

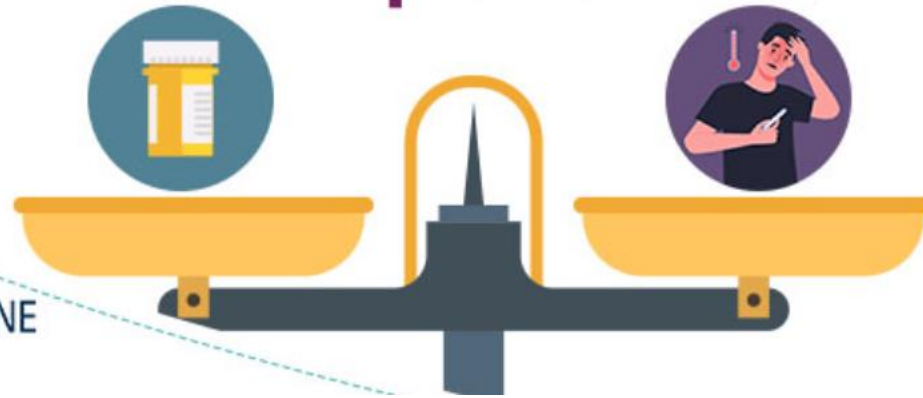
# A Pro/Con Debate on Fluoroquinolone Prophylaxis for Neutropenic Fever

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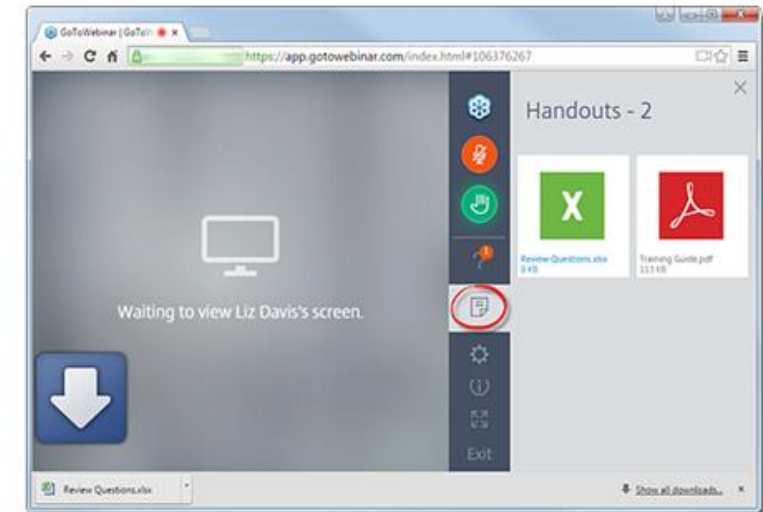
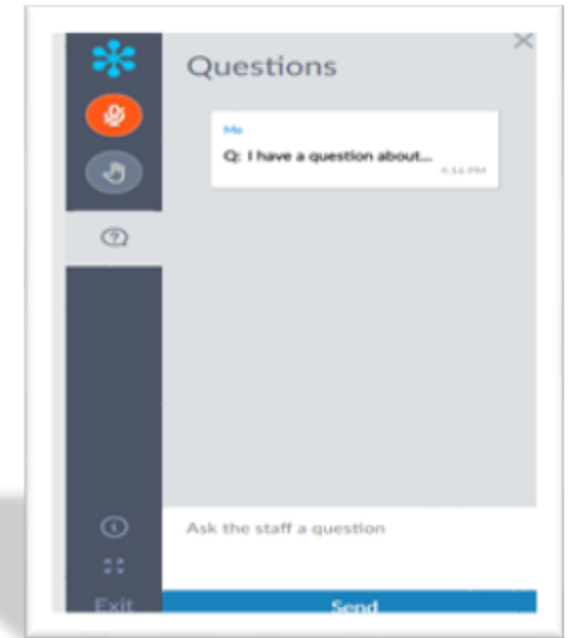
**Webinar**  
Jan. 25, 2023

## Continuing Education Webinar



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# Panelists



## **Erin K. McCreary, PharmD, BCPS, BCIDP - Moderator**

Director of Infectious Disease Improvement and Clinical Research Innovation, UPMC Clinical Assistant Professor, University of Pittsburgh, Infectious Disease Connect



## **Samuel Aitken, PharmD, MPH**

Clinical Pharmacist Specialist – Infectious Diseases, Michigan Medicine  
Adjunct Clinical Professor, University of Michigan College of Pharmacy



## **Ghady Haidar, M.D.**

Director of Research, Bone Marrow Transplant and Hematological Malignancy Infectious Disease, UPMC  
Assistant Professor of Medicine, Transplant ID Program,  
University of Pittsburgh and UPMC



# Disclosures

## Erin K. McCreary, PharmD, BCPS, BCIDP

- Advisory Boards: Abbvie, Cidara, Entasis, Ferring, La Jolla, Lab Simplify, MeMed, Merck Summit, Shionogi

## Sam Aitken, PharmD, MPH

- Advisory Boards: AstraZeneca, Entasis Therapeutics, F2G, GlaxoSmithKline, Shionogi
- Research Support: Melinta
- Honoraria: Shionogi

## Ghady Haidar, M.D.

- Advisory Boards: AstraZeneca, Karius
- Research Support: Allovir, AstraZeneca, Karius, National Institutes of Health
- Honoraria: International AID Society, MDOutlook



# Objectives

1. Discuss the pros of using Fluoroquinolone Prophylaxis for Neutropenic Fever
2. Describe the cons of using Fluoroquinolone Prophylaxis for Neutropenic Fever
3. Determine how microbiology laboratories and antimicrobial stewardship teams can collaborate to improve care of cancer patients with infections

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**PRO**  
**Dr. Samuel L. Aitken,**  
**PharmD, MPH**



# The eagles should have brought the hobbits to Mordor

Or, an argument for FQ prophylaxis

January 25<sup>th</sup>, 2023

Sam L. Aitken, PharmD, MPH



# Another Disclosure

## Personal Biases

- I am a pro-fluoroquinolone (FQ) pharmacist
- I hate meta-analyses but I use them to prove points (whoops)

# Points I will make

- Infection is a leading cause of death in patients with leukemia and hematopoietic cell transplant recipients (HCT)
- FQ prophylaxis reduces the risk of death relative to no FQ prophylaxis
- Benefits of FQ prophylaxis outweigh risks

# Infections are a major problem in leukemia

3. Changing patterns of fatal infection in acute leukemia.

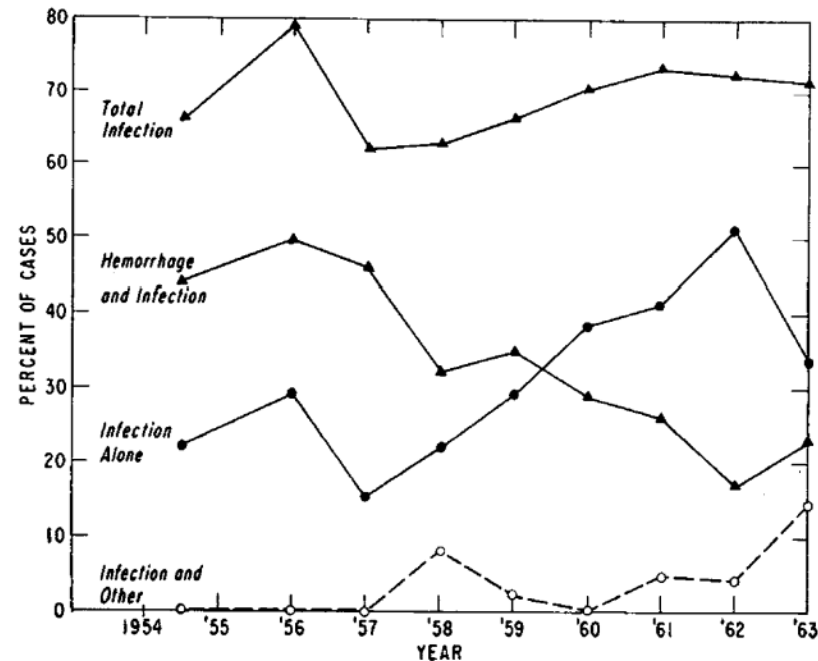


Table 6.—Organisms Identified in Cases of Septicemia

| Organism                       | 1954-1963<br>% | 1954-1959<br>% | 1960-1963<br>% |
|--------------------------------|----------------|----------------|----------------|
| <i>P aeruginosa</i>            | 29.3           | 24.6           | 34.4           |
| <i>E coli</i>                  | 17.4           | 21.6           | 12.8           |
| Fungi                          | 15.4           | 8.2            | 23.2*          |
| <i>S aureus</i>                | 14.7           | 23.9           | 4.8*           |
| <i>K pneumoniae</i>            | 9.3            | 6.7            | 12.0           |
| <i>Proteus</i> species         | 5.4            | 4.5            | 6.4            |
| <i>Paracolon</i> species       | 2.7            | 3.7            | 1.6            |
| <i>Clostridium perfringens</i> | 2.7            | 4.5            | 0.8            |
| Other organisms†               | 3.1            | 2.3            | 4.0            |
| Total number                   | 259            | 134            | 125            |

\*Significantly different incidence compared to 1954-1959  $P < .01$

†*Aerobacter aerogenes*, 3 isolations; *Diplococcus pneumoniae*, 2; *E freundii*, 1; *Bacteroides*, 1.

- Infections, primarily with Gram negative organisms, accounted for ~70% of all deaths in the early chemotherapy era

# Early prevention relied on protective isolation and enteral decontamination

Baltimore City Hospital

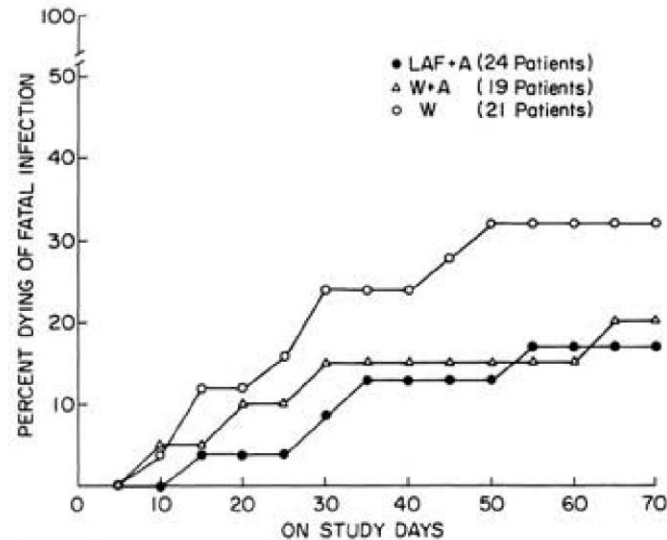


Figure 3. Onset of fatal infection. LAF + A = laminar air flow room reverse isolation plus oral, nonabsorbable antibiotics; W + A = routine hospital ward care plus oral, nonabsorbable antibiotics; W = routine hospital ward care.

National Cancer Institute

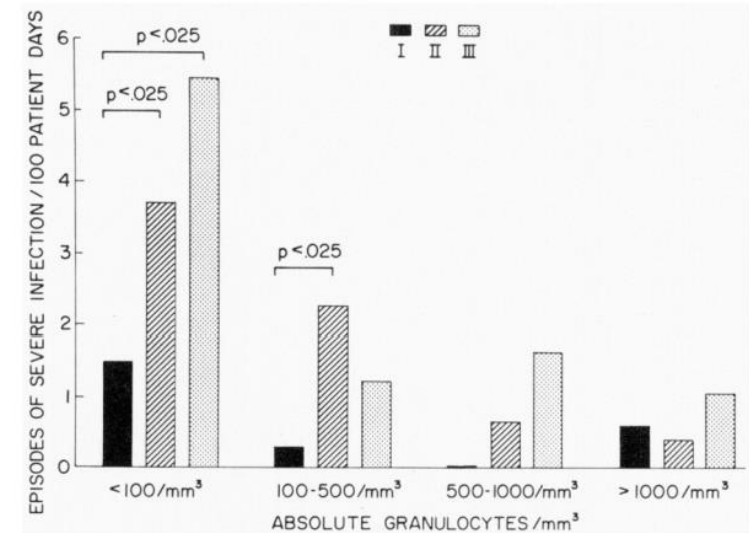


Figure 2. Total Number of Episodes of Severe Infection Occurring at Specified Granulocyte Levels Divided by Total Number of Patient-Days at Those Granulocyte Levels (Results Were Normalized to Episodes per 100 Patient-Days).

- Conflicting results on whether isolation, antibiotics, or both (or none) were better than another

# Protective isolation was a challenge!

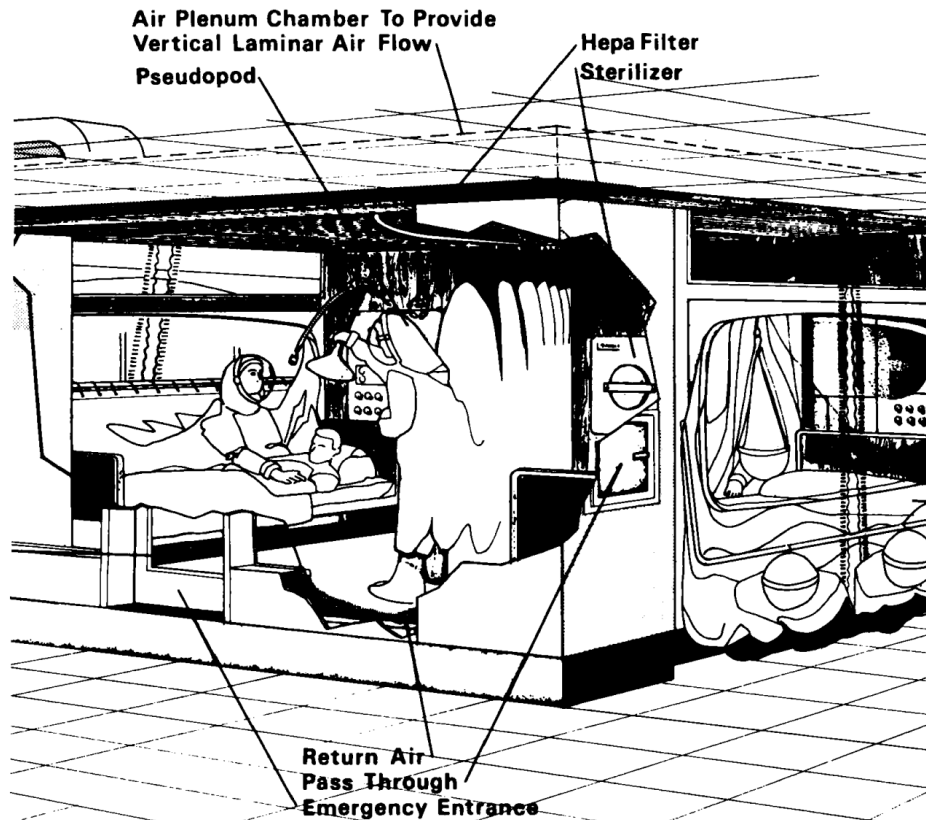


FIG. 1. Cutaway illustration of the double occupancy vertical laminar air flow room.

TABLE 2. Antimicrobial Prophylaxis

## Primary oral antibiotic regimen

|             |                          |                 |
|-------------|--------------------------|-----------------|
| Vancomycin  | 0.5 gm                   | } Every 6 hours |
| Gentamicin* | 200 mg                   |                 |
| Nystatin    | 500,000 u/m <sup>2</sup> |                 |

## Mouthwash and throat spray

|            |                                                                               |                                    |
|------------|-------------------------------------------------------------------------------|------------------------------------|
| Bacitracin | 8 mg/cc                                                                       | } 30 cc Q 4 hrs.<br>during the day |
| Neomycin   | 10 mg/cc                                                                      |                                    |
| Polymyxin  | 0.67 mg/cc                                                                    |                                    |
| Nystatin   | 10,000 µ/cc—added if mouth or<br>throat cultures persistently<br>yield monila |                                    |

## Nasal antibiotic ointment

|                       |           |
|-----------------------|-----------|
| Bacitracin            | 500 µ/gm  |
| Neomycin<br>sulphate  | 5 mg/gm   |
| Polymyxin<br>sulphate | 5000 µ/gm |

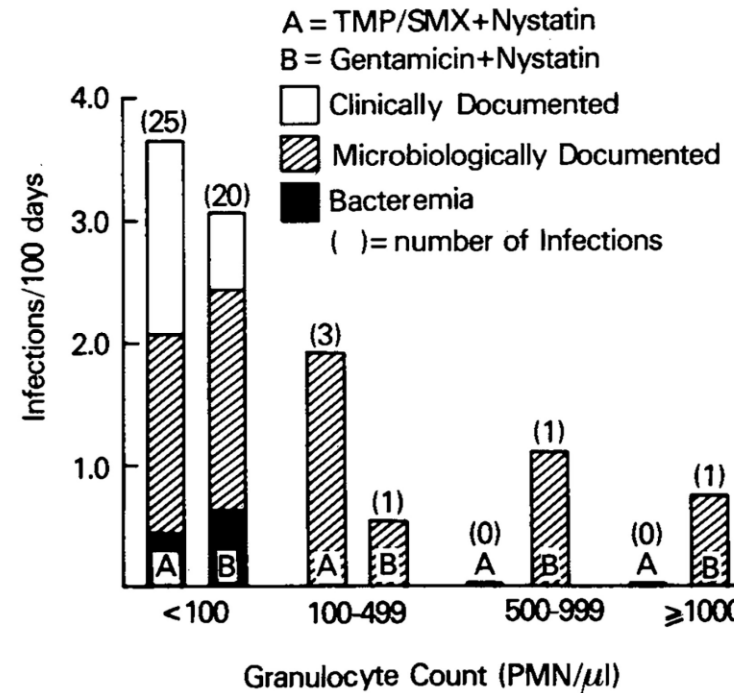
## Douche

|                  |                                         |
|------------------|-----------------------------------------|
| Povidone-iodine† | 15 cc in 1000 cc H <sub>2</sub> O daily |
|------------------|-----------------------------------------|

\* Gentamicin (Garamycin) supplied through the courtesy of Schering Corp., Bloomfield, N. J.

† Povidone-iodine (Betadine) supplied through the courtesy of Purdue Frederick Company, Yonkers, N.Y.

# Trimethoprim-sulfamethoxazole rapidly replaced non-absorbable antibiotics



- Better tolerated (although hints of hematologic toxicity) and easier to administer
- Mortality generally similar or reduced with TMP/SMX

# Nalidixic acid inferior to trimethoprim-sulfamethoxazole but less toxic

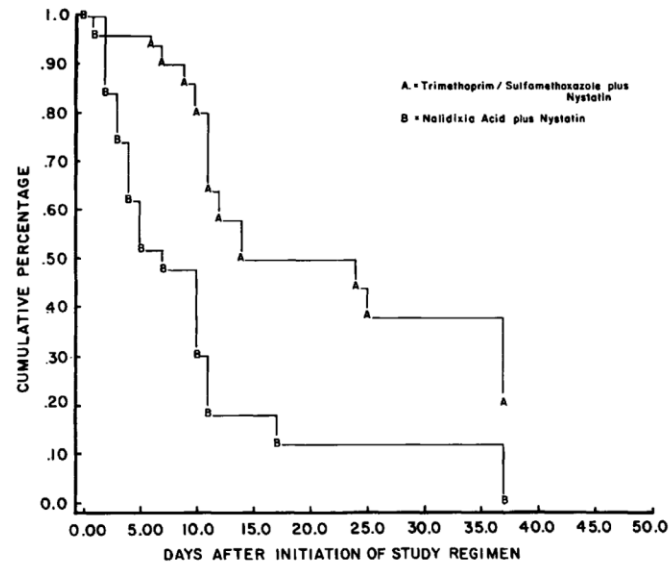


**Figure 1.** Cumulative percentage of patients with acute leukemia who were free of infection after initiation of prophylaxis against infection. The difference in the overall curve over time between the group given trimethoprim-sulfamethoxazole ( $n = 34$ ) and the group given nalidixic acid ( $n = 28$ ) was statistically significant ( $P = 0.0002$ ).

| Granulocyte count       | Initial induction                                |                                   |
|-------------------------|--------------------------------------------------|-----------------------------------|
|                         | Trimethoprim-sulfamethoxazole plus nystatin (17) | Nalidixic acid plus nystatin (15) |
| <100/mm <sup>3</sup>    | 22.6 ± 3.3*                                      | 13.6 ± 2.2*                       |
| 100–499/mm <sup>3</sup> | 6.9                                              | 8.6                               |
| 500–999/mm <sup>3</sup> | 4.4                                              | 4.6                               |
| ≥1,000/mm <sup>3</sup>  | 6.8                                              | 7.4                               |
| Total                   | 40.7 ± 4.2                                       | 34.2 ± 2.9                        |

- Duration of severe neutropenia nearly doubled in patients receiving TMP/SMX
- Increased rate of aspergillosis observed in TMP/SMX recipients

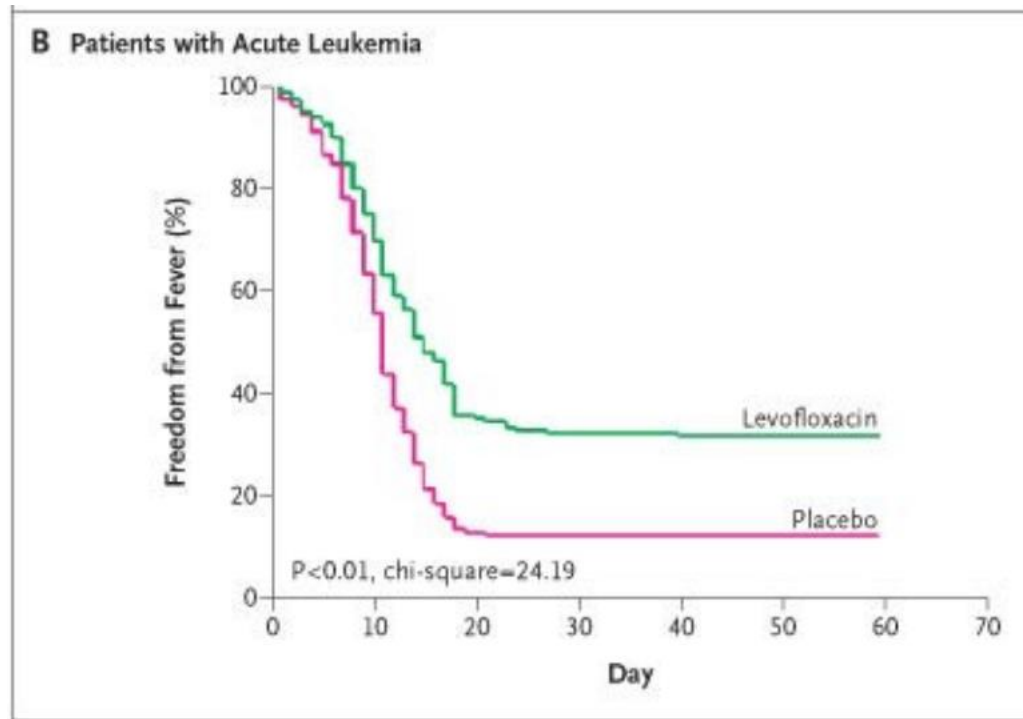
# Ofloxacin prophylaxis is superior to TMP/SMX

|                                                                           | Ofloxacin  | Trimethoprim-sulfamethoxazole |
|---------------------------------------------------------------------------|------------|-------------------------------|
| Granulocytopenic episodes without fever, n                                | 43 (42%)   | 25 (27%)                      |
| Proportion of granulocytopenic days spent febrile, % <sup>a</sup>         | 21%        | 28%                           |
| Patients remaining free of acquired infections, and febrile episodes, n   | 22 (31%)   | 9 (16%)                       |
| Median duration of fever for acquired episodes, days <sup>b</sup> (range) | 3.0 (0-40) | 7.0 (0-49)                    |
| Patients with acquired infections, n <sup>c</sup>                         | 36 (51%)   | 41 (71%)                      |
| Acquired infections, n                                                    | 47         | 57                            |
| Microbiologically documented (bacteremia)                                 | 22 (14)    | 39 (29)                       |
| Clinically documented                                                     | 25         | 18                            |
| Unexplained fever episodes, n                                             | 19         | 16                            |
| Fatal infections, n                                                       | 6          | 3                             |

|                                                              | Ofloxacin | Trimethoprim-sulfamethoxazole |
|--------------------------------------------------------------|-----------|-------------------------------|
| Patients with microbiologically documented infections, n (%) |           |                               |
| Gram-negative bacterial infection <sup>a</sup>               | 3 ( 4%)   | 15 (26%)                      |
| Gram-positive bacterial infection                            | 13 (19%)  | 13 (22%)                      |
| Fungal infection                                             | 5 ( 7%)   | 8 (14%)                       |
| Patients with bacteremia/fungemia, n (%)                     |           |                               |
| Gram-negative bacteremia <sup>a</sup>                        | 1 ( 1%)   | 13 (22%)                      |
| Gram-positive bacteremia                                     | 13 (19%)  | 12 (21%)                      |
| Fungemia                                                     | —         | 2 ( 3%)                       |

- Febrile neutropenia and microbiologically documented infections less common with ofloxacin
- Gram negative infection / colonization less common with ofloxacin

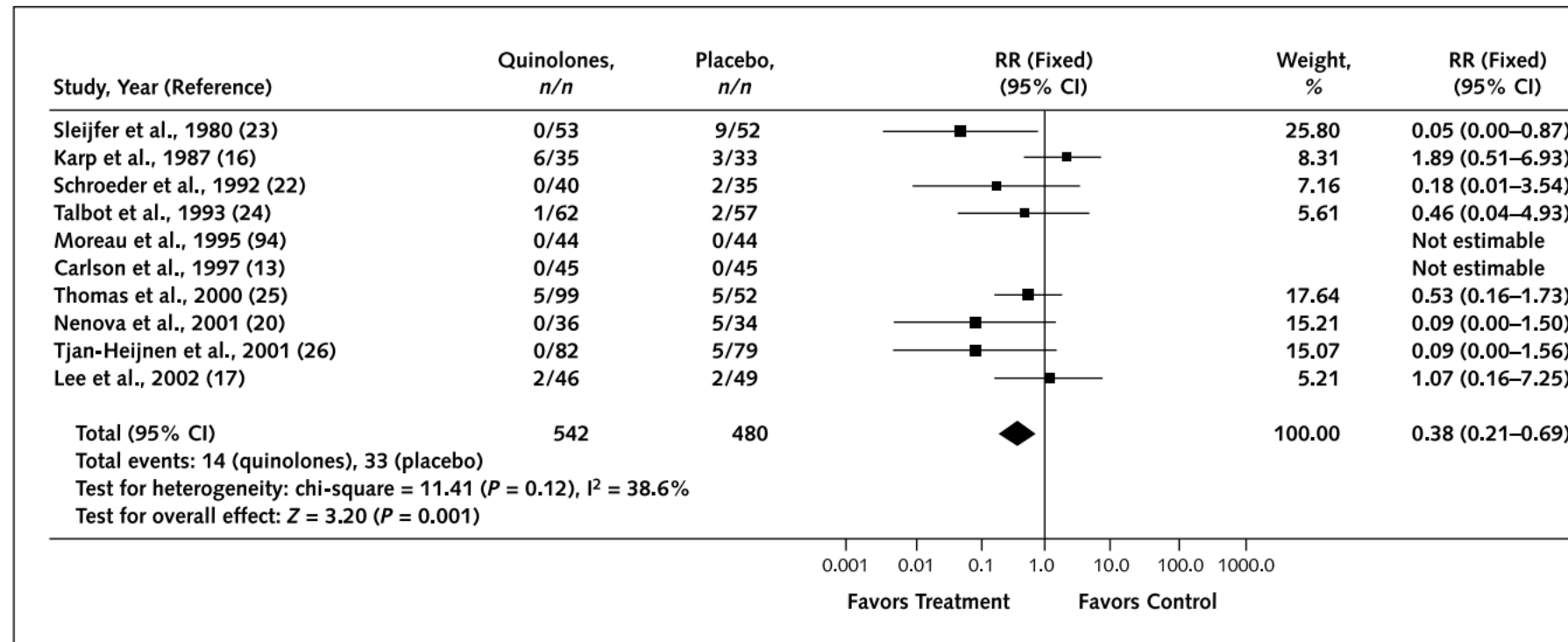
# Levofloxacin is superior to placebo



|                                                        |              |              |                        |  |
|--------------------------------------------------------|--------------|--------------|------------------------|--|
| Assessable patients with neutropenia $\geq 7$ days     |              |              |                        |  |
| Febrile episode                                        | 200/300 (67) | 252/280 (90) | -0.23 (-0.29 to -0.16) |  |
| <b>Acute leukemia</b>                                  |              |              |                        |  |
| Treated patients                                       |              |              |                        |  |
| Febrile episode                                        | 123/183 (67) | 154/179 (86) | -0.19 (-0.27 to -0.10) |  |
| Death                                                  | 9/182 (5)    | 13/179 (7)   | -0.02 (-0.07 to 0.02)  |  |
| Assessable patients                                    |              |              |                        |  |
| Febrile episode                                        | 113/165 (68) | 145/165 (88) | -0.20 (-0.28 to -0.10) |  |
| Microbiologically documented infection                 | 39/165 (24)  | 74/165 (45)  | -0.21 (-0.31 to -0.11) |  |
| Bacteremia                                             | 34/165 (21)  | 64/165 (39)  | -0.18 (-0.27 to -0.08) |  |
| Assessable patients with neutropenia for $\geq 7$ days |              |              |                        |  |
| Febrile episode                                        | 110/159 (69) | 138/151 (91) | -0.22 (-0.30 to -0.13) |  |

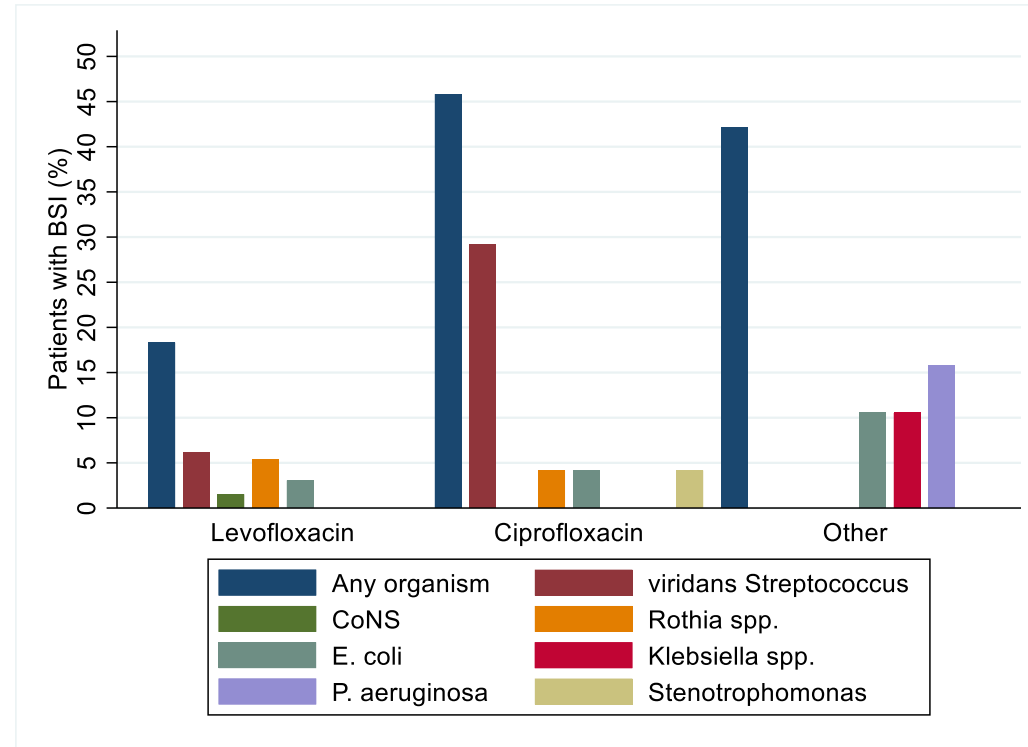
- Fever and microbiologically documented infections dramatically lower with levofloxacin
- Death reduced, but underpowered (despite n ~700)

# Quinolone prophylaxis reduces mortality!



- Mostly dramatically underpowered studies
- What harm outweighs reduced risk of death?

# Levofloxacin is associated with reduced bloodstream infection in patients receiving induction chemotherapy



- “Other” generally cefpodoxime
- Bloodstream infection, particularly Gram negative, dramatically reduced with levofloxacin prophylaxis at MD Anderson

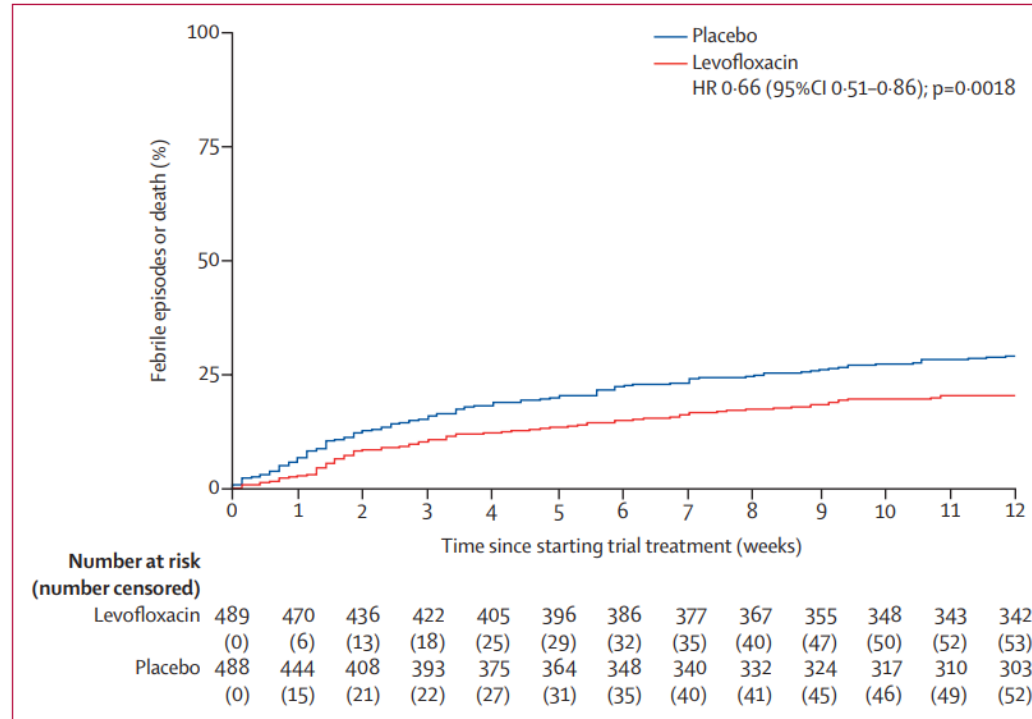
# Multicenter, contemporary studies confirm the protective effect

|                               | Mortality (n/N, %) |                |                    |
|-------------------------------|--------------------|----------------|--------------------|
|                               | FQ-px              | No FQ-px       | aSHR (95% CI)      |
| <b>Overall</b>                | 122/5302 (2.3)     | 110/3453 (3.2) | 0.72 (0.56 – 0.93) |
| <b>Allo-HSCT</b>              | 99/2857 (3.5)      | 65 /1366 (4.8) | 0.72 (0.53 – 0.99) |
| <b>Auto-HSCT</b>              | 11/1929 (0.6)      | 15/1673 (0.9)  | 0.64 (0.29 – 1.38) |
| <b>High-dose chemotherapy</b> | 12/516 (2.3)       | 30/414 (7.8)   | 0.30 (0.15 – 0.58) |

aSHR: adjusted subhazard ratio; HSCT: hematopoietic stem cell transplant; FQ: fluoroquinolone; px: prophylaxis

- Multi-national, observational cohort between 2009 – 2014 confirms FQ prophylaxis associated with reduced mortality

# A contemporary RCT in myeloma confirms benefit



- UK RCT of levofloxacin in nearly 1,000 patients with newly diagnosed myeloma
- 12-week mortality reduced from 3% to 1%
- ESBL colonization more common in placebo arm!

# A contemporary randomized trial in children confirms a benefit

Table 2. Comparison of Bacteremia Incidence per Patient During the Infection Observation Period and Bacteremia Rate per 1000 Patient-Days Between Randomized Groups for Acute Leukemia and HSCT Groups (N = 613)

|                                    | Bacteremia Incidence, No./Total (%)           |                              | Risk Difference, %<br>(95% CI) | Risk Ratio (95% CI)                          | P Value |
|------------------------------------|-----------------------------------------------|------------------------------|--------------------------------|----------------------------------------------|---------|
|                                    | Levofloxacin                                  | No Prophylaxis               |                                |                                              |         |
| Primary Analysis <sup>a</sup>      |                                               |                              |                                |                                              |         |
| Total acute leukemia               | 21/96 (21.9)                                  | 43/99 (43.4)                 | 21.6 (8.8-34.4)                | 0.50 (0.32-0.78)                             | .001    |
| AML                                | 15/64 (23.4)                                  | 25/63 (39.7)                 | 16.3 (0.3-32.2)                | 0.59 (0.35-1.01)                             | .05     |
| Relapsed ALL                       | 6/32 (18.8)                                   | 18/36 (50.0)                 | 31.2 (10.1-52.5)               | 0.38 (0.17-0.83)                             | .007    |
| Total HSCT                         | 23/210 (11.0)                                 | 36/208 (17.3)                | 6.3 (0.3-13.0)                 | 0.63 (0.39-1.03)                             | .06     |
| Autologous                         | 3/79 (3.8)                                    | 9/78 (11.5)                  | 7.7 (0.51-16.0)                | 0.33 (0.09-1.17)                             | .07     |
| Allogeneic                         | 20/131 (15.3)                                 | 27/130 (20.8)                | 5.5 (3.8-14.8)                 | 0.74 (0.43-1.24)                             | .25     |
| Post hoc Analysis <sup>b</sup>     |                                               |                              |                                |                                              |         |
|                                    | Bacteremia Rate/1000 Patient-Days<br>(95% CI) |                              |                                | Adjusted Rate Ratio<br>(95% CI) <sup>c</sup> |         |
| Total acute leukemia               | 4.9 (3.3-7.3) <sup>c</sup>                    | 9.4 (7.1-12.3) <sup>c</sup>  | 4.3 (1.3-7.4)                  | 0.52 (0.32-0.85)                             | .008    |
| Person-days of<br>observation, No. | 5327                                          | 5973                         |                                |                                              |         |
| Total HSCT                         | 5.3 (3.5-8.0) <sup>c</sup>                    | 10.0 (6.6-14.8) <sup>c</sup> | 5.2 (1.1-9.3)                  | 0.53 (0.32-0.88)                             | .02     |
| Person-days of<br>observation, No. | 4042                                          | 3766                         |                                |                                              |         |

- U.S. RCT of children with acute leukemia or undergoing HCT
- Resistance and *C. difficile* infection less common with prophylaxis!

Con argument #1: We can give antibiotics quickly!



## Con argument #2: There's no mortality benefit!



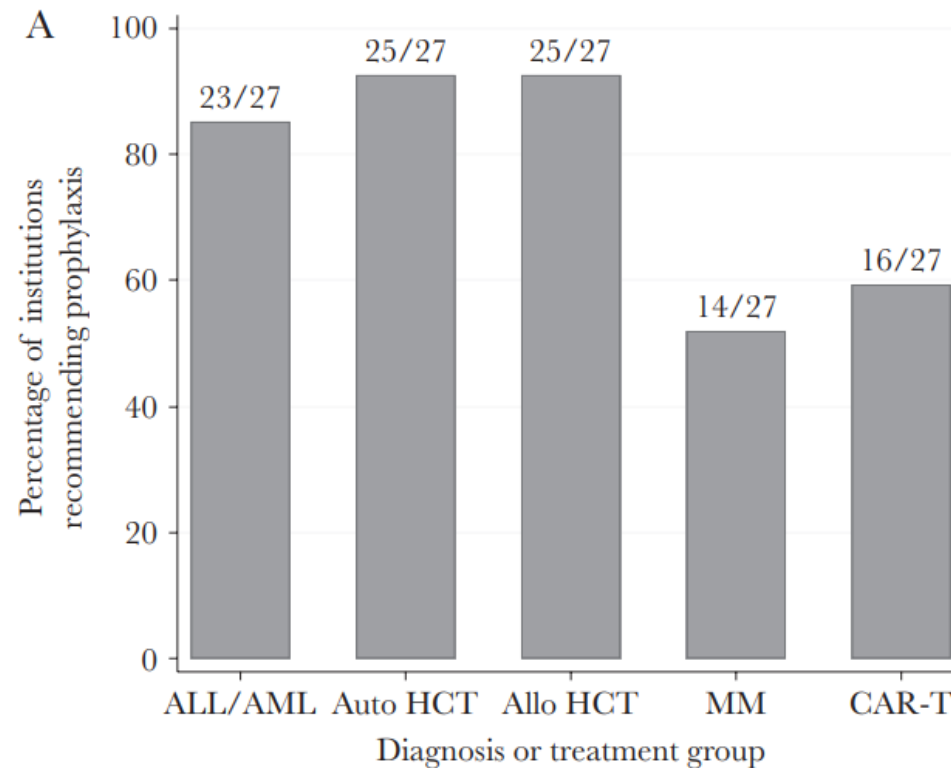
Con argument #3: Resistance! *C. diff*!



Con argument #4: Tendons, aortas, Diet Pepsi!



# Come on, everyone's doing it



- Overwhelming majority of U.S. cancer centers use FQ prophylaxis
- Since when have 9 out of 10 doctors been wrong?

# Points I made

- Infection is a leading cause of death in patients with leukemia and hematopoietic cell transplant recipients (HCT)
- FQ prophylaxis reduces the risk of death relative to no FQ prophylaxis
- Benefits of FQ prophylaxis outweigh risks

# The eagles should have brought the hobbits to Mordor

Or, an argument for FQ prophylaxis

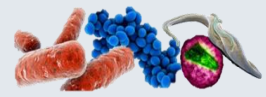
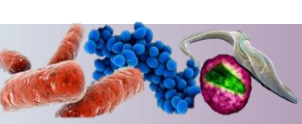
January 25<sup>th</sup>, 2023

Samuel L. Aitken, PharmD, MPH



**CON**  
**Ghady Haidar, M.D.**





# Perspectives on not using FQ prophylaxis in heme malignancy throughout the ages, aka...

*there and back again...*

Ghady Haidar, M.D.

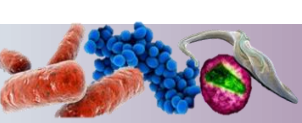
Assistant Professor of Medicine

Transplant Infectious Diseases Program

Director of Research, Heme Malignancy/BMT ID

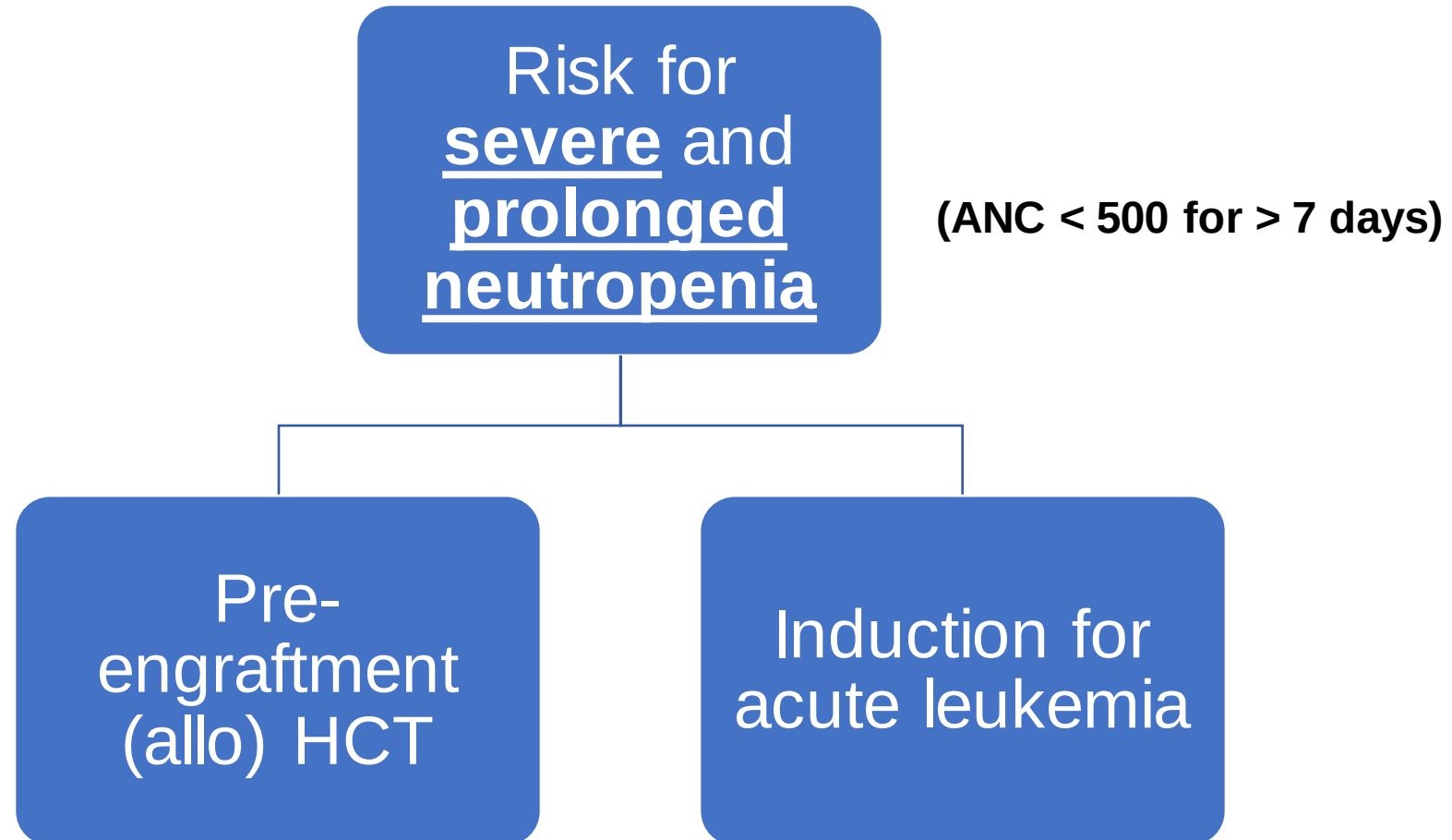
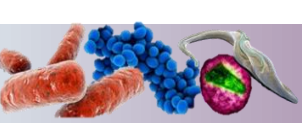
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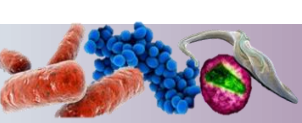




- Theory
- Historical perspectives and old arguments
- Contemporary perspectives
- Unpacking arguments against prophylaxis
- Closing remarks

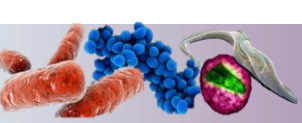






# Two perspectives

| Use FQ prophylaxis                                                                   | Do not use FQ prophylaxis     |
|--------------------------------------------------------------------------------------|-------------------------------|
| Reduce NF                                                                            | Resistance                    |
| Reduce infections                                                                    | Microbiome/aGVHD              |
| Probably reduce mortality (some but not all studies; some but not all meta-analyses) | Side effects                  |
| Drugs are overall safe                                                               | <i>C. difficile</i> infection |

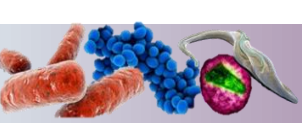


From the Infectious Diseases Society of America

## **Guidelines for the Use of Antimicrobial Agents in Neutropenic Patients with Unexplained Fever**

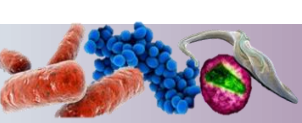
**(1990 - First one ever!)**

For afebrile patients expected to be profoundly neutropenic ( $<100$  cells/ $\mu$ l) for longer than 1 week, consideration should be given to the administration of an antibiotic prophylactically for the prevention of bacterial infections. At present,



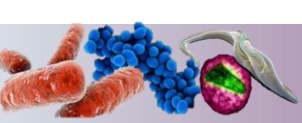
# 1990 – IDSA, themes being discussed

- Adverse effects of prophylaxis vs benefits
- "Preserving anaerobic flora" of GI tract vs "eliminating pathogenic GNR"
- TMP-SMX prophylaxis
- FQ prophylaxis (only 3 studies at the time)



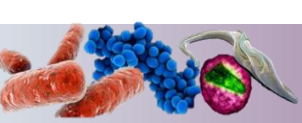
# 1990 – IDSA, TMP-SMX prophylaxis

- > 30 studies of prophylaxis
- **Significantly lowered infection vs placebo** in most cases
- Overall considered **“indicated” for prophylaxis**
- Controversies cited
  - What is the real impact on outcomes?
  - **Longer cytopenias**
  - **?More “fungal colonization,” oral candidiasis**
  - **“Other adverse events”**
  - No activity against *P. aeruginosa*
  - **Resistance**
  - **Cost**



# 1990 – IDSA, FQ prophylaxis

- Only 3 studies at the time
- All showed in a reduction in GNR bacteremia
- Some rise in GPC bacteremia
- No change in mortality
- **Not recommended**

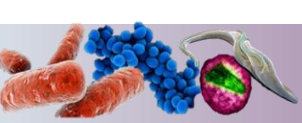


# 1996 – concerns from MSKCC

- Data at the time suggested (Cruciani et al Clin Infect Dis . 1996)
  - FQ prevent GNR bacteremia
  - FQ do not prevent
    - GPC bacteremia
    - Fever-related morbidity
    - Infection-related mortality

The headlong rush to embrace dubious strategies aimed at preventing bacterial infections in the granulocytopenic patient has a long and checkered history. The limitations of fluoroquinolone prophylaxis in the current management of neutropenic patients, together with the specter of the emergence of resistant clinical isolates, should give us pause for thought.

(Editorial comment, Maurice et al. CID 1997)



## GUIDELINES FROM THE INFECTIOUS DISEASES SOCIETY OF AMERICA

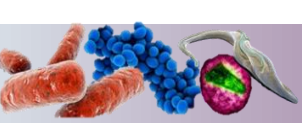
### 1997 Guidelines for the Use of Antimicrobial Agents in Neutropenic Patients with Unexplained Fever

***“Whatever benefit** may come from the administration of necessarily broad-spectrum antibiotics is countered by **deleterious effects** from **toxicity**, emergence of **antibiotic-resistant** bacteria, and **fungal overgrowth**. **Of special concern is the increasing prevalence of antibiotic-resistant bacteria.**”*



# 1997 – IDSA, recommendations

| Drug       | Neutropenic prophylaxis in 1997                  |                                                                                                                                                                          | VS 1990?                |
|------------|--------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
|            | Recommendation                                   | Rationale/notes                                                                                                                                                          |                         |
| TMP-SMX    | <u>“No sound consensus for routine use”</u>      | Mostly related to resistance<br><br><b>Reduces infection, not death</b>                                                                                                  | Not recommended anymore |
| Quinolones | <u>“Not recommended for routine prophylaxis”</u> | Emergence of resistance<br><br><b>Consider</b> for short periods in profound/persistent neutropenia if “ <b>potential for resistance is appreciated and outweighed</b> ” | Some nuance added       |



# 1997 – IDSA, paradox

The Panel's recommendation on routine prophylaxis is in a sense paradoxical. Data that support the efficacy of prophylaxis with TMP-SMZ and the quinolones in reducing the number of infectious episodes during the neutropenic period are adequate and would warrant a rating of (A, I) from the standpoint of efficacy alone. However, the Panel's concern about the problem of emerging drug-resistant bacteria due to extensive antibiotic use, plus the fact that such prophylaxis has not been shown to reduce mortality rates, led to the recommendation that routine prophylaxis with these antibiotics in neutropenic patients be avoided. Physicians should consider these issues in the treatment of individual patients.

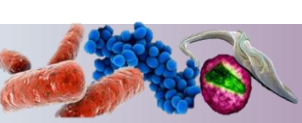
**TMP-SMX, FQ:**  
**Efficacy in**  
**reducing**  
**infections: A1**  
**grade!**

**Reasons why they**  
**chose not to**  
**recommend:**  
**resistance, no**  
**impact on death**



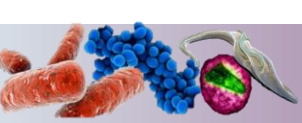
# 2002 – IDSA, recommendations

| Drug       | Neutropenic prophylaxis                                                                              |                                                                                                                                                                                                                                                                           | VS 1997                                                                    |
|------------|------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|
|            | Recommendation                                                                                       | Rationale/notes                                                                                                                                                                                                                                                           |                                                                            |
| TMP-SMX    | <p><b><u>No consensus to recommend for routine use for all afebrile neutropenic patients</u></b></p> | <p><b>Resistance concern</b></p> <p><b>Reduction in fever/infection, but not death established by meta-analyses</b></p>                                                                                                                                                   | <p><b>No change</b></p> <p><b>Same paradox as in 1997 acknowledged</b></p> |
| Quinolones |                                                                                                      | <p><i>“In some special cases, for patients with profound and prolonged neutropenia, a <b><u>quinolone plus penicillin or TMP-SMX</u></b> may be considered for critical periods of time, if the potential for resistant organisms is appreciated and outweighed.”</i></p> |                                                                            |

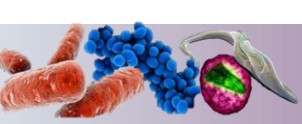


# Data between 2002 – current era

- More experience with quinolones
- Emergence meta-analyses finally showing mortality benefit with FQ prophylaxis (e.g., Gafer-Gvili A, Annals Int Med 2005)
  - Not all meta-analyses have shown this
- Shift in culture/guidelines



- **Do recommend FQ prophylaxis** in pre-engraftment adult HCT recipients
- Fine print
  - Be aware of local epi
  - Be aware of resistance to FQ
  - Be aware of “selection for” ESBL-E
  - Be aware of *C. difficile* infection



# Clinical Practice Guideline for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer: 2010 Update by the Infectious Diseases Society of America

2010 - IDSA

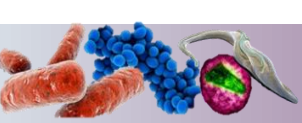
Alison G. Freifeld,<sup>1</sup> Eric J. Bow,<sup>9</sup> Kent A. Sepkowitz,<sup>2</sup> Michael J. Boeckh,<sup>4</sup> James I. Ito,<sup>5</sup> Craig A. Mullen,<sup>3</sup> Issam I. Raad,<sup>6</sup> Kenneth V. Rolston,<sup>6</sup> Jo-Anne H. Young,<sup>7</sup> and John R. Wingard<sup>8</sup>

- ~~TMP-SMX: no longer discussed~~
- Quinolones
  - Acknowledge that prior IDSA, CDC, German, Japanese, and ASBMT guidelines **do not recommend prophylaxis**
  - Acknowledge that **current NCCN and ASBMT guidelines DO recommend prophylaxis** in high risk



# 2010 – IDSA, recommendations

| Drug       | Neutropenic prophylaxis                                                                                   |                                                                                                                                                     | VS 2002                 |
|------------|-----------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
|            | Recommendation                                                                                            | Rationale and notes                                                                                                                                 |                         |
| TMP-SMX    | <u>Not mentioned</u>                                                                                      | NA                                                                                                                                                  | Removed                 |
| Quinolones | Should be considered for high-risk patients with expected durations of prolonged and profound neutropenia | <p>Cipro = levo</p> <p>Levo better if worried about mucositis/VGS</p> <p>No need to add GPC agent too</p> <p>Need to monitor FQ resistance, CDI</p> | <u>Now recommended!</u> |



- Highlight **conflicting mortality data** from meta-analyses
- Highlight **differing quality** of meta-analyses
- Emergence of **FQ-R GNR**
- Emergence of **VGS and other GPC with FQ prophylaxis**
- ***C. difficile* infection**
- Possibility of **increased MDROs → need for carbapenems for NF?**

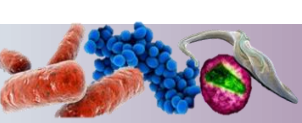
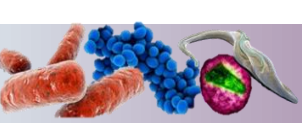


**Table 1** Key practice points – prophylaxis

- There is currently insufficient evidence to recommend routine use of FQ prophylaxis in patients at low risk of developing neutropenic fever (grade C)
- FQ prophylaxis should also not be routinely used in high-risk haematology patients (grade C)
- FQ prophylaxis could be considered in outpatient SCT and palliative patients with bone marrow failure (grade C)
- Appropriate surveillance (detailed within text) should be undertaken by centres using FO prophylaxis (grade C)
- When the prevalence of FQ resistance in *E. coli* in internal medicine patients at an institution approaches 20%, FQ prophylaxis is unlikely to be effective (grade C)

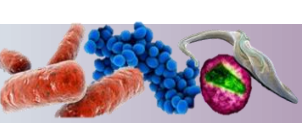
**When is prophy futile?**

SCT, stem cell transplant; FQ, fluoroquinolone.



- **2007:** ECIL recommended prophylaxis, but concerned about resistance
- **2017:** meta-analysis over span of 10 years

| Efficacy                                                                                                                                                                                                                                                | Resistance                                         |                                                                                  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|----------------------------------------------------------------------------------|
| Reduces BSI                                                                                                                                                                                                                                             | Laoprasopwattana et al, Pediatr Infect Dis J 2013: | Increase in colonization <b>with FQ-R Enterobacteriales from 20% to &gt; 80%</b> |
| Reduces NF                                                                                                                                                                                                                                              | Verlinden et al, Eur J Haematol 2014***            | <b>Stopping FQ prophylaxis was safe, less FQ resistance</b>                      |
| <b>Does not reduce mortality in this meta-analysis</b> , though do acknowledge that other meta-analyses have shown a mortality benefit (e.g., <i>Gafer-Gvili et al, Cochrane 2012 that would eventually be cited in the 2018 IDSA/ASCO guidelines</i> ) | Chong et al, PLoS ONE 2014                         | <b>Levofloxacin prophylaxis → no impact on resistance</b>                        |
|                                                                                                                                                                                                                                                         | Increase in FQ-R GNR BSI?                          | 20 studies, <b>3 showed + FQ-R GNR BSI</b> (14 no R, 4 no data)                  |
|                                                                                                                                                                                                                                                         | Increase in other MDRO BSI?                        | 11 studies, <b>4 showed + VRE or ESBL-E</b> (5 no MDRO, 2 no data)               |



## **Clinical and microbiological impact of discontinuation of fluoroquinolone prophylaxis in patients with prolonged profound neutropenia**

Anke Verlinden<sup>1</sup>, Hilde Jansens<sup>2</sup>, Herman Goossens<sup>2</sup>, Ann L. van de Velde<sup>1</sup>, Wilfried A. Schroyens<sup>1</sup>, Zwi N. Berneman<sup>1</sup>, Alain P. Gadisseur<sup>1</sup>

- Center (Belgium) had used FQ for decades
- Started observing FQ resistance
- This is what they did:
  - Stopped prophylaxis
  - Became worried about increased infections
  - Resumed prophylaxis after 8 months
  - Looked at outcomes x 2 years



## Clinical and microbiological impact of discontinuation of fluoroquinolone prophylaxis in patients with prolonged profound neutropenia

Anke Verlinden<sup>1</sup>, Hilde Jansens<sup>2</sup>, Herman Goossens<sup>2</sup>, Ann L. van de Velde<sup>1</sup>, Wilfried A. Schroyens<sup>1</sup>, Zwi N. Berneman<sup>1</sup>, Alain P. Gadisseur<sup>1</sup>

|                   | Prophy era | “Prophy stopped” era        | “Prophy resumed” era        |
|-------------------|------------|-----------------------------|-----------------------------|
| Neutropenic fever | 72%        | 80%                         | 72%                         |
|                   | SIMILAR    |                             |                             |
| Bacteremia        | 33%        | 33%                         | 33%                         |
|                   | SIMILAR    |                             |                             |
| Mortality         | 17%        | 0                           | 3.4%                        |
|                   | More       | Less (better overall care?) | Less (better overall care?) |

**Bottom line: stopping quinolone prophy was safe**



## Clinical and microbiological impact of discontinuation of fluoroquinolone prophylaxis in patients with prolonged profound neutropenia

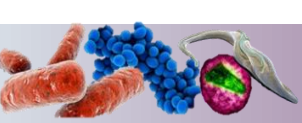
Anke Verlinden<sup>1</sup>, Hilde Jansens<sup>2</sup>, Herman Goossens<sup>2</sup>, Ann L. van de Velde<sup>1</sup>, Wilfried A. Schroyens<sup>1</sup>, Zwi N. Berneman<sup>1</sup>, Alain P. Gadisseur<sup>1</sup>

|                       | Long-standing prophylaxis<br>(n = 51) (%) | Discontinuation of prophylaxis<br>(n = 45) (%) | Reintroduction of prophylaxis<br>(n = 58) (%) | P      |
|-----------------------|-------------------------------------------|------------------------------------------------|-----------------------------------------------|--------|
| Bacteraemia           | 17 (33.3)                                 | 15 (33.3)                                      | 19 (32.8)                                     |        |
| Gram-positive         | 14 (27.5)                                 | 5 (11.1)                                       | 14 (24.1)                                     | 0.123  |
| Gram-negative         | 3 (5.9)                                   | 10 (22.2)                                      | 5 (8.6)                                       | 0.030  |
| Multisusceptible      | 0 (0)                                     | 5 (50)                                         | 0 (0)                                         | 0.063  |
| Quinolone-resistant   | 3 (100)                                   | 1 (10)                                         | 5 (100)                                       | 0.001  |
| Stool inventarisation | 19 (37.3)                                 | 39 (86.7)                                      | 32 (55.2)                                     | ≤0.001 |
| Multisusceptible      | 2 (10.5)                                  | 21 (53.8)                                      | 2 (6.3)                                       | ≤0.001 |
| Quinolone-resistant   | 14 (73.7)                                 | 3 (7.7)                                        | 24 (75)                                       | ≤0.001 |
| ESBL-producing        | 8 (42.1)                                  | 4 (10.3)                                       | 10 (31.2)                                     | 0.016  |

**More GNR BSI without FQ prophy...but more organisms were more S**

**Much less ESBL-E in stool without FQ prophy**

**Bottom line: stopping quinolone prophy → more GNR bacteremia, but less MDRO**



## Clinical and microbiological impact of discontinuation of fluoroquinolone prophylaxis in patients with prolonged profound neutropenia

Anke Verlinden<sup>1</sup>, Hilde Jansens<sup>2</sup>, Herman Goossens<sup>2</sup>, Ann L. van de Velde<sup>1</sup>, Wilfried A. Schroyens<sup>1</sup>, Zwi N. Berneman<sup>1</sup>, Alain P. Gadisseur<sup>1</sup>

In haematological patients at high risk of developing febrile neutropenia (expected profound neutropenia for more than 7 d), no clinically relevant short-term drawbacks were observed when the long-standing policy of routine use of fluoroquinolone prophylaxis was abandoned. No increase in occurrence of neutropenic fever, bacteraemia, severe sepsis or septic shock was observed after the policy change. Fluoroquinolone resistance as well as ESBL-producing isolates disappeared very rapidly after discontinuation and reappeared very quickly after reintroduction of prophylaxis. Analysis of this data has led us to suspend routine fluoroquinolone prophylaxis indefinitely. The local distribution of pathogens and their antimicrobial susceptibilities should always be taken into account when making decisions regarding antimicrobial prophylaxis.

- Nothing bad happened
- Deaths did not increase
- Less resistance

**Stopped FQ prophylaxis forever!**



# Long-term outcomes from same center

- Same center in Belgium, 7 years later

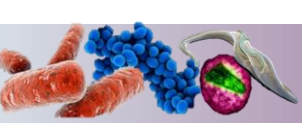
|                             | No prophy (589 pt) | Prophy (80 pt)     |
|-----------------------------|--------------------|--------------------|
| NF                          | 88% <b>(MORE)</b>  | 72% <b>(LESS)</b>  |
| “Sepsis”                    | 10% <b>(LESS)</b>  | 18% <b>(MORE)</b>  |
| FQ-R                        | 9% <b>(LESS)</b>   | 100% <b>(MORE)</b> |
| ESBL-E in stool             | 2% <b>(LESS)</b>   | 100% <b>(MORE)</b> |
| Bacteremia                  | <b>More GNR</b>    | <b>More GPC</b>    |
|                             | <b>SAME</b>        |                    |
| Infection-related mortality | 1.2%               | 2.8%               |
|                             | <b>SAME</b>        |                    |

- No safety signal → continue the same
- ?Less MDRO → less “sepsis”?
- Approach needs to be individualized based on center-specific variables



# 2017 – ECIL insights: downstream MDRO?

| What happened after these 2 centers <u>STARTED</u> FQ prophylaxis? |                                   |
|--------------------------------------------------------------------|-----------------------------------|
| Cumpston et al, Transplant ID 2012                                 | Macesic et al, Transplant ID 2014 |
| Less GNR BSI                                                       | Increase in FQ-R                  |
| More FQ-R GNR                                                      | Increase in ESBL-E                |
| Stable GPC BSI...but increase in VRE BSI                           | Increase in VRE                   |
| No changes in other MDROs                                          | Increase in BSI 2/2 MDRO          |
| No changes in <i>C. difficile</i> infection                        | Less overall bacteremias          |
| No changes in mortality                                            | No changes in mortality           |

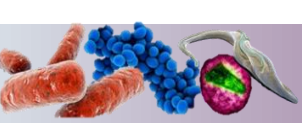


- No sufficient data to recommend reversing prior recommendations for prophylaxis
- Sounded the alarm
  - “Antibiotic pressure has been invariably linked to an increase in bacterial resistance”
  - “The potential benefit of lower rate of BSI is limited, has no evident impact on mortality and, most importantly, was demonstrated only in settings with low or moderate resistance”

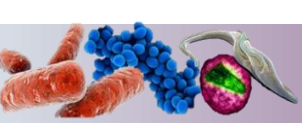


# 2018 – IDSA/ASCO, recommendations

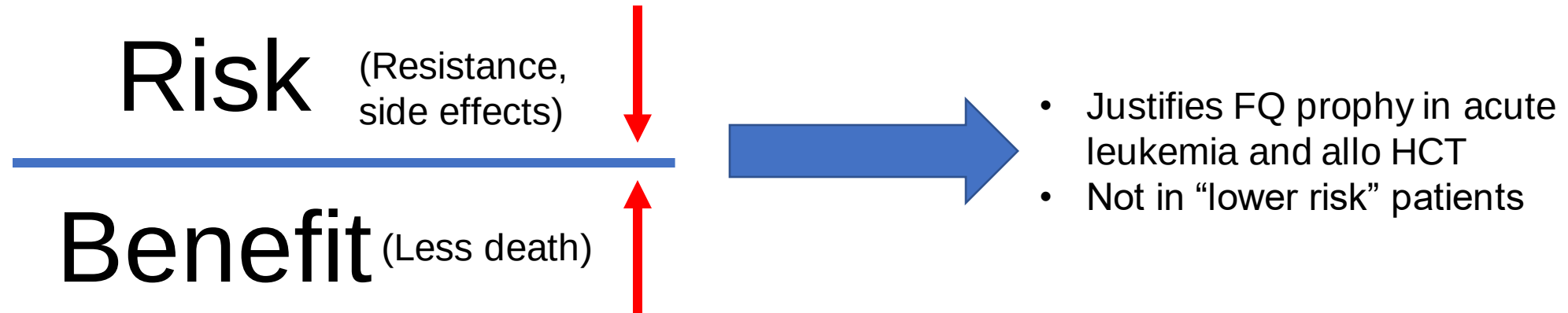
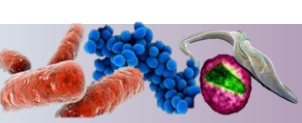
| Drug       | Neutropenic prophylaxis |                                                                                                                                                                                                                                                                    | VS 2010                                                                   |
|------------|-------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|
|            | Recommendation          | Rationale and notes                                                                                                                                                                                                                                                |                                                                           |
| Quinolones | <b>Recommended</b>      | <p><b>Reduction in mortality, febrile episodes, infections (<i>Gafer-Gvili et al, Cochrane 2012</i>)</b></p> <p>Cipro = levo</p> <p>Levo better if worried about mucositis/VGS</p> <p>No need to add GPC agent too</p> <p><b>Need to monitor FQ resistance</b></p> | <p><b><u>Changed from “should be considered” to “recommended”</u></b></p> |



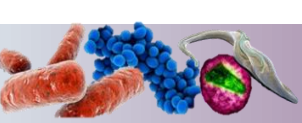
- FQ resistance very much acknowledged
- **< 1% to > 30%** between **1990 – 2009** (Enterobacterales)
- FQ resistance and ESBL phenotype go hand in hand
- No threshold of FQ resistance at which prophylaxis deemed futile
- Possibility of *C. difficile* infection, colonization with VRE
  - More VRE BSI?



- Highlight 2016 FDA warning about FQ
- “Disabling and potentially permanent adverse effects”
  - Tendons
  - Muscles
  - Joints
  - Peripheral nerves
  - CNS



no other treatment options.<sup>48</sup> In the context of this guideline, clinicians should consider the desired fluoroquinolone-driven treatment outcome, the subgroup of neutropenic patients in which the treatment outcome is desired, and these updated warnings.



## Colonization With Levofloxacin-resistant Extended-spectrum $\beta$ -Lactamase-producing Enterobacteriaceae and Risk of Bacteremia in Hematopoietic Stem Cell Transplant Recipients

Michael J. Satlin,<sup>1,a</sup> Kalyan D. Chavda,<sup>2,a</sup> Thomas M. Baker,<sup>1,3</sup> Liang Chen,<sup>2</sup> Elena Shashkina,<sup>2</sup> Rosemary Soave,<sup>1</sup> Catherine B. Small,<sup>1</sup> Samantha E. Jacobs,<sup>1,4</sup> Tsiporah B. Shore,<sup>5</sup> Koen van Besien,<sup>5</sup> Lars F. Westblade,<sup>1,6</sup> Audrey N. Schuetz,<sup>1,6,7</sup> Vance G. Fowler Jr,<sup>8</sup> Stephen G. Jenkins,<sup>1,6</sup> Thomas J. Walsh,<sup>1,9</sup> and Barry N. Kreiswirth<sup>2</sup>

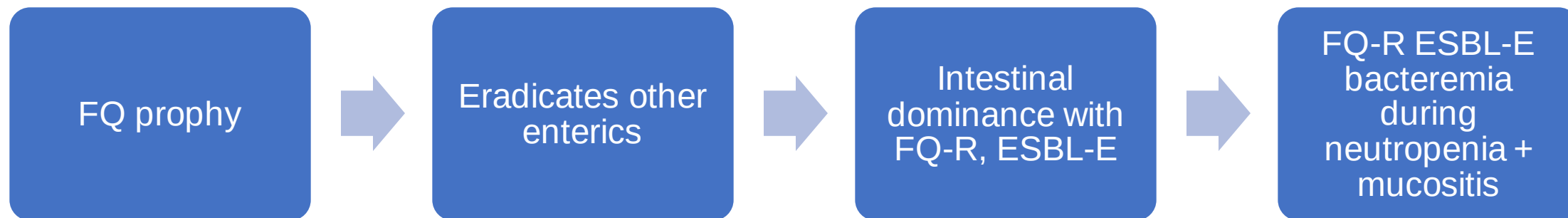
- 312 HCT recipients (allo + auto)
- All receiving levofloxacin prophylaxis
- 10%: perirectal colonization with ESBL-E pre-HCT
  - 25% S to levo
- **30% of ESBL-E-colonized patients → ESBL-E bacteremia; all FQ resistant** (ie there was no invasive disease with FQ-S ESBL-E)

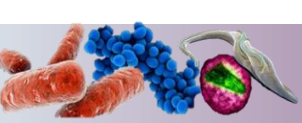


## Colonization With Levofloxacin-resistant Extended-spectrum $\beta$ -Lactamase-producing Enterobacteriaceae and Risk of Bacteremia in Hematopoietic Stem Cell Transplant Recipients

Michael J. Satlin,<sup>1,a</sup> Kalyan D. Chavda,<sup>2,a</sup> Thomas M. Baker,<sup>1,3</sup> Liang Chen,<sup>2</sup> Elena Shashkina,<sup>2</sup> Rosemary Soave,<sup>1</sup> Catherine B. Small,<sup>1</sup> Samantha E. Jacobs,<sup>1,4</sup> Tsiporah B. Shore,<sup>5</sup> Koen van Besien,<sup>5</sup> Lars F. Westblade,<sup>1,6</sup> Audrey N. Schuetz,<sup>1,6,7</sup> Vance G. Fowler Jr,<sup>8</sup> Stephen G. Jenkins,<sup>1,6</sup> Thomas J. Walsh,<sup>1,9</sup> and Barry N. Kreiswirth<sup>2</sup>

- In other words, only patients colonized with FQ-R ESBL-E developed invasive disease
- Authors hypothesized:

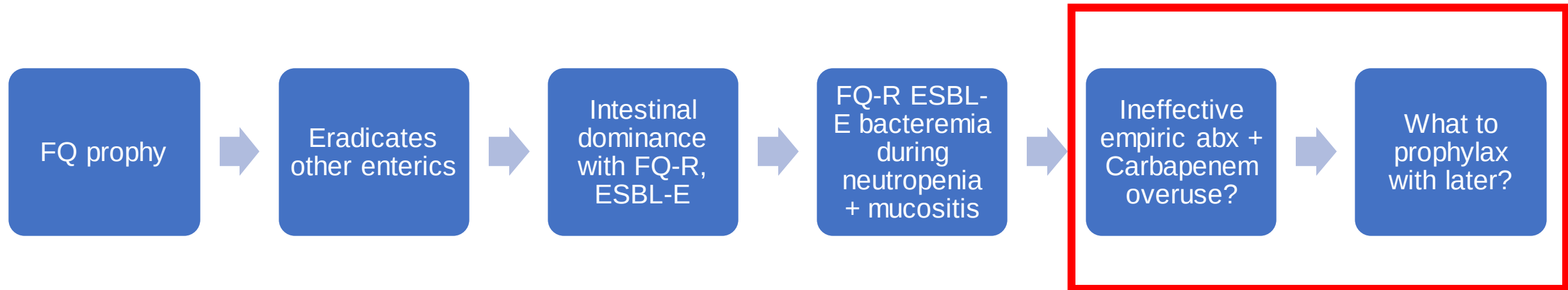


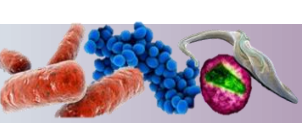


# Hypothetical bad scenario

How common is this really?

Is this really a nightmare scenario, or is it mostly manageable?





# 2019 – FQ and CR *P. aeruginosa*

## Fluoroquinolone Prophylaxis Selects for Meropenem-nonsusceptible *Pseudomonas aeruginosa* in Patients With Hematologic Malignancies and Hematopoietic Cell Transplant Recipients

Morgan Hakki,<sup>1</sup> Romney M. Humphries,<sup>2</sup> Peera Hemarajata,<sup>3</sup> Gregory B. Tallman,<sup>4</sup> Ryan K. Shields,<sup>5</sup> Roberta T. Mettus,<sup>5</sup> Yohei Doi,<sup>5,6</sup> and James S. Lewis II<sup>7</sup>

| All with <i>Pseudomonas</i> bacteremia | FQ prophy (n = 26) | No FQ prophy (n = 29) |
|----------------------------------------|--------------------|-----------------------|
| S to cipro                             | 0                  | 21 (72.4%)            |
| S to meropenem*                        | 4 (15.4)           | 21 (72.4)             |
| S to cefepime, TZP, CAZ                | SAME               |                       |

\*R = porin loss, upregulation of efflux pumps

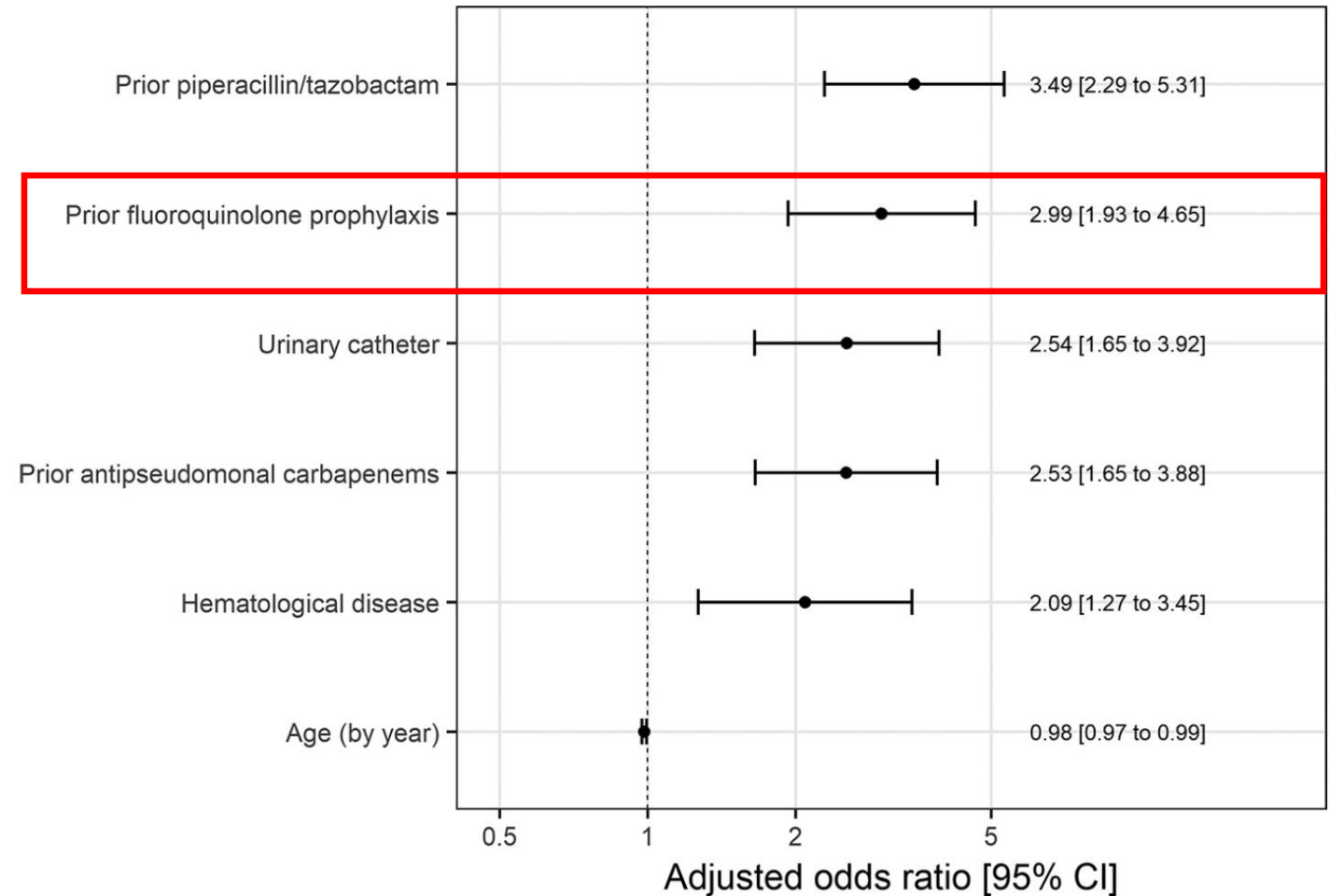


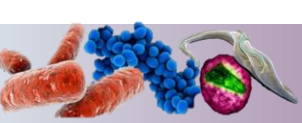
# 2020 – FQ and MDR *P. aeruginosa*

## Clinical Predictive Model of Multidrug Resistance in Neutropenic Cancer Patients with Bloodstream Infection Due to *Pseudomonas aeruginosa*

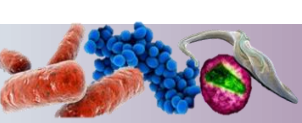
© C. Gudiol,<sup>a,b,nn</sup> A. Albasanz-Puig,<sup>a,nn</sup> J. Laporte-Amargós,<sup>a</sup> N. Pallarès,<sup>c</sup> A. Mussetti,<sup>d</sup> I. Ruiz-Camps,<sup>e,nn</sup> P. Puerta-Alca E. Abdala,<sup>a</sup> C. Oltolini,<sup>b</sup> M. Akova,<sup>f</sup> M. Montejo,<sup>j,nn</sup> M. Mikulska,<sup>k</sup> P. Martín-Dávila,<sup>l,nn</sup> F. Herrera,<sup>m</sup> O. Gasch,<sup>n,nn</sup> L. Drgo H. Paz Morales,<sup>p</sup> A.-S. Brunel,<sup>q</sup> E. García,<sup>r</sup> B. Isler,<sup>s</sup> W. V. Kern,<sup>t</sup> I. Morales,<sup>u,nn</sup> G. Maestro-de la Calle,<sup>v</sup> M. Montero,<sup>w,nn</sup> S. S. Kanj,<sup>x</sup> O. R. Sipahi,<sup>y</sup> S. Calik,<sup>z</sup> I. Márquez-Gómez,<sup>aa</sup> J. I. Marin,<sup>bb,cc</sup> © M. Z. R. Gomes,<sup>dd</sup> P. Hemmatti,<sup>ee</sup> R. Araos,<sup>ff,g</sup> M. Peghin,<sup>hh</sup> J. L. del Pozo,<sup>ii</sup> L. Yáñez,<sup>jj</sup> R. Tilley,<sup>kk</sup> A. Manzur,<sup>ll</sup> A. Novo,<sup>mm</sup> J. Carratalà,<sup>a,nn</sup> for the IRONIC Study Group

- >1000 patients, 12 centers
- **Use of FQ prophylaxis independently associated with future MDR *P. aeruginosa* bacteremia**



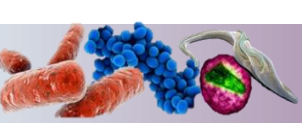


- FQ prophylaxis during neutropenia reduces Enterobacterales BSI in adults undergoing HCT
- **Resistance is a concern, but how much resistance do you need to have before FQ become ineffective?**
- **Also acknowledge risk of ESBL-E selection with FQ use**



# What about *C. difficile* infection?

**Concerns repeated in the literature...but conclusive data in this population are lacking, and studies specifically looking at this in leuk/HCT are lacking**



# What about *C. difficile* infection?

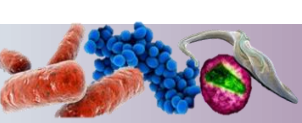
Open Forum Infectious Diseases

MAJOR ARTICLE



## Incidence Rates and Risk Factors of *Clostridioides difficile* Infection in Solid Organ and Hematopoietic Stem Cell Transplant Recipients

- 573 allo HCT in Denmark
- 20% developed CDI
- Myeloablative regimens only risk; **no effect of FQ**



# What about *C. difficile* infection?

Clinical Infectious Diseases

MAJOR ARTICLE



## Levofloxacin Prophylaxis During Induction Therapy for Pediatric Acute Lymphoblastic Leukemia

Joshua Wolf,<sup>1,2,3</sup> Li Tang,<sup>4</sup> Patricia M. Flynn,<sup>1,2</sup> Ching-Hon Pui,<sup>2,5,6</sup> Aditya H. Gaur,<sup>1,2</sup> Yilun Sun,<sup>4</sup> Hiroto Inaba,<sup>2,5</sup> Tracy Stewart,<sup>1</sup> Randall T. Hayden,<sup>6</sup> Hana Hakim,<sup>1</sup> and Sima Jeha<sup>2,5</sup>

| No prophy           | Levo prophy | Other prophy                                          |
|---------------------|-------------|-------------------------------------------------------|
| N = 173             |             | N = 102                                               |
| Shorter neutropenia |             | [Cefepime*, cipro, vanc + cipro, vanc + cefepime (?)] |

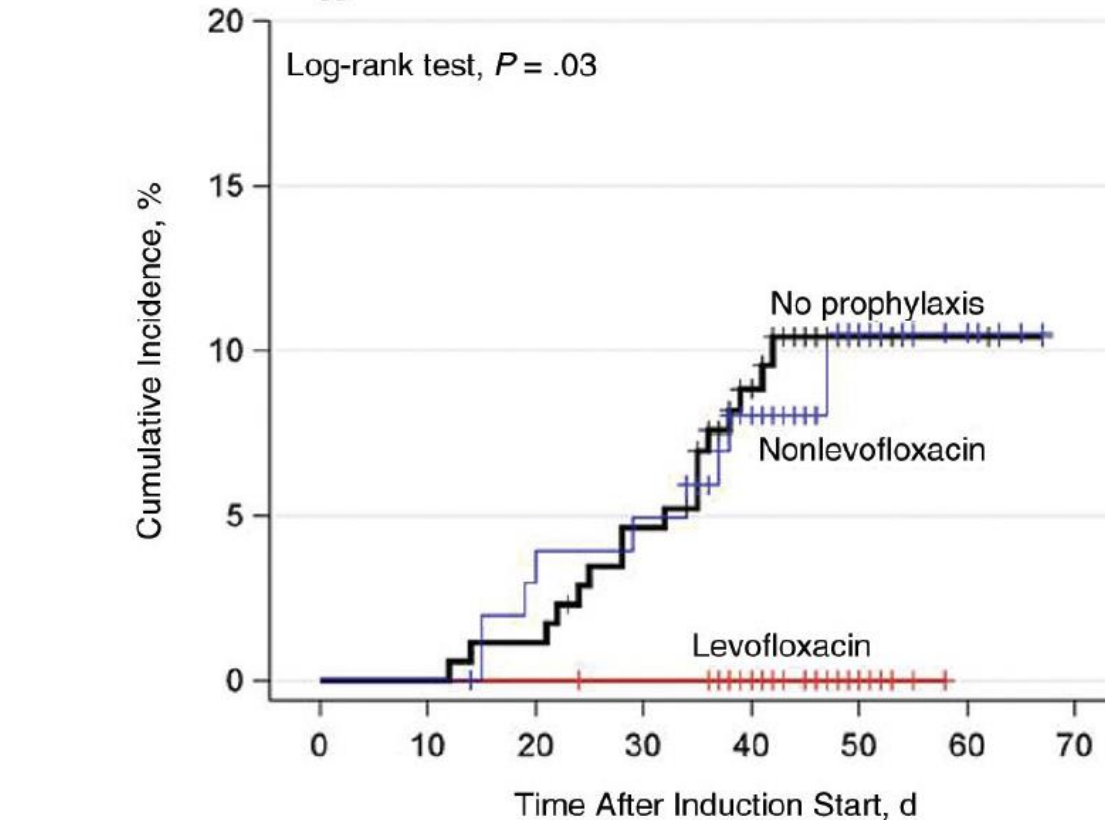
\*actually, cefepime prophy was associated with a higher rate of CDI

Maybe CDI risk was reduced by reducing the need for other abx?



# What about *C. difficile* infection?

## A *Clostridium difficile* infection



*C. difficile* infection vs regimen

| No. at risk     | 0   | 10  | 20  | 30  | 40  | 50 | 60 | 70 |
|-----------------|-----|-----|-----|-----|-----|----|----|----|
| Levofloxacin    | 69  | 69  | 69  | 68  | 57  | 9  | 0  |    |
| No prophylaxis  | 173 | 173 | 171 | 164 | 137 | 22 | 3  | 0  |
| Nonlevofloxacin | 102 | 102 | 98  | 96  | 83  | 25 | 5  | 0  |

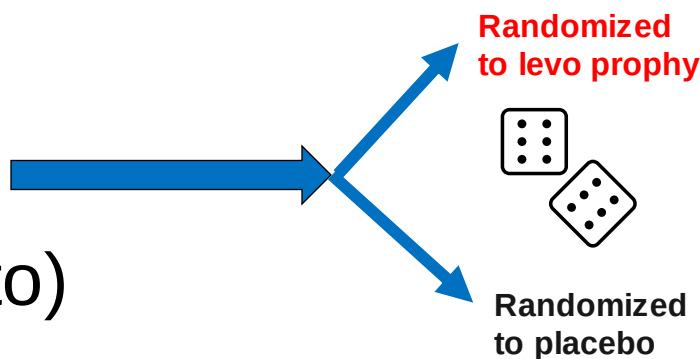


# What about *C. difficile* infection?

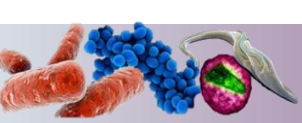
JAMA | Original Investigation

## Effect of Levofloxacin Prophylaxis on Bacteremia in Children With Acute Leukemia or Undergoing Hematopoietic Stem Cell Transplantation A Randomized Clinical Trial

- Children
- 200 acute leuk
- 424 HCT (allo > auto)



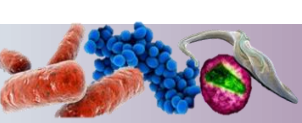
- Leuk: less bacteremia
- HCT: same bacteremia
- **Same rate of CDI**
- **Same rate of musculoskeletal adverse events**



## Intestinal Domination and the Risk of Bacteremia in Patients Undergoing Allogeneic Hematopoietic Stem Cell Transplantation

Ying Taur,<sup>1,2</sup> Joao B. Xavier,<sup>2,3</sup> Lauren Lipuma,<sup>2</sup> Carles Ubeda,<sup>5</sup> Jenna Goldberg,<sup>4</sup> Asia Gobourne,<sup>2</sup> Yeon Joo Lee,<sup>1</sup> Krista A. Dubin,<sup>2</sup> Nicholas D. Socci,<sup>3</sup> Agnes Viale,<sup>6</sup> Miguel-Angel Perales,<sup>4</sup> Robert R. Jenq,<sup>4</sup> Marcel R. M. van den Brink,<sup>4,5</sup> and Eric G. Pamer<sup>1,2,5</sup>

- Marked shifts in gut bacterial populations following allo-HCT
- Metronidazole → VRE dominance (3x) → more VRE BSI
- **FQ → 10X reduction in Proteobacteria (ie Enterobacterales)**
- **So FQ reduce GNR BSI by affecting the microbiome...but are there actually any downstream consequences of this?**



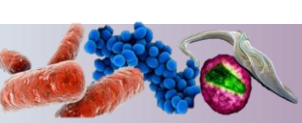
## Omitting Ciprofloxacin Prophylaxis in Patients Undergoing Allogeneic Hematopoietic Stem Cell Transplantation and Its Impact on Clinical Outcomes and Microbiome Structure

Haneen Daoud-Asfour <sup>1</sup>, Israel Henig <sup>2</sup>, Itai Ghersin <sup>3</sup>, Stav Rakedzon <sup>4</sup>, Anat Stern <sup>5</sup>, Milena Pitashny <sup>3</sup>, Tsila Zuckerman <sup>2, 6</sup>, Haggai Bar-Yoseph <sup>3, 6</sup> ✉

**Very limited studies looking at this**



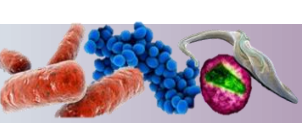
- Pre/post analysis of allo-HCT recipients before and after stopping cipro prophylaxis
- ***“Omitting prophylactic ciprofloxacin during allo-HSCT did not affect microbiome composition, lower GI-GVHD rate, or other significant clinical outcomes”***



## FDA Drug Safety Podcast: FDA updates warnings for oral and injectable fluoroquinolone antibiotics due to disabling side effects



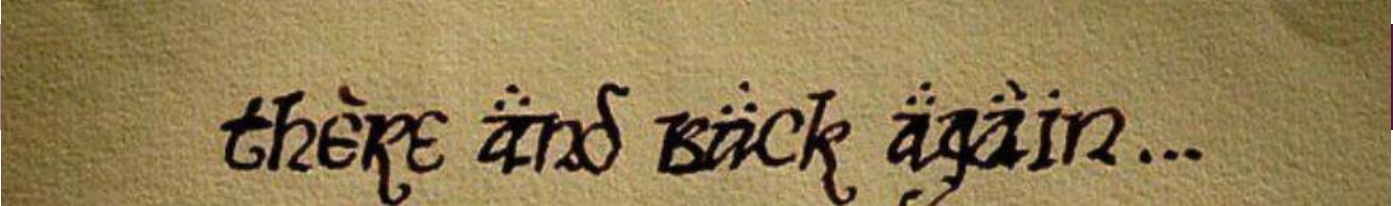
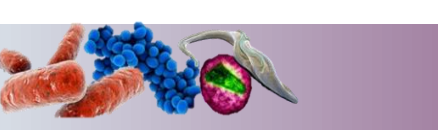
- Very few studies specifically address this in mal heme
- Existing studies: **no safety signal**
  - Karol et al, Cancer Med. 2020: **no neuropathy**
  - Gardner et al, TCT 2021: **no cardiac/QTc issues (also no increased CDI or aGVHD risk)**
  - Alexander et al, JAMA 2018: **no tendon issues**



# There and back again...

| Use FQ prophylaxis                                                                   | Do not use FQ prophylaxis     |
|--------------------------------------------------------------------------------------|-------------------------------|
| Reduce NF                                                                            | Resistance                    |
| Reduce infections                                                                    | Microbiome/aGVHD              |
| Probably reduce mortality (some but not all studies; some but not all meta-analyses) | Side effects                  |
| Drugs are overall safe                                                               | <i>C. difficile</i> infection |

Most of these are “talking points”  
Repeated over the decades  
Not supported by data



- Arguments for/against prophylaxis started with concerns of AMR with prophylaxis in the 90s
- Prophylaxis widely accepted now
- 30+ years later...some of the concerns about resistance are coming true, maybe
- Rest of concerns not really supported by the literature

| Use FQ prophylaxis                                                                   | Do not use FQ prophylaxis                                                                                                                        | Final assessment                                     |
|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------|
| Reduce NF                                                                            | <b>Resistance (ESBL-E, VRE, MDR <i>Pseudomonas</i>; more so than just FQ-R GNR)</b>                                                              | <b>Valid concern</b>                                 |
| Reduce infections                                                                    | Microbiome and aGVHD risk...too many unknowns                                                                                                    | ? (data do not support)                              |
| Probably reduce mortality (some but not all studies; some but not all meta-analyses) | Side effects: FDA warnings noted, but no safety signals in studies of mal heme                                                                   | Not supported by data                                |
| Drugs are overall safe                                                               | <i>C. difficile</i> infection: data do not appear to higher than "background"                                                                    | Risk is probably there, just not worse than expected |
|                                                                                      | Ultimately, prophylaxis is safe, but if you choose not to prophylaxis, there are data showing that this is safe and that your patients won't die |                                                      |

# Additional CE Information

- Learners can claim credit for today's live CE activity by completing a MAD-ID evaluation before February 25, 2023
- You will receive an email tomorrow from [IDInsights@idcteamed.com](mailto:IDInsights@idcteamed.com) that provides a link to the required MAD-ID CE evaluation
- Future learners can claim CE credit by watching the recorded webinar and completing an enduring event MAD-ID CE evaluation. Both will be available on ID Connect's website under News & Resources starting 1/26/23

**Thank you!**

**We will now begin  
moderated Q&A**



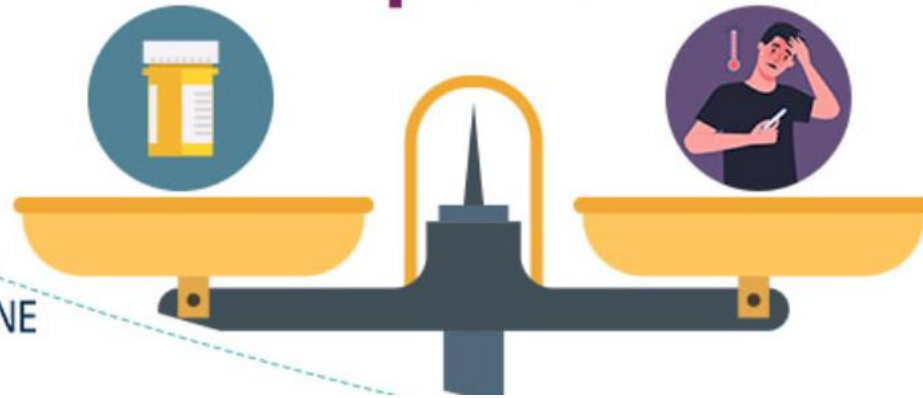
# A Pro/Con Debate on Fluoroquinolone Prophylaxis for Neutropenic Fever

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