



Diverticular Disease: Where We Are in 2023

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Disclosures

- Advisory Board Member
 - Ardelyx Pharmaceuticals, Phathom Pharmaceuticals
- Consultant
 - Ardelyx Pharmaceuticals, Phathom Pharmaceuticals, Vertex Pharmaceuticals
- Speaker
 - Exegi Pharma, Salix Pharmaceuticals

An aerial photograph of a city skyline, likely Atlanta, Georgia, featuring prominent skyscrapers like the Bank of America Tower. The image is overlaid with a large, semi-transparent blue geometric shape that tapers from the top left towards the bottom right. The text is centered within this blue area.

In Its Proper Time, the
Unknown Becomes the Known.

What Is Known and Not Known About Diverticular Disease of the Colon

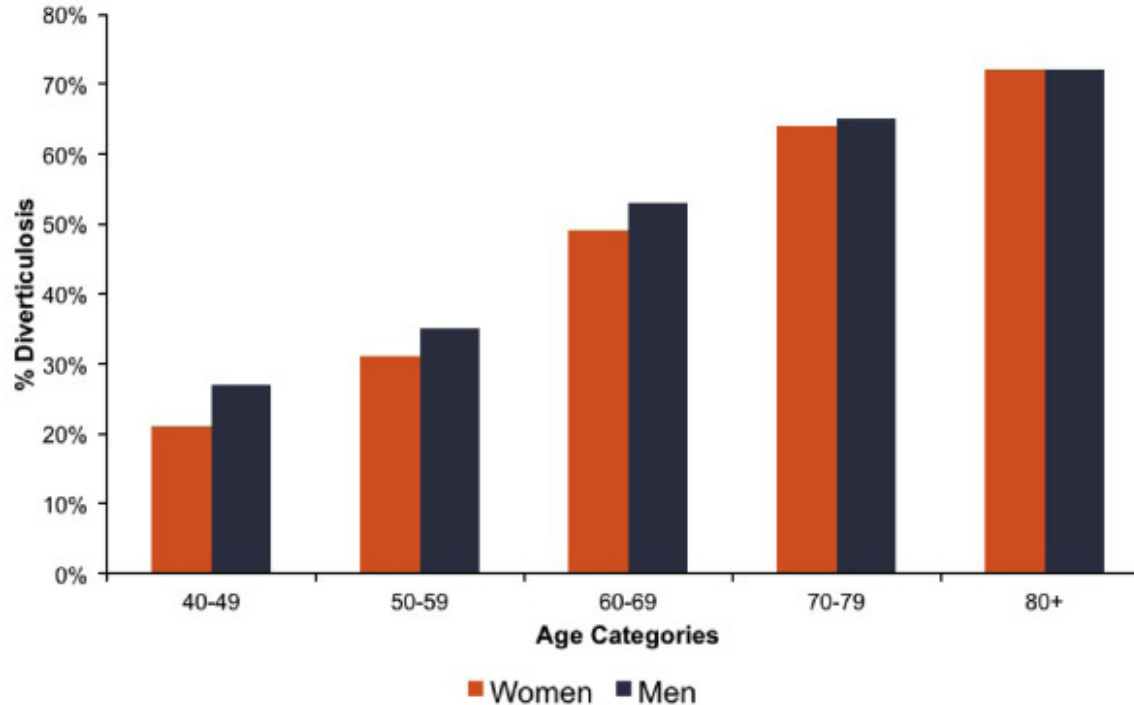
- **Known**

- Diverticulosis is a common finding
- More common than it used to be
- More common as people age
- More common in “Western” countries (i.e., USA, Europe) and people consuming “Western” diet
- Complicated by inflammation (“diverticulitis”), abscess, perforation, and hemorrhage

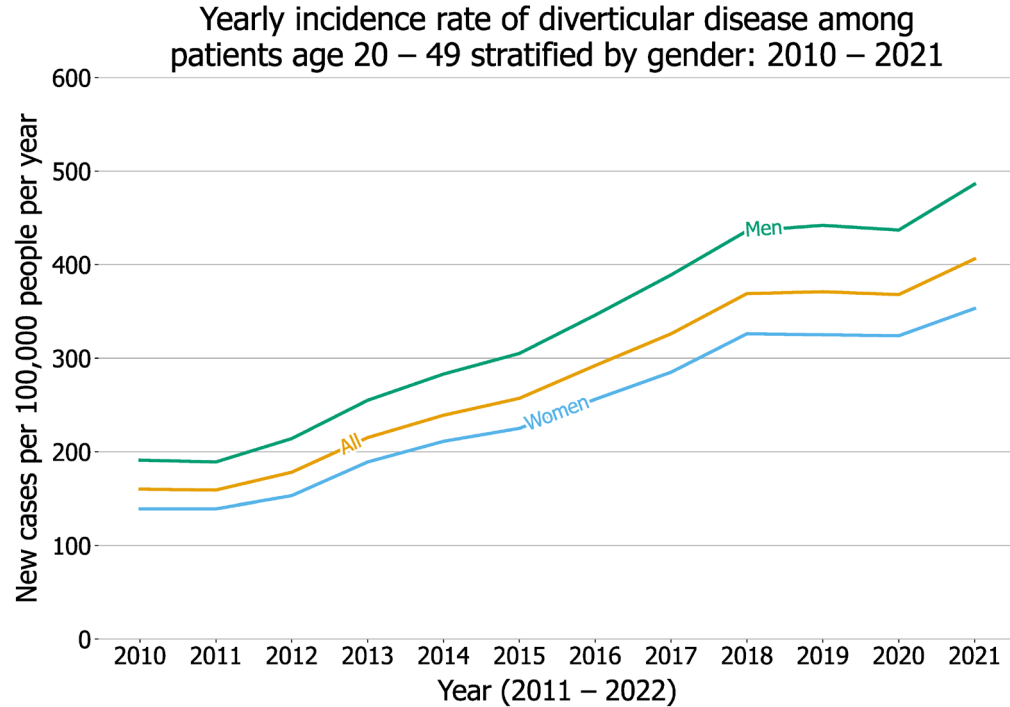
- **Not known**

- Why diverticula form?
- What is pathogenesis of complications?
- What is the role (if any) of the colonic microbiota?
- How to distinguish “symptomatic uncomplicated diverticular disease” (SUDD) from IBS + diverticulosis?
- High-quality evidence-based management advice

Prevalence of Diverticulosis at Colonoscopy



Incidence of Diverticular Disease in Young Adults



From TriNetX database of 100 million unique US patients in 68 healthcare systems;
Wang L, Xu R, Kaelber DC, Berger NA. Time Trend and Association of Early-Onset Colorectal Cancer with Diverticular Disease in the United States: 2010–2021. *Cancers*. 2022; 14(19):4948.

Pathophysiology of Formation of Diverticula

Schylling PANIC PETE SQUEEZE TOY



INCREASED INTRALUMINAL PRESSURE



Pathophysiology of Formation of Diverticula

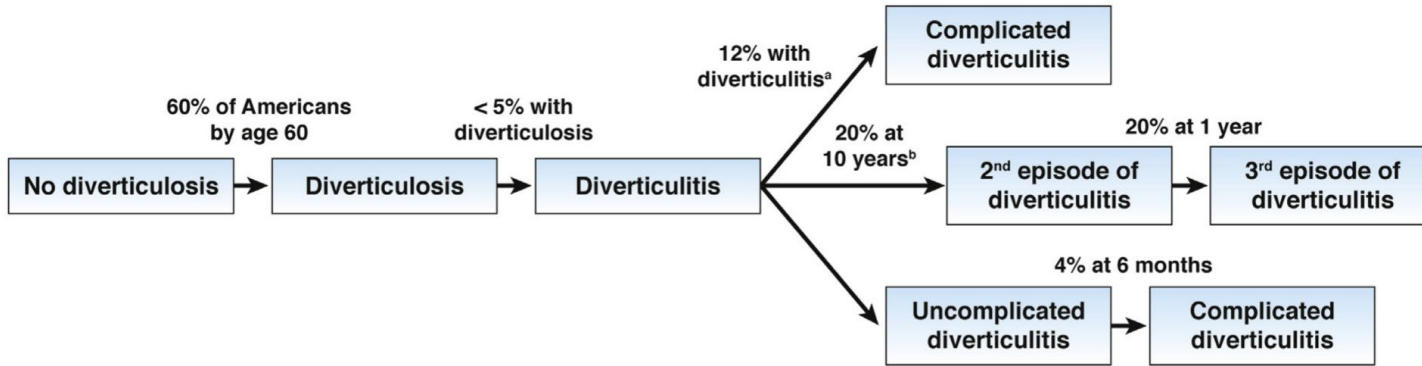
- In Western countries, more common in left colon (more in right colon in Asians)
- Occur at weak points in colon wall where blood vessels penetrate through colon wall
 - Pseudodiverticula: mucosa only
- Altered collagen or elastin deposition
- Altered motility
- Genetics?
- Diet: fiber hypothesis proposed by Denis Burkett in 1966—1972
- Abnormal connective tissue metabolism (matrix metalloproteinases and their inhibitors)
- “Aging”

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STILL UNKNOWN

Natural History of Diverticular Disease



- Risk of recurrent diverticulitis 8% in year after first attack
- Risk of recurrent diverticulitis increases with subsequent episodes
- Risk of complications (phlegmon/abscess, peritonitis, obstruction) highest with *first* episode

Natural History of Diverticular Disease

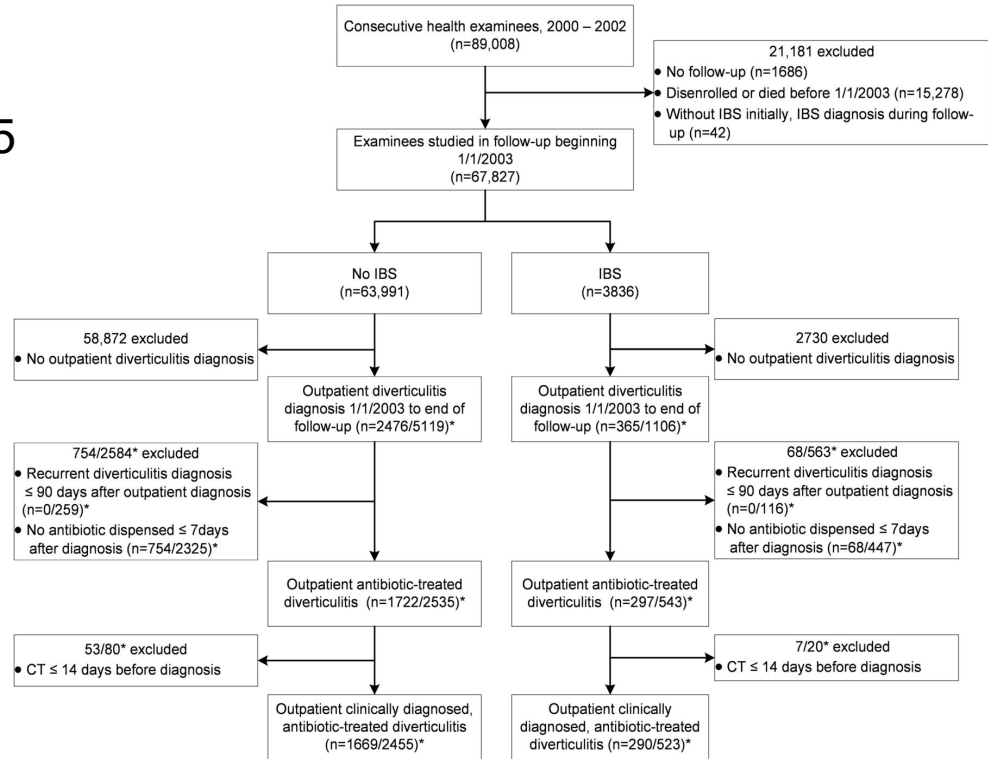
- Patients with **complicated** diverticulitis treated medically do NOT seem to have greater likelihood of recurrence than **uncomplicated** diverticulitis
- The risk of recurrence is significantly lower for patients treated surgically for complicated diverticulitis

Natural History of Diverticular Disease

- **Symptomatic Uncomplicated Diverticular Disease (=SUDD)**
 - “Gastrointestinal symptoms in the setting of diverticular disease without evidence of overt inflammation or diverticulitis”
 - Does diverticulosis cause chronic symptoms?
 - If so, which ones?
 - Does diverticulitis cause chronic symptoms?
 - Can this be distinguished from IBS?
- Studies are disputable and conflicting
 - IBS → diverticulitis
 - Diverticulitis → IBS

Does IBS → Diverticulitis?

- Retrospective study of IBS and non-IBS cohorts from 2003—2015
- “Diverticulitis” diagnosed in:
 - 2.6% of non-IBS group
 - 7.6% of IBS group
- 3-fold increase in relative risk of diagnosis
 - Misdiagnosis in 25% of IBS cohort

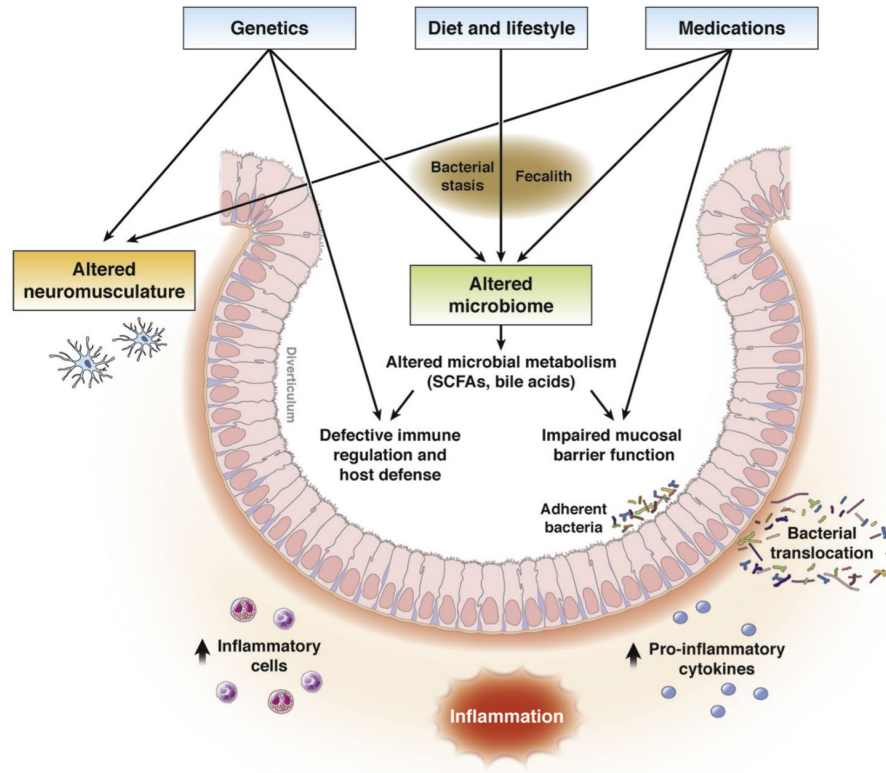


Risk Factors for Diverticulitis

- Western diet (high red meat, fat, refined grain)
 - May account for 75% of risk for diverticulitis
- Obesity (especially central obesity)
- Smoking
- Medications
 - NSAIDs >ASA
 - Immunosuppressive drugs
- Family history

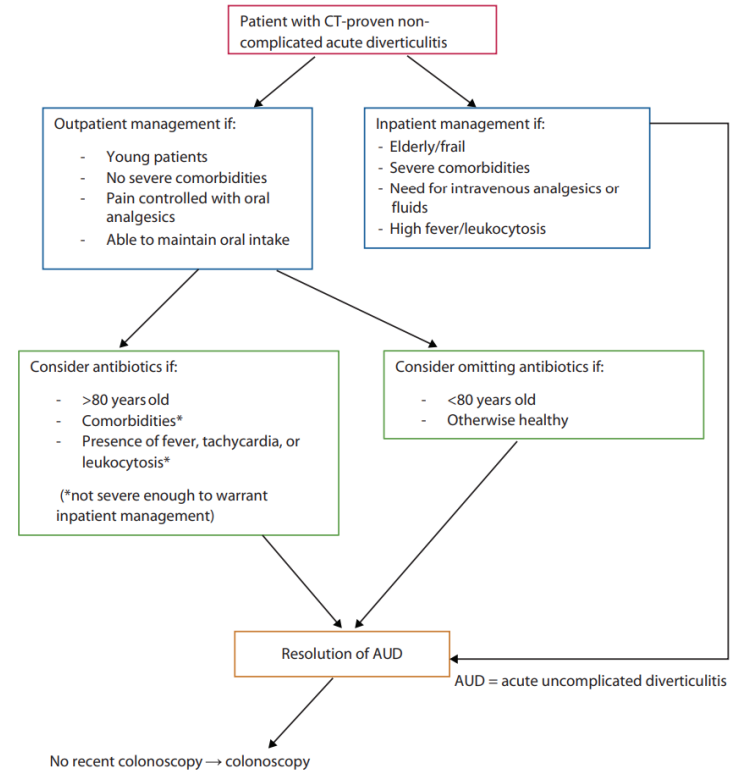
Risk factor	Category	RR/OR ^a
Diet		
Fiber	Highest quintile	0.57–0.75
Nuts	>2 times/wk	0.80
Popcorn	>2 times/wk	0.72
Vegetarian diet	Yes/no	0.69
Prudent dietary pattern ^b	Highest quintile	0.74
Western dietary pattern ^c	Highest quintile	1.55
Red meat	Highest quintile	1.58
Lifestyle		
Physical activity	Highest quintile	0.63–0.75
BMI	BMI ≥30 kg/m ²	1.33–4.4
Waist-to-hip ratio	Highest quintile	1.62
Smoking	Current or ≥15 cigarettes/d	1.23–1.89
Medications		
Non-aspirin NSAIDs	≥2 times/wk	1.72
Aspirin	Ever or ≥2 times/wk	1.25–1.32
All NSAIDs	≥2 times/wk	1.62
Corticosteroids	Current use	2.74
Opiate analgesics	Current use	2.16
Statins	Current use	0.44
Vitamin D	Highest quintile	0.49
Sibling with diverticular disease	Yes/no	2.92

Pathogenesis of Diverticulitis



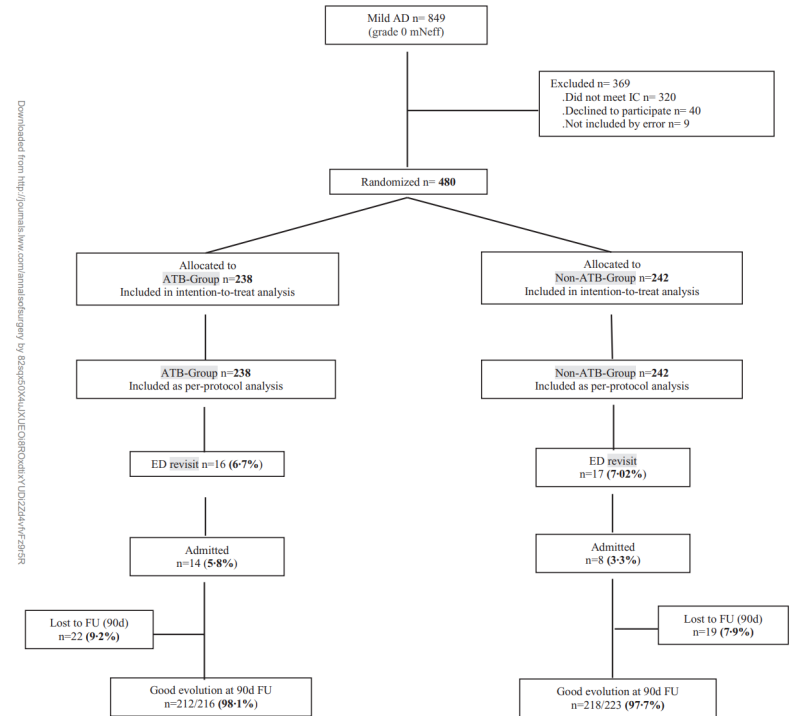
Management of Acute Uncomplicated Diverticulitis

- Confirm diagnosis with imaging
- Decide whether inpatient or outpatient management is right
- Consider antibiotic therapy
- After resolution:
 - Colonoscopy (if not done recently)
 - Consider resection if immunosuppressed, repeated episodes
 - Prevention of recurrence
 - High fiber diet (?)
 - Smoking cessation (?)



Antibiotic Therapy for Acute Uncomplicated Diverticulitis

- Spanish multicenter, open-label, non-inferiority study
- Uncomplicated diverticulitis on CT scan, no episode within 3 mo., no significant comorbidities, immunocompetent, no recent antibiotics, ~normal vital signs, adequate symptom control in ED
- Randomized to oral ibuprofen or oral amoxicillin-clavulanic acid



Antibiotic Therapy for Acute Uncomplicated Diverticulitis

- Trials suggest that antibiotics do not expedite recovery from acute uncomplicated diverticulitis & may not prevent complications
 - Guidelines suggest avoiding antibiotics in selected immunocompetent patients with mild disease
 - Immunocompromised patients, “sick” patients should receive antibiotics
- Traditional antibiotic combination: metronidazole + fluoroquinolone
 - Potential alternate therapy for outpatient management: amoxicillin-clavulanate
- Elective surgery no longer automatically recommended after two episodes of recovered, uncomplicated diverticulitis

Management of Complicated Diverticulitis

- Abscess, phlegmon
 - IR drainage
 - Antibiotics
 - Resection (?)
- Hemorrhage
 - Colonoscopy, angiography
- Peritonitis
 - Antibiotics
 - Surgery
- Obstruction, fistula
 - Surgery

What Colonic Resection Can and Cannot Do

- Quality of life improves in most patients with diverticulitis with ongoing inflammation or recurrence, if QOL was reduced
- Reduces (but does not eliminate) risk of recurrence by 75% at 5 years (15% vs. 61% with medical therapy)
- Chronic abdominal pain persists in >50%!
 - Pain without recurrence or complications should not be an indication for surgery
- Ostomies are created in 10–18% of elective resections for diverticulitis; only 50% are ever reversed

Summary

- Colonic diverticulosis is a common (and idiopathic) diagnosis
- Pathophysiology remains unproven
- Diverticulitis and complications of diverticulitis are common clinical problems in patients with diverticulosis
- Natural history is better appreciated; bad outcomes in minority
- History and physical examination are not sufficient for diagnosis; imaging is necessary
- Antibiotics not needed in all cases
- Use of elective surgery should be individualized

Selected References

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