MONTHLY FEATURE CPG SOPR SUMMARY

CPG Citation: *Qaseem A, Etxeandia-Ikobaltzeta I, Lin JS, Fitterman N, Shamliyan T, Wilt TJ for the Clinical Guidelines Committee of the American College of Physicians. Diagnosis and Management of Acute Left-Sided Colonic Diverticulitis: A Clinical Guideline From the American College of Physicians. Ann Intern Med. 2022;175:399-415. doi:10.7326/M21-2710.*

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**Accompanying Systematic Review: Balk EM, Adam GP, Bhuma MR, et al. Diagnostic imaging and medical management of acute left-sided colonic diverticulitis. A systematic review. Ann Intern Med. 2022; 175: 379-387. doi:10.7326/M21-1645

Scope of Guideline: All clinicians who care for patients with acute colonic diverticulitis.

Inclusion: Patients with suspected or confirmed acute colonic diverticulitis.

Exclusion: Patients with right- or complicated left-sided diverticulitis, SIRS/sepsis, immunosuppression, unstable comorbidities, concurrent antibiotics usage, need immediate surgery, acute renal injury, other sinister colonic pathology.

Key Words: acute colonic diverticulitis, antibiotics, imaging, outpatient management.

Key Recommendations: *Each recommendation is accompanied by the "strength" of recommendation and the level of evidence (LoE) supporting that recommendation*

Recommendations	Strength, LoE
FOR Clinical Action	
Clinicians **could** use abdominal CT imaging when there is diagnostic uncertainty in a patient with suspected acute left-sided colonic diverticulitis.	Conditional, Low
Clinicians **could** manage most patients with acute uncomplicated left-sided colonic diverticulitis in an outpatient setting.	Conditional, Low
Clinicians initially **could** manage select patients with acute uncomplicated left-sided colonic diverticulitis without antibiotics.	Conditional, Low

CLINICAL COMMENTARY:

About 5-10% of patients with diverticulosis will develop acute colonic diverticulitis (ACD), and risk increases with age. Prevalence of right-sided ACD is higher in Asian countries, whereas left-sided disease is more common in Western countries. About 12% of cases are complicated by inflammatory fistulae, abscess, phlegmon, obstruction, bleeding or perforations. The recurrence rates at 10yrs are about 22% after an initial event, and up to 55% after secondary attacks. The annual hospitalization costs for ACD have reached upwards of $USD8billion in recent years.

Many ED patients with abdominal pain (acute, recurrent) receive invasive investigations, and repeat CT scans which can result in long-term harms. Updates on managing low-risk recurrent abdominal pain have been recently reviewed in the Society for Academic Medicine GRACE-2 (Guidelines for Reasonable & Appropriate Care in Emergency room) publication

(May 2022; downloadable at https://onlinelibrary.wiley.com/doi/10.1111/acem.14495) [DISCLOSURE: S. Upadhye is an author on GRACE-2 guidelines].

Benefits of Recommendations: Given the low certainty of evidence supporting CPG questions, ED physicians **could** consider following the stated Recs, but there is not higher supporting evidence guiding physicians as to what they **should** do…

This CPG made a **deliberate effort to solicit and rank Patient-Relevant Outcomes (PROs)** amongst panelists (including public/patient stakeholders); these are summarized in **Table 1.**

The **diagnostic accuracy of contrast CT for acute left-sided diverticulitis from pooled studies was Sens 94% (95%CI 87-97%), and Spec 99% (90-99%), which is corresponds to a LR+ 94 and LR- 0.06**, confirming that this is a very useful diagnostic discriminatory test. Based on a prevalence range from 10-70%, 6-42 per 1000 patients would have false negative results, and 3-9 per 1000 patients would have a false abnormal finding. These are summarized in **Figure 2** below.

Managing low-risk patients in an outpatient setting was not unsafe compared to inpatient treatment (OR 0.85, 0.5-1.43), when considering outcomes of elective surgery or recurrence rates (low certainty evidence, 6 studies).

Low-certainty evidence (5 studies) **comparing antibiotics Rx with no Abx showed no significant differences** in need for surgery at 6-12mo (ARD -2.0% to 0.4%), complications at 1mo (1.1% vs 1.8%) and 1yr (2.1% vs 4.0%), and quality of life at 3/6/12/24months. These studies mostly enrolled immunocompetent adults with uncomplicated left ACD, however. There was insufficient evidence re: comparing Abx regimens for all important outcomes and durations of therapy. **There was a strong preference to treatment without Abx by patient participants.**

Harms/Adverse Effects of Recommendations: There is always a risk of detecting clinically insignificant findings, which may lead to different diagnostic/treatment decisions that may not be relevant for morbidity, mortality or patient quality of life.

Potential harms from CT scanning include radiation exposure, detecting incidental findings that are clinically irrelevant, and contrast dye reactions.

Studies typically didn't report on harms, adverse events or side effects of infections (nosocomial, other), Abx usage (eg. C. Diff infections, resistance) or adverse procedure events (eg. bleeding, catheter infections).

Barriers to Uptake: Geographic distance from definitive care and caregiver supports may be an important consideration in decisions re: imaging, therapies and out-patient care. The **costs** of a contrast CT abdo were considerably variable based on US Medicare vs uninsured patient status ($USD 56-94 vs. $USD 580-4900). There was **no summarized evidence relevant to the following PROs**: progression to complicated ACD/mortality, return to normal bowel function, missed work/employment/school, and opioid misuse.

Facilitators of Uptake: The **majority of included studies were conducted in ED settings**, increasing the generalizability of findings to ED ACD patients.

There are **absolute cost savings for treating ACD patients as outpatients** vs admission (generally 1/3 cost). **Table 3** showed the relative Abx-costs for IV vs oral Abx treatment routes; oral Ciprofloxacin was the cheapest oral agent listed for patient out-of-pocket costs.

Non-Abx care of "select" patients focuses on supportive care to reduce bowel inflammation (analgesia, hydration, bowel rest). Select patients for non-Abx care = immunocompetent, uncomplicated left ACD, no SIRS/sepsis criteria, not medically frail/needing hospitalization for other reasons, have supportive social/family supports, and

can follow-up with outpatient supervision. **This decision will likely be the most contentious for ED physicians discharging patients with surgical follow-up, and should likely be made in conjuction with follow-up surgeons and patients/caregivers.**

In the absence of accessible abdominal CT scan, it is reasonable to consider abdominal US or MRI scans to confirm ACD diagnosis. Clinicians should err on the side of imaging if there is **risk of ACD progression to complicated disease; these include symptoms >5days duration, systemic comorbidities, high WBC > 13.5 or CRP level >140mg/L, or CT signs of perforation, GI bleeding, obstruction (vomiting), abscess/phlegmon or a longer inflamed colon segment (cutoff?).**

Table 1. Outcome Ratings for the Diagnosis and Management of Acute Colonic Diverticulitis*

Outcomes Rated as Critical	Outcomes Rated as Important
Use of CT imaging in the diagnosis of acute colonic diverticulitis	
Falsely normal CT findings	Future episode of complicated diverticulitis
Falsely abnormal CT findings	Length of hospital stay
Conversion to complicated diverticulitis	Recurrent diverticulitis
Diverticulitis-related complications	Sequelae related to incidental findings
Diverticulitis-related mortality	Time to resolution
Change in management	
Harms of overtreatment	
Harms of undertreatment	
Management of acute colonic diverticulitis	
Avoidance of surgery	Antibiotic resistance
Clostridioides difficile infection	Health care-based infections
Conversion to complicated diverticulitis	Missed work or school
Diverticulitis-related complications	Need for second procedures or revisions
Length of hospital stay	Opioid misuse
Mortality	Return to normal bowel function
Quality of life	Resource use
Resolution of diverticulitis	Recurrence of diverticulitis
Rehospitalization	Side effects/adverse events
Treatment failure	

CT = computed tomography.
* Rated a priori by clinician and nonclinician public members of the Clinical Guidelines Committee and the Clinical Guidelines Committee Public Panel.

Table 3. Estimated Antibiotic Unit Costs for Interventions Included in the Studies*

Drug	Range of Estimated 7-d Pharmacy Costs (Patient Out-of-Pocket Cost), $	Estimated 7-d Cost, Veterans Affairs (System Perspective), $	Range of Estimated 7-d Costs, CMS (System Perspective), $
Intravenous route			
Cefotaxime	96–128	NA	37
Cefuroxime	87–111	73	24
Ertapenem	283–665	336–735	44–199
Imipenem	1448	157	29–126
Meropenem	145–205	38	18–308
Metronidazole	1.3–1.7	2	0.6–1.1
Piperacillin–tazobactam	305–354	106	16–315
Oral route			
Cefadroxil	17–45	14	3–6
Ciprofloxacin	7–22	3	1–2
Metronidazole	13–19	8	1–3
Amoxicillin–clavulanate	23–30	3	9–91

CMS = Centers for Medicare & Medicaid Services; NA = not available.
* Data from www.medicaid.gov/medicaid/prescription-drugs/pharmacy-pricing/index.html, www.va.gov/opal/nac/fss/pharmPrices.asp, https://hcai.ca.gov/visualizations/prescription-drug-wholesale-acquisition-cost-increases, www.goodrx.com, and www.drugs.com (patient perspective). When drug doses were not reported, we used doses recommended by drug labels or clinical guidelines dosing in adults with intraabdominal infections.

CPG Quality/ Trustworthiness Standards

Amalgamated from AGREE-II/NEATS instruments.

Quality/Trustworthiness Domain	
1. The clinical practice guideline (CPG) discloses and states explicitly its funding source.	✓
2. Financial conflicts of interest of guideline development group (GDG) members have been disclosed and managed.	✓
3. The CPG development group includes all of the relevant multidisciplinary stakeholders, including clinicians, methodologists and patients/caregivers.	✓
4. The CPG objectives, health questions, scope of relevant providers and target recipients of care are clearly defined.	✓
5. Values/preferences of patients, caregivers, advocates and/or the public with experience with the clinical disease management has been sought/integrated into CPG development (reported clearly). **PROs listed in Table 1.**	✓
6. The search strategy for evidence is thoroughly developed and described.	✓
7. The criteria for selecting relevant studies/evidence are clearly described.	✓
8. The quality, strengths and limitations of the body of evidence are clearly described (e.g., GRADE, **Cochrane**, etc.). Summaries of evidence tables are provided. **Yes (in accompanying systematic review).**	✓
9. The health benefits, side effects, and risks were considered in formulating the recommendations.	✓
10. There is an explicit approach linking the evidence to formulate the recommendations.	✓
11. The strength of recommendations is clearly reported, including confidence in underlying evidence.	✓
12. Recommendations are clear and unambiguous, and easily identified in the CPG publication.	✓
13. Different options for management for managing the health questions are clearly presented.	✓
14. Experts externally reviewed the guideline prior to its publication.	✓
15. The CPG describes a procedure to update the guideline, and provides advice, tools and/or clinical pathways for easy adoption/adaptation into practice. **Expires within 5yrs. No tools to facilitate uptake.**	?
16. The CPG describes barriers and facilitators to implement recommendations.	X
17. Performance metrics for monitoring implementation of recommendations for audit/feedback have been defined appropriately.	X
18. Resource implications for implementing CPG recommendations have been discussed. **Multiple economics databases searched for relevant resources/costing information.**	✓

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***Conflicts of Interested*:** **(**Reported) Declared and managed. One panelist recused from voting and authorship due to advisory board status with an ongoing trial.

*****EVIDENCE Profiles from supporting Systematic Review (Balk et al, Annals Int Med 2022)***

Table 1. Evidence Profile for Outpatient Versus Inpatient Management of Uncomplicated Acute Diverticulitis

Outcome	Studies (Participants), *n*	Risk of Bias	Consistency	Precision	Directness	Other Limitations	Overall SoE	Conclusions
Death	3 (1009)	Low	Consistent	Imprecise	Direct	Sparse	Insufficient	No conclusion Rare event
Emergency surgery	2 (208)	Low	Consistent	Imprecise	Direct	Sparse	Insufficient	No conclusion Rare event
Treatment failure	2 (697)	Low	Inconsistent	Unclear	Direct	None	Insufficient	No conclusion
Elective surgery (~8–55 mo)	3 (755)	High	Consistent	Precise	Direct	Unadjusted	Low	No difference found (unadjusted OR, 0.76 [95% CI, 0.21–2.77])
Quality of life	1 (132)	Low	NA	Precise	Direct	Sparse	Insufficient	No conclusion
Recurrence (~8–55 mo)	4 (791)	High	Consistent	Precise	Direct	Unadjusted	Low	No difference found (unadjusted OR, 0.85 [CI, 0.50–1.43])

NA = not applicable; OR = odds ratio; SoE = strength of evidence.

Table 1 Summary: The evidence comparing out-patient vs. in-patient management of uncomplicated ACD is sparse and inconclusive to push a Recommendation in either direction. Shared decision-making with patients, caregivers and follow-up surgeons should be undertaken to generate an individual care plan.

Table 2. Evidence Profile for Antibiotic Treatment of Acute Diverticulitis

Topic and Outcome	Studies (Participants), *n*	Risk of Bias	Consistency	Precision	Directness	Other Limitations	Overall SoE	Conclusions
Antibiotics vs. no antibiotics								
Death	3 (1329)	Moderate	Consistent	Imprecise	Direct	Sparse events	Insufficient	No conclusion Rare event
Treatment failure	2 (1109)	Low	Consistent	Precise	Indirect*	Post hoc IPD MA†	Low	No evidence of a difference 5.0% vs. 7.2% (*P* = 0.062)†
Length of hospital stay	3 (1329)	Moderate	Inconsistent	Precise	Direct	None	Low	No evidence of a difference Difference, −7.7 h (95% CI, −20.2 to 4.8 h)
Rehospitalization	2 (706)	Moderate	Consistent	Precise	Direct	Sparse‡	Insufficient	No conclusion
Surgery at 6–12 mo	2 (1110)	Moderate	Consistent	Imprecise	Direct	None	Low	No evidence of a difference, but possible trend toward lower risk with antibiotics (OR, 0.33 [CI, 0.07 to 1.63])§
Diverticulitis-related complications	2 (1151)	Moderate	Consistent	Precise	Direct	Post hoc IPD MA	Low	No evidence of a difference 1.1% vs. 1.8% (1 mo) and 2.1% vs. 4.0% (1 y)
Quality of life	2 (732)	Moderate	Consistent	Precise	Direct	Sparse, per analysis	Low	No evidence of a difference
Recurrence	4 (1633)	Moderate	Consistent	Precise	Indirect‖	None	Low	No evidence of a difference (summary OR, 1.06 [CI, 0.69 to 1.64])
Adverse events	1 (623)	Moderate	NA	Precise	Direct	Sparse	Insufficient	No conclusion
Various antibiotic regimens								
All	8 (141 098)¶	Moderate	NA	Imprecise	Direct	Sparse, per analysis**	Insufficient	No conclusion

IPD MA = individual patient data meta-analysis; NA = not applicable; OR = odds ratio; SoE = strength of evidence.

Table 2 Summary: Sparse evidence found no difference in risks for treatment failures, elective surgery, ACD recurrence, hospital length-of-stay, quality of life or ACD complications. There was insufficient evidence presented to inform comparative risks of death, rehospitalizations, or Abx-related adverse events (largely because of rare events).

Figure 2. Summary of the ACP recommendation on diagnosis of acute left-sided colonic diverticulitis.

ACP American College of Physicians Leading Internal Medicine, Improving Lives

Role of CT Imaging in the Diagnosis of Acute Left-Sided Colonic Diverticulitis

Background

Acute colonic diverticulitis is inflammation of diverticula, abnormal outpouchings of the large intestine. Given that abdominal CT imaging is widely used to evaluate individuals with suspected diverticulitis, many patients with acute abdominal pain will undergo CT scans each year. However, questions exist about the diagnostic accuracy, effect on clinical management, and downstream outcomes.

Patient Population
Adults with suspected or known diagnosis of acute left-sided colonic diverticulitis

Interventions Evaluated
CT scan with or without IV, oral, or rectal contrast vs. no CT scanning

Outcomes Evaluated (Clinical Management)

CRITICAL OUTCOMES		
Appropriate management (good clinical sequelae)	Abdominal CT scan may be associated with appropriate management of adults with suspected acute left-sided colonic diverticulitis.	Certainty of evidence **LOW** ⊕○○
Inappropriate management (poor clinical sequelae)	Falsely normal or abnormal findings on abdominal CT scan resulting in inappropriate management (poor clinical sequelae) may be rare in adults with suspected acute left-sided colonic diverticulitis, although the included studies did not report patient outcomes associated with misdiagnosis.	Certainty of evidence **LOW** ⊕○○
IMPORTANT OUTCOMES		
Detection of incidental findings	In adults with suspected acute diverticulitis, abdominal CT scan may commonly detect incidental findings (findings not related to diverticulitis), but the clinical significance of the incidental findings is unclear.	Certainty of evidence **LOW** ⊕○○

Outcomes Evaluated (Test Accuracy)

Sensitivity: 94% **Specificity: 99%**	*Prevalence 10%*	*Falsely normal findings per 1000 patients*	*6*	Certainty of evidence **MODERATE** ⊕⊕○
		Falsely abnormal findings per 1000 patients	*9*	
	Prevalence 70%	*Falsely normal findings per 1000 patients*	*42*	
		Falsely abnormal findings per 1000 patients	*3*	

Evidence Gaps

Evidence is inconclusive to assess the association between **CT imaging and diverticulitis-related patient health outcomes.**

Values and Preferences

Values and preferences may vary according to individuals. No literature was identified that assessed patient values and preferences for the diagnosis of acute left-sided colonic diverticulitis, and feedback from the CGC Public Panel showed variability in preferences for undergoing abdominal CT imaging to diagnose acute left-sided colonic diverticulitis.

Recommendation

RECOMMENDATION 1

ACP suggests that clinicians use abdominal CT imaging when there is diagnostic uncertainty in a patient with suspected acute left-sided colonic diverticulitis (conditional recommendation; low-certainty evidence).

RATIONALE: A detailed history, physical examination, and laboratory findings are the first steps in diagnosing acute colonic diverticulitis in most patients with abdominal pain or tenderness primarily in the left lower quadrant. In patients for whom diagnostic uncertainty remains, abdominal CT imaging can be used to complement the history, examination, and laboratory findings to establish the diagnosis of diverticulitis. Moderate-certainty evidence showed that CT imaging is associated with very high sensitivity and specificity. Low-certainty evidence from studies performed in emergency department or equivalent settings showed that misdiagnoses with CT may not be associated with downstream adverse sequelae, although the effect on patient outcomes is unclear.

Clinical Considerations

- Potential harms from CT imaging include incidental findings, radiation exposure, and side effects of or allergic reactions to any contrast used.
- Informed decision making with patients should include discussion of potential patient burdens related to CT imaging, including contraindications to use of contrast agents or limited access to CT imaging. Abdominal ultrasonography can be considered when CT cannot be obtained. Abdominal magnetic resonance imaging can be considered when ultrasonography provides inconclusive results (for example, in obese patients and those with severe abdominal pain or extensive bowel gas).
- Clinicians should err on the side of imaging in patients with predictors of progression to complicated diverticulitis. These include a symptom duration before clinical presentation of longer than 5 days and signs of perforation, bleeding, obstruction, or abscess.
- The diagnostic accuracy of CT to differentiate between colorectal cancer and complicated diverticulitis is not considered here; the additional value of early cancer detection with follow-up colonoscopy after resolved episodes of acute complicated diverticulitis is discussed in another guideline.

Outcomes Evaluated (Antibiotics vs. No Antibiotics)

CRITICAL OUTCOMES		
Diverticulitis-related complications	There may be no differences in diverticulitis-related complications at 1 month and at 1 year when comparing antibiotic vs. no antibiotic treatment.	Certainty of evidence **LOW** ⊕◯◯
Treatment failure (assessed as no return to normal bowel function)	7 people per 100 without antibiotic treatment 0 10 20 30 40 50 60 70 80 90 100 5 people per 100 with antibiotic treatment	Certainty of evidence **LOW** ⊕◯◯
Quality of life	There may be no difference in quality of life when comparing antibiotic vs. no antibiotic treatment (mean difference scale scores ranged from 0.7 worse to 0.8 better).	Certainty of evidence **LOW** ⊕◯◯
Surgery at 6 to 12 months	There may be no difference in the need for surgery at 6 to 12 months when comparing antibiotic vs. no antibiotic treatment (absolute risk difference range, −2.0% to −0.4%).	Certainty of evidence **LOW** ⊕◯◯
IMPORTANT OUTCOMES		
Length of hospital stay	Evidence showed that there may be no difference in length of hospital stay when comparing antibiotic vs. no antibiotic treatment (mean difference, −7.7 hours [CI, −20.2 to 4.8 hours]).	Certainty of evidence **LOW** ⊕◯◯
Recurrence	9 people per 100 without antibiotic treatment 0 10 20 30 40 50 60 70 80 90 100 10 people per 100 with antibiotic treatment	Certainty of evidence **LOW** ⊕◯◯

Evidence was very uncertain (insufficient) for the following outcomes:
Critical outcomes: **mortality**
Important outcomes: **any adverse event, rehospitalization**

Evidence Gaps

Evidence is very uncertain (insufficient) to assess the benefits and harms on **comparative effectiveness of antibiotic regimens** and **percutaneous drainage of abscess versus conservative management.** Evidence was inconclusive or unavailable to assess the management of **acute complicated left-sided colonic diverticulitis with antibiotics or in outpatient settings.**

Values and Preferences

Values and preferences may vary according to individuals. No literature was identified that assessed patient values and preferences for the management of acute left-sided colonic diverticulitis. Feedback from the CGC Public Panel showed a preference for outpatient management and a strong preference for management without antibiotics.

Recommendations

RECOMMENDATION 2

ACP suggests that clinicians manage most patients with acute uncomplicated left-sided colonic diverticulitis in an outpatient setting (conditional recommendation; low-certainty evidence).

RATIONALE: In the absence of evidence suggesting a benefit of routine hospitalization for patients with acute uncomplicated diverticulitis, the initial (default) management of uncomplicated diverticulitis can be as an outpatient. This applies to most immunocompetent patients with acute uncomplicated left-sided diverticulitis who have no evidence of systemic inflammatory response and can continue treatment at home under medical supervision with adequate family and social support and follow-up. Low-certainty evidence showed that there may be no differences in risk for elective surgery or long-term diverticulitis recurrence for outpatient compared with inpatient management.

RECOMMENDATION 3

ACP suggests that clinicians initially manage select patients with acute uncomplicated left-sided colonic diverticulitis without antibiotics (conditional recommendation; low-certainty evidence).

RATIONALE: "Select" patients are defined as immunocompetent patients with uncomplicated left-sided diverticulitis, with no systemic inflammatory response or immunosuppression, who are not medically frail, do not require hospitalization, and can follow up as an outpatient under medical supervision with social and family support. For these patients, low-certainty evidence showed that there may be no differences in diverticulitis-related complications (such as abscess, fistula, stenosis, and obstruction), quality of life, need for surgery, or long-term recurrence between those receiving and those not receiving antibiotics. The use of antibiotics without evidence of important benefit to the patient may incur potential harms and costs, and inappropriate use of antibiotics contributes to antibiotic resistance, a major individual and public health threat.

Clinical Considerations

Uncomplicated diverticulitis refers to localized inflammation, whereas complicated diverticulitis refers to inflammation associated with an abscess, a phlegmon, a fistula, an obstruction, bleeding, or perforation.

Predictors of progression to complicated disease among patients with uncomplicated acute diverticulitis: symptoms >5 days, vomiting, systemic comorbidity, high C-reactive protein levels (>140 mg/L), CT findings of pericolic extraluminal air, fluid collection, or a longer inflamed colon segment (69, 70).

Management in Outpatient vs. Inpatient Settings

- This recommendation does not apply to patients with suspected complicated diverticulitis, recent antibiotic use, concomitant unstable comorbid conditions, immunosuppression, or signs of sepsis, given that these populations were excluded from the reviewed studies.

Antibiotics vs. No Antibiotics

- This recommendation does not apply to patients with complicated diverticulitis, systemic inflammatory response, immunosuppression, or ongoing or recent antibiotic treatment.
- Initial management without antibiotics should be coupled with watchful waiting and ability to continue monitoring patient status, based on individual clinical judgment. The included studies did not report how many patients randomly assigned to watchful waiting needed antibiotics at follow-up (6, 12, 24 months and 11 years), but antibiotics did not reduce the risk for any critical or important outcomes.
- Implementation of this recommendation does not require a CT-confirmed diagnosis, but clinicians should err on the side of imaging in patients presenting with signs and symptoms consistent with perforation, bleeding, obstruction, or abscess.