio (95% CI)

Surgical Site Infection or Abscess within 90 Days

Surgical Site Infection or Abscess within 90 Days



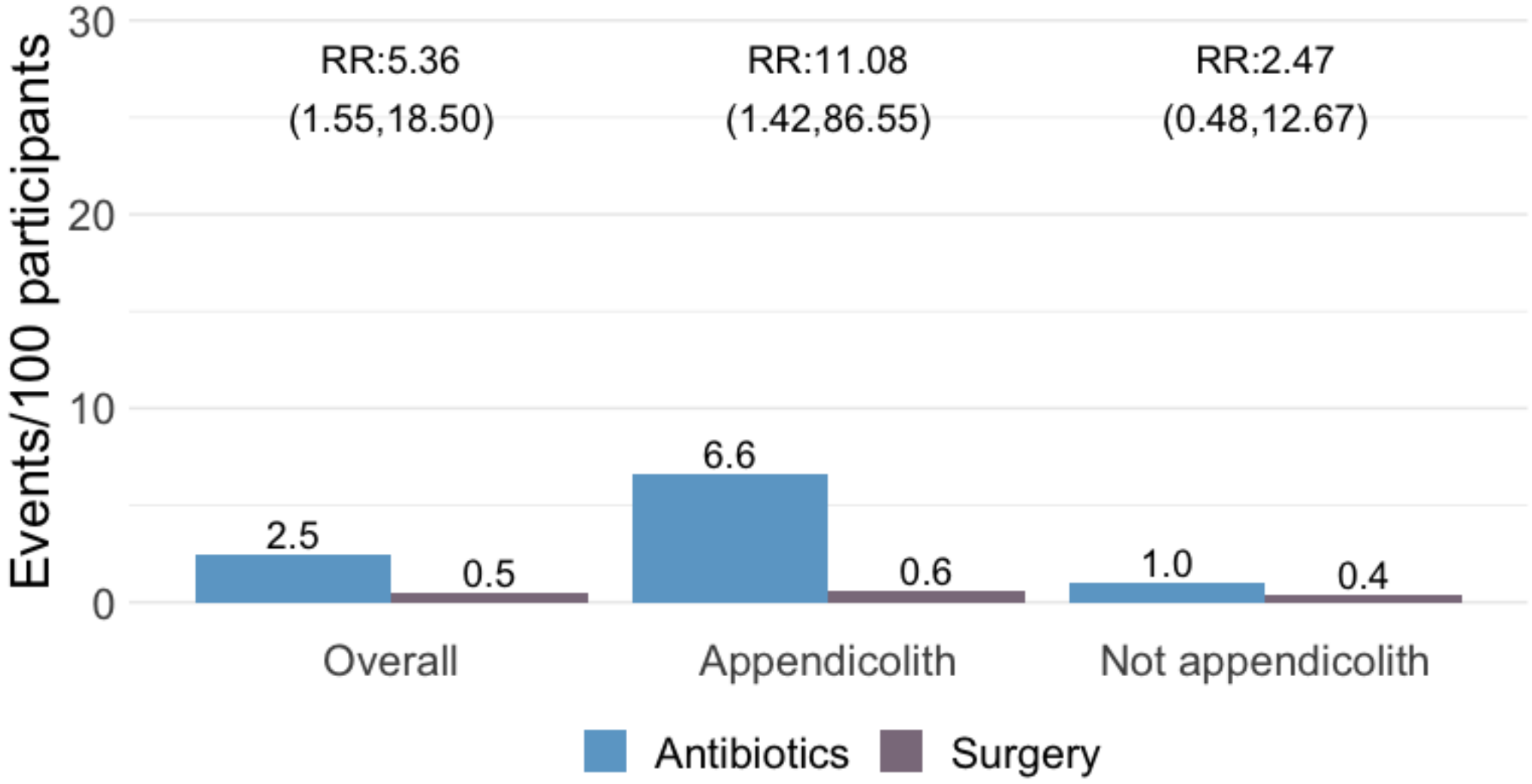
Surgical Site Infection or Abscess within 90 Days



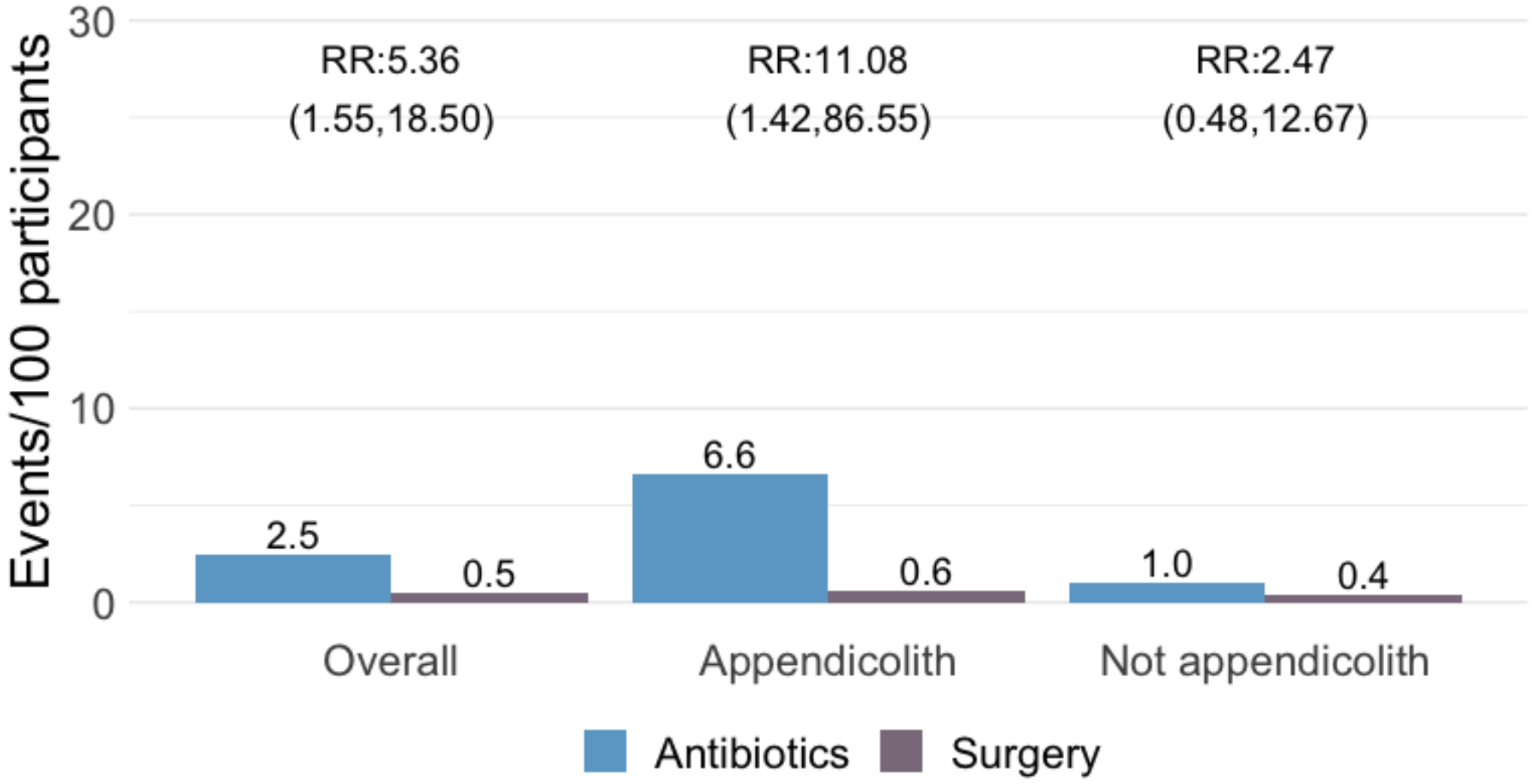
RR=Rate Ratio (95% CI)

Percutaneous Drainage within 90 Days

Percutaneous Drainage within 90 Days



Percutaneous Drainage within 90 Days



RR=Rate Ratio (95% CI)

Neoplasm

Neoplasm

- 9 Identified by 90 days

Neoplasm

- 9 Identified by 90 days
  - 7 in appendectomy arm and 2 in antibiotic arm

Neoplasm

- 9 Identified by 90 days
  - 7 in appendectomy arm and 2 in antibiotic arm
  - 8 were carcinomas and 1 was a mucocele

Neoplasm

- 9 Identified by 90 days
  - 7 in appendectomy arm and 2 in antibiotic arm
  - 8 were carcinomas and 1 was a mucocele
- Mean age 47 (SD 17), with a range of 21-74 years

Neoplasm

- 9 Identified by 90 days
  - 7 in appendectomy arm and 2 in antibiotic arm
  - 8 were carcinomas and 1 was a mucocele
- Mean age 47 (SD 17), with a range of 21-74 years

Limitations

Limitations

- Early report: appendectomy for recurrence likely to increase with longer follow up

Limitations

- Early report: appendectomy for recurrence likely to increase with longer follow up
- Pragmatic trials: strengths and weaknesses

Limitations

- Early report: appendectomy for recurrence likely to increase with longer follow up
- Pragmatic trials: strengths and weaknesses
  - Technique not standardized

Limitations

- Early report: appendectomy for recurrence likely to increase with longer follow up
- Pragmatic trials: strengths and weaknesses
  - Technique not standardized
  - Indication for appendectomy in antibiotics arm

Limitations

- Early report: appendectomy for recurrence likely to increase with longer follow up
- Pragmatic trials: strengths and weaknesses
  - Technique not standardized
  - Indication for appendectomy in antibiotics arm
  - ED-to-home antibiotics: confounding and selection bias

Limitations

- Early report: appendectomy for recurrence likely to increase with longer follow up
- Pragmatic trials: strengths and weaknesses
  - Technique not standardized
  - Indication for appendectomy in antibiotics arm
  - ED-to-home antibiotics: confounding and selection bias
- Lack of blinding and subjective outcomes

Limitations

- Early report: appendectomy for recurrence likely to increase with longer follow up
- Pragmatic trials: strengths and weaknesses
  - Technique not standardized
  - Indication for appendectomy in antibiotics arm
  - ED-to-home antibiotics: confounding and selection bias
- Lack of blinding and subjective outcomes
  - Parallel observational study reported separately

Limitations

- Early report: appendectomy for recurrence likely to increase with longer follow up
- Pragmatic trials: strengths and weaknesses
  - Technique not standardized
  - Indication for appendectomy in antibiotics arm
  - ED-to-home antibiotics: confounding and selection bias
- Lack of blinding and subjective outcomes
  - Parallel observational study reported separately
- Sex distribution

Summary of findings

Summary of findings

- “Will I Feel Better?”

Summary of findings

- “Will I Feel Better?”
  - At least at 30 days, antibiotics non-inferior based on a health status measure

Summary of findings

- “Will I Feel Better?”
  - At least at 30 days, antibiotics non-inferior based on a health status measure
  - Time until resolution of signs and symptoms similar between groups

Summary of findings

- “Will I Feel Better?”
  - At least at 30 days, antibiotics non-inferior based on a health status measure
  - Time until resolution of signs and symptoms similar between groups
  - If receiving antibiotics,

Summary of findings

- “Will I Feel Better?”
  - At least at 30 days, antibiotics non-inferior based on a health status measure
  - Time until resolution of signs and symptoms similar between groups
  - If receiving antibiotics,
    - ~3 in 10 overall undergo appendectomy

Summary of findings

- “Will I Feel Better?”
  - At least at 30 days, antibiotics non-inferior based on a health status measure
  - Time until resolution of signs and symptoms similar between groups
  - If receiving antibiotics,
    - ~3 in 10 overall undergo appendectomy
    - ~4 in 10 if there is an appendicolith

Summary of findings

- “Will I Feel Better?”
  - At least at 30 days, antibiotics non-inferior based on a health status measure
  - Time until resolution of signs and symptoms similar between groups
  - If receiving antibiotics,
    - ~3 in 10 overall undergo appendectomy
    - ~4 in 10 if there is an appendicolith
- “Safety?”

Summary of findings

- “Will I Feel Better?”
  - At least at 30 days, antibiotics non-inferior based on a health status measure
  - Time until resolution of signs and symptoms similar between groups
  - If receiving antibiotics,
    - ~3 in 10 overall undergo appendectomy
    - ~4 in 10 if there is an appendicolith
- “Safety?”
  - Non-appendicolith group: no difference in safety/complications

Summary of findings

- “Will I Feel Better?”
  - At least at 30 days, antibiotics non-inferior based on a health status measure
  - Time until resolution of signs and symptoms similar between groups
  - If receiving antibiotics,
    - ~3 in 10 overall undergo appendectomy
    - ~4 in 10 if there is an appendicolith
- “Safety?”
  - Non-appendicolith group: no difference in safety/complications
  - Appendicolith group: higher risk of complications and safety events with antibiotics

Summary of findings

- “Will I Feel Better?”
  - At least at 30 days, antibiotics non-inferior based on a health status measure
  - Time until resolution of signs and symptoms similar between groups
  - If receiving antibiotics,
    - ~3 in 10 overall undergo appendectomy
    - ~4 in 10 if there is an appendicolith
- “Safety?”
  - Non-appendicolith group: no difference in safety/complications
  - Appendicolith group: higher risk of complications and safety events with antibiotics
- “Time in healthcare/Return to work?”

Summary of findings

- “Will I Feel Better?”
  - At least at 30 days, antibiotics non-inferior based on a health status measure
  - Time until resolution of signs and symptoms similar between groups
  - If receiving antibiotics,
    - ~3 in 10 overall undergo appendectomy
    - ~4 in 10 if there is an appendicolith
- “Safety?”
  - Non-appendicolith group: no difference in safety/complications
  - Appendicolith group: higher risk of complications and safety events with antibiotics
- “Time in healthcare/Return to work?”
  - Antibiotics: more visits (ED and hospital) but quicker return to work

Acknowledgments

Acknowledgments

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

Acknowledgments

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

NIH NIDDK T32 grant: 5T32DK070555-09

Acknowledgments

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

NIH NIDDK T32 grant: 5T32DK070555-09

AHRQ grant to fund CERTAIN: R01HS22959

Acknowledgments

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

NIH NIDDK T32 grant: 5T32DK070555-09

AHRQ grant to fund CERTAIN: R01HS22959

The views presented in this presentation are solely the responsibility of the author(s) and do not necessarily represent the views of the Patient-Centered Outcomes Research Institute® (PCORI®), its Board of Governors or Methodology Committee

Acknowledgements

We are especially appreciative of the generosity and altruism of all the participants who participated in this trial.

Executive Committee: Bonnie Bizzell, MBA, MEd (Chair, Patient Advisory Board); Bryan Comstock, MS (Operations Director, Data Coordinating Center); Giana Davidson, MD MPH (Chair, Clinical Coordinating Center); Erin Fannon (Senior Project Manager); David R. Flum, MD, MPH (Co-Principal Investigator); Patrick J. Heagerty, PhD, MS (Director, Data Coordinating Center); Larry G. Kessler, ScD (Chair, Executive Committee); Anusha Krishnadasan, PhD (Project Manager, California); Danielle C. Lavallee, PharmD, PhD (Director, Stakeholder Coordinating Center); Sarah Monsell, MS (Lead Biostatistician); Kelsey Pullar, MPH (Research Coordinator Lead); David A. Talan, MD (Co-Principal Investigator); Erika Wolff, PhD (UW)

Patient Advisory Board: Meridith Weiss, Kimberly Deeney, Heather VanDusen, Elliott Skopin, Mary Guiden, Miriam Hernandez

National Advisory Board: Emily E. Anderson, PhD, MPH; Darrell A. Campbell, Jr., MD; Fergal Fleming, MD; David B. Hoyt, MD; J.J. Tepas III, MD (Deceased); Richard W. Whitten, MD; SreyRam Kuy, MD; Daniel S. Lessler, MD, MHA

Data Safety and Monitoring Board: Karla Ballman, PhD; Thomas Diflo, MD; Bruce Wolfe, MD; Arden Morris, MD; Donald Yealy, MD. Patient Advisors: Kathleen O’Connor, EdD; Olga Owens, N-PC

CODA Collaborative

Midwest:

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

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

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

South:

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

CERTAIN™

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Trial Comparing Antibiotics with Appendectomy for Appendicitis

David R. Flum, M.D., M.P.H., Giana H. Davidson, M.D., M.P.H., Sarah E. Monsell, M.S., Nathan I. Shapiro, M.D., M.P.H., Stephen R. Odom, M.D., Sabrina E. Sanchez, M.D., M.P.H., F. Thurston Drake, M.D., M.P.H., Katherine Fischkoff, M.D., Jeffrey Johnson, M.D., Joe H. Patton, M.D., Heather Evans, M.D., Joseph Cuschieri, M.D., et al., for the CODA Collaborative*

CODA: Site Investigators

Bellevue NYU School of Medicine
Onaona Gurney, MD
William Chiang, MD
Patricia Ayoung-Chee, MD, MPH

Beth Israel Deaconess Medical Center
Charles Parsons, MD
Nathan Shapiro, MD, MPH

Boston University Medical Center
Thurston Drake, MD, MPH
Sabrina Sanchez, MD, MPH

Columbia University Medical Center
Katherine Fischkoff, MD
Aleksandr Tichter, MD, MS

Harbor-UCLA Medical Center
Daniel A. DeUgarte, MD
Amy Kaji, MD, PhD

Harborview Medical Center
Joe Cuschieri, MD
Amber K Sabbatini, MD, MPH
Heather Evans, MD

Henry Ford Health Hospital
Jeffrey Johnson, MD
Joe Patton, MD

Madigan Army Medical Center
Vance Sohn, MD
Karen McGrane, MD

Maine Medical Center
Damien Carter, MD

The Ohio State University
Jon Wisler, MD
Amy Rushing, MD

Olive View-UCLA Medical Center
Darin Saltzman, MD, PhD
David Talan, MD
Gregory Moran, MD

Providence Regional Medical Center
Careen Foster, MD
Brandon Tudor, MD

Rush University Medical Center
Thea P Price, MD

Swedish Medical Center
Katherine Mandell, MD, MPH

Tisch NYU Langone Medical Center
Onaona Gurney, MD
William Chiang, MD

UCHealth University of Colorado
Lisa Ferrigno, MD, MPH
Matthew Salzberg, MD, MBA

University of Iowa Healthcare
Dionne Skeete, MD
Brett Faine, PharmD, MS

University of Michigan Medical Center
Pauline Park, MD
Hasan Alam, MD

University of Mississippi
Matthew Kutcher, MD, MS
Alan Jones, MD

University of Texas at Houston
Lillian Kao, MD, MS

University of Texas LBJ
Mike Liang, MD

University of Washington
Giana H. Davidson, MD, MPH
Amber K Sabbatini, MD, MPH

Vanderbilt University Medical Center
Wesley Self, MD, MPH
Callie Thompson, MD

Virginia Mason Medical Center
Abigal Wiebusch, MD
Juliana Yu, MD

Weill Cornell Medical Center
Robert Winchell, MD
Sunday Clark, ScD, MPH

CERTAIN™

CODA “take home points”

CODA “take home points”

- Largest trial to date

CODA “take home points”

- Largest trial to date
  - Includes historically “at risk” patients

CODA “take home points”

- Largest trial to date
  - Includes historically “at risk” patients
- ED-to-home antibiotics-used in 47%

CODA “take home points”

- Largest trial to date
  - Includes historically “at risk” patients
- ED-to-home antibiotics-used in 47%
- 3-in-10 undergo appendectomy (higher in the appendicolith group) / 7-in-10 avoid surgery

CODA “take home points”

- Largest trial to date
  - Includes historically “at risk” patients
- ED-to-home antibiotics-used in 47%
- 3-in-10 undergo appendectomy (higher in the appendicolith group) / 7-in-10 avoid surgery
- Multiple outcomes favor one treatment or the other

CODA “take home points”

- Largest trial to date
  - Includes historically “at risk” patients
- ED-to-home antibiotics-used in 47%
- 3-in-10 undergo appendectomy (higher in the appendicolith group) / 7-in-10 avoid surgery
- Multiple outcomes favor one treatment or the other
- Complication rate

CODA “take home points”

- Largest trial to date
  - Includes historically “at risk” patients
- ED-to-home antibiotics-used in 47%
- 3-in-10 undergo appendectomy (higher in the appendicolith group) / 7-in-10 avoid surgery
- Multiple outcomes favor one treatment or the other
- Complication rate
  - Higher overall for antibiotics-driven by appendicolith subgroup

CODA “take home points”

- Largest trial to date
  - Includes historically “at risk” patients
- ED-to-home antibiotics-used in 47%
- 3-in-10 undergo appendectomy (higher in the appendicolith group) / 7-in-10 avoid surgery
- Multiple outcomes favor one treatment or the other
- Complication rate
  - Higher overall for antibiotics-driven by appendicolith subgroup
  - No increase in complications in non-appendicolith group

CODA “take home points”

- Largest trial to date
  - Includes historically “at risk” patients
- ED-to-home antibiotics-used in 47%
- 3-in-10 undergo appendectomy (higher in the appendicolith group) / 7-in-10 avoid surgery
- Multiple outcomes favor one treatment or the other
- Complication rate
  - Higher overall for antibiotics-driven by appendicolith subgroup
  - No increase in complications in non-appendicolith group
- Decision makers must weigh characteristics, preferences and circumstances: “one size does not fit all”

CODA “take home points”

- Largest trial to date
  - Includes historically “at risk” patients
- ED-to-home antibiotics-used in 47%
- 3-in-10 undergo appendectomy (higher in the appendicolith group) / 7-in-10 avoid surgery
- Multiple outcomes favor one treatment or the other
- Complication rate
  - Higher overall for antibiotics-driven by appendicolith subgroup
  - No increase in complications in non-appendicolith group
- Decision makers must weigh characteristics, preferences and circumstances: “one size does not fit all”
- Antibiotics for appendicitis: a good choice for some, probably not all