Supplementary Material for the 2024 Clinical Practice Guideline by the Infectious Diseases Society of America on Complicated Intra-abdominal Infections: Utility of Intra-abdominal Fluid Cultures in Adults, Children, and Pregnant People

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METHODS

Panel formation and conflicts of interest

The chair of the guideline panel was selected by the leadership of IDSA. Fifteen additional panelists comprised the full panel. The panel included clinicians with expertise in infectious diseases, pediatric infectious diseases, surgery, emergency medicine, microbiology, and pharmacology. Panelists were diverse in gender, geographic distribution, and years of clinical experience. Guideline methodologists oversaw all methodological aspects of the guideline development and identified and summarized the scientific evidence for each clinical question. IDSA staff oversaw all administrative and logistic issues related to the guideline panel.

All members of the expert panel complied with the IDSA policy on conflict of interest (COI), which requires disclosure of any financial, intellectual, or other interest that might be construed as constituting an actual, potential, or apparent conflict. Evaluation of such relationships as potential conflicts of interest was determined by a review process which included assessment by the Standards and Practice Guideline Committee (SPGC) Chair, the SPGC liaison to the Guideline panel and the Board of Directors liaison to the SPGC, and if necessary, the Conflicts of Interests Task Force of the Board. This assessment of disclosed relationships for possible COI was based on the relative weight of the financial relationship (i.e., monetary amount) and the relevance of the relationship (i.e., the degree to which an independent

observer might reasonably interpret an association as related to the topic or recommendation of consideration). The reader of these guidelines should be mindful of this when the list of disclosures is reviewed. See the Notes section at the end of this guideline for the disclosures reported to IDSA.

Practice recommendations

Clinical Practice Guidelines are statements that include recommendations intended to optimize patient care by assisting practitioners and patients in making shared decisions about appropriate health care for specific clinical circumstances. These are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options [IOM 2011]. The "IDSA Handbook on Clinical Practice Guideline Development" provides more detailed information on the processes followed throughout the development of this guideline [IDSA CPG Handbook].

Review and approval process

Feedback was obtained from five external individual peer expert reviewers as well as the endorsing organizations. The IDSA Standards and Practice Guidelines Subcommittee (SPGS) and Board of Directors reviewed and approved the guideline prior to publication.

Process for updating

IDSA guidelines are regularly reviewed for currency. The need for updates to the guideline is determined by a scan of current literature and the likelihood that any new data would impact the recommendations. Any changes to the guideline will be submitted for review and approval to the appropriate Committees and Board of IDSA.

Clinical questions

Each clinical question was formatted according to the PICO style: Patient/Population (P), Intervention/Indicator (I), Comparator/Control (C), Outcome (O). For each PICO question, outcomes of interest were identified a priori and rated for their relative importance for decision-making.

Literature search

A medical librarian designed the literature searches and MeSH terms for Ovid Medline, Embase, and Cochrane Library. Searches were limited to studies published in English. The initial formal literature searches were performed in July to November 2018, and updated literature searches were conducted in March 2021 and October 2022. To supplement the electronic searches, reference lists of related articles and guidelines were reviewed for relevance.

MEDLINE

#1 exp Intraabdominal Infections/

#2 ((intraabdom?n* or abdom?n* or appendix or appendectom* or appendic* or peritonitis* or typhlitis* or diverticul* or subdiaphragmat* or subphren* or sub-diaphragmat* or sub-phren* or peritoneal* or pericolon* or peri-colon* or periappendic* or phlegmon*) adj2 (complicated or infect* or candidias* or bacteremia* or abscess* or abcess* or sepsis or septic or shock*)).tw,kf.

#3 1 or 2

#4 ((fluid* or ascit*) adj10 culture*).tw,kf.

#5 ((fluid* or ascit*) adj5 (tapping* or analy*)).tw,kf.

#6 Ascitic Fluid/mi

#7 *Body Fluids/mi

#8 or/4-7

#9 3 and 8

#10 (culture* and ((intraabdom?n* or abdom?n* or appendix or appendectom* or appendic* or peritonitis* or typhlitis* or diverticul* or subdiaphragmat* or subphren* or sub-diaphragmat* or sub-phren* or peritoneal* or pericolon* or peri-colon* or periappendic* or phlegmon*) adj5 (fluid* or ascit*))).tw,kf.

#11 9 or 10

#12 Animals/ not (Animals/ and Humans/)

#13 ((animal or animals or canine* or cat or cats or dog or dogs or feline or hamster* or mice or monkey or monkeys or mouse or murine or pig or pigs or piglet* or porcine or primate* or rabbit* or rats or rat or rodent* or sheep*) not (human* or patient*)).tw,kf.

#14 11 not (12 or 13)

#15 limit 14 to (comment or editorial or letter or case reports or congress or clinical conference or consensus development conference or consensus development conference, nih)

#16 14 not 15

#17 limit 16 to english

#18 remove duplicates from 17

EMBASE

#1 exp abdominal infection/

#2 ((intraabdom?n* or abdom?n* or appendix or appendectom* or appendic* or peritonitis* or typhlitis* or diverticul* or subdiaphragmat* or subphren* or sub-diaphragmat* or sub-phren* or peritoneal* or pericolon* or peri-colon* or periappendic* or phlegmon*) adj2 (complicated or infect* or candidias* or bacteremia* or abscess* or abcess* or sepsis or septic or shock*)).tw,kw,kf.

#3 1 or 2

#4 ((fluid* or ascit*) adj10 culture*).tw,kw,kf.

#5 ((fluid* or ascit*) adj5 (tapping* or analy*)).tw,kw,kf.

#6 4 or 5

#7 3 and 6

#8 ascites fluid/

#9 body fluid/

#10 8 or 9

#11 exp microbiology/

#12 10 and 11

#13 3 and 12

#14 7 or 13

#15 (culture* and ((intraabdom?n* or abdom?n* or appendix or appendectom* or appendic* or peritonitis* or typhlitis* or diverticul* or subdiaphragmat* or subphren* or sub-diaphragmat* or sub-phren* or peritoneal* or pericolon* or peri-colon* or periappendic* or phlegmon*) adj5 (fluid* or ascit*))).tw,kw,kf.

#16 14 or 15

#17 (exp animal/ or exp juvenile animal/ or adult animal/ or animal cell/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not human/

#18 ((animal or animals or canine* or cat or cats or dog or dogs or feline or hamster* or mice or monkey or monkeys or mouse or murine or pig or pigs or piglet* or porcine or primate* or rabbit* or rats or rat or rodent* or sheep*) not (human* or patient*)).tw,kw,kf.

#19 16 not (17 or 18)

#20 case report/

#21 19 not 20

#22 limit 21 to (books or "book review" or chapter or conference abstract or conference paper or "conference review" or editorial or letter or note)

#23 21 not 22

#24 limit 23 to english

#25 limit 24 to yr="2021 -Current"

#26 remove duplicates from 25

COCHRANE

#1 ((intraabdom?n* or abdom?n* or appendix or appendectom* or appendic* or peritonitis* or typhlitis* or diverticul* or subdiaphragmat* or subphren* or sub-diaphragmat* or sub-phren* or peritoneal* or pericolon* or peri-colon* or periappendic* or phlegmon*) NEAR/2 (complicated or infect* or candidias* or bacteremia* or abscess* or abcess* or sepsis or septic or shock*)):ti,ab,kw

#2 ((fluid* or ascit*) NEAR/10 (culture*)):ti,ab,kw

#3 ((fluid* or ascit*) NEAR/5 (tapping* or analy*)):ti,ab,kw

#4 #2 OR #3

#5 #1 AND #4

#6 (culture* and ((intraabdom?n* or abdom?n* or appendix or appendectom* or appendic* or peritonitis* or typhlitis* or diverticul* or subdiaphragmat* or subphren* or sub-diaphragmat* or sub-phren* or peritoneal* or pericolon* or peri-colon* or periappendic* or phlegmon*) NEAR/5 (fluid* or ascit*))):ti,ab,kw

#7 #5 OR #6

Study selection

Titles and abstracts were screened in duplicate for all identified citations using Rayyan [Ouzzani 2016]. All potentially relevant citations were subjected to a full-text review, using predefined inclusion and exclusion criteria tailored to meet the specific population, intervention, and comparator of each clinical question. The steps of the literature selection process were supervised and reviewed by a guideline methodologist for the final selection of the relevant articles.

The following eligibility criteria were used:

Inclusion criteria:

- *Patient population*- Adults, children, or pregnant people admitted to the hospital/emergency department and receiving a culture of intra-abdominal fluid
- *Intervention*- Fluid culture
- *Comparator*- N/A
- *Outcomes*- Change in antimicrobial therapy or clinical management, mortality, true positivity and contamination rates (secondary)
- *Study design*- Randomized controlled trials (RCTs) with no date limit, observational studies published 2005-present, no minimum number of study participants

Exclusion criteria:

- *Patient population*- Patients with spontaneous bacterial peritonitis or cirrhosis
- *Intervention*- N/A
- *Comparator*- N/A
- *Study design*- Observational studies published prior to 2005 (cutoff decided on in 2020 for the question on antimicrobials and associated questions, to capture 15 years of data), abstracts and conference proceedings, letters to the editor, editorials, and review articles

Data extraction and analysis

A guideline methodologist in conjunction with panelists extracted the data for each pre-determined patient-important outcome. If a relevant publication was missing raw data for an outcome prioritized by the panel, an attempt was made to contact the author(s) for the missing data. Where applicable, data were pooled using random-effects model (fixed effects model for pooling of rates) using RevMan [RevMan].

Evidence to decision

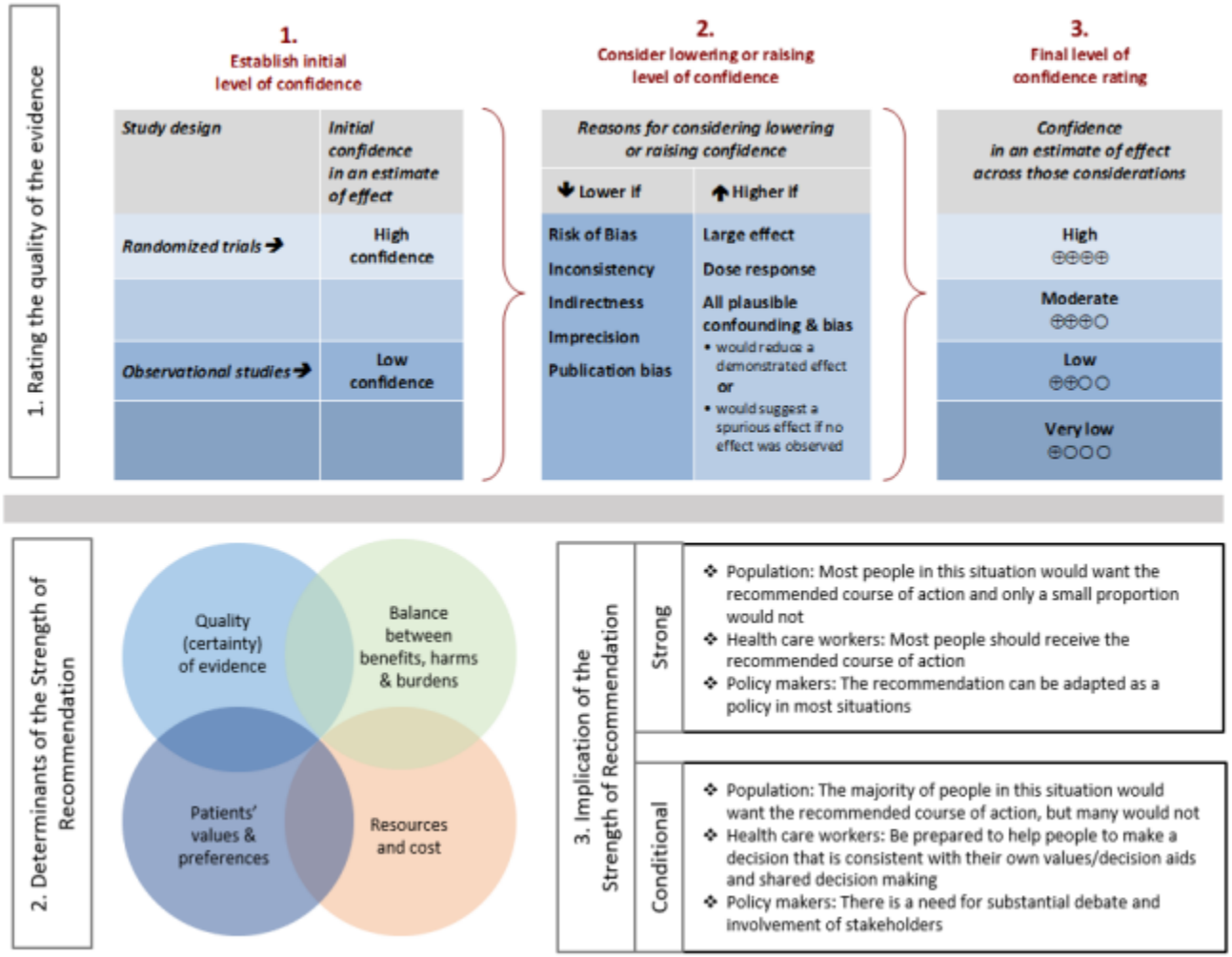
Guideline methodologists prepared the evidence summaries for each question and assessed the risk of bias and the certainty of evidence. Risk of bias was assessed by using the QUIPS tool for studies addressing risk/prognostic factors [Hayden 2013] and the QUADAS-2 tool for diagnostic test accuracy studies [Whiting 2011]. The certainty of evidence was determined first for each critical and important outcome and then for each recommendation using the GRADE approach for rating the confidence in the evidence [Guyatt 2008, GRADE Handbook]. Evidence profiles were developed using the GRADEpro Guideline Development Tool [Guyatt 2008] and reviewed by panel members responsible for each PICO.

The Evidence to Decision framework [GRADEpro] was used to translate the evidence summaries into practice recommendations. All recommendations were labeled as either “strong” or “conditional” according to the GRADE approach [IDSA CPG Handbook]. The words “we recommend” indicate strong recommendations and “we suggest” indicate conditional recommendations. Supplementary Figure 1 provides the suggested interpretation of strong and conditional recommendations for patients, clinicians, and healthcare policymakers. For recommendations where the comparator treatment or tests are not formally stated, the comparison of interest is implicitly referred to as “not using the intervention” (either not using a specific treatment or a diagnostic test).

All members of the panel participated in the preparation of the draft guideline and approved the recommendations.

TABLES AND FIGURES

Supplementary Figure 1. Approach and implications to rating the quality of evidence and strength of recommendations using GRADE methodology (unrestricted use of figure granted by the U.S. GRADE Network)



Supplementary Table 1. Characteristics of included studies for fluid cultures

Author, year of publication	Location, years of data collection	Study design	Number of patients and age	Population included	Intervention
Foo 2008	UK A 3-year period; years not stated	Retrospective cohort study	652 patients (435 with intraoperative swabs) Median age 20 years (range 1 month-81 years)	Adult and pediatric patients undergoing emergency appendicectomy (simple and complicated)	Intraoperative swabs
Kening 2013	Poland 2007-2013	Retrospective cohort study	369 patients (236 with intraoperative cultures) Mean age 35.8 years (range 16-92)	Patients undergoing appendectomy (laparoscopic and open)	Swabs; routinely obtained for open appendectomies but not for laparoscopic
Khan 2007	UK 2002-2003	Retrospective cohort study	137 patients (109 with peritoneal cultures) Median age 19 years (range 5-61)	Patients undergoing appendectomy (simple and complicated)	Intraoperative peritoneal swabs
Moawad 2006	UK 2.5-year period; years not stated	Retrospective cohort study	498 patients (117 with intraperitoneal cultures) Median age 22 years (range 3-91)	Patients undergoing appendectomy (laparoscopic and open)	Intraoperative peritoneal swabs
Theodorou 2021	USA 2015-2019	Retrospective comparative study	255 patients (149 with intraoperative cultures) Median age 8.5 years (range 1.2-17.6)	Patients <18 years undergoing appendectomy (laparoscopic or open) for perforated appendicitis *High rates of *Pseudomonas* reported	Intraoperative culture Culture positivity rate not stated. 50/149 had antibiotics changed.
Tocchioni 2016	Italy 2012	Prospective cohort study	36 children Mean age 12 years (range 3-17)	Children undergoing appendectomy, complicated appendicitis only (most laparoscopic)	Peritoneal fluid or pus swabs
Tsuchiya 2019	Japan 2014-2016	Retrospective cohort study	41,495 adults (16,303 with intra-abdominal cultures) Mean 62.3 years	Adults with complicated intra-abdominal infection who had undergone source control procedures (open or laparoscopic or percutaneous transhepatic biliary drainage) on the first day of admission	Intra-abdominal cultures
Viel-Theriault 2019	Canada 2017-2018	Retrospective cohort study	133 children (53 with peritoneal fluid cultures) Median age 10 years for those with culture performed (range 8-13)	Children undergoing appendectomy or IR drainage for complicated appendicitis	Peritoneal fluid specimens sampled using a trap or container; swabs discouraged
Wakeman 2022	USA 2020	Quality improvement, pre-/post-intervention study	41 children in the post-intervention cohort, 40 of whom had cultures obtained Mean age 9.1 years	Children with complicated appendicitis who, as part of the post-implementation cohort, had aerobic and anaerobic cultures of intra-abdominal fluid collected at the time of (mostly laparascopic) appendectomy	Intra-abdominal fluid cultures Fluid culture yield: 33/40 (83%) 13 had home antibiotic regimen changed (32%).

Supplementary Table 2. Risk of bias for included studies

Supplementary Table 3. GRADE Evidence Profile: Do cultures of intra-abdominal fluid result in a meaningful change in antibiotic therapy or prevention of mortality?

Outcome (risk factor)	No. of studies	Certainty Assessment						Effect							Certainty
								No. of Individuals							
		Study Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	No. with fluid culture	No. without fluid culture/ control	With cx: change in therapy	Without cx: change in therapy	Effect Measure	Adjusted Effect Estimate	95% CI	
Change in therapy for uncomplicated appendicitis (Khan 2007)	1	cohort study	very serious	not serious	not serious	not serious	none	67 (19 positive)	N/A	0	N/A	Proportion	0.00		⊕⊕◯◯ LOW
Change in therapy for complicated appendicitis (Khan 2007, Tocchioni 2016, Viel-Theriault 2019, Wakeman 2022)	4	cohort studies	very serious	serious	not serious	not serious	none	171 (115 positive)	N/A	14	N/A	Proportion	0.09		⊕⊕◯◯ LOW
Change in therapy for both uncomplicated and complicated appendicitis (Foo 2008, Kening 2013, Moawad 2006)	3	cohort studies	very serious	not serious	not serious	not serious	none	787 (289 positive)	N/A	1	N/A	Proportion	0.01		⊕⊕◯◯ LOW
Change in therapy for complicated intra-abdominal infection (Tsuchiya 2019)	1	cohort study	not serious	not serious	serious	not serious	none	16280 (culture positivity not provided)	24511	1154	1091	OR	1.56	(1.42-1.72)	⊕⊕⊕◯ MODERATE
Mortality for complicated intra-abdominal infection (Tsuchiya 2019)	1	observational study	not serious	not serious	not serious	not serious	none	16280 (culture positivity not provided)	24511	1154	1091	OR	0.85	(0.77-0.95)	⊕⊕⊕⊕ HIGH

Supplementary Figure 2. Proportion of patients with a change in therapy due to culture results (Foo 2008, Kening 2013, Khan 2007, Moawad 2006, Tocchioni 2016, Viel-Theriault 2019, Wakeman 2022)

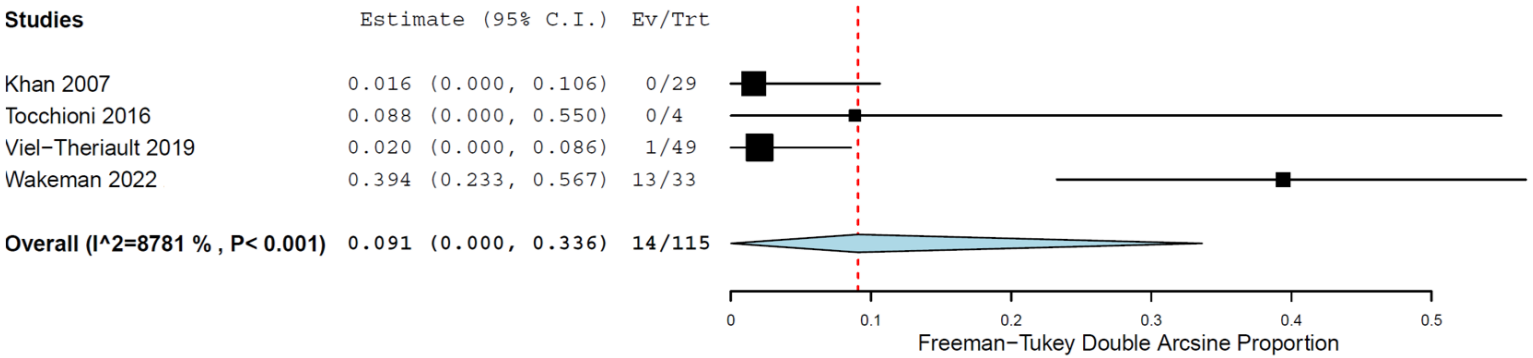
Fluid culture yield ranged from 11%-92%, with most ~40-50% (assumed 45% for modeling below).

a) Uncomplicated appendicitis

Khan 2007: 0/19 changes in therapy in patients with positive fluid culture

Modeling: Start with 100 patients who had fluid cultures obtained. Assuming a fluid culture yield of 45%, 45 return positive cultures… of those 45, X (some unspecified number) are contaminated or false positives… 0 result in a change in therapy ((0/67)*100 = 0).

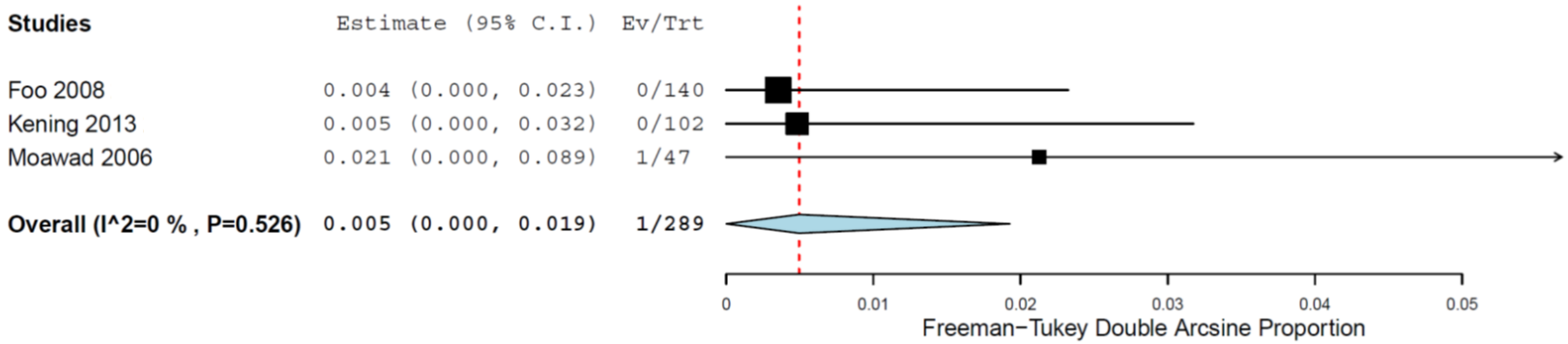
b) Complicated appendicitis



Modeling: Start with 100 patients who had fluid cultures obtained. Assuming a fluid culture yield of 45%, 45 return positive cultures… of those 45, X (some unspecified number) are contaminated or false positives. At most, 4 result in a change in therapy (45*0.091).

One additional study (not included above) indicated that 50/149 patients undergoing appendectomy for perforated appendicitis had antibiotics changed as a result of intraoperative cultures; however, the rate of *Pseudomonas* in this study was quite high (22% of those cultured) [Theodorou 2021].

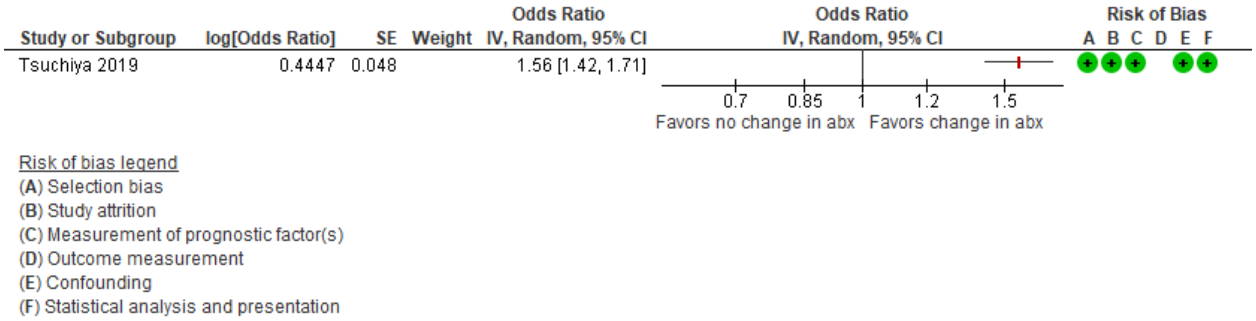
c) Both uncomplicated and complicated appendicitis



Modeling: Start with 100 patients who had fluid cultures obtained. Assuming a fluid culture yield of 45%, 45 return positive cultures… of those 45, X (some unspecified number) are contaminated or false positives… 0-1 result in a change in therapy (45*0.002).

Risk of Bias: High
Indirectness: Moderate (swabs)
Imprecision: None
Inconsistency: None

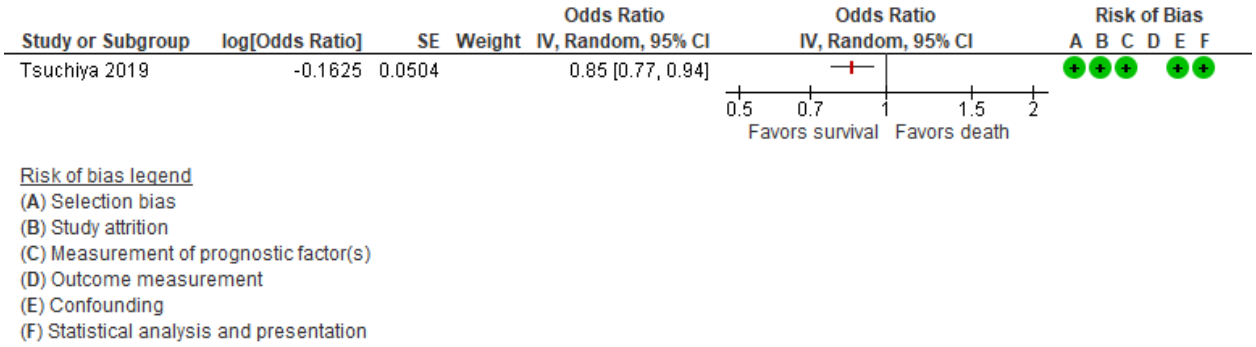
Supplementary Figure 3. Fluid culture as a predictor of change in therapy [Tsuchiya 2019]



Modeling: Start with 100 patients who had fluid cultures obtained… 45 return positive cultures… of those 45, X (some unspecified number) are contaminated or false positives… an *additional* ~3% (7.1% vs. 4.5% in the culture and no culture groups of Tsuchiya 2019) would have therapy changed = ~1-2 *additional* changes in therapy

Risk of Bias- Change in therapy: None (QUIPS=low)
Indirectness- Change in therapy: Serious (no cx positivity rate provided; authors unable to distinguish change in therapy due to cx vs. clinical picture, so the outcome is indirect)
Imprecision- Change in therapy: None
Inconsistency- Change in therapy: N/A

Supplementary Figure 4. Fluid culture as a predictor of mortality (Tsuchiya 2019)



Risk of Bias- Mortality: None (QUIPS=low)
Indirectness- Mortality: None
Imprecision- Mortality: None
Inconsistency- Mortality: N/A

REFERENCES

Foo FJ, Beckingham IJ, Ahmed I. Intra-operative culture swabs in acute appendicitis: a waste of resources. Surgeon, **2008**; 6(5): 278-281.

McMaster University and Evidence Prime Inc. GRADEpro GDT. Available at: https://gradepro.org/. Accessed 24 May 2020.

Guyatt GH, Oxman AD, Vist GE, et al.; GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ, **2008**; 336:924-926.

Hayden JA, van der Windt DA, Cartwright JL, Cote P, Bombardier C. Assessing bias in studies of prognostic factors. Ann Intern Med, **2013**; 158(4): 280-286.

Infectious Diseases Society of America. IDSA Handbook on Clinical Practice Guideline Development. Available at: https://www.idsociety.org/practice-guideline/clinical-practice-guidelines-development-training-and-resources/. Accessed May 1, 2021.

IOM (Institute of Medicine). Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press, **2011**.

Kenig J, Richter P. The need for culture swabs in laparoscopically treated appendicitis. Wideochir Inne Tech Maloinwazyjne, **2013**; 8(4): 310-314.

Khan MN, Vidya R, Lee RE. Are routine peritoneal fluid cultures during appendicectomy justified? Ir J Med Sci, **2007**; 176(1): 37-40.

Moawad MR, Dasmohapatra S, Justin T, Keeling N. Value of intraoperative abdominal cavity culture in appendicectomy: a retrospective study. Int J Clin Pract, **2006**; 60(12): 1588-1590.

Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev, **2016**; 5(1): 210.

Review Manager 5 (RevMan 5). 5.4 ed. Copenhagen: The Cochrane Collaboration, 2020.

Schünemann H, Brożek J, Guyatt GH, Oxman A. Introduction to GRADE Handbook. Available at: https://gdt.gradepro.org/app/handbook/handbook.html. Accessed 25 May 2020.

Theodorou CM, Stokes SC, Hegazi MS, Brown EG, Saadai P. Is Pseudomonas infection associated with worse outcomes in pediatric perforated appendicitis? J Pediatr Surg **2021**; 56(10): 1826-30.

Tocchioni F, Tani C, Bartolini L, et al. The role of DNA amplification and cultural growth in complicated acute appendicitis. Pediatr Rep, **2016**; 8(3): 6487.

Tsuchiya A, Yasunaga H, Tsutsumi Y, Kawahara T, Matsui H, Fushimi K. Nationwide observational study of mortality from complicated intra-abdominal infections and the role of bacterial cultures. Br J Surg, **2019**; 106(5): 606-615.

Viel-Theriault I, Bettolli M, Toye B, Harrison MA, Le Saux N. Contemporary microbiology and antimicrobial treatment of complicated appendicitis: the value of a short-term study. Pediatr Infect Dis J, **2019**; 38(11): e290-e294.

Wakeman D, Livingston MH, Levatino E, et al. Reduction of surgical site infections in pediatric patients with complicated appendicitis: utilization of antibiotic stewardship principles and quality improvement methodology. J Pediatr Surg, **2022**; 57(1): 63-73.

Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med **2011**; 155(8): 529-536.