Some Important ID Publications With Implications for Clinical Management – 2023 (so far)

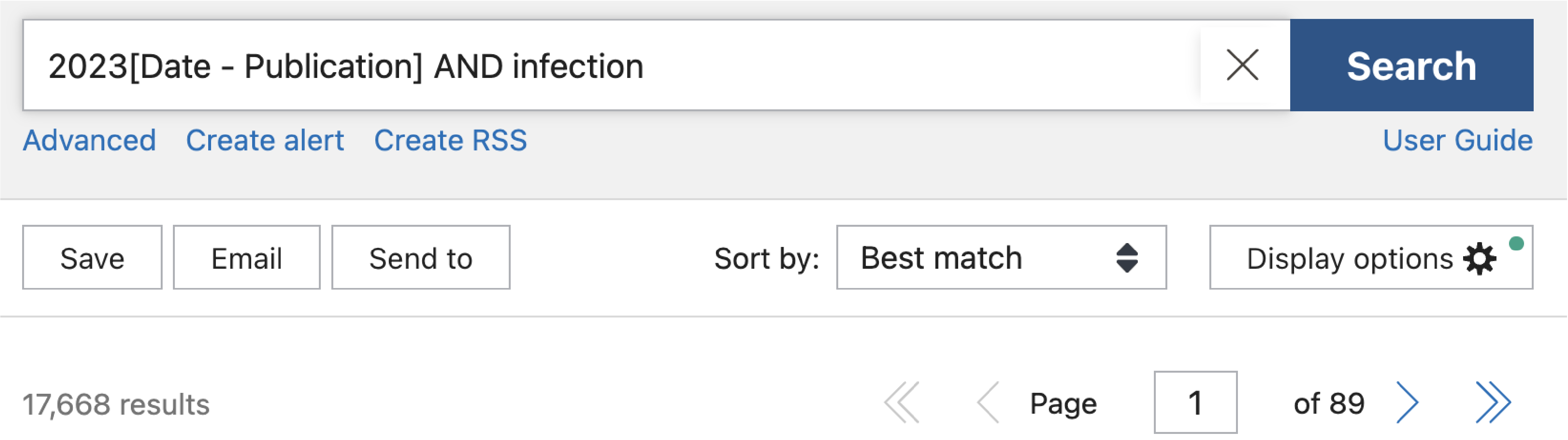
Stan Deresinski

Stanford University

4 November 2023

Papers with “Infection” in the title published in 2023 as of 11 AM on Friday, November 3

N = 17,668



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Inhaled Amikacin to Prevent Ventilator-Associated Pneumonia

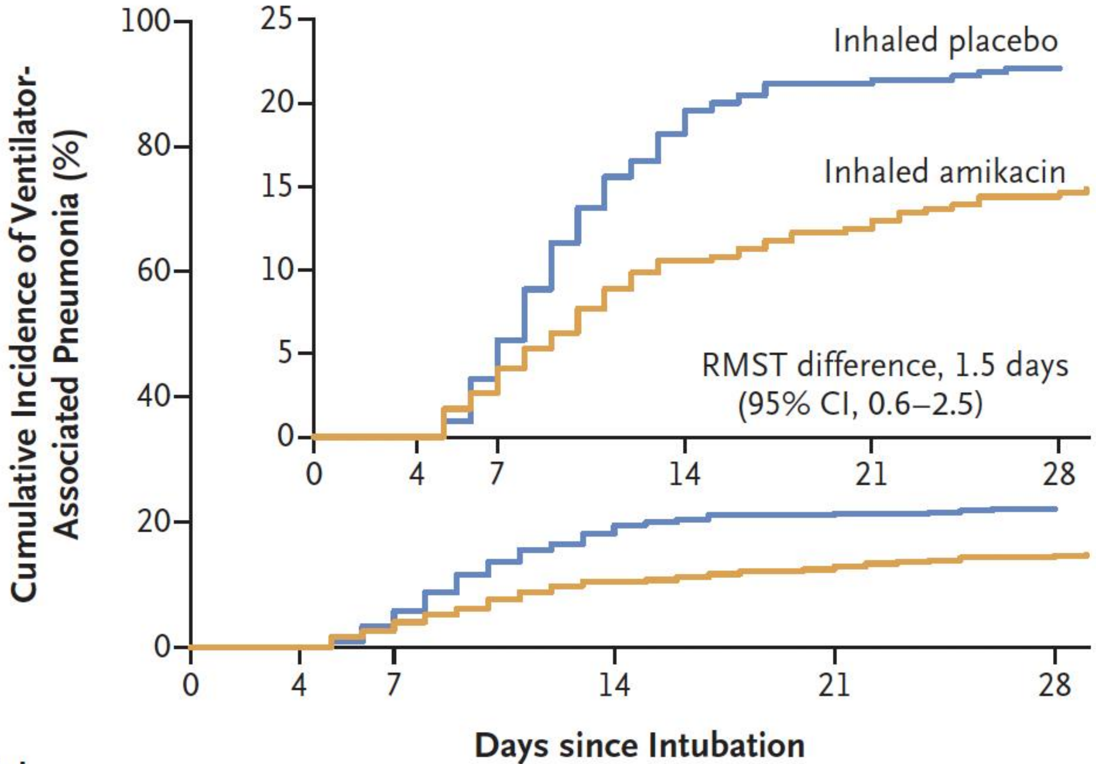
October 25, 2023
DOI: 10.1056/NEJMoa2310307

Inhaled Amikacin to Prevent VAP

- Randomized, double-blind, placebo-controlled superiority trial – 19 French ICUs
- MV for 72-96 hours
- Exclusions:
  - Suspected or confirmed VAP, RRT, GFR<30, trach tube, imminent extubation, systemic aminoglycoside
- Randomized (stratified by center & systemic antibiotics) to 20 mg/kg amikacin or equivalent volume NS - each daily for 3 consecutive days
- Primary outcome: 1st episode VAP to day 28
  - Blinded adjudication: VAP = positive quantitative culture plus $\geq$2 of hyperleukocytosis, leukopenia, fever, purulent secretions with new infiltrate
- 850 patients needed for 80% power with 2-sided alpha = 0.05 with estimated outcomes of 6% & 12%

DOI: 10.1056/NEJMoa2310307

Inhaled Amikacin to Prevent VAP



No. at Risk	0	4	7	14	21	28
Inhaled placebo		430	288	85	40	18
Inhaled amikacin		420	269	120	60	28
No. of Deaths						
Inhaled placebo		0	21	65	85	106
Inhaled amikacin		0	20	47	78	92

DOI: 10.1056/NEJMoa2310307

<u>VAP</u>

Amikacin N = 62 (15%)

Placebo N=95 (22%)

Difference in RMST:

1.5 days (95% CI 0.6t o 2.5; P=0.004)

<u>In-Hospital Deaths</u>

Amikacin 123 (29%).

Placebo 136 (32%)

HR 0.91 (0.71 to 1.16)

Beta-Lactam -Prolonged Infusion
Official Recommendations

Surviving Sepsis – 2021

For adults with sepsis or septic shock, we suggest using prolonged infusion of beta-lactams for maintenance (after an initial bolus) over conventional bolus infusion.

Critical Care Medicine 49(11):p e1063-e1143, November2021. | *DOI:* 10.1097/CCM.0000000000005337

Beta-Lactam -Prolonged Infusion Official Recommendations

International consensus recommendations for the use of prolonged-infusion beta-lactam antibiotics -2023
(Endorsed by 7 organizations, including IDSA, SIDP, ESCMID)

We suggest PI β-lactam antibiotics over SI to reduce mortality or increase clinical cure among severely ill adult patients, particularly those with gram-negative infections.

Conditional recommendation; very low certainty of evidence. (Panel vote 17–0 in favor of this recommendation)

Pharmacotherapy 2023 Aug;43(8):736-739. doi: 10.1002/phar.2844

Prolonged/Continuous Beta-Lactam Infusions Systematic Reviews/Metanalyses

- Vardakas et al (1)
  - 22 randomized trials
  - 1876 subjects with sepsis
  - Anti-pseudomonal BLs
  - Primary endpoint: all-cause mortality
  - Prolonged ($\geq$3h) or continuous infusion Vs short ($\leq$1h)- risk ratio: 0.70 (95% CI, 0.56 – 0.87)
- Rhodes et al (2)
  - 18 studies: 9 prospective, 9 retrospective, randomized
    - 8 critically ill with sepsis, severe sepsis, septic shock; 3 HAP or VAP
  - 3401 subjects
  - Piperacillin-tazobactam
  - Primary endpoint: all-cause mortality
  - Prolonged (3-4 h) or continuous infusion Vs 0.5 h – risk ratio: 0.69 (95% CI, 0.56 -0.84)

1. Lancet Infect Dis. 2018;18(1):108-120. doi:10.1016/S1473-3099(17)30615-1

2. Crit Care Med. 2018;46(2):236-243. doi:10.1097/CCM.0000000000002836

June 16, 2023

Continuous vs Intermittent Meropenem Administration in Critically Ill Patients With Sepsis

The MERCY Randomized Clinical Trial

Giacomo Monti, MD[1,2]; Nikola Bradić, MD[3,4]; Matteo Marzaroli, MD[1]; et al

Author Affiliations | Article Information

JAMA. 2023;330(2):141-151. doi:10.1001/jama.2023.10598

MERCY: Meropenem CI Vs Intermittent

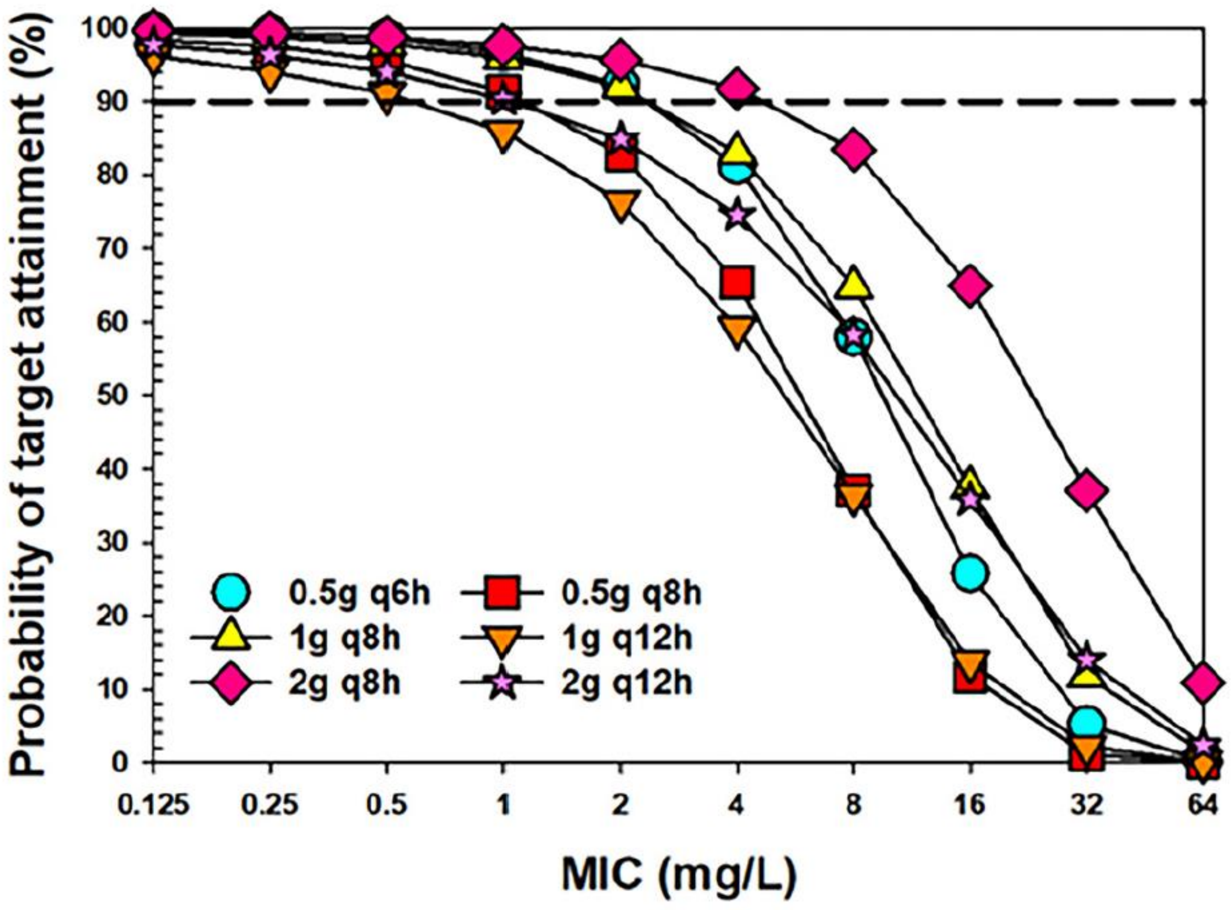
- Critically ill (N = 607) with sepsis/septic shock who had been prescribed meropenem
- Excluded severe immunosuppression (eg, AIDS, etc)
- Randomized, double-blind; N=607
  - 1 gram loading dose, then either
    - 3 grams CI over 24 hours OR
    - 1 gram every 8 hours each over 30—60 minutes
- Primary outcome: composite of all-cause mortality & emergence of pan- or XDR-resistance
- $\geq$80% power to detect 12% absolute risk reduction with alpha = 0.05

JAMA 2023; 330:141-151.

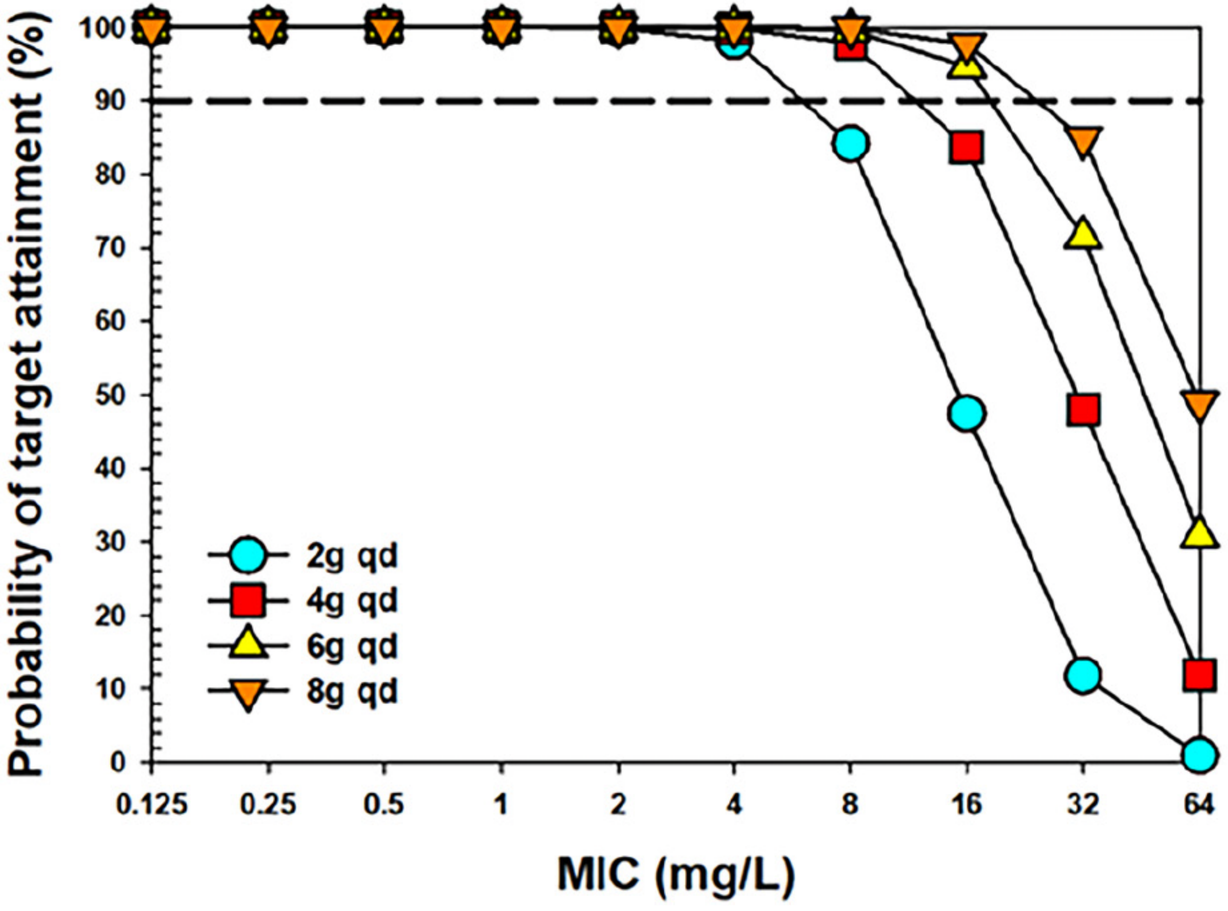
Meropenem PK/PD Target Attainment

Target: 100% $f\mathrm{T}_{>\mathrm{MIC}}$

Intermittent infusion (30-minute infusion)



Continuous infusion (24-hour infusion)



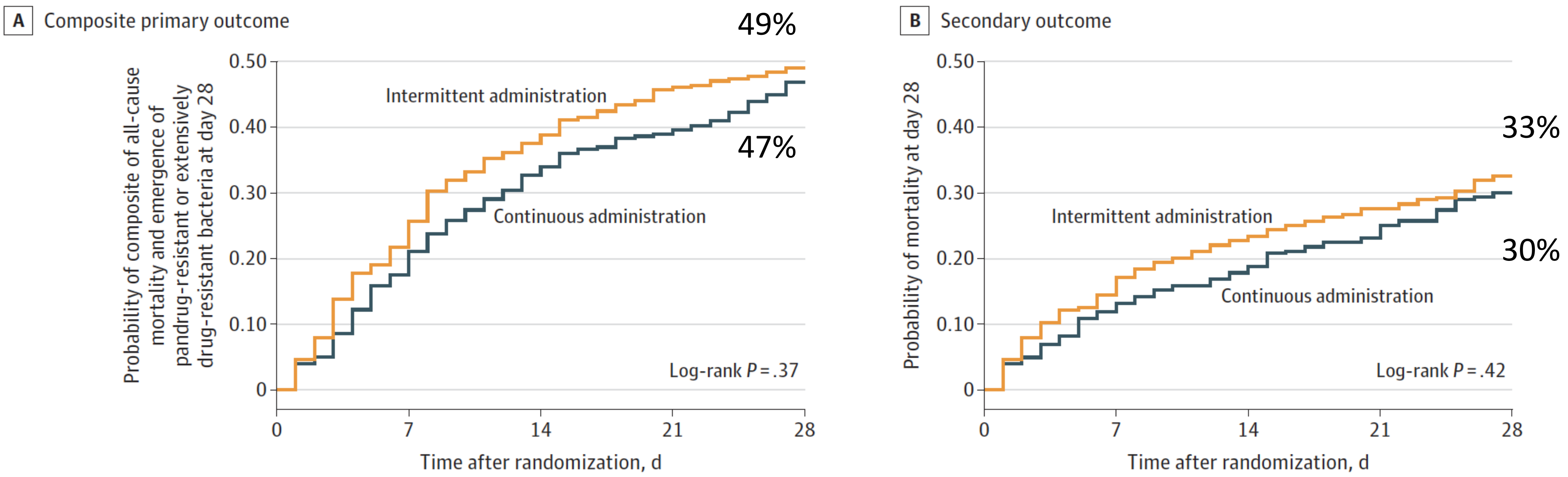
EUCAST ≤2/>8

CLSI ≤1/2/≥4 Target of 100% $f\mathrm{T}_{>\mathrm{MIC}}$

AAC 2023; 67:7-13

MERCY: Meropenem CI Vs Intermittent

Figure 2. Kaplan-Meier Analysis for the Composite Primary Outcome and the Secondary Outcome of Probability of Mortality at Day 28



No. at risk										
Continuous administration	303	250	204	185	161	303	267	249	233	212
Intermittent administration	304	238	190	165	155	304	260	235	220	205

RR 0.96, 95% CI 0.81 TO 1.13; P=0.60

RR 0.92, 95% CI 0.73 to 1.17; P=0.50

Potential issues: Not all GNR (77.9%), Only 10% had BSI, Concurrent antibiotics in three-fourths

JAMA 2023; 330:141-151.

BLING III

ACTIVE, NOT RECRUITING

Beta-Lactam InfusioN Group Study (BLING III)

ClinicalTrials.gov ID NCT03213990

Sponsor The George Institute

Information provided by The George Institute (Responsible Party)

Last Update Posted 2023-01-25

A Phase III Randomised Controlled Trial of Continuous Beta-lactam Infusion Compared With Intermittent Beta-lactam Dosing in Critically Ill Patients

- Piperacillin OR meropenem
- Primary endpoint – all-cause mortality
- Planned enrollment: 7000 patients (70 ICUs worldwide; 35 Australia, New Zealand

Actual enrollment as of 1 January 2023: 7203

Artificial Intelligence & Infectious Diseases

Leveraging Artificial Intelligence in the Fight against Infectious Diseases.

- Major challenges in AI ID:
- Pathogen outbreaks & pandemics
- Antimicrobial resistance & anti-infective drug discovery
- Neglected, persistent & difficult to treat infection

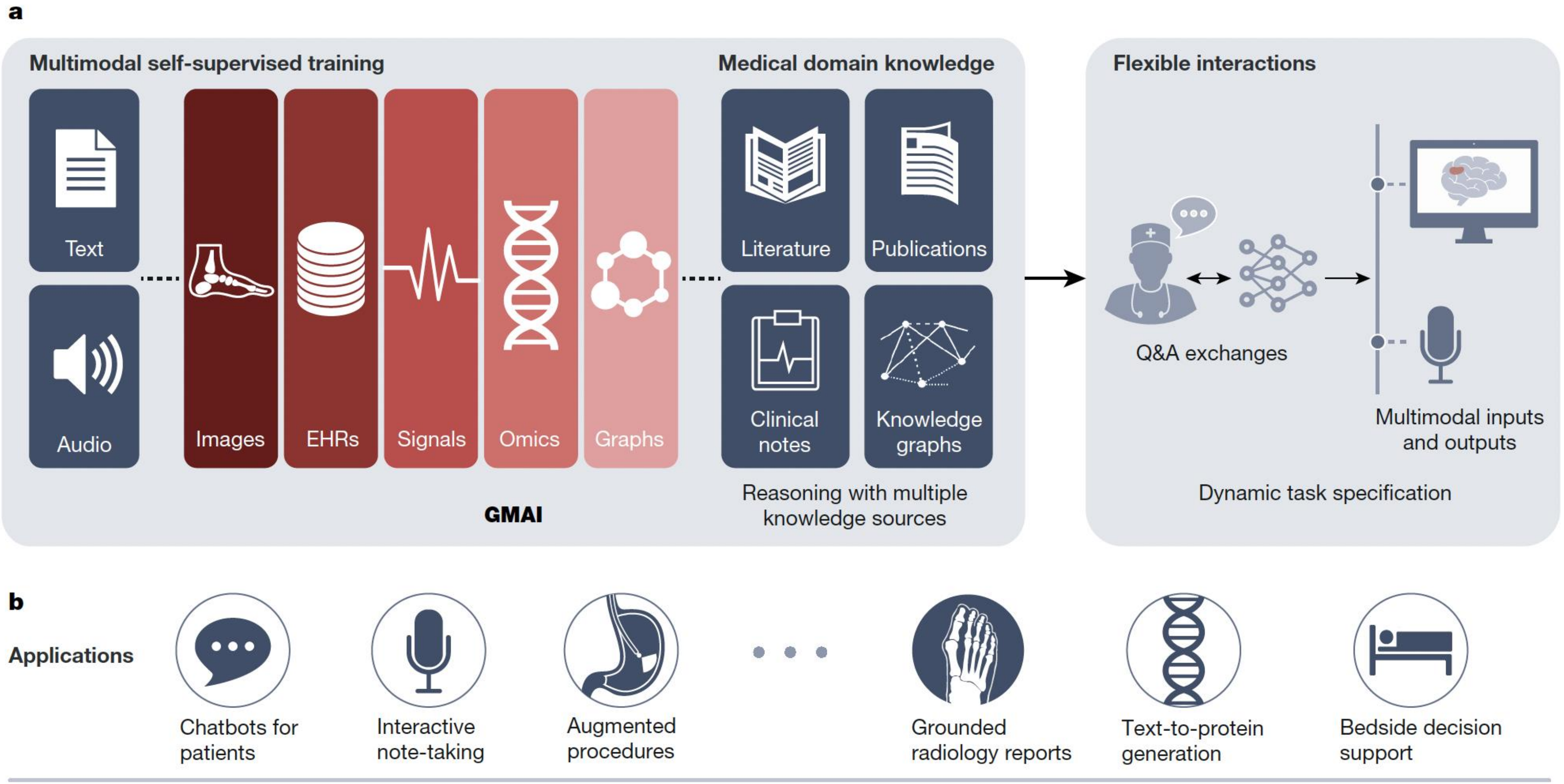
Science 381, 164–170 (2023) 14 July 2023

Advances in Artificial Intelligence for Infectious Disease Surveillance

- Early Warning
  - Outbreaks - natural language processing of news (eg HealthMap)
  - Novel infections - machine learning and social media
- Pathogen classification, type, AMR
- Source ID – eg EMR mining, WGS
- Risk Assessment

NEJM 388;17 April 27, 2023

Foundation Models for Generalist Medical Artificial Intelligence



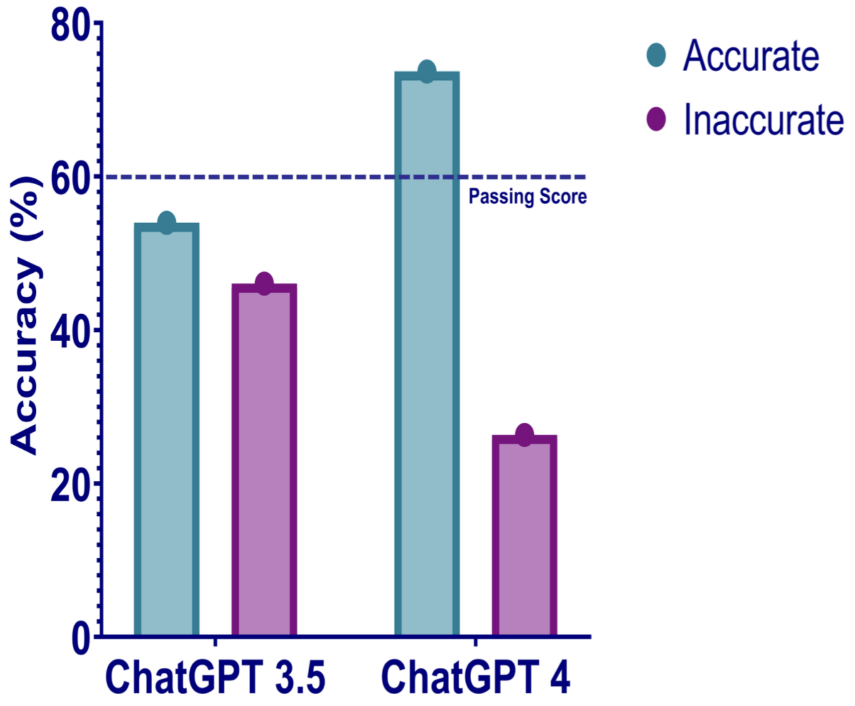
Some ChatBots: Claude, ChatGPT, GPT-4, Bard

Nature | *Vol 616* | *13 April 2023* | *259*

(GPT = Generative Pre-trained Transformer)

ChatGPT Performance in the Brazilian Infectious Disease Specialty Examination

Results



ChatGPT-3.5 accuracy = 53.95%

ChatGPT-4 accuracy = 73.68%

"Although ChatGPT-4 surpassed the passing score on the multiple-choice test, its 26.32% error rate limits its current clinical use, as patient care information must be reliable."

IDWeek 2023 Abstract 102

IDSA Infectious Diseases Society of America
hivma hiv medicine association
OXFORD

Clinical Infectious Diseases

MAJOR ARTICLE

Can Chatbot artificial intelligence replace infectious disease physicians in the management of bloodstream infections? A prospective cohort study.

Queried Chat GPT-4 for diagnosis, management plans for 44 consecutive patients with first positive blood cultures

Conclusion:

> "The management plans of ChatGPT-4 for a first positive blood-culture episode were considered **optimal in 2%, satisfactory in 39%, and harmful in 16% of cases**: its use without consultant input remains hazardous in this setting."

Clin Infect Dis. 2023 Oct 12:ciad632. doi: 10.1093/cid/ciad632

THE LANCET
Infectious Diseases

CORRESPONDENCE | VOLUME 23, ISSUE 4, P405-406, APRIL 2023

ChatGPT and antimicrobial advice: the end of the consulting infection doctor?

Alex Howard • William Hope • Alessandro Gerada

Published: February 20, 2023 • DOI: https://doi.org/10.1016/S1473-3099(23)00113-5

2022: Methylprednisolone Severe CAP

- Randomized, double blind, placebo controlled
- Severe CAP – ICU; N = 584 - 96% male (VA study)
- Placebo vs. methylprednisolone 40 mg bolus then 40 mg/day thru day 7 with taper – total duration 20 days
- Primary outcome: 60 d mortality
  - Methylprednisolone: 47/286 16% (95% CI,)
  - Placebo: 50/277 18% (95% CI,)
  - Absolute Diff (unadjusted): -2% (95% CI, -8% to 5%); P=0.6

Study stopped due to poor enrollment; 1406 needed to have 86% power to achieve 7% difference in mortality.

Intensive Care Med 48, 1009–1023 (2022). https://doi.org/10.1007/s00134-022-06684-3

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 25, 2023 VOL. 388 NO. 21

Hydrocortisone in Severe Community-Acquired Pneumonia

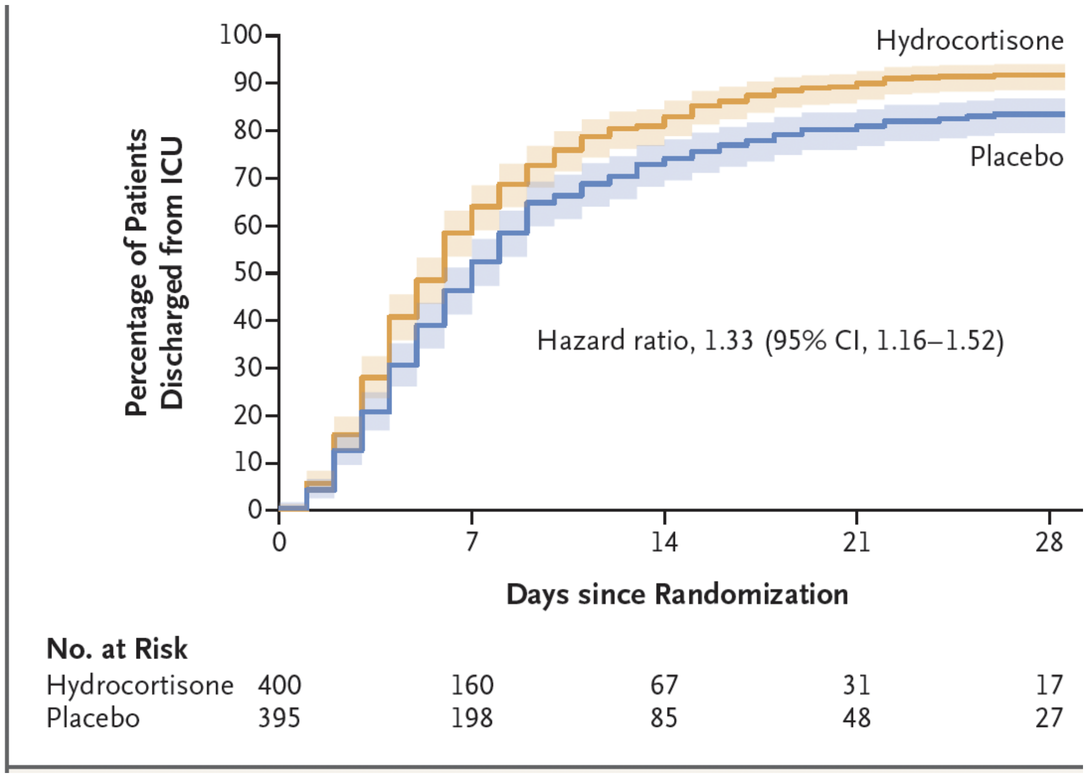
Hydrocortisone in Severe CAP

- Randomized, double blind, placebo controlled in French ICUs
- October 28, 2015 – March 11, 2020
- Severe CAP requiring ICU care; N = 795
- Placebo vs. hydrocortisone 200 mg IV/d for 8-14 d (depending on predefined criteria) with taper
- Primary outcome: 28 d mortality
  - Hydrocortisone: 25/400 **6.2%** (95% CI, 3.9 – 8.6)
  - Placebo: 47/395 **11.9%** (95% CI, 8.7 – 15.1)
  - Absolute Diff: -5.6% (95% CI, -9.6 to -1.7) **P=0.0006**

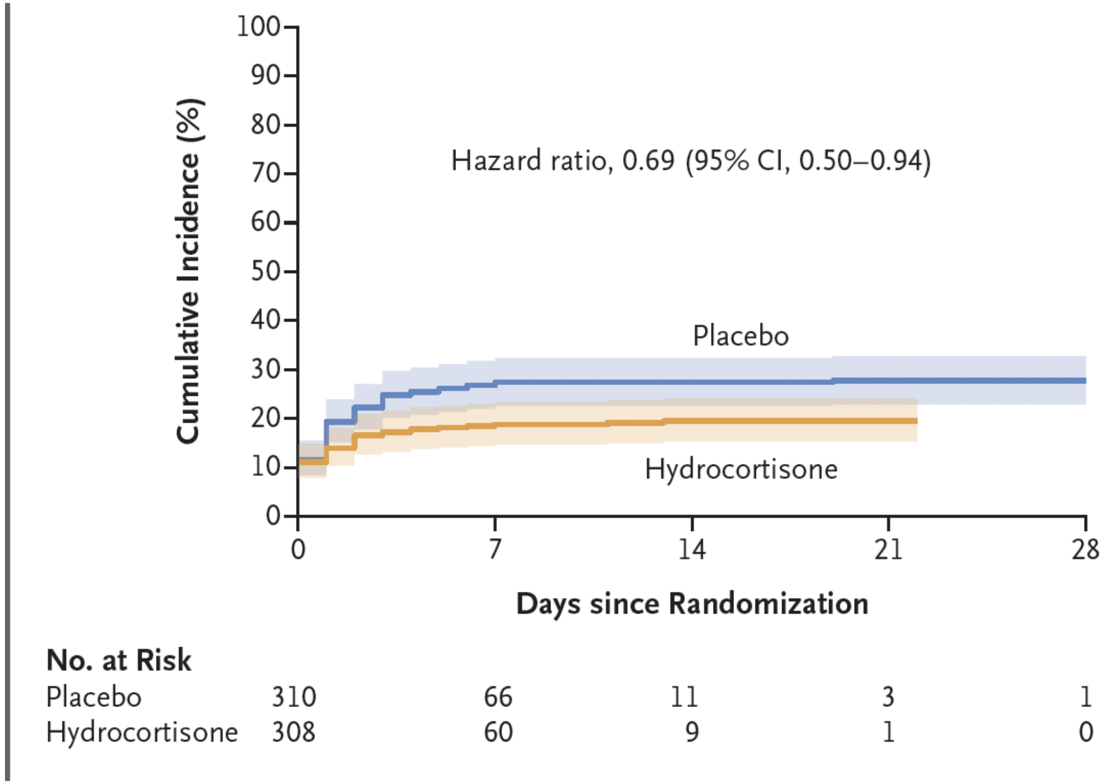
N Engl J Med. 2023 May 25;388(21):1931-1941.

Hydrocortisone in Severe CAP

Discharge from ICU by Day 28



New Intubation



N Engl J Med. 2023 May 25;388(21):1931-1941.

Corticosteroids for CAP: Meta-Analysis & Meta-Regression of Randomized, Controlled Trials

15 trials

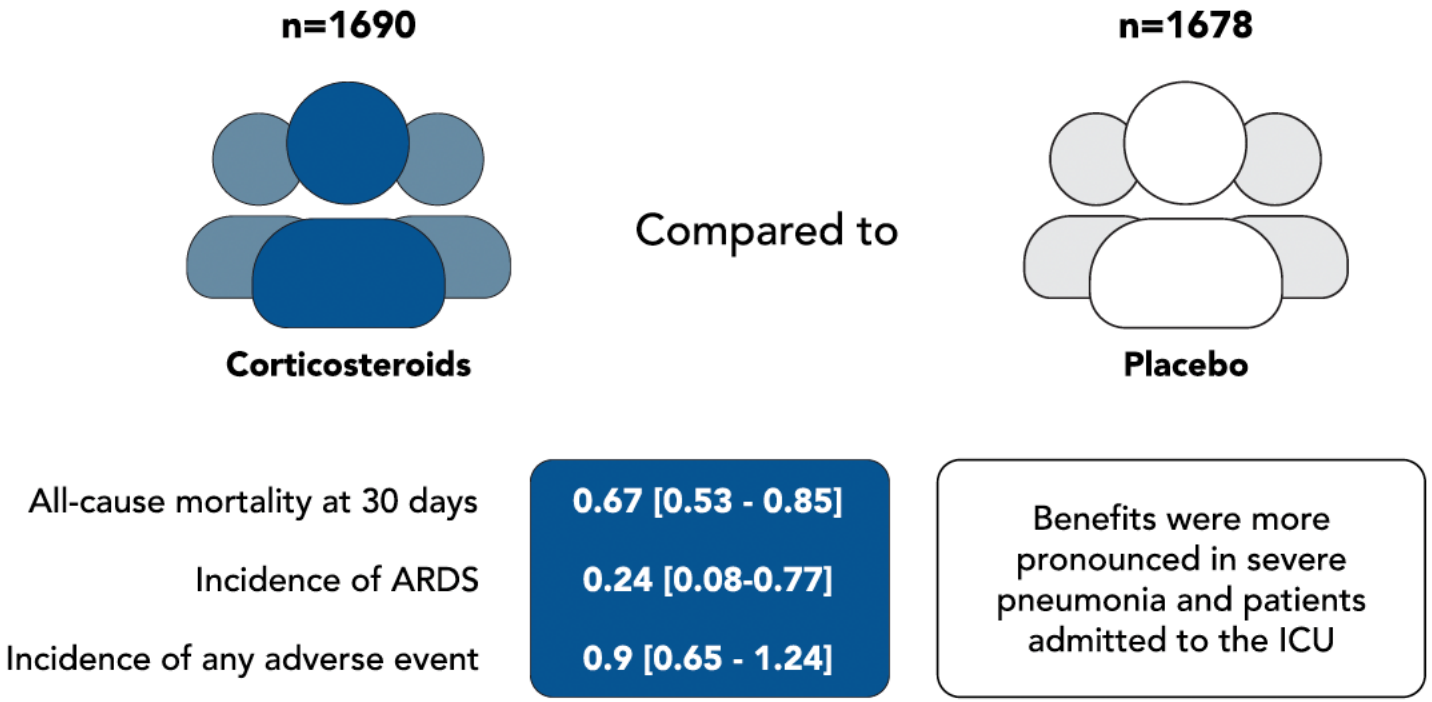
30-day all cause **mortality**:

Corticosteroids: 104/1690 (**6.15%**)

Controls: 152/1677 (**9.06%**)

95% CI, 0.53 to 0.85**; P=0.001**

\



Time to clinical stability (4 studies)

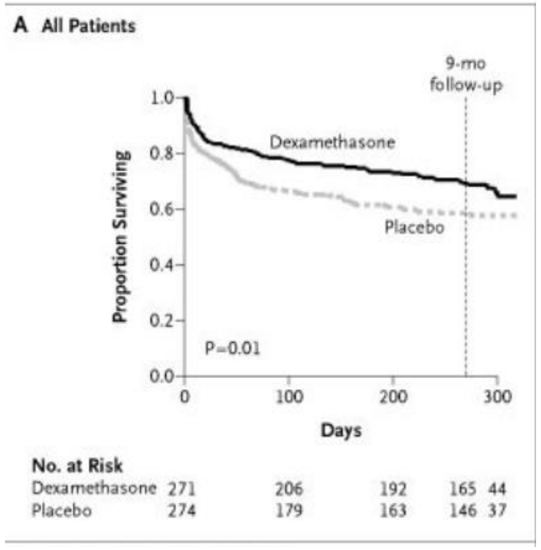
−1.46 days; :

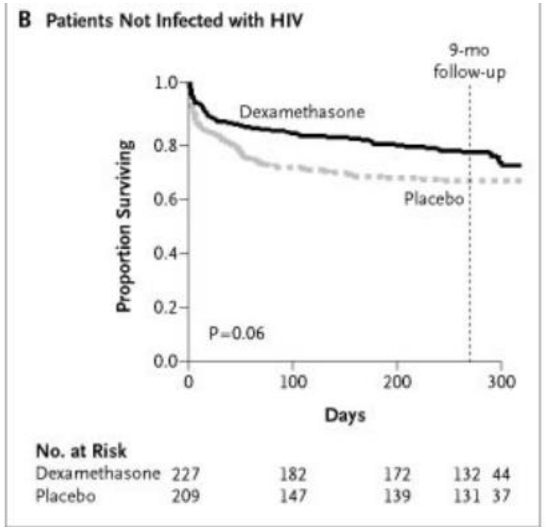
95% CI, −1.51 to −1.41 days; P < .001;

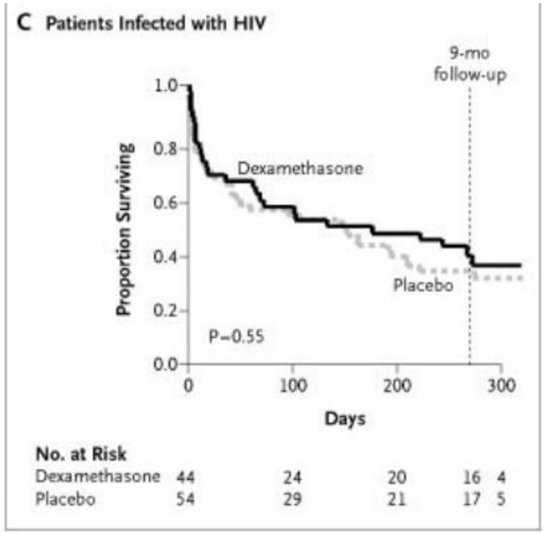
Clin Infect Dis, ciad496, https://doi.org/10.1093/cid/ciad496 Oct 23, 2023

2004: Adjunctive Dexamethasone in Tuberculous Meningitis – In Adolescents& Adults

- 545 randomized
- “Adjunctive treatment with dexamethasone **improves survival** in patients over 14 years of age with tuberculous meningitis but probably does not prevent severe disability.”
- **Only 98/545 HIV infected**







N Engl J Med 2004;351:1741-1751.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Adjunctive Dexamethasone for Tuberculous Meningitis in HIV-Positive Adults

October 12, 2023
N Engl J Med 2023; 389:1357-1367
DOI: 10.1056/NEJMoa221621

Adjunctive Dexamethasone for Tuberculous Meningitis in HIV-Positive Adults

- 520 patients randomized in Ho Chi Minh City & Jakarta
  - 80% power for 2-sided 5% significance level assuming 5% loss to follow-up.
- Stratified by site and severity
- 255/520 (49.0%) ART-naïve
  - ART started 6-8 weeks after initiation of anti-TB Rx
- 251/484 (51.9%) CD4 $\leq 50/mm^3$
  - 15.1% $>200/mm^3$
- Primary endpoint: All-cause mortality

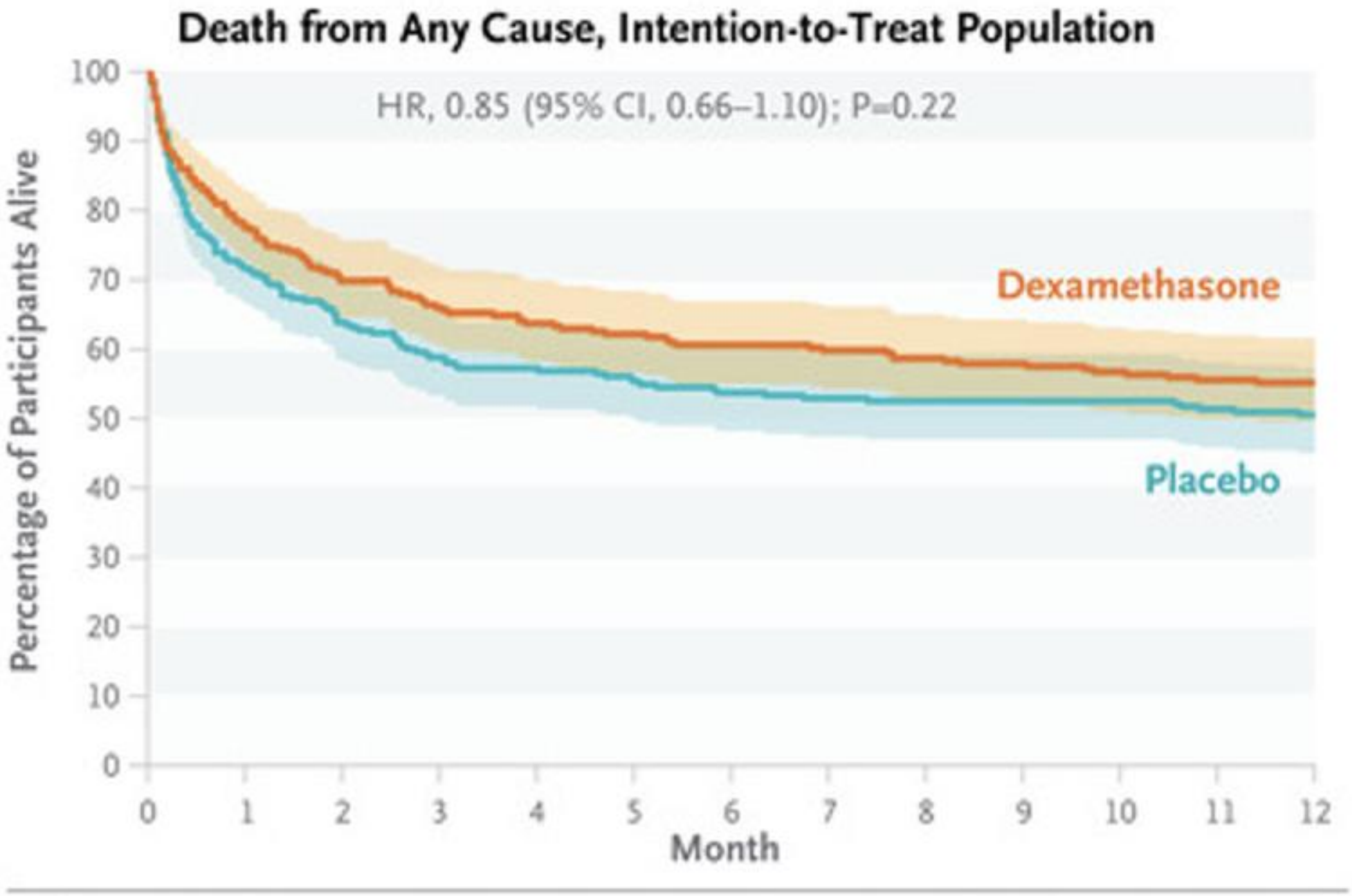
N Engl J Med 2023; 389:1357-1367. DOI: 10.1056/NEJMoa2216218

Adjunctive Dexamethasone for Tuberculous Meningitis in HIV-Positive Adults - Desath

Dexamethasone:
116/263 (**44.1%**)

Placebo:
126/251 (**49.0%)**

HR 0.85, 95% CI 0.66-1.10.
P =0.22



N Engl J Med 2023; 389:1357-1367

Adjunctive Dexamethasone for Tuberculous Meningitis in HIV-Positive Adults

Some possible confounders:

- Approximately ¼ (26.5%) in each group received corticosteroids off-label.

- Observed HR less than anticipated – affecting power calculation.

- Advanced HIV – what about patients with controlled HIV infection?

N Engl J Med 2023; 389:1357-1367. DOI: 10.1056/NEJMoa2216218

Clinical Infectious Diseases

VIEWPOINTS

Infectious Diseases Society of America

hiv medicine association

OXFORD

The 2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis: Updating the Modified Duke Criteria

https://doi.org/10.1093/cid/ciad271

The 2023 Duke International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis: Updating the Modified Duke Criteria

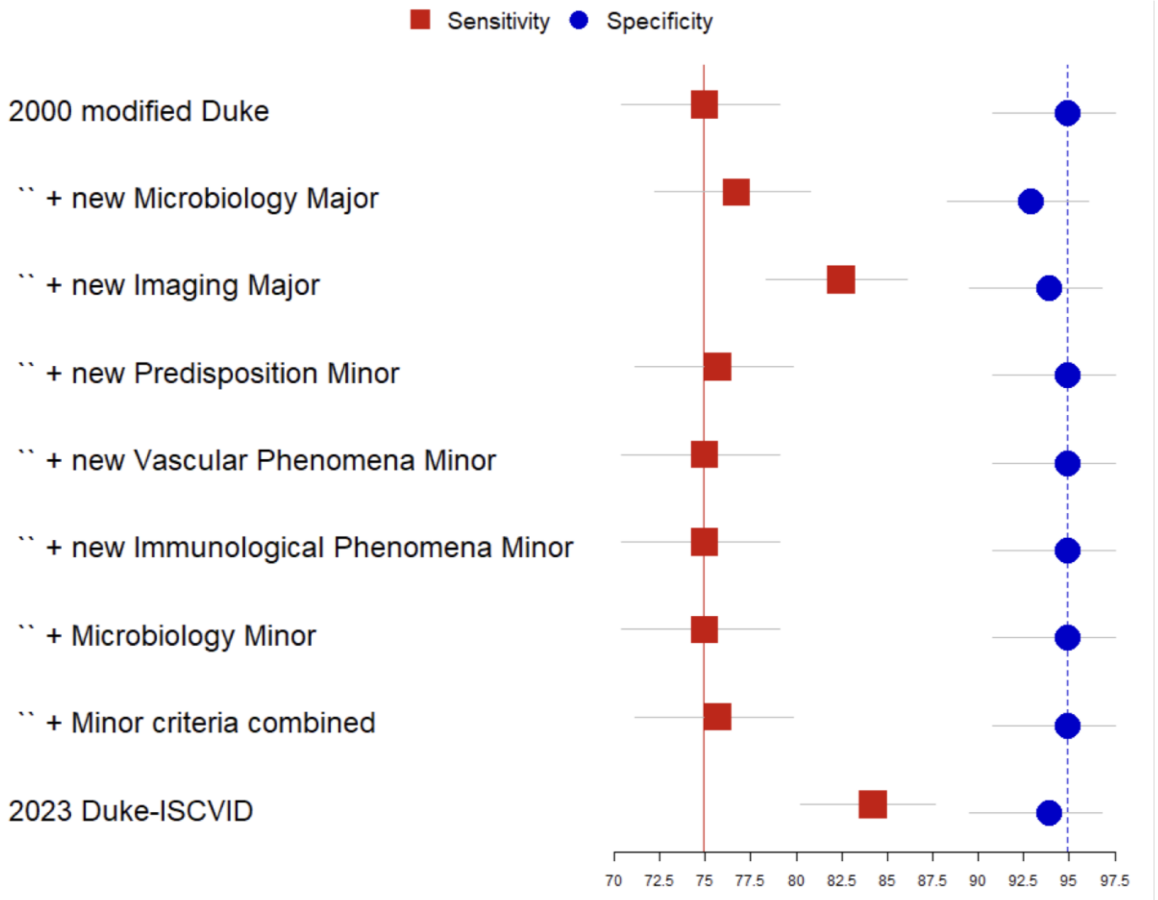
A Selective Sampling of Changes:

- Expanded the list of “typical pathogens”to include, e.g., *Staphylococcus lugdenensis*, *Graniculatella*, *Abiotrophia*, etc.
- In presence of intracardiac prosthetic material, list expanded to include, e.g., *Corynebacterium striatum*, *Cutibacterium acnes*
- “…requirements for blood cultures specifying timing and separate venipunctures should be discontinued” & separate venipunctures no longer required
- Added NAA tests on blood for *Coxiella*, *Bartonella*, *Tropheryma* & IFA for *Bartonella*
- Cardiac CT, PET CT

External Validation of 2023 Duke-ISCVID Criteria for Infective Endocarditis

Diagnostic accuracy

	Sensitivity (95% CI)	Specificity (95% CI)	P-value (sensitivity) vs Duke-ISCVID	P-value (specificity) vs Duke-ISCVID
2000 Modified Duke Criteria	74.9 (70.4 - 79.1)	94.9 (90.8 - 97.5)	<0.001	0.16
2015 ESC Criteria	80.0 (75.7 - 83.8)	93.9 (89.6 - 96.8)	<0.001	1
2023 Duke-ISCVID Criteria	84.2 (80.3 - 87.7)	93.9 (89.6 - 96.8)	-	-



ID Week 2023, Boston, Abstract 963

Endocarditis – 95 Pages From Europe

ESC
European Society of Cardiology

European Heart Journal (2023) **00**, 1–95
https://doi.org/10.1093/eurheartj/ehad193

ESC GUIDELINES

2023 ESC Guidelines for the management of endocarditis

Developed by the task force on the management of endocarditis of the European Society of Cardiology (ESC)

THE LANCET

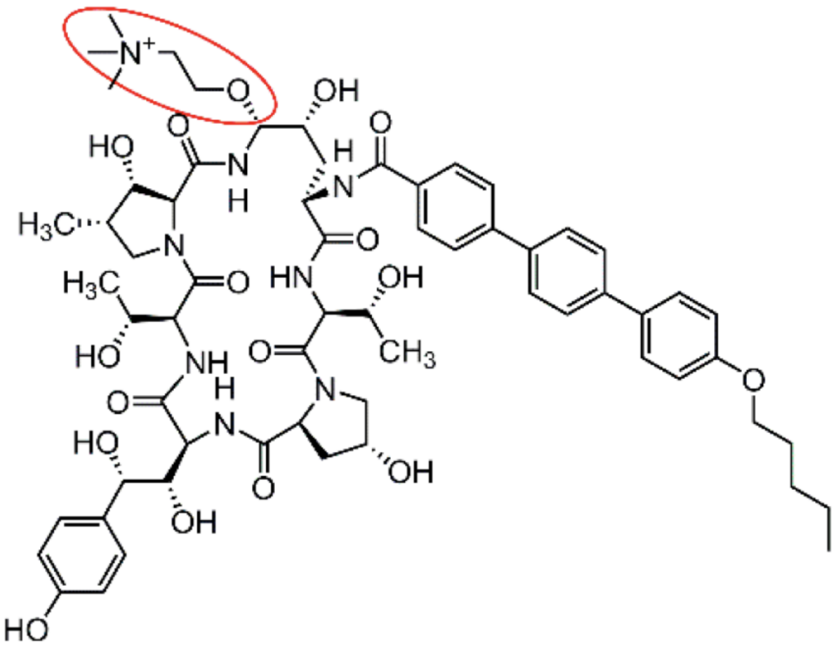
Volume 401, Issue 10370, 7–13 January 2023, Pages 49-59

Articles

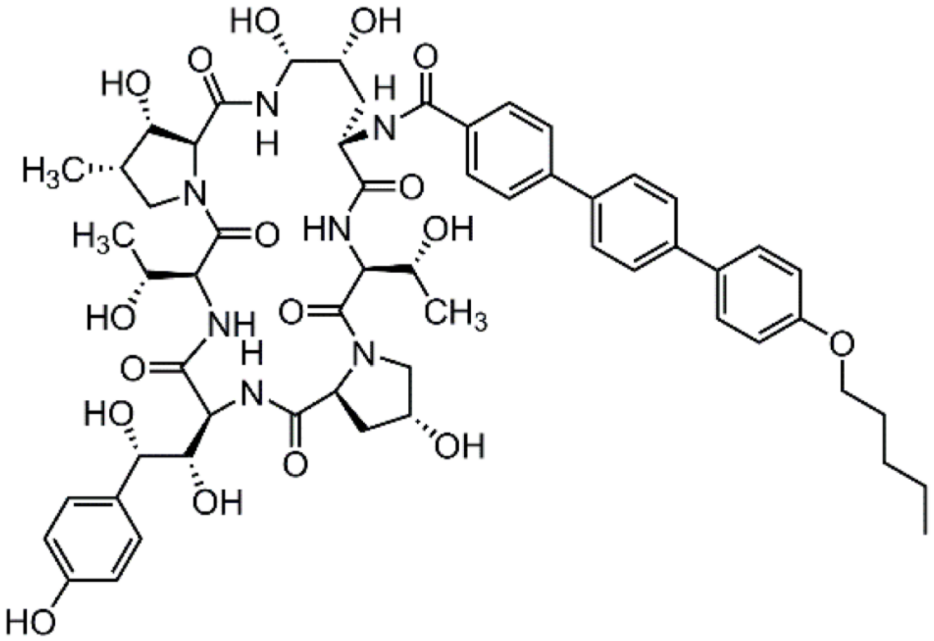
Rezafungin versus caspofungin for treatment of candidaemia and invasive candidiasis (ReSTORE): a multicentre, double-blind, double-dummy, randomised phase 3 trial

REZAFUNGIN

Anidulafungin with a choline moiety at the C5 ornithine position

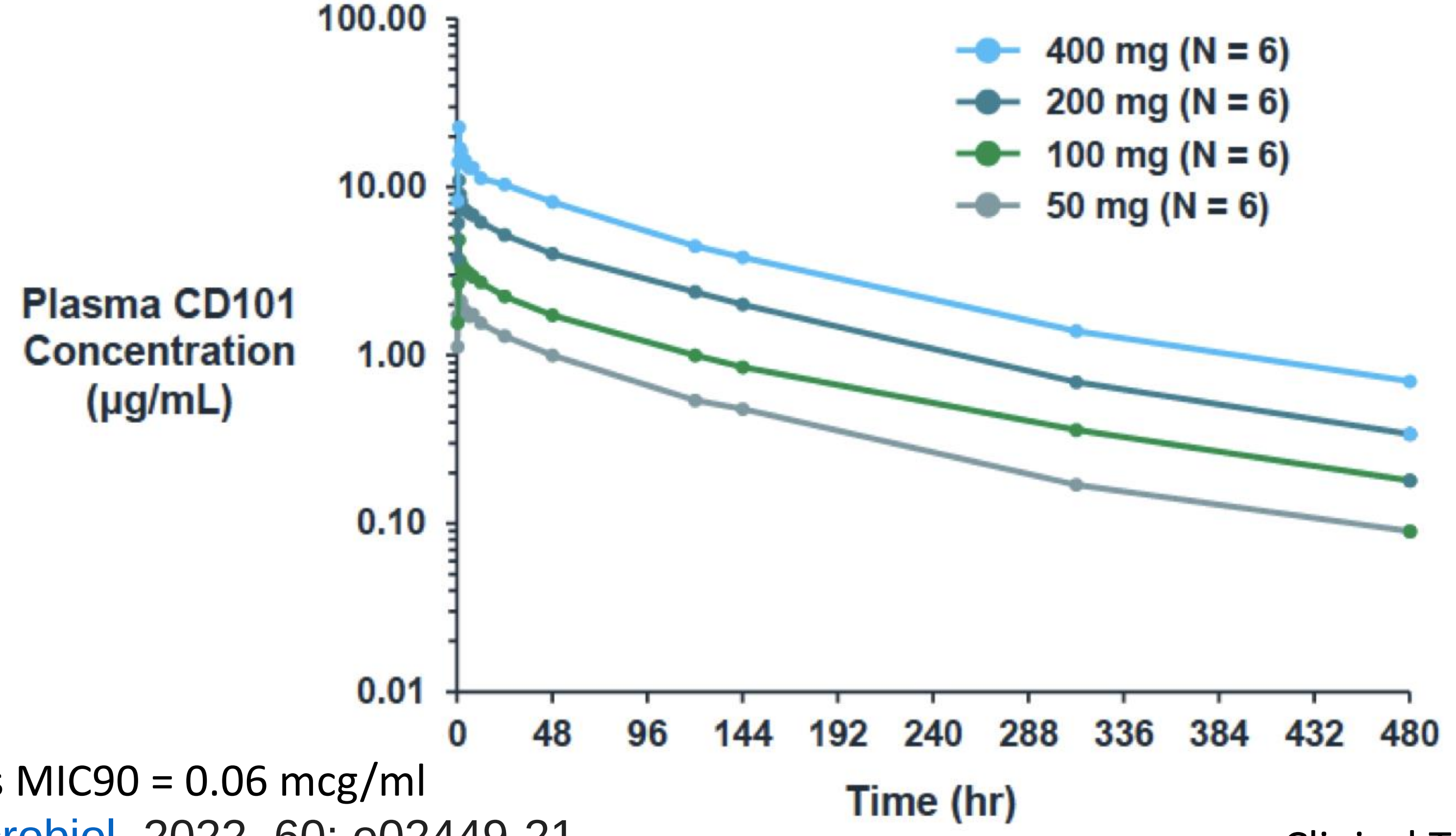


rezafungin



anidulafungin

Figure 9: Single-Dose Pharmacokinetics of IV Rezafungin



<u>Mean Terminal Half-Lives (h)</u>

Rezafungin	127-146
Anidulafungin	23
Caspofungin	10.7-17.2

C. Albicans MIC90 = 0.06 mcg/ml
J Clin Microbiol. 2022, 60: e02449-21

Clinical Trial Dosing: **400 mg then 100 mg wkly**
One week = 168 hours

https://www.fda.gov/media/164668/download

Rezafungin versus Caspofungin for Treatment of Candidaemia and Invasive Candidiasis (ReSTORE)

- 199 randomized; stratified by BSI (70%) or IC, APACHE II, ANC
- Rezafungin: 400 mg IV -→ 100 mg q week for 2-4 weeks*
- Caspofungin: 70 mg IV -→ 50 mg daily for <u><</u>4 weeks (fluconazole step-down allowed)*
- Primary endpoints:
  - Global (clinical, radiologic, mycological cure – as appropriate) – Day 14
  - Mortality – Day 30

*The median duration IV + PO in each group was 14 days.

Lancet 2023; 401: 49–59.

Rezafungin Vs. Caspofungin

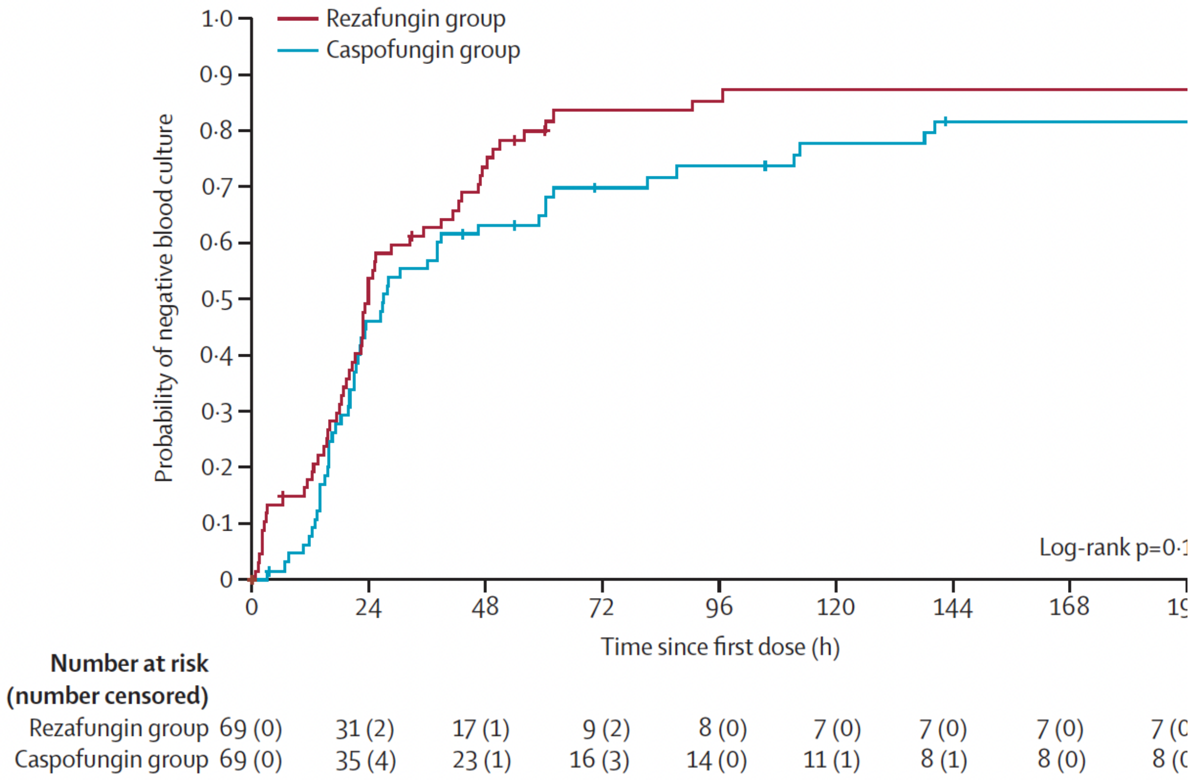
Global Success

Rezafungin	**55/93**	**59%**
Caspofungin	57/94	61%

Mortality

Rezafungin	**22/93**	**24%**
Caspofungin	20/94	21%

Time to Negative Blood Culture

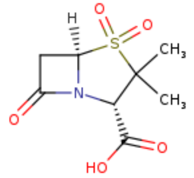


Median time to a negative blood culture was **23·9 h** (IQR 15·4–48·3) for the rezafungin group and **27·0 h** (16·4–111·3) for the caspofungin group (p=0·18;

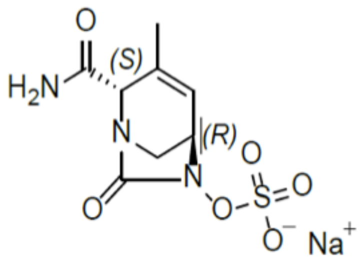
Lancet 2023; 401: 49–59.

Sulbactam-Durlobactam

- Sulbactam BLI with antibacterial activity against Acinetobacter PB1, PBP3



- Durlobactam – diazabicyclooctane serine BLI inhibitor of Ambler class A, C, and D β-lactamases not MLB



- BLI protecting a BLI!

- 2.3% - 3.7% resistance in *Acinetobacter baumanii* complex (ABC)
  - due to PBP3 mutations, MBL:

doi: 10.3390/antibiotics11121793

Clinical Trial > Lancet Infect Dis. 2023 Sep;23(9):1072-1084.
doi: 10.1016/S1473-3099(23)00184-6. Epub 2023 May 11.

Efficacy and safety of sulbactam-durlobactam versus colistin for the treatment of patients with serious infections caused by Acinetobacter baumannii-calcoaceticus complex: a multicentre, randomised, active-controlled, phase 3, non-inferiority clinical trial (ATTACK)

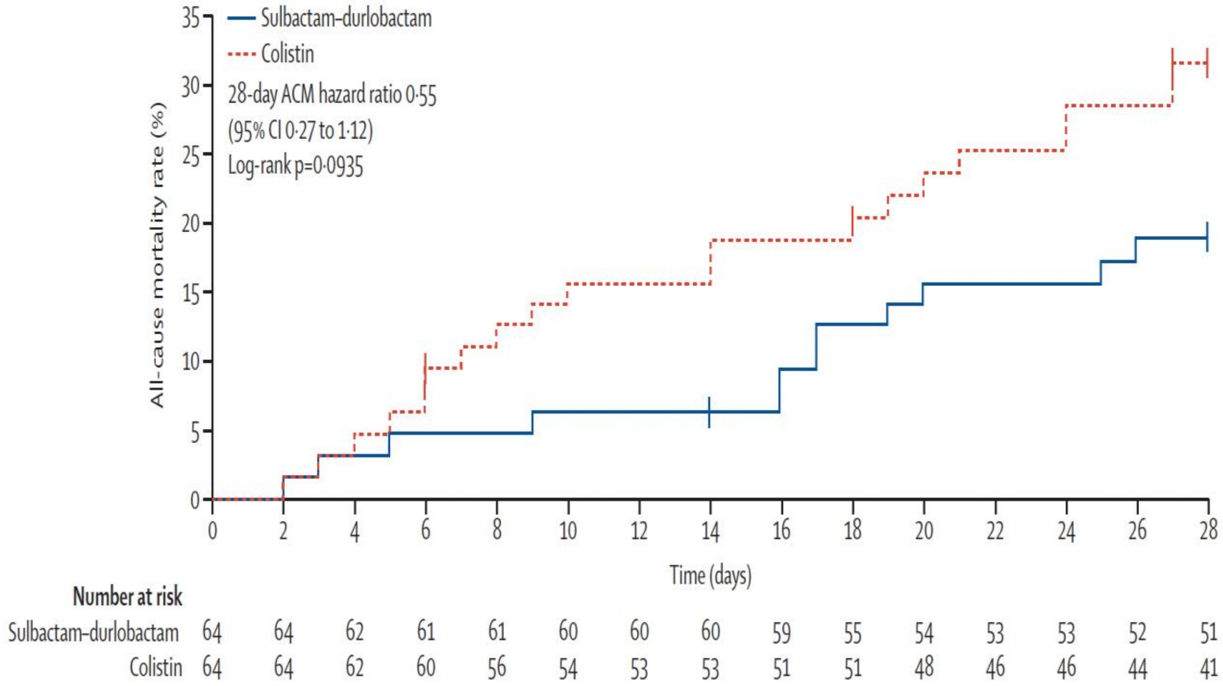
Sulbactam-Durlobactam Vs. Colistin in *Acinetobacter baumannii–calcoaceticus* complex (ABC) Infections

- 186 patients (175 pneumonia, 5 BSI)
- 125/186 with confirmed carbapenem-resistant ABC infections in primary outcome (28 d mortality) analysis.
- All received imipenem; randomized to sulbactam-durlobactam or colistin
- Non-inferiority:
  - If upper bound of 95% CI for Rx difference less than +20%

Lancet Infect Dis 2023; 23: 1072–84

Sulbactam-Durlobactam Vs. Colistin in *Acinetobacter baumannii–calcoaceticus* complex (ABC) Infections

All-Cause Mortality



28-day all cause mortality:

Colistin: 20/62 (32%).
Sul/Durl: 12/63 (19%)

Difference: -13% (95% CI, -30.0 to 3.5)

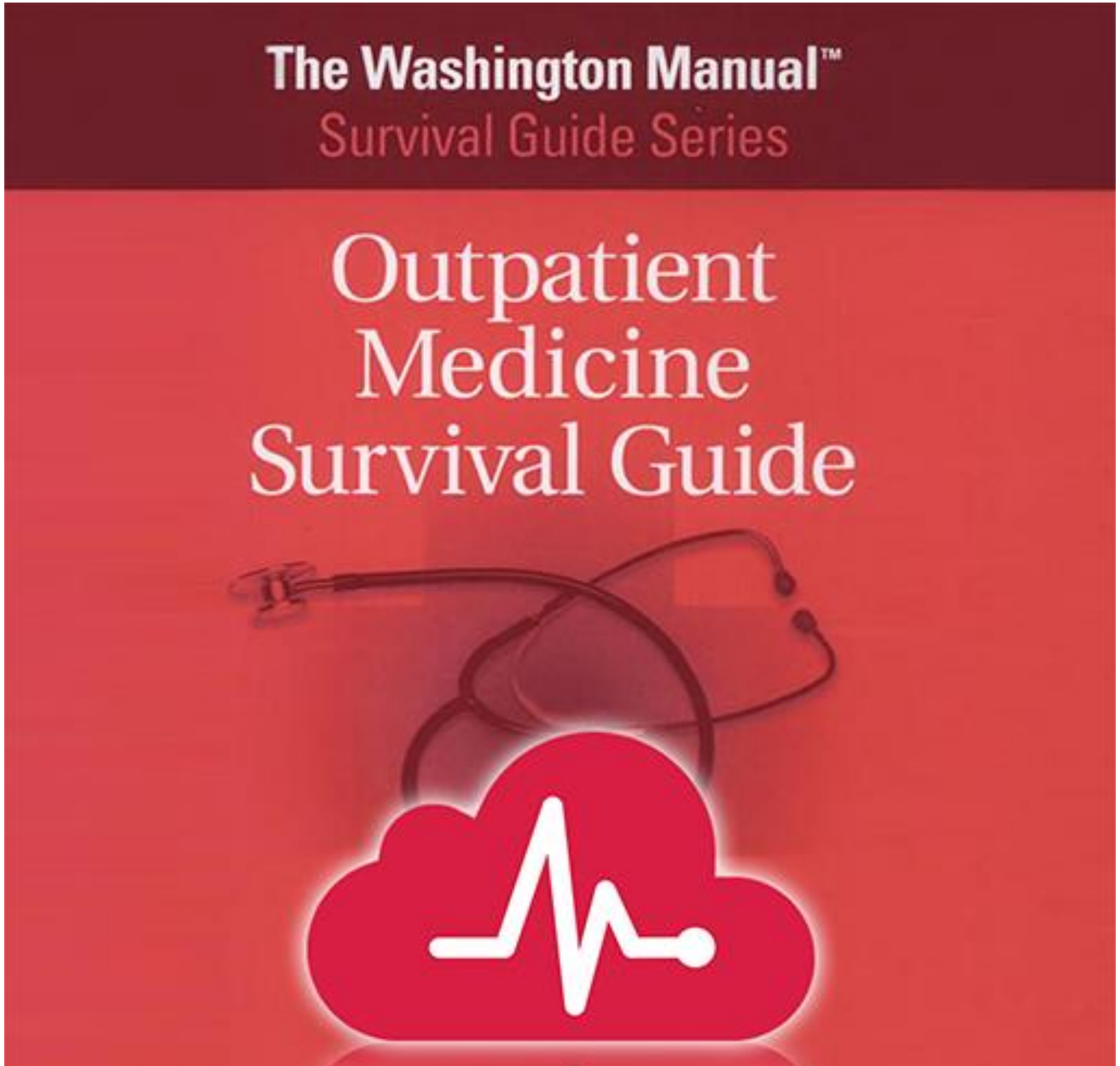
Nephrotoxicity:

Colistin: 32/85 (38%)
Sul/Durl: 12/91 (13%).

P<0.001

All patients also received imipenem.

Lancet Infect Dis 2023; 23: 1072–84


The Washington Manual™
Survival Guide Series
Outpatient
Medicine
Survival Guide

1969

RESPIRATORY SYNCYTIAL VIRUS DISEASE IN INFANTS DESPITE PRIOR ADMINISTRATION OF ANTIGENIC INACTIVATED VACCINE[1, 2]

HYUN WHA KIM, JOSE G. CANCHOLA[3], CARL D. BRANDT, GLORIA PYLES, ROBERT M. CHANOCK, KEITH JENSEN, AND ROBERT H. PARROTT[4]

(Received for publication August 8, 1968)

- Formalin-inactivated vaccine
- 80% of 85 who developed RSV required hospitalization – majority with pneumonia and or bronchiolitis
  - 5% in controls (parainfluenza type 1 vaccine)

Am J Epidemiol. 1969 Apr;89(4):422-34.

RSV Prevention – Vaccines, Monoclonals

- Vaccines for Older Adults
  - Arexvy (GSK; adjuvanted); Abrysvo (Pfizer)

    N Engl J Med 2023;388:595-608.

    N Engl J Med 2023;388:1465-77.

- Immunizations to Protect Infants and Children
  - Maternal vaccination – Abrysvo (Pfizer) at 32-36 weeks

    N Engl J Med 2023; 388:1451

  OR
  - Monoclonal antibody – nirsevimab (pavilizumab)

    N Engl J Med 2023;388:1533-1534

https://www.cdc.gov/rsv/clinical/index.html

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Single-Dose Rifapentine in Household Contacts of Patients with Leprosy

- Why should we care?
- WHO: Present in >120 countries with 200,000 new cases/year
- United States: 159 new diagnoses in 2020 with 6 states accounting for 69% of cases – Florida, California, Louisiana, Hawaii, New York , Texas
- California – ???autochthonous transmission??? – 6 cases:
  - Belzer et al Autochthonous leprosy in the United States. N Engl J Med 2023;388:2485-2487..

N Engl J Med 2023;388:1843-52.
DOI: 10.1056/NEJMoa2205487

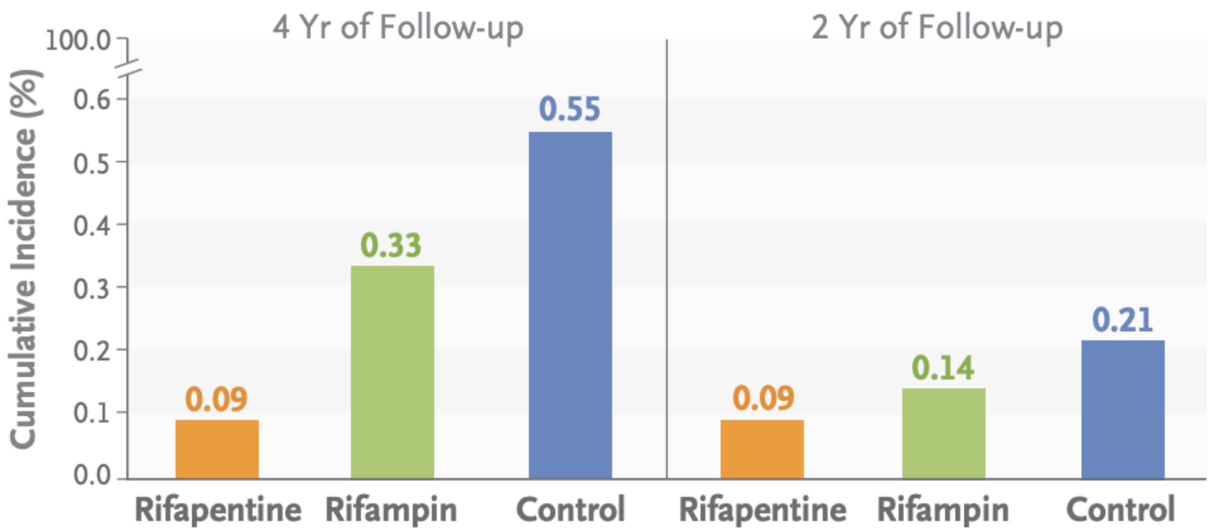
Single Dose Rifapentine in Household Contacts of Patients with Leprosy

- Cluster-randomized trial in Southwest China
- 207 clusters with 7450 household contacts randomized to single dose rifampin, single dose rifapentine, or no intervention
- Primary outcome: 4-year cumulative incidence of leprosy in household contacts
- 86.7% of index cases were multibacillary
  - Median 3 (IQR 2-4) contacts per index case

N Engl J Med 2023;388:1843-52.

Single Dose Rifapentine in Household Contacts of Patients with Leprosy

Cumulative Incidence of Leprosy



Outcome	No. of Cases of Leprosy	Cumulative Incidence (95% CI) *percent*	Cumulative Incidence Ratio (95% CI)	P Value
4-Yr cumulative incidence				
Control	13	0.55 (0.32–0.95)	1.00	
Rifapentine	2	0.09 (0.02–0.34)	0.16 (0.03–0.87)	0.02
Rifampin	9	0.33 (0.17–0.63)	0.59 (0.22–1.57)	0.23

N Engl J Med 2023;388:1843-52.

Idiopathic CD4 Lymphoctopenia - The History

- 1981 – Gay men with PCP, KS – low CD4
- 1983 – HIV identified
- 1985 – HIV antibody test approved
- 1987 – Zidovudine approved
- 1992 - "Unexplained CD4+ T-lymphocyte depletion in persons without evident HIV infection" 21 cases reported in MMWR
  - "AIDS without HIV"
  - Idiopathic CD4 lymphocytopenia (ICL)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Reappraisal of Idiopathic CD4 Lymphocytopenia at 30 Years

- Adults with CD4 <300 or <20% & twice previously at least 6 weeks apart in absence of disease or therapy causing lymphocytopenia
- 108 enrolled, 91 included – median age 48 years, 51% male
  - Among reasons for exclusion: CVI, chemotherapy for lymphoma, autoimmune disease, inborn errors of immunity with genetic variants in *NFKB1, P13CD, FAS, IL2RG, COCK8,* or *CD4*.
- Median cell counts (IQR): CD4 80 (25-168), CD8 130 (58-317)
- Infection at enrollment or during follow-up (median, 3 yrs) in 69%; Autoimmune condition in 36%.

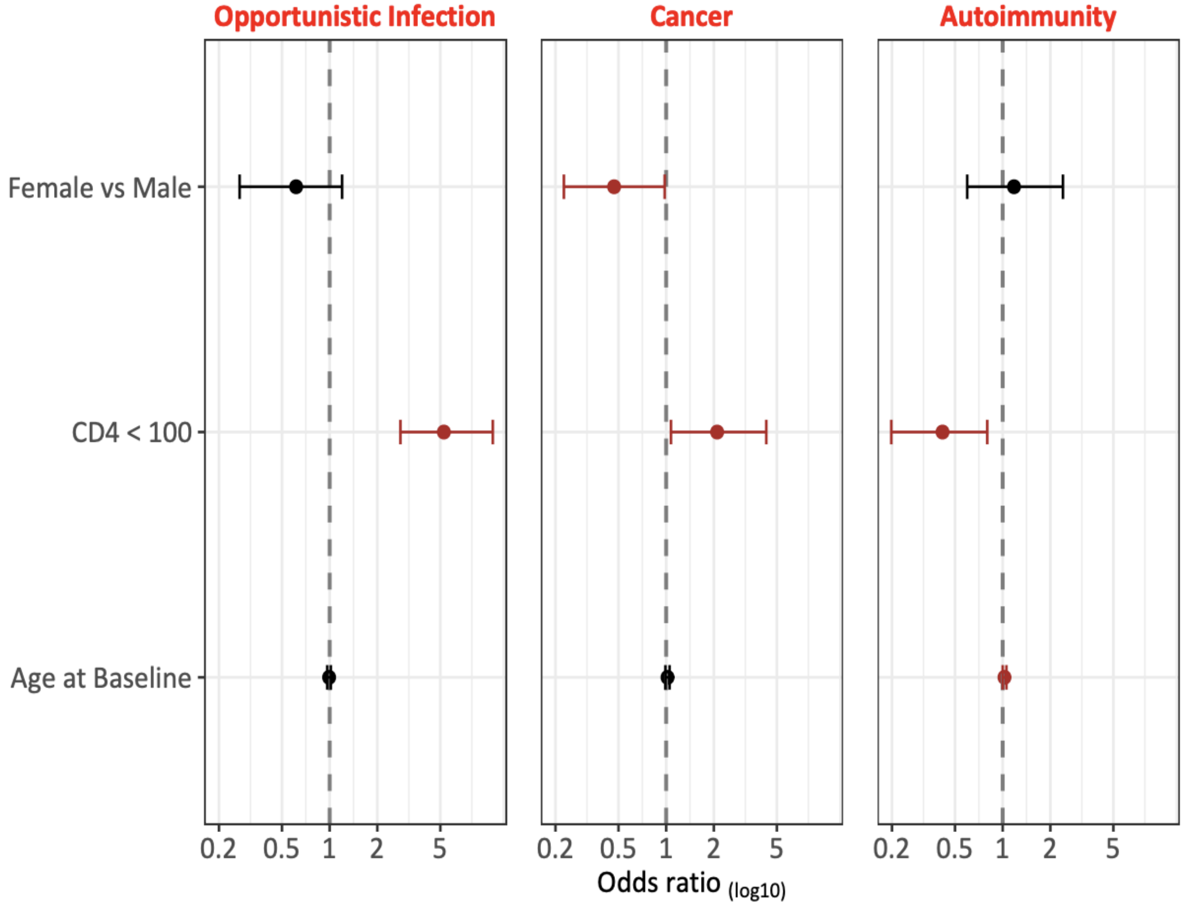
N Engl J Med 2023;388:1680-91.

Reapprasial of Idiopathic CD4 Lymphocytopenia - Infections

- $\geq$1 infectious complication: 63/91 (69%)
- $\geq$1 OI "of clinical significance": 53/91 (58%); 49/53 at screening
  - Severe skin or anogenital HPV – 27 (29%
  - Cryptococcal infection - 22 (24%); 16/22 meningitis, 4 pneumonia, 2 disseminated skin/musculoskeletal
  - Molluscum contagiosum – 8
  - NTM – 5
  - Histoplasmosis – 4; 1 pulmonary, 3 disseminated
  - PML - 3
  - Multi-dermatomal or complication and herpes zoster, CMV – 2 each

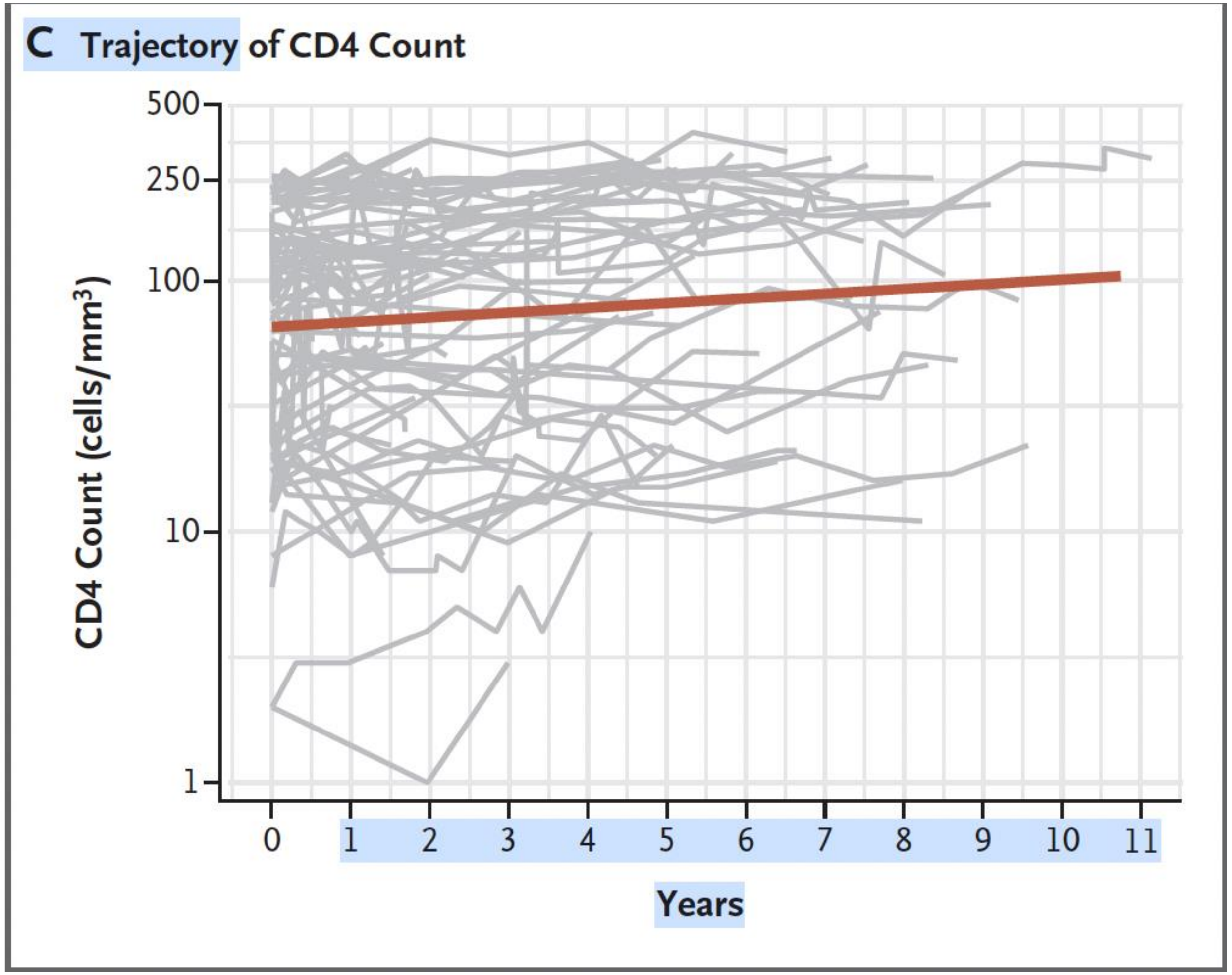
  - 55% received OI prophylaxis, mostly for PJP but also some azithromycin, fluconazole

Idiopathic CD4 Lymphocytopenia – NIH CD4 & Complications



- Most common opportunistic pathogens: HPV, Cryptococcus
- Prevalence of 6 cancers higher than general population:
  - anal, vulvovaginal, oral cavity or pharynx, papillary thyroid carcinoma, non-Hodgkin's lymphoma, and Kaposi's sarcoma
- 44 autoimmune diseases in 33 patients
  - 30 at enrollment, 14 during follow-up

Course of CD4 Lymphocytopenia



- CD4 Increased by factor of 1.044/y
- Death rate over 374 patient-years of follow-up was similar to general population:
  - 1.337 deaths per 100 person-years [5 deaths in 91 patients] and 0.854 deaths per 100 person-years, respectively

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections

N Engl J Med 2023;388:1296-306.
DOI: 10.1056/NEJMoa2211934

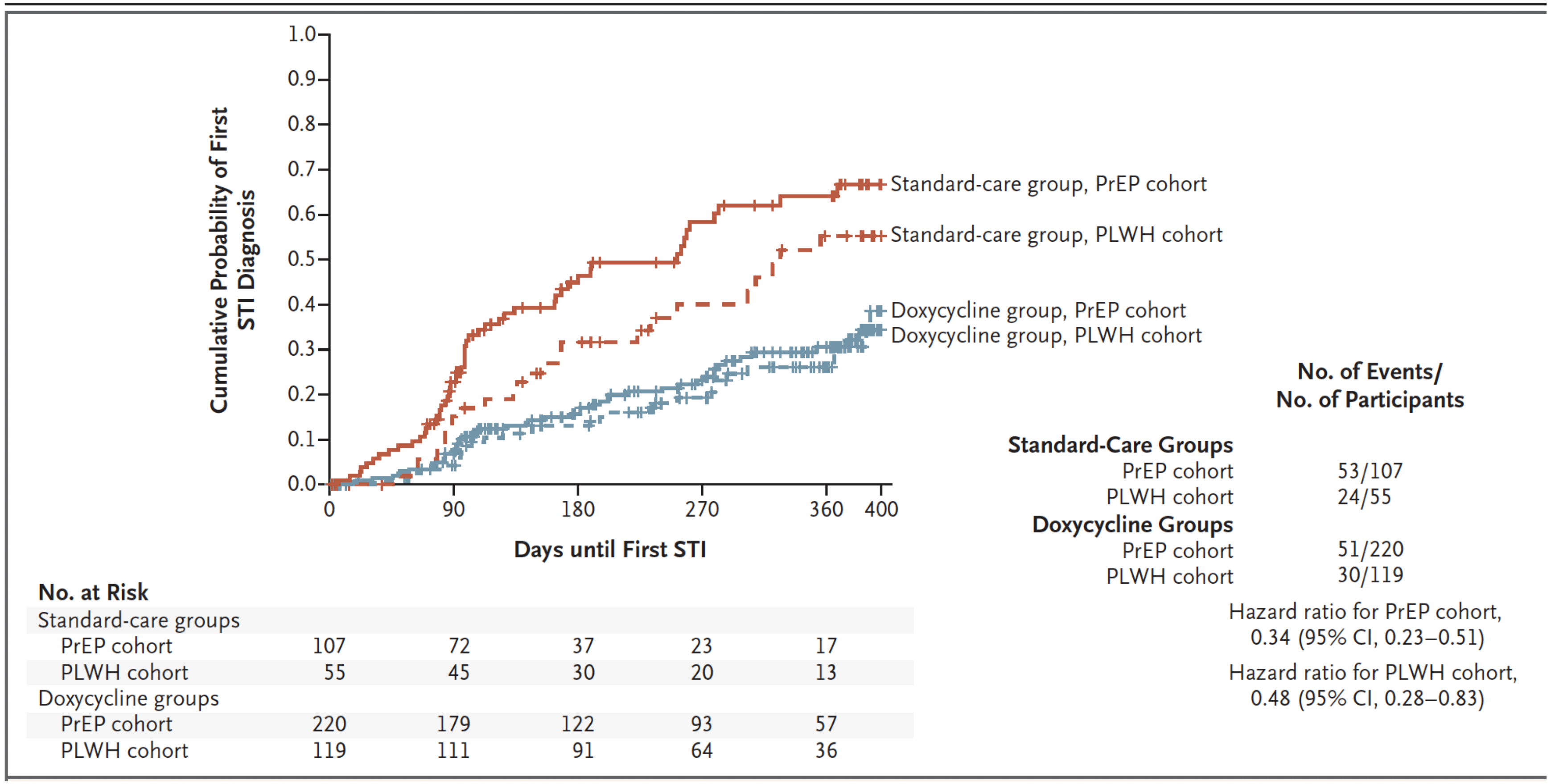
DOXY-PEP

DOXY-PEP Randomized Trial

- Assigned **male** at birth
- **HIV and/or PrEP**, protected sex with male in last 12 months, & gonorrhea, chlamydia, or early syphilis in last 12 months
- Randomized: Standard care or **200 mg doxycycline within 72 h** (ideally within 24 h) after unprotected anogenital, vaginal, or oral sex
- **Quarterly** blood tests for syphilis and PCR testing of pharynx, rectum & urine for gonorrhea and chlamydia with culture of gonorrhea positive specimens for susceptibility testing
- **Primary efficacy endpoint: incidence of at least one STI per follow-up quarter**

N Engl J Med 2023;388:1296-306

DOXY-PEP:Time to First STI Diagnosis



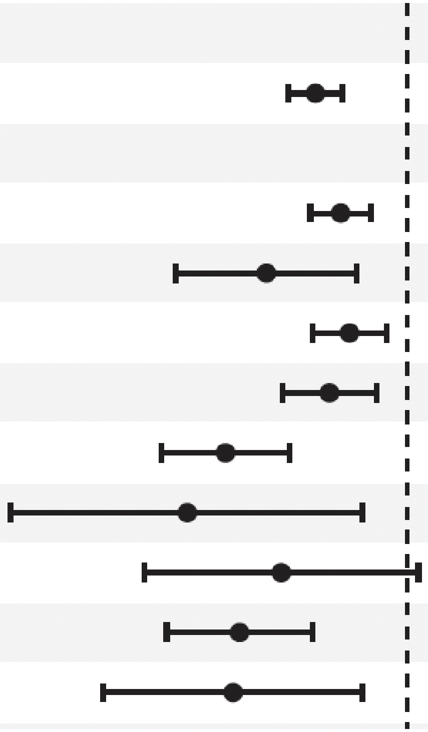
Of the participants with gonorrhea culture available, tetracycline-resistant gonorrhea occurred in 5 of 13 in the doxycycline groups and 2 of 16 in the standard-care groups.

N Engl J Med 2023;388:1296-306

DOXY-PEP - PrEP Cohort

A PrEP Cohort

Analyses	Doxycycline	Standard Care	Relative Risk (95% CI)	P Value
	no. of quarterly visits with event /total no. of visits (%)			
Primary analysis				<0.001
Any STI	61/570 (10.7)	82/257 (31.9)	0.34 (0.24–0.46)	
Secondary analysis				
Any gonorrhea	52/570 (9.1)	52/257 (20.2)	0.45 (0.32–0.65)	
Urethral	5/570 (0.9)	12/257 (4.7)	0.19 (0.06–0.55)	
Pharyngeal	38/570 (6.7)	34/257 (13.2)	0.50 (0.32–0.78)	
Rectal	25/570 (4.4)	29/257 (11.3)	0.40 (0.23–0.69)	
Any chlamydia	8/570 (1.4)	31/257 (12.1)	0.12 (0.05–0.25)	
Urethral	1/570 (0.2)	6/257 (2.3)	0.07 (0.01–0.59)	
Pharyngeal	2/570 (0.4)	4/257 (1.6)	0.22 (0.04–1.14)	
Rectal	7/570 (1.2)	23/257 (8.9)	0.14 (0.06–0.32)	
Any early syphilis	2/570 (0.4)	7/257 (2.7)	0.13 (0.03–0.59)	



DOXY-PEP:Time to First STI Diagnosis

FEDERAL REGISTER

The Daily Journal of the United States Government

Notice

Guidelines for the Use of Doxycycline Post-Exposure Prophylaxis for Bacterial Sexually Transmitted Infection (STI) Prevention; Request for Comment and Informational Presentation

A Notice by the Centers for Disease Control and Prevention on 10/02/2023

https://www.federalregister.gov/documents/2023/10/02/2023-21725/guidelines-for-the-use-of-doxycycline-post-exposure-prophylaxis-for-bacterial-sexually-transmitted

Comments Close:11/16/2023

Doxycycline PEP, when offered, should be implemented in the context of a comprehensive sexual health approach including risk reduction counseling, STI screening and treatment, recommended vaccination, and linkage to HIV pre-exposure prophylaxis (PrEP), HIV care, or other services, as appropriate.

About CROI Abstracts Presenters

CROI
Conference on Retroviruses and Opportunistic Infections

Attendees Scholarships Program

DOXYCYCLINE POSTEXPOSURE PROPHYLAXIS FOR PREVENTION OF STIs AMONG CISGENDER WOMEN

Feb 2023

- 449 cisgender women in Kenya, median age 24 yrs; 36.7% reported transactional sex
- STI at enrollment in 17.9%: 14.1% C. trachomatis, 3.8% NI gonorrheae, 0.4% T. pallidum
- Randomized to DOXY-PEP or SOC
- 80% power to detect 50% incident STI
- Incident STI: **RR 0.88, 95% CI 0.60-1.29; P =0.51**

https://www.croiconference.org/abstract/doxycycline-postexposure-prophylaxis-for-prevention-of-stis-among-cisgender-women

"I'M SORRY BUT THERE ARE NOW 16,000 MEDICAL JOURNALS, AND I NO LONGER HAVE TIME TO SEE ANY PATIENTS."