Clostridium difficile infections: Challenges and Scenarios

Courtesy of American College of Surgeons Division of Education
Clinical Congress 2015

Brian S. Zuckerbraun, MD, FACS

Henry T. Bahnson Professor of Surgery
Chief, Trauma And Acute Care Surgery
University of Pittsburgh Medical Center
General Surgery, VA Pittsburgh Healthcare System

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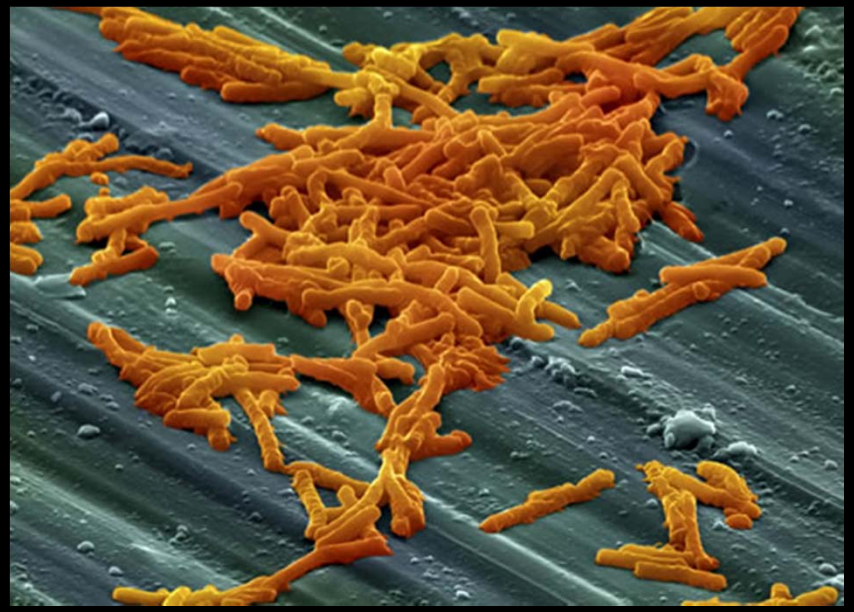
Background

-*Clostridium difficile:*
anaerobic,
gram positive,
spore forming,
bacillus



-Estimated $3.2 billion/year in expenditures

-Mortality estimated to be ~4-8%

-Surgical Treatment In Complicated Cases

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58 yo female calls your office after being discharged from the hospital from laparoscopic hysterectomy. Now POD 6, states she has diarrhea for one day (17 loose BM) and feels lousy.

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B. Send her for C diff testing and start therapy if positive.
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67 yo female in the hospital on the medical service for community acquired pneumonia treated with ceftriaxone 1 g IV q24h plus azithromycin 500 mg IV q24h for past 4 days, now with WBC increase to 15 and diarrhea. No abdominal tenderness, normal creatinine and labs otherwise WNL. C diff PCR +

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A. Stop or change antibiotics for pneumonia if possible and start treatment with metronidazole 500 PO q8h.
B. Stop or change antibiotics for pneumonia if possible and start treatment with vancomycin 125 mg IV q6h.
C. Start vancomycin 125 mg po q6h.
D. Start fidaxomicin 200 mg PO q12h.

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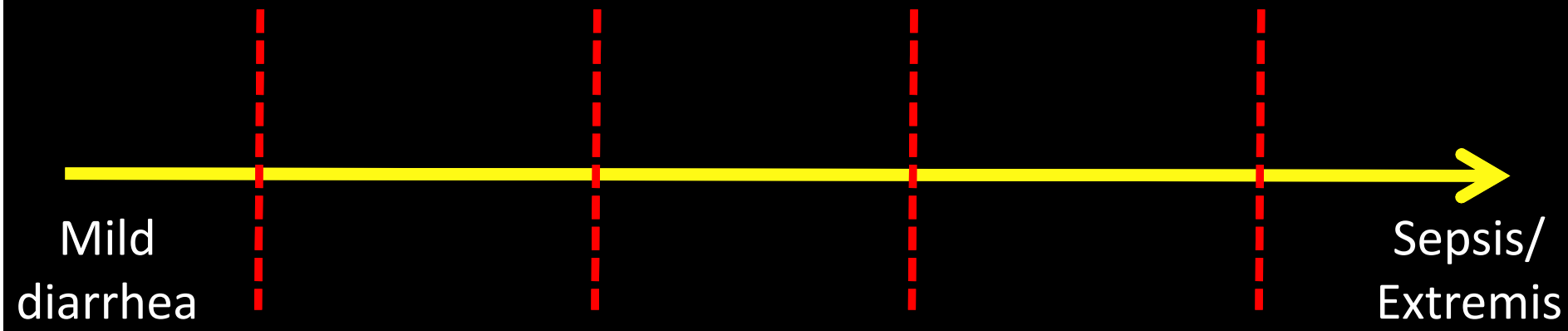
Severity Scoring and Treatment



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Practice Guidelines

The American Journal of Gastroenterology , (26 February 2013) | doi:10.1038/ajg.2013.4

Guidelines for Diagnosis, Treatment, and Prevention of Clostridium difficile Infections

Christina M Surawicz, Lawrence J Brandt, David G Binion, Ashwin N Ananthakrishnan, Scott R Curry, Peter H Gilligan, Lynne V McFarland, Mark Mellow and Brian S Zuckerbraun

ACG Severity Scoring and Treatment

Severity	Criteria
Mild:	Diarrhea
Moderate:	Diarrhea plus any additional signs or symptoms not meeting severe or complicated criteria
Severe:	Any two of the following: -WBC≥ 15000cells/mm^3 -Serum albumin <3 g/dL -Abdominal tenderness

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ACG Severity Scoring and Treatment

Severity	Criteria
Complicated:	Any one of the following: -Admission to ICU for CDI -Hypotension with or without required use of vasopressors -End organ failure (Mechanical ventilation, Renal failure, etc) -Mental status changes -Fever ≥38.5° -Ileus or significant abdominal distention/tender -WBC≥ 35,000 cells/mm^3 ate levels greater than 2.2 mmol/Liter

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ACG Severity Scoring and Treatment

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Moderate:	Diarrhea plus any additional signs or symptoms not meeting severe or complicated criteria	
Severe:	Any two of the following: -WBC≥ 15000cells/mm^3 -Serum albumin <3 g/dL -Abdominal tenderness	Vancomycin 125mg PO qid

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Metronidazole v. Vancomycin

Metronidazole

-effective as intravenous or enteral form

-Does not reach colon at effective MIC unless diarrhea

-Both dosing regimens dependent upon GI motility

Vancomycin

-Intravenous not effective

-Enteral (oral, tube, rectal) reaches colon at effective MIC in both diarrheal and non-diarrheal stool

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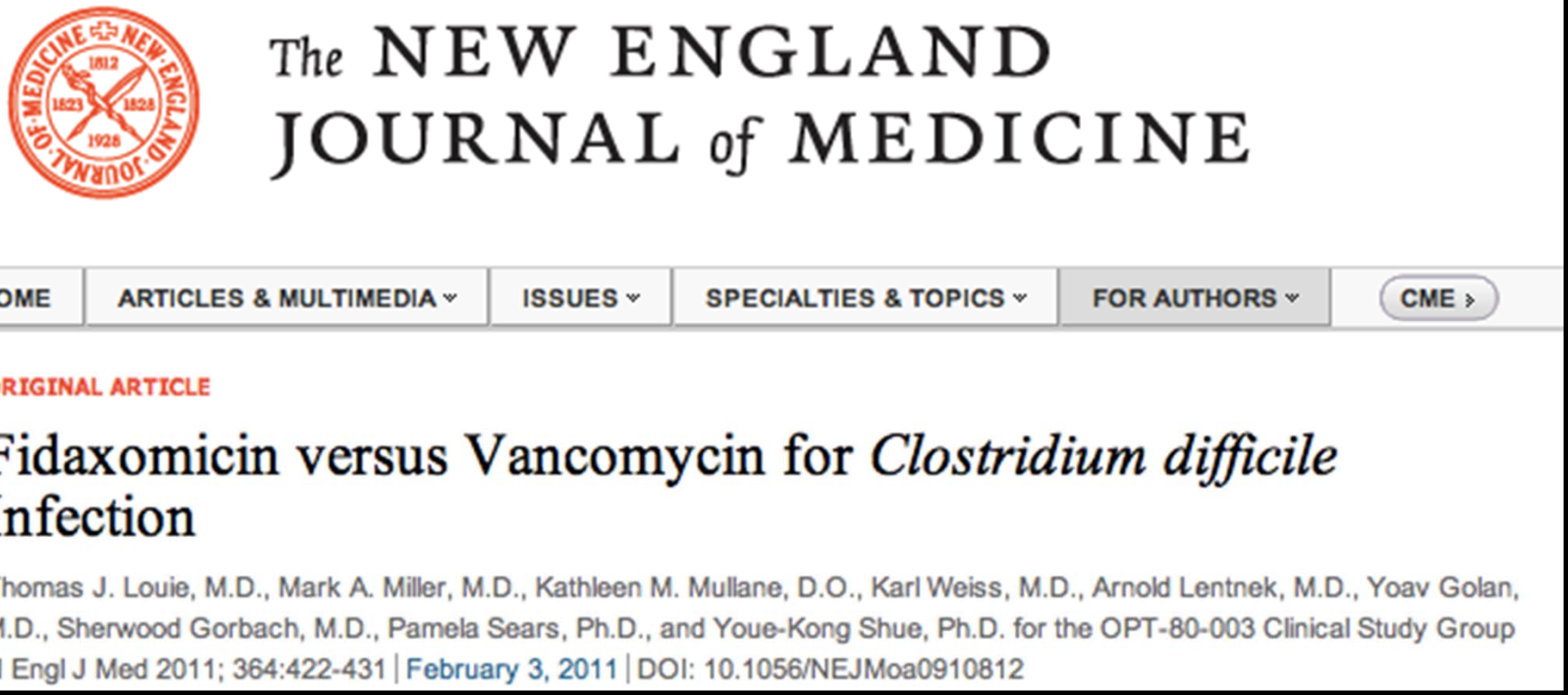
Metronidazole v. Vancomycin

-No antimicrobial agent is clearly superior for the initial cure of C. difficile infection

-Three randomized control trials have compared metronidazole to vancomycin

*One trial demonstrated vanco superior in severe disease (Zar et al, Clinical Infectious Disease, 2007)
(evidence considered insufficient)



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ORIGINAL ARTICLE

Fidaxomicin versus Vancomycin for *Clostridium difficile* Infection

Thomas J. Louie, M.D., Mark A. Miller, M.D., Kathleen M. Mullane, D.O., Karl Weiss, M.D., Arnold Lentnek, M.D., Yoav Golan, M.D., Sherwood Gorbach, M.D., Pamela Sears, Ph.D., and Youe-Kong Shue, Ph.D. for the OPT-80-003 Clinical Study Group

N Engl J Med 2011; 364:422-431 | February 3, 2011 | DOI: 10.1056/NEJMoa0910812

-Non-inferior to vancomycin for cure rate
-Lower recurrence rate compared to vanco
-expensive
-Use in setting of recurrences

Probiotics

Data does not support the use of probiotics as a treatment for C Diff infection.

Studies suggest a trend for prevention or to limit recurrences.

Courtesy of American College of Surgeons Division of Education
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72 yo male s/p total hip whose post-op course was complicated by the development of C diff infection treated with a 10 day course of vancomycin 125 mg PO q6h X 10 days. Was discharged 4 days into the course with clinical resolution of diarrhea. Initial post-op visit was doing well. Calls 3 weeks later (POD 38) with new onset diarrhea. "Just like in hospital." No fevers, mild cramping.

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A. Treat with second course vancomycin for 10 days
B. Treat with 7 week pulse and taper of vanc
C. Treat with fidaxomicin for 10 day course.
D. Treat with metronidazole and followed by probiotics.

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Recommended for recurrent disease

1st Recurrence: Vancomycin

2nd Recurrence: Vancomycin 7 week taper

3rd Recurrence: Fecal Microbiota Therapy

Courtesy of American College of Surgeons Division of Education Clinical Congress 2015

ORIGINAL ARTICLE

Duodenal Infusion of Donor Feces for Recurrent *Clostridium difficile*

Els van Nood, M.D., Anne Vrieze, M.D., Max Nieuwdorp, M.D., Ph.D., Susana Fuentes, Ph.D., Erwin G. Zoetendal, Ph.D., Willem M. de Vos, Ph.D., Caroline E. Visser, M.D., Ph.D., Ed J. Kuijper, M.D., Ph.D., Joep F.W.M. Bartelsman, M.D., Jan G.P. Tijssen, Ph.D., Peter Speelman, M.D., Ph.D., Marcel G.W. Dijkgraaf, Ph.D., and Josbert J. Keller, M.D., Ph.D.

N Engl J Med 2013; 368:407-415 | January 31, 2013 | DOI: 10.1056/NEJMoa1205037

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Hot Topics: Health Data Connected Care

U.S.'s first stool bank supplies hospitals with fecal transplants for C. difficile treatment

February 22, 2014 8:00 am by Deanna Pogorelc | 1 Comments

Rebiotix
Microbiota Restoration Therapy

Courtesy of American College of Surgeons Division of Education
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81 yo transferred to MICU from another institution with known c diff infection treated for 5 days with vancomycin on norepinephrine at 0.4mcg/kg/min, creatinine 3.2, intubated and ventilated. Next step…

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A. Resuscitate, add metronidazole and watch clinical response.
B. Resuscitate, add vancomycin enemas and watch clinical response.
C. Resuscitate, add metronidazole, vanc enemas, and give patient 24 hours to improve.
D. Immediate surgical consultation and immediate operative intervention.

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Severity Scoring and Treatment

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Courtesy of American College of Surgeons Division of Education Clinical Congress 2015

TIME MATTERS!

Courtesy of American College of Surgeons Division of Education
Clinical Congress 2015

Sailhamer et al, Fulminant Clostridium difficile colitis: patterns of care and predictors of mortality., Archives of Surgery 2009.

Ferrada et al, Timing and type of surgical treatment of Clostridium difficile-associated disease: a practice management guideline from the Eastern Association for the Surgery of Trauma. J Trauma Acute Care Surg. 2014

A diagnosis of CDAD as determined by one of the following:

1. Positive C Diff test
2. Endoscopic findings
3. CT scan consistent with CDAD

Plus any one of the following criteria:

1. Peritonitis
2. Perforation
3. Worsening abdominal distention/pain
4. Severe Sepsis
5. Intubation
6. Ongoing Vasopressor requirement
7. Mental status changes
8. Unexplained clinical deterioration
9. Renal Failure
10. Lactate > 5mmol/L
11. White blood cell count greater or equal to 50,000
12. Abdominal compartment syndrome
13. Not improving after ? Days

Courtesy of American College of Surgeons Division of Education Clinical Congress 2015

Hypothesis: Therapy to decrease bacterial counts and toxin levels throughout the whole colon will adequately treat severe, complicated CDAD.

Not C Diff Colon

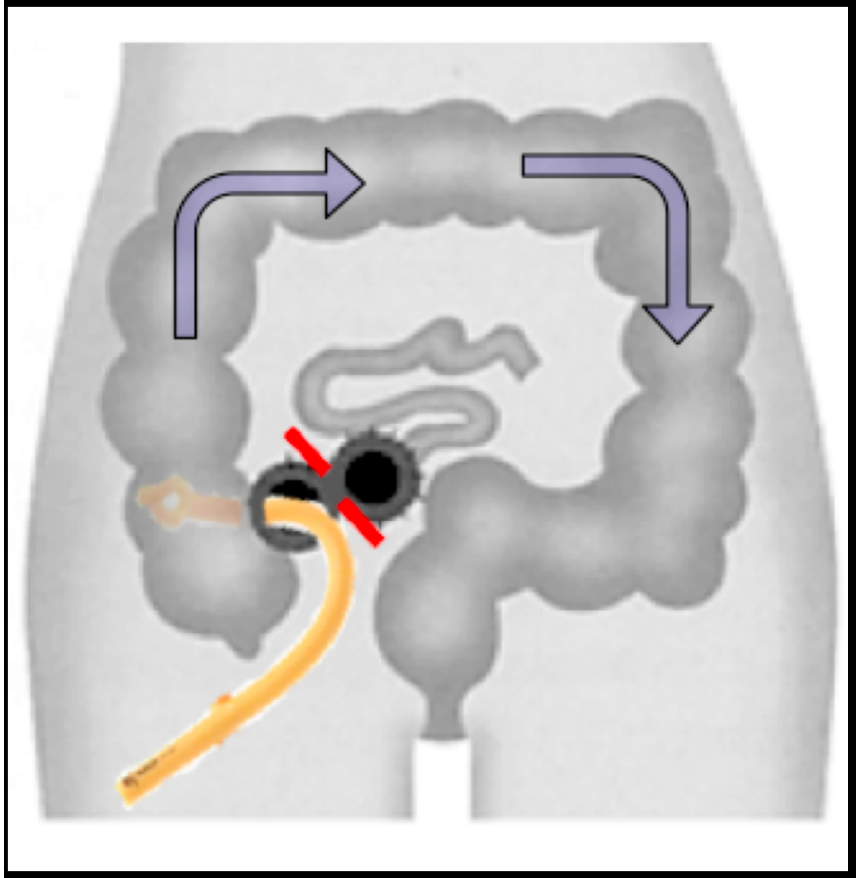
Diverting Loop Ileostomy and Colonic Lavage: An Alternative to Total Abdominal Colectomy for the Treatment of Severe, Complicated Clostridium difficile Associated Disease

Neal MD, Alverdy JC, Hall DE, Simmons RL, Zuckerbraun BS

Ann Surg. 2011;254:423-429

Courtesy of American College of Surgeons Division of Education Clinical Congress 2015

Methods



1. Exploratory laparoscopy/laparotomy
2. Creation of diverting loop ileostomy
3. Colonic lavage with 8 liters of warm PEG3350/balanced electrolyte solution (Go-Lightly™) via ileostomy
4. Post-op antegrade vancomycin flushes via ileostomy (500mg in 500ml tid) for 10 days

Courtesy of American College of Surgeons Division of Education
Clinical Congress 2015

Loop ileostomy/colonic lavage patients have improved survival compared to total abdominal colectomy (historical controls) for severe, complicated *C. Diff*.

	Ileostomy/washout	colectomy
APACHE-II (mean±S.D.)	29.7±10.8	29.9±8.9
Post-Operative Death	22/100* (22%)	49/100 (49%)

-3 patients not offered this therapy and offered colectomy
-7/100 had subsequent colectomy.

Courtesy of American College of Surgeons Division of Education Clinical Congress 2015

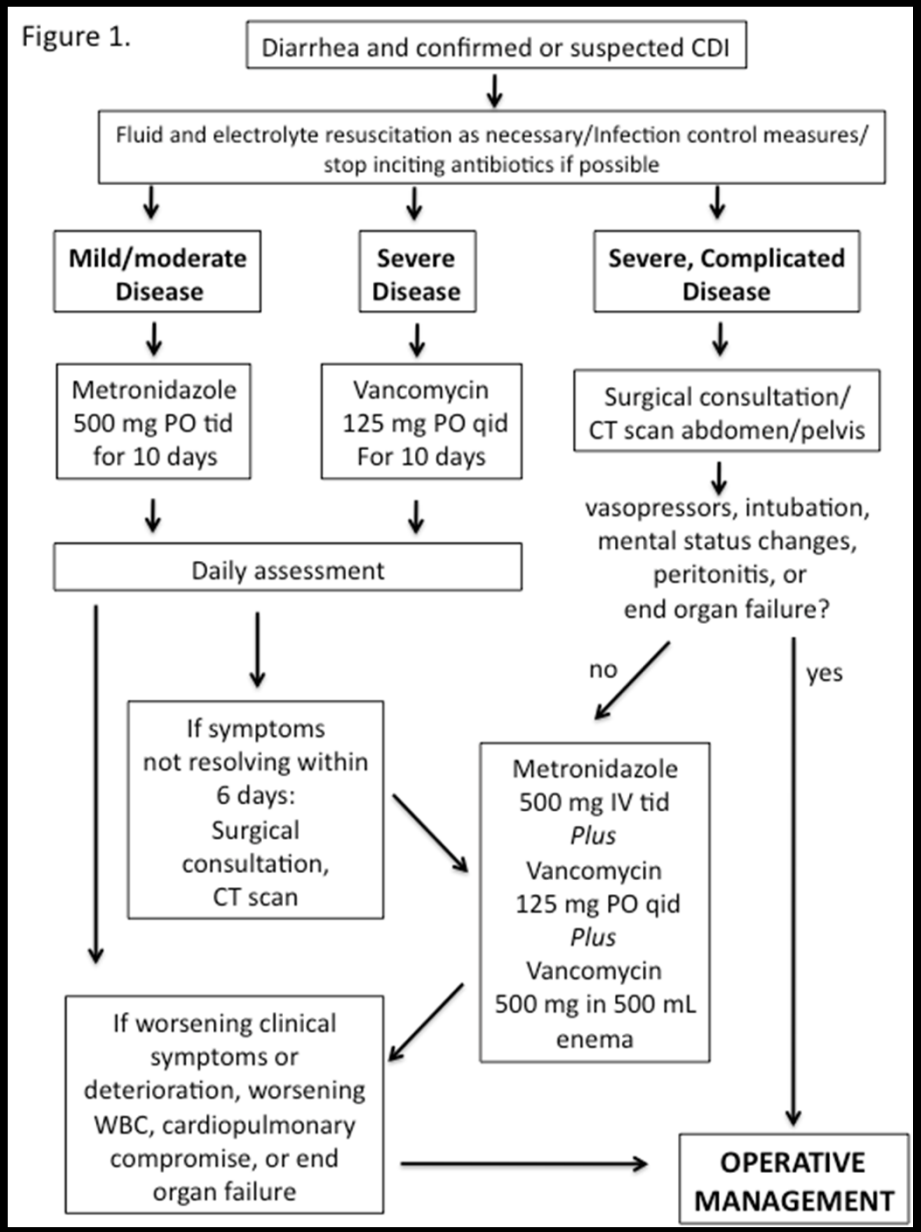
Loop ileostomy/colonic lavage has an improved one-year survival and restoration of GI continuity in patients that were discharged to home following surgery

	Ileostomy/washout	colectomy
Alive at 1 year	58/67 (87%)	36/51(71%)
Restoration of GI continuity*	49/58 (84%)	8/36 (22%)

*Data for patients followed for greater than 12 months

Loop ileostomy/lavage patients had similar APACHE-II scores as colectomy patients, however there was earlier consultation & surgical management compared to historical colectomy controls

	Ileostomy/washout	colectomy
APACHE-II (mean±S.D.)	29.7±10.8	29.9±8.9
Time from presentation to surgical consultation	11±9 hours	32±12 hours
Time from surgical consultation to operative intervention	9±6 hours	29±12 hours



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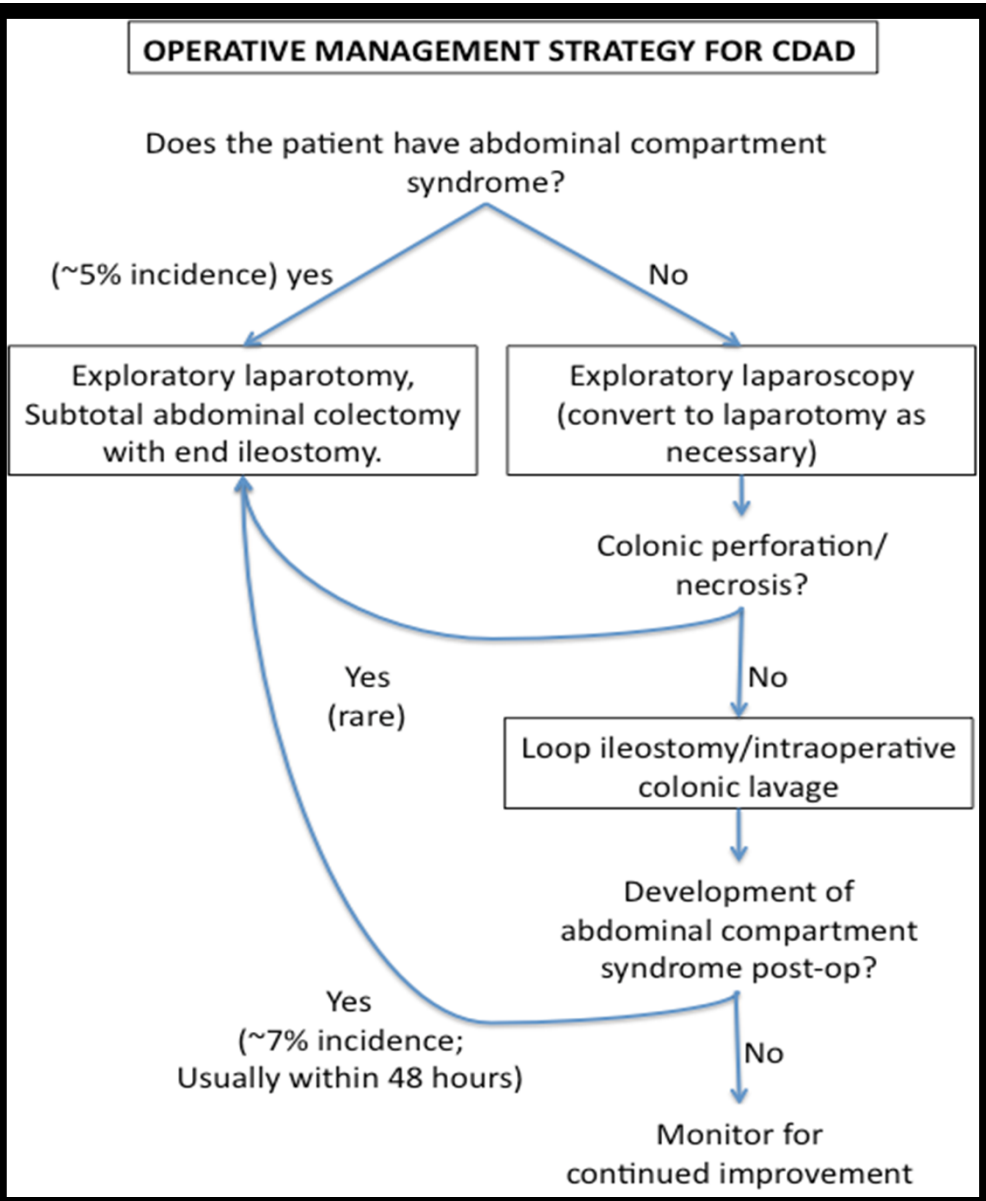

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72 yo male 3 weeks s/p an esophagectomy readmitted to the thoracic service with abdominal pain and diarrhea (15 per day for 3 days). Admitted to ICU.

-Abdomen mildly tender and distended.
-WBC 23
-Cr 2.7 (baseline 1.1)
-Albumin 2.4
-SBP 90.
-Started on fluids (total of 5 liters)
-Initially on NE gtts, but weaned off

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-C diff testing sent off
-Started on metronidazole 500 mg IV q8h and vancomycin 500 mg PO q6h
-General Surgery team consulted

72 yo male 3 weeks s/p an esophagectomy readmitted to the thoracic service with abdominal pain and diarrhea (15 per day for 3 days). Admitted to ICU.

Next day…

-Continued diarrhea
-No hypotension
-WBC down to 15 (23)
-Cr down to 1.6 (2.7)

Was making continued progress until 3 days later…

-Mild increase in pain and tenderness
-Continue 10 BM per day
-No hypotension
-WBC back up to 21, 42% bands
-Good urine output, hemodynamics normal, normal MS

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-Mild increase in pain and tenderness
-Continue 10 BM per day
-No hypotension
-WBC back up to 21, 42% bands
-Good urine output, hemodynamics normal, normal MS

-Added vancomycin enemas (500 mg in 500 mL q8)
-Increased frequency of serial exams

Pain and tenderness improved by next day. Still with 8-10 BM/day. WBC 20 (14% bands).

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-Increased pain, distention, and tenderness
-No hypotension
-WBC 22

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-Increased pain, distention, and tenderness
-No hypotension
-WBC 22

Took to OR for laparoscopy, diverting loop ileostomy/colonic lavage. D/C to SNF after 8 days.

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