Centers for Disease Control and Prevention
National Center for Emerging and Zoonotic Infectious Diseases

Decolonizing Approaches: Current State and Future Needs

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Centers for Disease Control and Prevention

Drug Development Considerations for the Prevention of Healthcare-Associated Infections—
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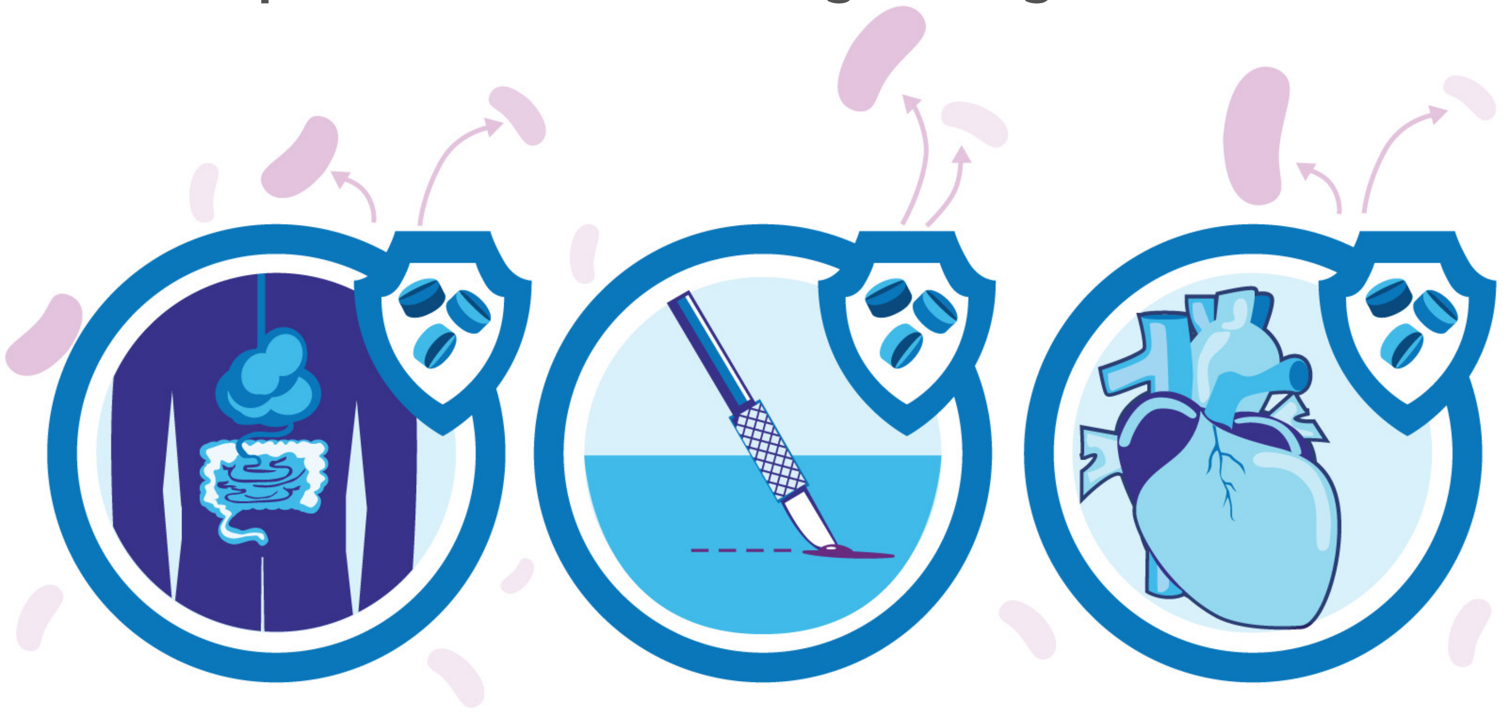
The findings and conclusions in this presentation are those of the author and do not necessarily represent the official position of the Centers for Disease Control and Prevention

Take-home messages

- Decolonization and pathogen reduction are already widely used for prevention in some forms of antimicrobial prophylaxis
- We can learn from unfolding failings of antimicrobial prophylaxis
- Future decolonization strategies should possess specific attributes
- Current and future products span various compositions and modes of action
- There is a central role for the human microbiome in colonization resistance that should be considered in all decolonization strategies
- A tolerable safety margin is impacted by local vs. systemic distribution and targeted vs. risk-based strategies
- It is important to tailor the intervention and its timing to the duration and timing of maximum risk of infection

Decolonization and pathogen reduction is already widespread in some forms of antimicrobial prophylaxis

Antimicrobial prophylaxis involves localized or systemic administration to prevent infection through a range of mechanisms



Decolonization/ pathogen reduction

Prevention of invasion/ translocation

Prevention of pathogen attachment to establish infection

Antimicrobial prophylaxis that works through decolonization or pathogen reduction as examples of the effectiveness of approach Evidence-based practice recommendations

- **US and International**
  - Pre-operative application of nasal mupirocin to prevent *S. aureus* infections following cardiac and orthopedic surgery[1,2,3]
    - ACS/SIS SSI Guidelines, 2016 Update: Decision about whether to implement screening and decolonization protocols should depend on baseline SSI and MRSA rates.[3]
    - CDC Surgical Site Infection Guideline (2017) did not address issue[4]
  - Pre-operative administration of non-absorbable antimicrobials, along with mechanical bowel preparation, to prevent surgical infection and anastomotic leaks following bowel surgery[1,2,3,5]
  - Prevention of secondary cases of meningococcal disease (oral rifampicin or other agents)[6]
- **Netherlands**
  - From onset of ICU care, selective digestive decontamination (SDD) and selective oral decontamination (SOD) to prevent infections and reduce mortality[7]

[1] ASHP, IDSA, SIS, and SHEA Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery. Surgical Infecitons. 2013; 14(1): 73-156.
[2] Global guidelines for the prevention of surgical site infection. World Health Organization. Available at http://apps.who.int/iris/bitstream/handle/10665/250680/9789241549882-eng.pdf?sequence=8
[3] Ban KA, et al. Executive Summary of the American College of Surgeons/Surgical Infection Society Surgical Site Infection Guidelines-2016 Update. Surg Infect. 2017; 18(4):379-382.
[4] Berrios-Torres SI et al. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. JAMA Surg. 2017;152(8):784-791.
[5] Rollins KE et al. The Role of Oral Antibiotic Preparation in Elective Colorectal Surgery. Ann Surg 2019;270:43–5.
[6] Telisinghe L et al. Chemoprophylaxis and vaccination in preventing subsequent cases of meningococcal disease in household contacts of a case of meningococcal disease: a systematic review. Epidemiol. Infect. (2015), 143, 2259–2268.
[7] Wittekamp, BH et al. Selective decontamination of the digestive tract (SDD) in critically ill patients: a narrative review. Intensive Care Med (2020) 46:343–349

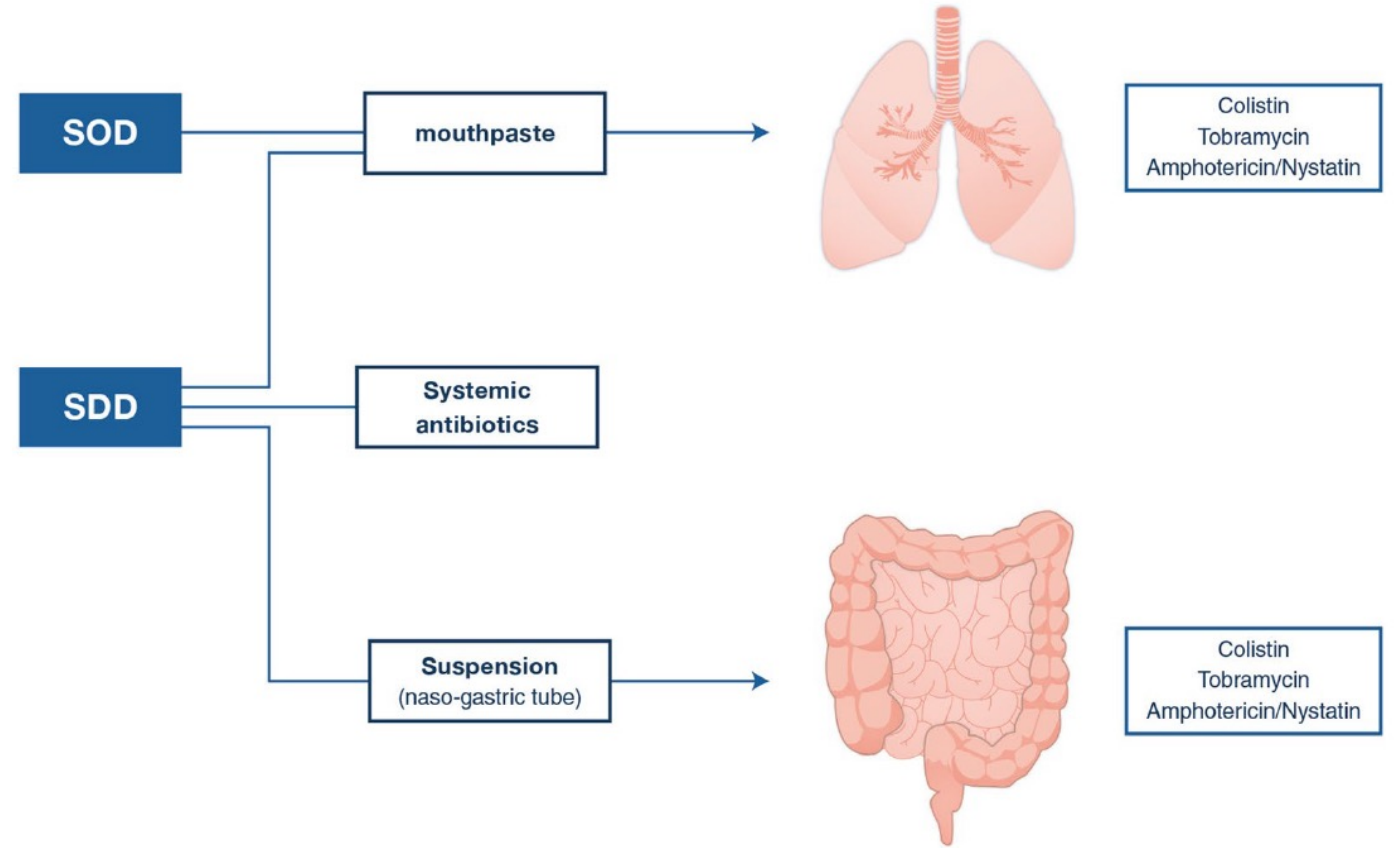


Fig. 1 Components of SDD and SOD. *SDD* selective digestive tract decontamination, *SOD* selective oropharyngeal decontamination

Wittekamp, BH et al. Selective decontamination of the digestive tract (SDD) in critically ill patients: a narrative review. Intensive Care Med (2020) 46:343–349

Take-home message

In settings with low prevalence of antibiotic resistance, SDD is consistently associated with less antibiotic resistance and with improved patient outcome. In settings with moderate-to-high prevalence of antibiotic resistance, benefits of SDD on clinically relevant patient outcomes remain to be demonstrated.

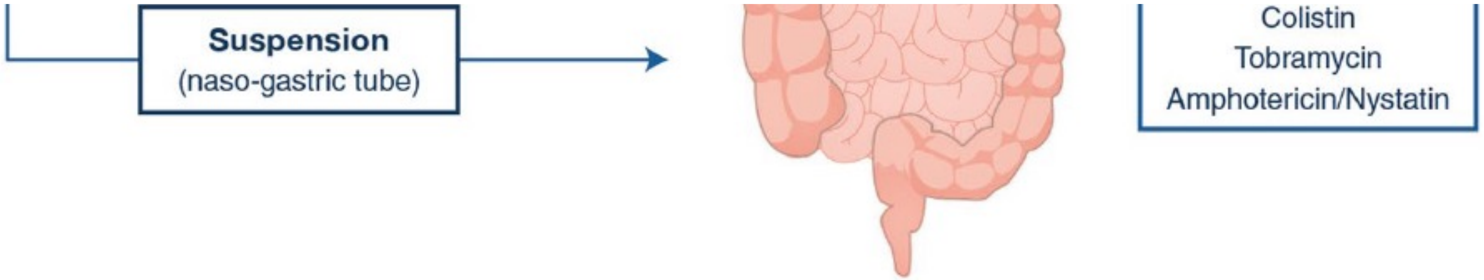


Fig. 1 Components of SDD and SOD. *SDD* selective digestive tract decontamination, *SOD* selective oropharyngeal decontamination

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Antimicrobial prophylaxis: learning from unfolding failings where decolonization plays a variable role

- **Systemic fluoroquinolones to prevent infections following transrectal prostate biopsy[1]**
  - Some studies indicate improved prevention with administration beginning one day before procedure[2]
  - Recent worldwide increases in breakthrough post-biopsy infections[1]
  - Intestinal colonization with fluoroquinolone-resistant gram-negative pathogens increases risk of breakthrough infection[1]
- **Systemic fluoroquinolones to prevent bloodstream infections in neutropenic patients[4]**
  - Increasing reports of clusters of breakthrough infections[5]
  - Intestinal domination by gram-negative pathogens (proteobacteria) is associated with bloodstream infection[6]
  - Fluoroquinolone normally prevents intestinal domination by gram-negative pathogens (proteobacteria)[6]
  - Intestinal colonization with fluoroquinolone-resistant gram-negative pathogens increases risk of breakthrough infection[5]

[1]Pilatz A et al. Antibiotic Prophylaxis for the Prevention of Infectious Complications following Prostate Biopsy: A Systematic Review and Meta-Analysis. J Urol . 2020 Aug;204(2):224-230
[2]Manecksha RP et al. Prospective Study of Antibiotic Prophylaxis for Prostate Biopsy Involving >1100 Men. ScientificWorldJournal . 2012;2012:650858
[3]Liss MA et al: An update of the American Urological Association white paper on the prevention and treatment of the more common complications related to prostate biopsy. J Urol 2017; 198: 329
[4]Mikulska M et al. Fluoroquinolone prophylaxis in haematological cancer patients with neutropenia: ECIL critical appraisal of previous guidelines. J Infect. 2018 Jan;76(1):20-37
[5]Satlin MJ et al. Colonization With Fluoroquinolone-Resistant Enterobacterales Decreases the Effectiveness of Fluoroquinolone Prophylaxis in Hematopoietic Cell Transplant Recipients. Clin Infect Dis. 2021 Oct 5;73(7):1257-1265
[6]Taur Y et al. Intestinal Domination and the Risk of Bacteremia in Patients Undergoing Allogeneic Hematopoietic Stem Cell Transplantation. Clin Infect Dis 2012;55(7):905–14

Intestinal domination by gram-negative pathogens (proteobacteria) is associated with bloodstream infection in hematopoietic cell transplant recipients

	VRE Bacteremia		Gram-negative Bacteremia	
Dominating Taxon[b]	HR (95% CI)	*P*	HR (95% CI)	*P*
Enterococcus	9.35 (2.43–45.44)	.001	1.35 (.25–5.08)	.690
Streptococcus	0.21 (.00–1.75)	.184	0.82 (.09–3.65)	.823
Proteobacteria	0.75 (.01–6.14)	.837	5.46 (1.03–19.91)	.047

Intestinal domination: >30% of composition of gut microbiota by single genus

Taur Y et al. Intestinal Domination and the Risk of Bacteremia in Patients Undergoing Allogeneic Hematopoietic Stem Cell Transplantation. Clin Infect Dis 2012;55(7):905–14

Fluoroquinolone prophylaxis normally prevents intestinal domination by gram negative pathogens (proteobacteria) in hematopoietic cell transplant recipients

Table 2. Clinical Predictors of Intestinal Domination

	Enterococcus Domination		*Streptococcus* Domination		Proteobacteria Domination	
Predictor	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Age, years	1.00 (.98–1.04)	.790	0.99 (.97–1.03)	.681	1.00 (.95–1.05)	.978
Female sex	0.84 (.42–1.64)	.611	1.07 (.50–2.27)	.852	1.12 (.33–3.78)	.854
Underlying diagnosis (leukemia vs other)	3.22 (1.60–6.94)	.001	0.71 (.32–1.51)	.375	0.66 (.18–2.19)	.498
Prior antibiotics (14 days)[a]	1.49 (.77–2.94)	.237	1.03 (.48–2.17)	.945	1.31 (.39–4.44)	.651
Conditioning regimen (myeloablative or reduced intensity vs non-myeloablative)	1.01 (.44–2.84)	.977	0.61 (.25–1.75)	.329	0.98 (.22–9.25)	.983
T-cell depleted graft	0.81 (.40–1.61)	.551	0.91 (.39–2.00)	.812	1.07 (.29–3.62)	.910
Stem cell source (cord vs other)	1.22 (.55–2.52)	.607	0.54 (.19–1.34)	.196	1.36 (.36–4.69)	.633
Fever[b]	1.68 (.78–3.74)	.182	0.90 (.36–2.39)	.826	1.28 (.30–6.34)	.747
Antibiotics[b]						
Vancomycin	2.12 (.67–10.21)	.222	0.95 (.33–3.77)	.938	5.17 (.52–707.15)	.192
Metronidazole	3.38 (1.65–6.73)	.001	1.94 (.81–4.30)	.131	1.73 (.41–6.03)	.426
Fluoroquinolones[c]	1.09 (.49–2.24)	.832	1.19 (.51–2.60)	.677	0.09 (.00–.75)	.020
Beta-lactam[d]	1.64 (.74–3.99)	.232	1.69 (.62–5.64)	.319	1.23 (.27–7.50)	.800

Abbreviations: CI, confidence interval; HR, hazard ratio.

[a] Defined as administration of any antibacterial drug within 14 days prior to observation period.

[b] Analyzed as a time-varying predictor.

[c] Fluoroquinolones consist of ciprofloxacin and levofloxacin.

[d] Beta-lactams include cephalosporins, beta-lactam–beta-lactamase combinations, and carbapenems.

Intestinal domination: >30% of composition of gut microbiota by single genus

Taur Y et al. Intestinal Domination and the Risk of Bacteremia in Patients Undergoing Allogeneic Hematopoietic Stem Cell Transplantation. Clin Infect Dis 2012;55(7):905–14

Colonization with fluoroquinolone-resistant gram-negative pathogens (Enterobacterales) increases risk for bloodstream infection in hematopoietic cell transplant recipients

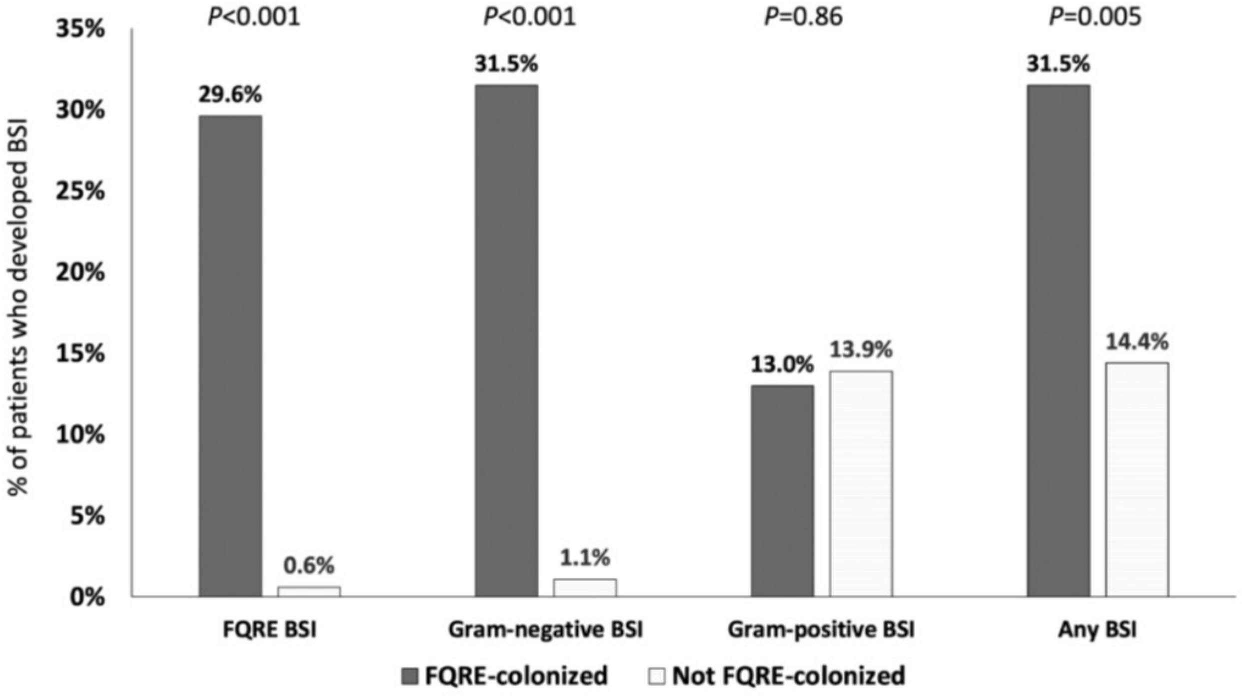


Figure 2. Proportion of patients who developed fluoroquinolone-resistant Enterobacterales (FQRE) bloodstream infection (BSI), gram-negative BSI, gram-positive BSI, and any BSI, stratified by pretransplant FQRE colonization status. *P* values represent comparisons between FQRE-colonized and noncolonized patients.

Satlin MJ et al. Colonization With Fluoroquinolone-Resistant Enterobacterales Decreases the Effectiveness of Fluoroquinolone Prophylaxis in Hematopoietic Cell Transplant Recipients. Clin Infect Dis. 2021 Oct 5;73(7):1257-1265

Rethinking the mechanisms of fluoroquinolone prophylaxis in neutropenia and improved approaches

Intestinal domination by gram-negative pathogens is associated with subsequent bloodstream infection

-AND-

Fluoroquinolone prophylaxis normally reduces the risk of intestinal domination by gram-negative pathogens

-AND-

Colonization with fluoroquinolone-resistant gram-negative pathogens increases risk for breakthrough infection

-THEREFORE-

The protection from fluoroquinolone prophylaxis is mediated at least in part through pathogen reduction

-AND-

Fluoroquinolone resistance leads to breakthrough infections through breakthrough intestinal dominance

Rethinking the mechanisms of fluoroquinolone prophylaxis in neutropenia and improved approaches

Fluoroquinolones were developed for short term treatment of local infection through systemic administration and not specifically for decolonization or pathogen reduction:

1. High oral absorption
2. Excellent body site distribution and tissue penetration
3. Increasingly recognized toxicity
4. Although high fecal levels achieved (15-94 ug/g for levofloxacin),[1] resistance commonly leads to high MICs (> 32 ug/ml)[2]
5. Although initially thought to have little impact on anaerobic microbiota and gut microbiome,[3] selection of resistance in anaerobes (e.g., C. difficile)[4] and microbiome disruption increasingly recognized

[1]Edlund C et al. Comparative effects of levofloxacin and ofloxacin on the normal oral and intestinal microflora. Scand J Infect Dis . 1997;29(4):383-6
[2]Satlin MJ et al. Colonization With Fluoroquinolone-Resistant Enterobacterales Decreases the Effectiveness of Fluoroquinolone Prophylaxis in Hematopoietic Cell Transplant Recipients. Clin Infect Dis. 2021 Oct 5;73(7):1257-1265
[3]Murray BE. Quinolones and the Gastrointestinal TractEur. J. Clin. Microbiol. Infect. Dis., December 1989, p. 1093-1102
[4]McDonald LC et al. An epidemic, toxin gene-variant strain of Clostridium difficile. N Engl J Med. 2005 Dec 8;353(23):2433-41.

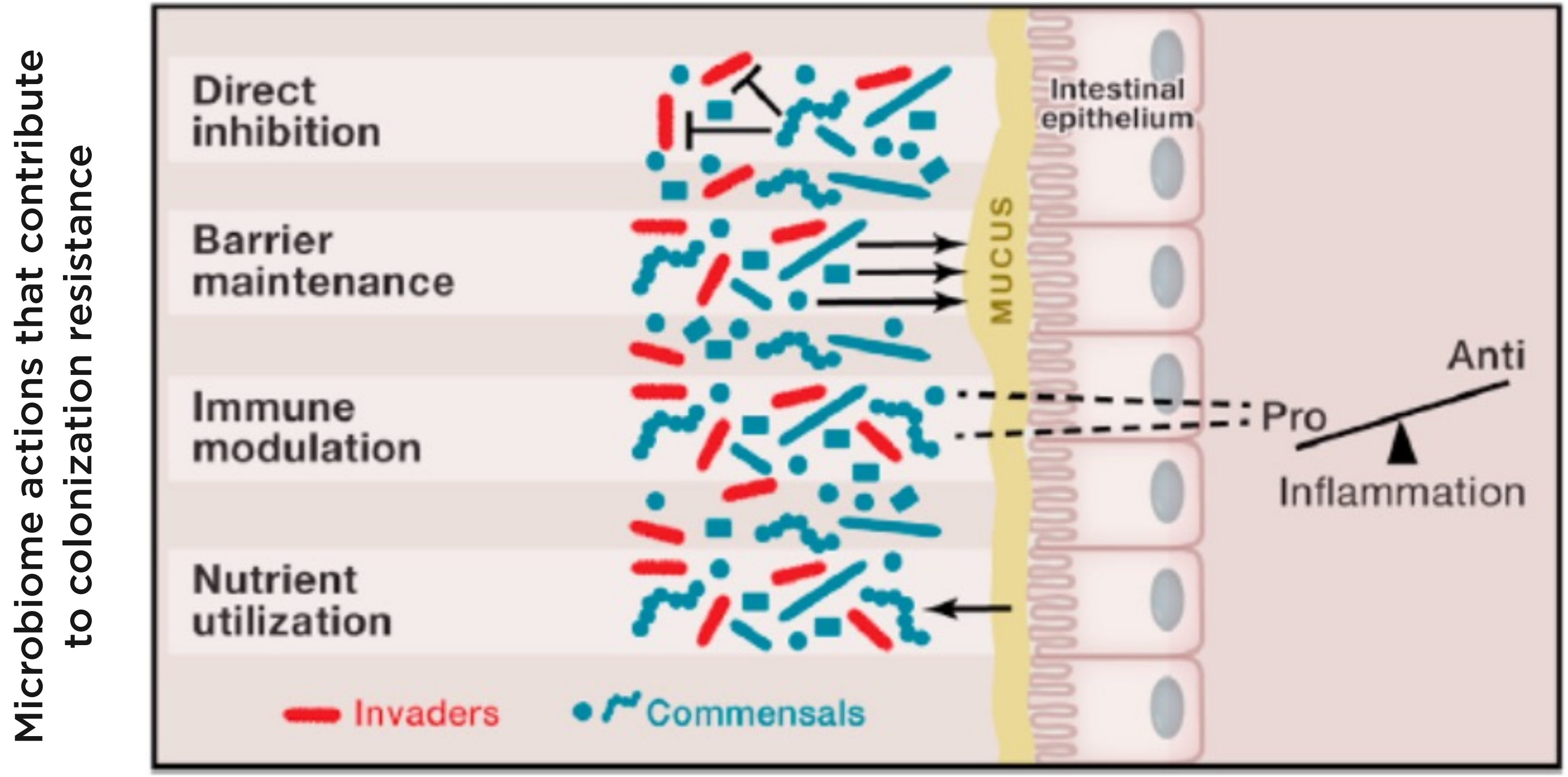
Future decolonization strategies should possess specific attributes

- **Narrow spectrum and limited body site distribution**
  - To improve drug safety and reduce collateral damage to microbiome
  - Non-absorbable narrow-spectrum agent for enteral, topical, or other local application
- **Favorable pharmacokinetics**
  - To reduce emergence of resistance through local evolution
  - High levels achievable locally relative to minimum inhibitory (MIC) or even bactericidal concentration (MBC)
- **Unlikely to evoke cross resistance through markedly different mechanisms of action**
  - Antiseptics generally less likely to evoke cross resistance to antimicrobials, although co-selection still possible via genetic linkage or strain selection
- **Leveraging colonization resistance afforded by the microbiome**
  - Through microbiome sparing, protection, or restoration
- **Durability**
  - Phage or live biotherapeutics may extend duration of decolonization or colonization resistance through their replication

Current and future products span various compositions and modes of action

- **Small molecule antimicrobial**
  - Current use: Mupirocin, non-absorbable antibiotics used for gut decontamination
- **Bacteriocins, and local (monoclonal) antibodies**
  - Under development: Lysostaphin
- **Topical antiseptics—decontaminating agents**
  - Current use: Alcohol, chlorhexidine
- **Microbiome protectants**
  - Under development: Activated charcoal, beta-lactamase enzyme
- **Microbiome restoratives**
  - Current use (under enforcement discretion for rCDI): Fecal microbiota transplantation (FMT)
  - Under development: pathogen reduced or processed FMT or derivative, defined microbiota consortium
- **Phage**
  - Under development: single or in cocktail form

There is a central role for the human microbiome in colonization resistance that should be considered in all decolonization strategies



McKenney PT and Pamer EG. From Hype to Hope: The Gut Microbiota in Enteric Infectious Disease. Cell 2015 (163): 1326-32

Broad reach of microbiome: reduced bloodstream infection, hospital stay, and deaths in recurrent *C. difficile* infection treated with FMT

Table 2. Outcome Data in the Original Cohort and in the Propensity Score-Matched Cohort

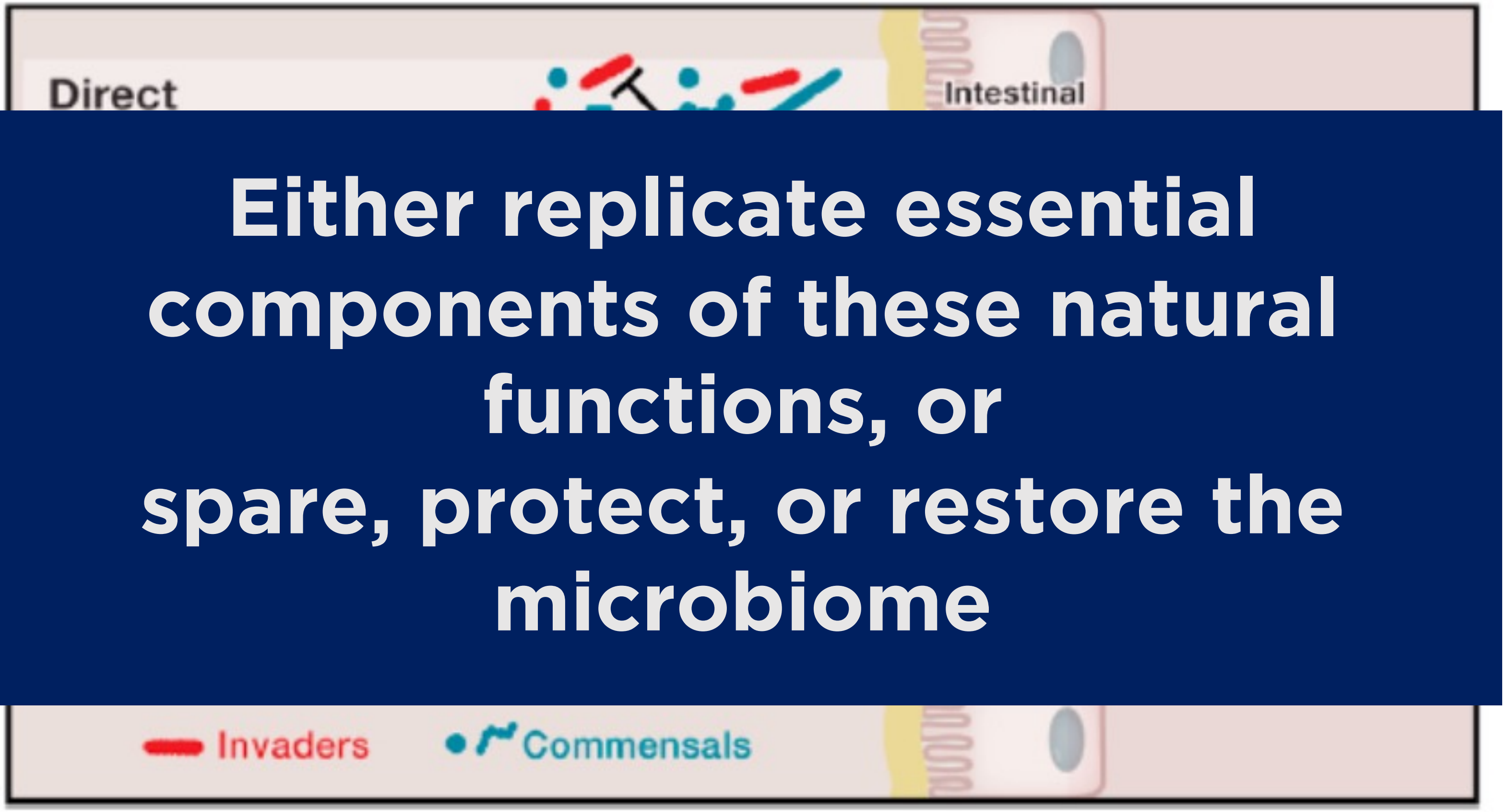
Variable	Original Cohort			After Propensity Score Matching		
	Treated With FMT	**Treated With Antibiotics**	**Difference, %**	**Treated With FMT**	**Treated With Antibiotics**	**Difference (95% CI), %**
Patients, *n*	109	181	–	57	57	–
Primary outcomes, *n* (%)						
BSI	5 (5)	40 (22)	16	2 (4)	15 (26)	23 (10–35)
Polymicrobial*	1 (1)	11 (6)	–	0 (0)	0 (0)	–
Bacterial	5 (5)	28 (15)	–	2 (4)	8 (14)	–
Fungal	0 (0)	12 (7)	–	0 (0)	7 (12)	–
Secondary outcomes						
Length of hospitalization	–	–	24	–	–	14 (9–20)
Mean (SD), *d*	13.3 (14.8)	29.7 (22.6)	–	13.4 (13.7)	27.8 (17.6)	–
Median (interquartile range), *d*	8 (2–20)	22 (14–39)	–	9 (2–21)	22 (14–40)	–
Overall survival at 90 d	–	–	30	–	–	32 (16–47)
Alive after 90 d, *n (%)*	100 (92)	111 (61)	–	51 (89)	33 (58)	–
Total deaths within 90 d, *n (%)*	9 (8)	70 (39)	–	6 (11)	22 (39)	–
Deaths in days 0–30, *n*	5	53	–	3	15	–
Deaths in days 31–90, *n*	4	17	–	3	7	–

BSI = bloodstream infection; FMT = fecal microbiota transplantation.
* 12 of 45 patients developed a polymicrobial BSI (from multiple bacteria in 10 patients and from fungal and bacterial organisms in 2 patients).

Ianiro G et al. Incidence of Bloodstream Infections, Length of Hospital Stay, and Survival in Patients With Recurrent Clostridioides difficile Infection Treated With Fecal Microbiota Transplantation or Antibiotics. Ann Intern Med. 2019;171:695-702.

There is a central role for the human microbiome in colonization resistance that should be considered in all decolonization strategies

Microbiome actions that contribute to colonization resistance



Either replicate essential components of these natural functions, or spare, protect, or restore the microbiome

Read more [About Microbial Ecology | CDC]

McKenney PT and Pamer EG. From Hype to Hope: The Gut Microbiota in Enteric Infectious Disease. Cell 2015 (163): 1326-32

A tolerable safety margin is impacted by local vs. systemic distribution and targeted vs. risk-based strategies

- **Local body site distribution, for example an orally administered non-absorbed agent, limits end-organ exposure to potential toxicities**
  - However, getting the locally-acting agent to its site of action may slow onset of action, for example oral ingestion requiring small-bowel transit to reach site of action in the large intestine
- **Targeted:**
  - Rapid screening for colonization with a specific pathogen
  - Generally smaller population exposure[1,]
  - Examples:
    - Pre-operative application of nasal mupirocin to prevent *S. aureus* infections following cardiac and orthopedic surgery[1]
    - Targeted (known colonized) MRSA decolonization on discharge (CLEAR study)[3]

—versus—

- **Risk-based:**
  - Administration to all patients fitting a particular risk profile or patient care area
  - Generally larger population exposure
  - Examples:
    - SDD as recommended in the Netherlands for all ventilated ICU patients[4]
    - Mupirocin and chlorhexidine decolonization as recommended for ICU patients and hospitalized adults with central venous catheters to prevent *S. aureus* bloodstream infection [5]

[1]Huang SS et al. Targeted versus Universal Decolonization to Prevent ICU Infection. N Engl J Med 2013;368:2255-65.
[2]Global guidelines for the prevention of surgical site infection. World Health Organization. Available at http://apps.who.int/iris/bitstream/handle/10665/250680/9789241549882-eng.pdf?sequence=8
[3]Huang SS et al. Decolonization to Reduce Postdischarge Infection Risk among MRSA Carriers. N Engl J Med. 2019 February 14; 380(7): 638–650.
[4]Wittekamp, BH et al. Selective decontamination of the digestive tract (SDD) in critically ill patients: a narrative review. Intensive Care Med (2020) 46:343–349
[5]CDC. Strategies to Prevent Hospital-onset Staphylococcus aureus Bloodstream Infections in Acute Care Facilities. https://www.cdc.gov/hai/prevent/staph-prevention-strategies.html

It is important to tailor the intervention and its timing to the duration and timing of maximum risk

- **Need to integrate screening (or risk stratification) with onset of action of the intervention**
  - If targeted application, need rapid turnaround screening methods[1,2]

- **Speed of decolonization relative to onset of risk**
  - SDD/SOD, when extended to Europe, may have been hampered by removal of 3rd gen cephalosporin, if decolonization or pathogen reduction could not be achieved rapidly enough[3]

- **Duration of decolonization relative to duration of risk**
  - Pre-partum decolonization (vs. intrapartum antibiotics) of Group B *Streptococcus* is not recommended as a prevention strategy for early onset infection of neonates because it cannot be achieved or maintained up to time of birth using available antibiotics[4, 5]

[1]Global guidelines for the prevention of surgical site infection. World Health Organization. Available at http://apps.who.int/iris/bitstream/handle/10665/250680/9789241549882-eng.pdf?sequence=8
[2]Huang SS et al. Targeted versus Universal Decolonization to Prevent ICU Infection. N Engl J Med 2013;368:2255-65
[3]Wittekamp, BH et al. Selective decontamination of the digestive tract (SDD) in critically ill patients: a narrative review. Intensive Care Med (2020) 46:343–349
[4]Baecher L and Grobman W. Prenatal antibiotic treatment does not decrease group B streptococcus colonization at delivery. Int J Gynaecol Obstet. 2008 May;101(2):125-8.
[5]ACOG Committee Opinion, Number 797. Prevention of Group B streptococcal early-onset disease in newborns. Obstet Gynecol . 2020 Feb;135(2):e51-e72.

Take-home messages

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Thank you

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Supplementary Slides

Selective decontamination of the digestive tract (SDD) in critically ill patients

- The main goal of SDD is to prevent ICU-acquired infections (and thereby improve patient outcomes)
  - Patients with an expected ICU stay of at least 2 or 3 days, and receiving mechanical ventilation
  - Preferred moment to start SDD is immediately upon ICU admission
  - In most studies, SDD was continued until ICU discharge and in some until extubation
  - Later, as an alternative to SDD, selective oropharyngeal decontamination (SOD) was proposed, based on clinical studies suggesting a more important role of upper respiratory tract colonization in the pathogenesis of ventilator-associated pneumonia than intestinal carriage
- Until 2000, most studies were individually randomized trials
  - Recognition that individual randomization may reduce the generalizability of study results and is suboptimal if cross-transmission occurs, artificially reducing the effect size afforded by indirect protection in settings where SDD applied uniformly
  - To overcome this, investigators adopted cluster designs
- Complicating factor: requirement of informed consent
  - Practically precludes enrollment of all eligible patients and will delay the start of SDD in many that do consent
  - In three recent cluster-randomized studies, waivers for informed consent were granted in the Netherlands, Belgium, Spain, Portugal, Italy, Slovenia, and the UK
    - SDD was considered part of daily ICU practice in each country
    - True equipoise on the effects of SDD, leading to marked differences in practice between ICUs
    - SDD (and SOD) were considered safe and it was acknowledged that a cluster-randomized study would not be feasible without such a waiver
    - Waivers allowed an immediate start of SDD after ICU admission and enrollment of 6000 patients and more

Wittekamp, BH et al. Selective decontamination of the digestive tract (SDD) in critically ill patients: a narrative review. Intensive Care Med (2020) 46:343–349

Overview of recent SDD studies using a cluster-randomized design

Author	Study period	Design	Countries	Study Outcome(s)	Patient numbers	Effect size	Antibiotic resistance
Jonge et al. (1)	1999-2001	CRCT, comparing SC to SDD	Netherlands	ICU and hospital mortality	SDD n=466 SC n=468	ICU mortality (SDD vs. SC): - 69 (15%) / 107 (23%) (P=0,002). Hospital mortality (SDD vs. SC): - 113 (24%) vs 146 (31%) (P=0,02).	During SDD acquired carriage was lower for Pseudomonas aeruginosa resistant to ceftazidime, ciprofloxacin and imipenem, and for other Gram-negative bacteria resistant to other Gram-negative bacteria resistant to ciprofloxacin, imipenem and tobramycin.
Smet et al. (2)	2004-2006	CRCT, comparing SC to SDD and SOD	Netherlands	Mortality at day 28	SDD n=2045 SOD n=1904 SC n=1990	Adjusted Odds ratio for mortality at day 28: SDD vs. SC: 0.83 (95% CI, 0.72 to 0.97) SOD vs. SC: 0.86 (95% CI 0.74 to 0.99)	Average prevalence of rectal carriage with Gram-negative bacteria resistant to gentamicin/tobramycin + ciprofloxacin or ceftazidime SDD 0.5% SOD 2.3% (P <0.05 to SDD) SC 2.2% (P <0.05 to SDD)
Oostdijk et al. (3)	2009-2013	CRCT, comparing SDD to SOD	Netherlands	Unit-wide prevalence of specific antibiotic-resistant microorganisms Mortality at day 28	SDD n=6.116 SOD n=5.881	Proportions colonized with rectal with HRMO SDD vs. SOD: 12.7% (IQR 11.2-14.2) vs. 7.3% (IQR 6.1-8.4); P =0.008 Adjusted odds ratio for mortality at day 28: SDD vs. SOD, 0.85 (95% CI, 0.77-0.93); P =0,001	Prevalence of rectal carriage of aminoglycoside-resistant gram-negative bacteria increased 7% per month (95%CI, 1%-13%) during SDD (P = .02) and 4% per month (95%CI, 0%-8%) during SOD (P =0.046; P =0.40 for difference).
Wittekamp et al. (4)	2013-2017	CRCT, comparing SC to SDD*, SOD and CHX	Spain, Italy, Portugal, Belgium, UK, Slovenia	ICU-acquired BSI with MDR-GNB Mortality at day 28	SDD n=2082 SOD n=2224 CHX n=2108 SC n=2251	Adjusted hazard ratios for ICU-acquired BSI with MDR-GNB SDD vs SC: 0.70 (95% CI, 0.43-1.14) SOD vs SC: 0.89 (95% CI 0.55-1.45) CHX vs SC: 1.13 (95% CI 0.68-1.88) Adjusted hazard ratios for mortality at day 28: -Adjusted odds ratio SDD vs. SC: 1.03 (95% CI 0.80-1.32) -Adjusted odds ratio SOD vs. SC: 1.05 (95% CI 0.85-1.29) -Adjusted odds ratio CHX vs. SC: 1.07 (95% CI 0.86-1.32)	Adjusted Relative Risk for unit-wide rectal carriage with MDR-GNB SDD vs SC: 1.01 (95% CI 0.64-1.58) SOD vs SC: 0.80 (95% CI 0.49-1.30) CHX vs SC: 0.80 (95% CI 0.50-1.27)

References
1. de Jonge E, Schultz MJ, Spanjaard L, Bossuyt PM, et al (2003) Effects of selective decontamination of digestive tract on mortality and acquisition of resistant bacteria in intensive care: a randomised controlled trial. Lancet (London, England) 362 (9389):1011-1016. doi:10.1016/s0140-6736(03)14409-1
2. de Smet AM, Kluytmans JA, Cooper BS, Mascini EM, et al (2009) Decontamination of the digestive tract and oropharynx in ICU patients. The New England journal of medicine 360 (1):20-31. doi:10.1056/NEJMoa0800394
3. Oostdijk EA, Kesecioglu J, Schultz MJ, Visser CE, et al (2014) Effects of decontamination of the oropharynx and intestinal tract on antibiotic resistance in ICUs: a randomized clinical trial. Jama 312 (14):1429-1437. doi:10.1001/jama.2014.7247
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- Ongoing cluster, cross-over RCT (clinicaltrials. gov NCT02389036)
  - Currently recruiting 12,000-15,000 patients in Canada, UK, and Australia
  - Patients not already receiving intravenous therapeutic antibiotic: 4-day course of intravenous cephalosporin

Wittekamp, BH et al. Selective decontamination of the digestive tract (SDD) in critically ill patients: a narrative review. Intensive Care Med (2020) 46:343–349

Examples of antimicrobial prophylaxis with little role for decolonization and pathogen reduction: missed opportunities?

- Targeting only prevention of invasion/translocation or pathogen attachment
- Systemic surgical or endocarditis prophylaxis administered prior to procedure
  - Clean or clean-contaminated surgical procedures or dental work
  - Targeting a variety of gram-positive skin or oral aerobes
  - As currently practiced, little to no time to decolonize or pathogen reduce with drug achieving relatively low levels at sites of colonization—focus is on achieving high blood levels at time of procedure
- Systemic intrapartum prophylaxis for prevention of early-onset group B streptococcus (GBS) infection in neonates
  - Rectal GBS colonization in mother is pre-requisite for infection; heavy rectal colonization or GBS bacteriuria carries increased risk[1]
  - Early attempts suggested pre-partum maintenance of decolonization was not possible[2] Current guidance primarily targets administration based on screening at up to 5 weeks before delivery, risk-based administration if screening missed[1]
  - Systemic prophylaxis administered in about half of all U.S. births, crossing the placental barrier and leading to significant population impact on early life microbiome development[3]

[1]ACOG Committee Opinion, Number 797. Prevention of Group B streptococcal early-onset disease in newborns. Obstet Gynecol . 2020 Feb;135(2):e51-e72.
[2]Baecher L and Grobman W. Prenatal antibiotic treatment does not decrease group B streptococcus colonization at delivery. Int J Gynaecol Obstet. 2008 May;101(2):125-8.
[3] Prescott S et al. Impact of intrapartum antibiotic prophylaxis on offspring microbiota. Front. Pediatr. 9:754013.

Broad reach of microbiome: reduced bloodstream infection, hospital stay, and deaths in recurrent C. difficile infection treated with FMT

Table 3. Organisms Involved in BSIs in the Original Study Cohort

Microbes	Total Patients, *n*	FMT Group, *n*	Antibiotic Group, *n*
Bacteria			
XDR *Acinetobacter baumannii*	2	0	2
Escherichia coli	3	0	3
Enterococcus faecalis	3	1	2
VR *E faecium*	3	0	3
Klebsiella oxytoca	1	1	0
K pneumoniae	3	1	2
CRE *K pneumoniae*	3	0	3
ESBL *K pneumoniae*	1	1	0
Staphylococcus species	7	1	6
S aureus	1	0	1
MR *S aureus*	1	0	1
Proteus mirabilis	1	0	1
XDR *P mirabilis*	1	0	1
Corynebacterium species	1	0	1
Total	31	5	26
Fungi			
Candida albicans	9	0	9
C parapsilosis	4	0	4
C tropicalis	1	0	1
Total	14	0	14
Overall	45*	5	40

BSI = bloodstream infection; CRE = carbapenem-resistant Enterobacteriaceae; ESBL = extended-spectrum β-lactamase–producing; FMT = fecal microbiota transplantation; MR = methicillin-resistant; VR = vancomycin-resistant; XDR = extensively drug-resistant.
* 12 of 45 patients developed a polymicrobial BSI (from multiple bacteria in 10 patients and from fungal and bacterial organisms in 2 patients).

Ianiro G et al. Incidence of Bloodstream Infections, Length of Hospital Stay, and Survival in Patients With Recurrent Clostridioides difficile Infection Treated With Fecal Microbiota Transplantation or Antibiotics. Ann Intern Med. 2019;171:695-702.