Top ID papers of 2025

Prof Josh Davis, February 2026

THE UNIVERSITY OF NEWCASTLE AUSTRALIA

NSW GOVERNMENT Health Hunter New England Local Health District

HMRI Hunter Medical Research Institute

Criteria

- IMHO
- Published during 2025
- Deal with diagnosis or treatment of infectious diseases
- Relevant to (my) clinical practice
- Practice-changing, paradigm-shifting, or dogma-challenging.
- **In alphabetical order by first author**

Honorable Mentions

Guglielmetti	EndTB oral MDR trial	**NEJM**	https://www.nejm.org/doi/full/10.1056/NEJMoa2400327
St Peter	Appendicectomy vs Abs in kids	**Lancet**	https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(24)02420-6/fulltext
Durban	Mosdenevir prophylaxis dengue CHIM	**NEJM**	https://www.nejm.org/doi/full/10.1056/NEJMoa2500179
Pomirchy	VZV vaccine and dementia quasi-experimental study	**JAMA**	https://jamanetwork.com/journals/jama/fullarticle/2833335
Liesenfeld	SEPSIS-SHIELD study	**Nature Med**	https://www.nature.com/articles/s41591-025-03933-y
Burdet	CloCEBA trial	**Lancet**	Lancet. 2025 Oct 17; doi:10.1016/S0140-6736(25)01624-1
Paterson	GAME CHANGER trial	**Lancet ID**	Lancet Infect Dis. 2025 Oct 7; doi:10.1016/S1473-3099(25)00469-4

Honorable mentions implications

- Burdet – Cefazolin is *probably* as good as flucloxacillin for MSSA-BSI
- Durban – We may have finally found a drug that works against dengue
- Gugielmetti – All oral 9/12 regimens as good as “standard” 18/12 for Rif-R TB
- Liesenfeld – Getting closer to biomarkers to distinguish sterile SIRS from sepsis
- Paterson – Ceficerocol has not lived up to its promise for CREs
- Pomirchy – Zoster vaccines probably decrease risk of dementia
- St Peter – Appendicectomy should be 1st line Rx in kids with appendicitis

- https://www.escmid.org/guidelines-journals/escmid-journals/communicable-podcast/

Negative pressure wound therapy versus usual care in patients with surgical wound healing by secondary intention in the UK (SWHSI-2): an open-label, multicentre, parallel-group, randomised controlled trial

*Catherine Arundel, Laura Mandefield, Caroline Fairhurst, Kalpita Baird, Athanasios Gkekas, Pedro Saramago, Ian Chetter, on behalf of the SWHSI-2 Trial Investigators**

- WHY
  - Dogma-challenging
- WHAT/HOW
- KEY FINDINGS

Lancet 2024; 405: 1689–99

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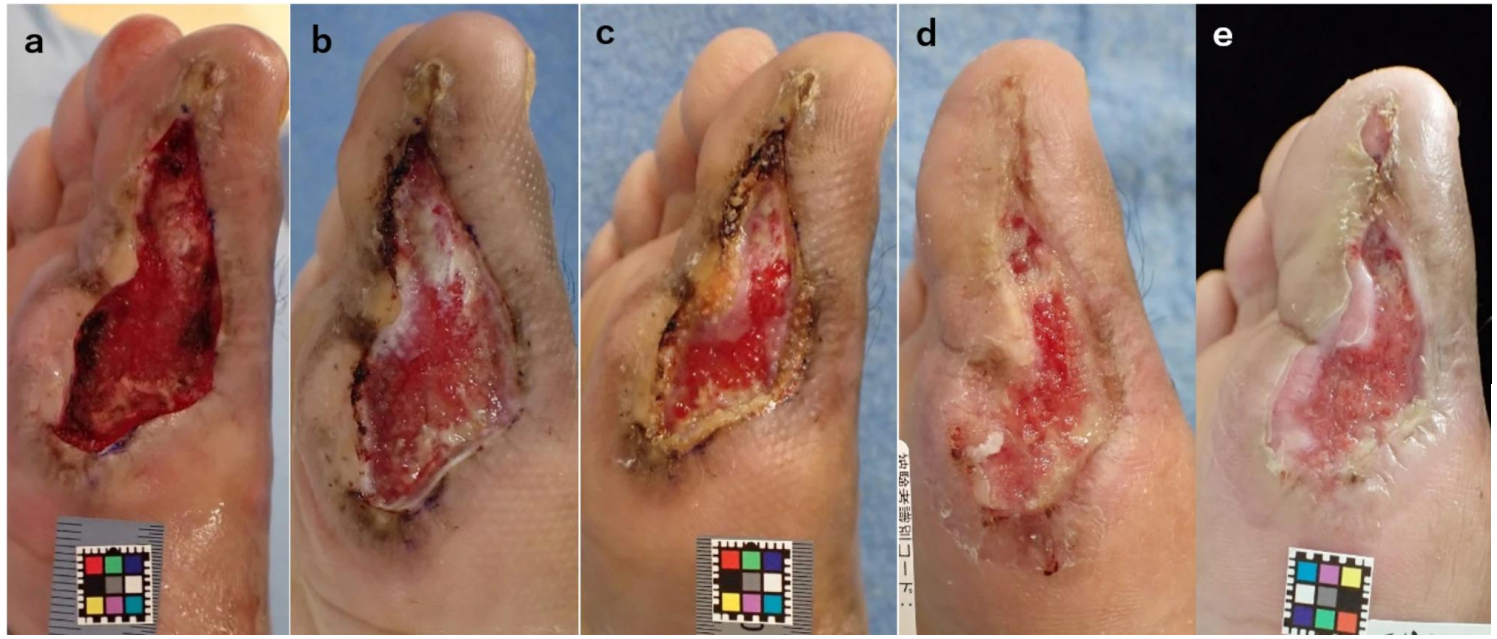
- WHY
  - Dogma-challenging
- WHAT/HOW
  - Note first published 15/4/2025
  - Open label individually randomised RCT in 29 UK hospitals
  - P – Adults with surgical wound healing by 2ry intention
  - I/C – Negative pressure wound therapy (NPWT) or usual care
  - O – Time to wound healing
  - 686 patients randomised. 80% had DM, 80% foot, 90% vascular surgery

Lancet 2024; 405: 1689–99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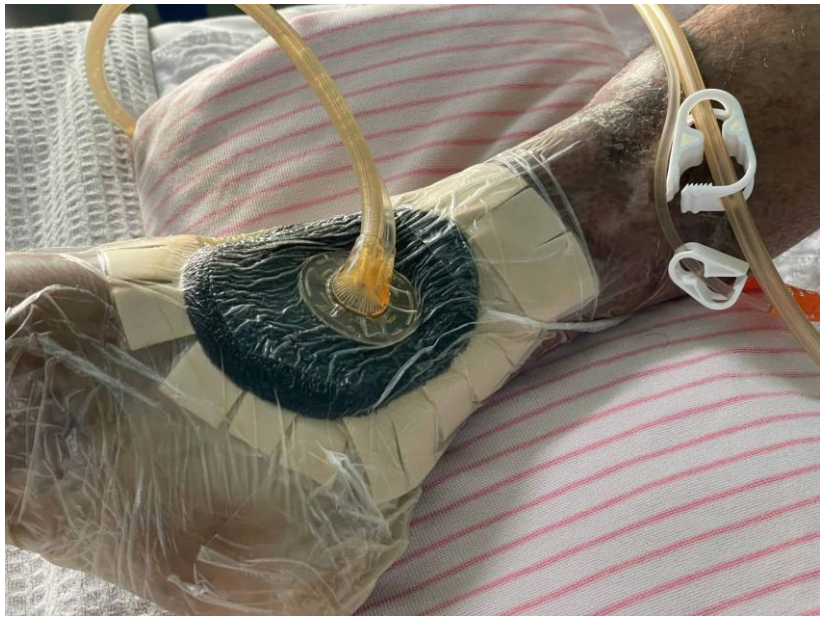
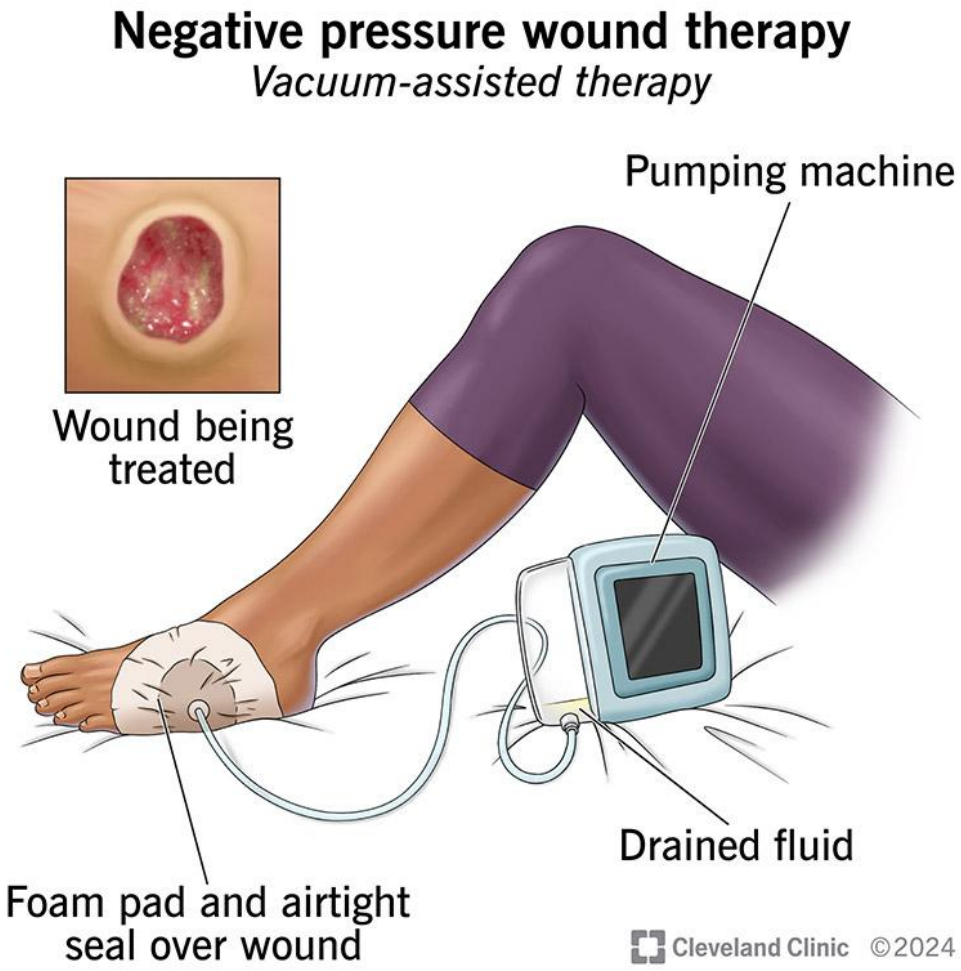
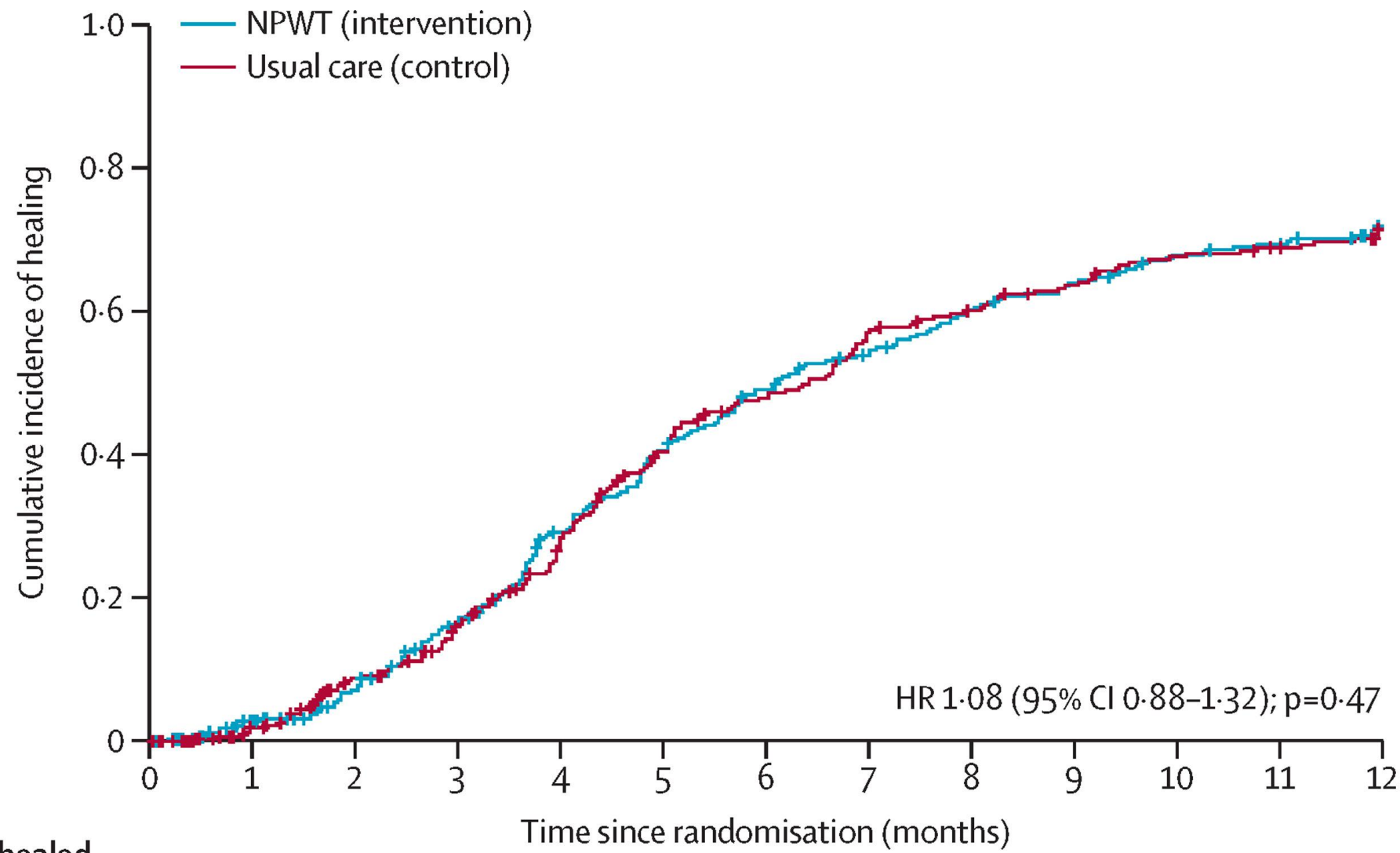



Negative pressure wound therapy
Vacuum-assisted therapy
Pumping machine
Wound being treated
Drained fluid
Foam pad and airtight seal over wound
Cleveland Clinic ©2024



Number unhealed (number censored)													
NPWT (intervention)	349	303	278	243	200	167	141	124	106	95	83	78	67
	(0)	(38)	(49)	(56)	(63)	(64)	(66)	(70)	(71)	(72)	(74)	(76)	(147)
Usual care (control)	337	307	270	242	204	160	137	113	102	91	80	75	68
	(0)	(24)	(40)	(47)	(55)	(61)	(64)	(64)	(67)	(69)	(70)	(73)	(141)

	NPWT group	Usual care group	Treatment difference (95% CI)*	p value
Primary analysis population	n=349; median time to healing 187 days (95% CI 169 to 226)	n=337; median time to healing 195 days (95% CI 158 to 213)	HR 1·08 (0·88 to 1·32)	0·47
Time to healing as assessed by masked outcome assessment†	n=349; 157 days (95% CI 140 to 188)	n=337; 158 days (95% CI 134 to 203)	HR 1·13 (0·87 to 1·47)	0·36
Hospital admission‡	n=320; 63 (19·7%)	n=320; 58 (18·1%)	OR 1·13 (0·76 to 1·69)	0·54
Reoperation‡	n=320; 78 (24·4%)	n=320; 69 (21·6%)	OR 1·20 (0·82 to 1·74)	0·35
Amputation‡	n=320; 35 (10·9%)	n=320; 36 (11·2%)	OR 0·98 (0·60 to 1·62)	0·95
Wound infection‡	n=320; 102 (31·9%)	n=320; 100 (31·2%)	OR 1·05 (0·75 to 1·48)	0·77
Antibiotic use (for SWHSI)‡	n=320; 211 (65·9%)	n=320; 210 (65·6%)	OR 1·01 (0·70 to 1·45)	0·96
Death‡	n=349; 40 (11·5%)	n=337; 43 (12·8%)	OR 0·89 (0·56 to 1·41)	0·61
WHQ at 3 months§	n=195; mean 7·01 (5·08)	n=190; mean 7·15 (5·72)	Mean adjusted difference 0·29 (–1·01 to 1·58)	0·66
WHQ at 6 months§	n=132; mean 4·71 (4·33)	n=118; mean 4·94 (5·67)	Mean adjusted difference 0·29 (–1·19 to 1·77)	0·70
WHQ at 12 months§	n=86; mean 5·75 (5·76)	n=74; mean 5·52 (5·60)	Mean adjusted difference 1·09 (–0·65 to 2·83)	0·22
Wound pain at 3 months§	n=197; mean 18·9 (24·7)	n=202; mean 17·4 (23·1)	Mean adjusted difference –0·58 (–6·45 to 5·30)	0·85
Wound pain at 6 months§	n=139; mean 17·6 (27·3)	n=124; mean 15·3 (24·3)	Mean adjusted difference –0·28 (–7·11 to 6·54)	0·94
Wound pain at 12 months§	n=90; mean 15·9 (24·4)	n=83; mean 11·5 (18·3)	Mean adjusted difference 1·03 (–7·02 to 9·08)	0·80

HR=hazard ratio. NPWT=negative pressure wound therapy. OR=odds ratio. SWHSI=surgical wound healing by secondary intention. WHQ=Bluebelle Wound Healing Questionnaire. *Adjusted for wound size, duration of wound, and wound location as fixed effects and centre as a random effect. †Cox's proportional hazards regression. Data are 25th percentiles as fewer than half of the participants had healing confirmed in this analysis set so a median could not be reported. ‡Logistic regression using events over 12 months of follow-up. §Linear regression.

Table 2: **Primary and secondary outcomes for NPWT and usual care groups for the intention-to-treat population**

Negative pressure wound therapy versus usual care in patients with surgical wound healing by secondary intention in the UK (SWHSI-2): an open-label, multicentre, parallel-group, randomised controlled trial

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- WHY
  - Dogma-challenging
- IMPLICATIONS
  - Unclear if generalisable beyond diabetic foot post-operative wounds
  - 2 prev v.small RCTs and 48 observational studies suggested faster wound healing
  - Manufacturers' guides and clinical guidelines also recommend NPWT
  - Clinical practice and guidelines should be based on large well designed RCTs
  - NPWT should not be routinely used or recommended in foot ulcers post-op

Lancet 2024; 405: 1689–99

1

- WHY
  - Paradigm-shifting
- WHAT/HOW
- KEY FINDINGS

ORIGINAL ARTICLE

Ivermectin to Control Malaria — A Cluster-Randomized Trial

C. Chaccour,[1,3] M. Maia,[4,5] M. Kariuki,[6] P. Ruiz-Castillo,[1] C. Wanjiku,[4] L. Kasiwa,[4] A. Brazeal,[4] A. Casellas,[1] M. Ngama,[6] T. Onyango,[4] E. Elobolobo,[7] K. Kazungu,[4] M. Mael,[1] W. Wangari,[4] K. Nuru,[4] R. Otuko,[4] A. Sanz,[1] I. Ringera,[4] A. Matano,[6] S. Mitora,[6] M. Ribes,[1] J. Brew,[7] N. Gorski,[1] P. Nicolas,[1] S. Stanulovic,[1] I. Omondi,[4] J. Furnival-Adams,[1] L. Túnez,[1] J. Mbarak,[6] V. Vegove,[8] E. Yaa,[6] S. Mramba,[6] Y. Kibet,[6] N. Nyambura,[6] C. Rotich,[6] S. Wanjiru,[6] M. Vura,[6] F. Wanjiku,[6] L. Sam,[9] L. Collins,[10] K. Xia,[11] F. Hammann,[12] F. Saúte,[13] M. Rudd,[14] C. Rist,[11] C. Jones,[4,5] J. Mwangangi,[6,15] and N.R. Rabinovich[1,16]

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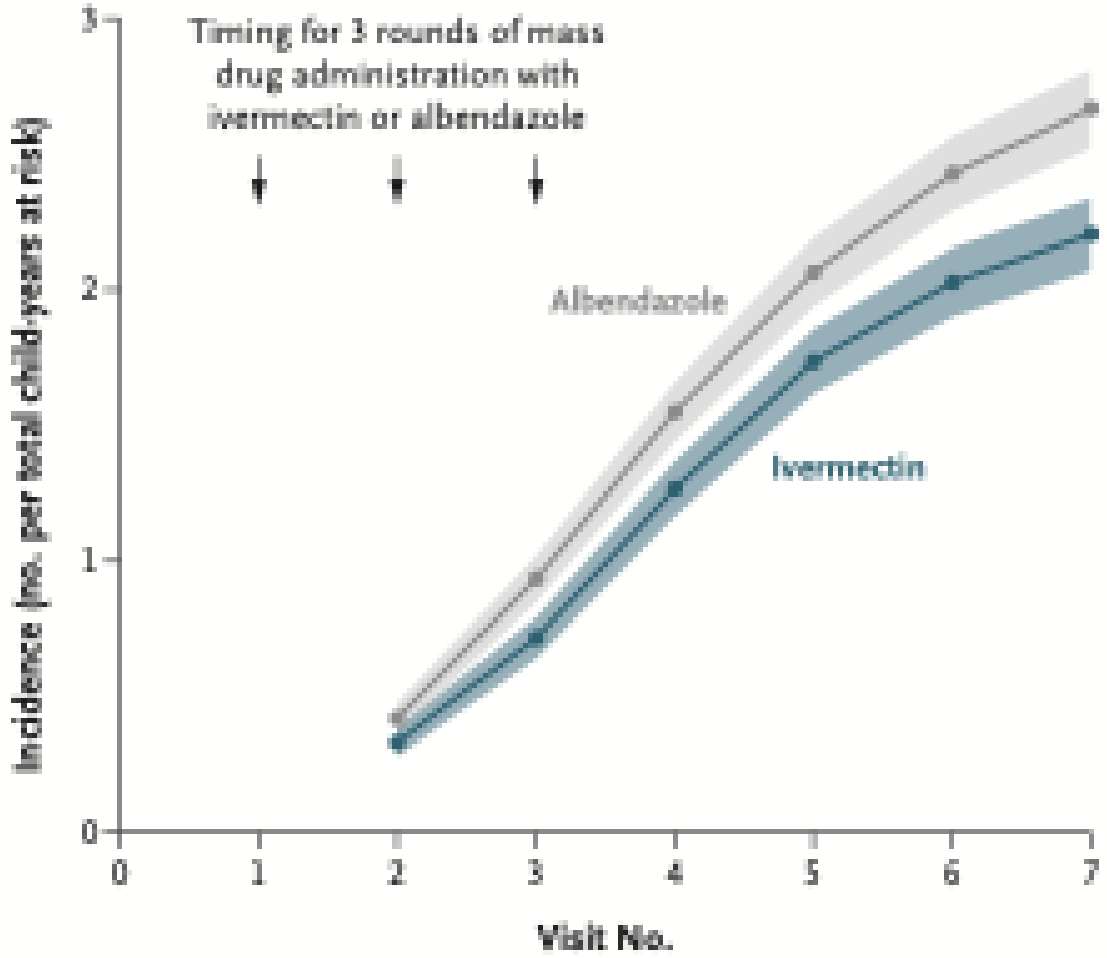
- WHY
  - Paradigm-shifting
- WHAT/HOW
  - Academic-sponsored, open label, assessor blinded cluster RCT in Kwale, Kenya
  - P – Patients (all >15kg not pregnant)) living in household clusters
    - Clusters=84, participants=30,727, outcome-assessed children=2,871
  - I – Ivermectin 400mcg/kg monthly for 3 months early wet season
  - C – Albendazole 400mg as above
  - O – Cumulative incidence of malaria infection among children aged 5-15 over 6 months period following intervention

N ENGL J MED [illegible] NEJM.ORG JULY 24, 2025

Table 2. Results for the Incidence of Malaria Infection.*

Characteristic	Incidence Rate Ratio, Ivermectin vs. Albendazole (95% CI)	
	All Covariates	Final Model
Trial-group assignment		
Albendazole	Reference	Reference
Ivermectin	0.69 (0.53–0.90)	0.74 (0.58–0.95)†



Albendazole							
No. of children tested	1255	1154	1108	1121	1086	1068	1009
Cumulative no. of cases		203	453	751	1000	1177	1292
Ivermectin							
No. of children tested	1180	1135	1061	1069	1075	1051	978
Cumulative no. of cases		157	341	602	825	964	1048

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- WHY
  - Paradigm-shifting
- IMPLICATIONS
  - Note high baseline coverage of insecticide-impregnated bednets
  - Malaria incidence was 26% lower with ivermectin than albendazole
  - It is feasible to decrease malaria incidence by targeting mosquitoes via human treatment – overcomes insecticide resistance and human behavior changes

N ENGL J MED 393;4 NEJM.ORG JULY 24, 2025

ORIGINAL ARTICLE

One Dose versus Three Doses of Benzathine Penicillin G in Early Syphilis

E.W. Hook III,[1] J.A. Dionne,[1] K. Workowski,[2] C.J. McNeil,[3] S.N. Taylor,[4] T.A. Batteiger,[5] J.C. Dombrowski,[6] K.H. Mayer,[7,8] A.C. Seña,[9] M.M. Hamill,[10] H.C. Wiesenfeld,[11,12] C. Zhu,[13] C. Perlowski,[14] J.E. Mejia-Galvis,[15] and L.M. Newman[15]

- WHY
  - Practice-changing
- WHAT/HOW
- KEY FINDINGS

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- WHY
  - Practice-changing
- WHAT/HOW
  - Open, label, NIH-sponsored, individually randomised non-inf trial at 10 US sites
  - P – Adults with 1ry, 2ry or early latent syphilis
  - I/C – Benzathine penicllin G 2.4M U IM once or x3 at weekly intervals
  - O – Decrease in RPR by >=2 dilutions (or to –ve) at 6 months

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Table 2. Serologic Response to Treatment with Benzathine Penicillin G at Month 6, According to Syphilis Stage.

Syphilis Stage	Intention-to-Treat Analysis			Per-Protocol Analysis		
	One Dose*	Three Doses	Total	One Dose†	Three Doses	Total
	number/total number (percent)					
Primary	20/25 (80)	16/23 (70)	36/48 (75)	19/21 (90)	14/20 (70)	33/41 (80)
Secondary	45/58 (78)	46/59 (78)	91/117 (78)	40/52 (77)	32/45 (71)	72/97 (74)
Primary and secondary	65/83 (78)	62/82 (76)	127/165 (77)	59/73 (81)	46/65 (71)	105/138 (76)
Early latent	29/41 (71)	25/42 (60)	54/83 (65)	23/33 (70)	20/28 (71)	43/61 (70)

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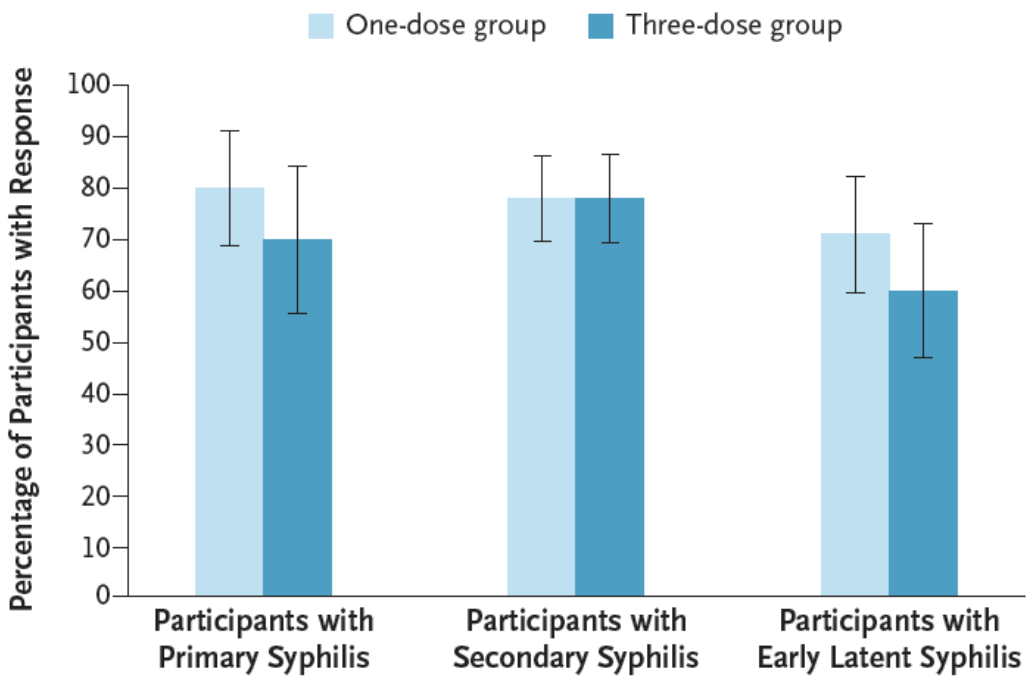

Figure 2. Serologic Response to Treatment with Benzathine Penicillin G.

Table 3. Serologic Response to Treatment with Benzathine Penicillin G at Month 6, According to Other Factors.

Factor and Analysis	One-Dose Group		Three-Dose Group		Total	
	no. with response/ total no.	*percent (95% CI)*	*no. with response/ total no.*	*percent (95% CI)*	*no. with response/ total no.*	*percent (95% CI)*
HIV status						
Intention-to-treat analysis						
Positive	53/70	76 (65–84)	59/83	71 (61–80)	112/153	73 (66–80)
Negative	39/51	76 (63–86)	28/40	70 (55–82)	67/91	74 (64–82)
Per-protocol analysis						
Positive	46/64	72 (60–81)	45/66	68 (56–78)	91/130	70 (62–77)
Negative	36/42	86 (72–93)	21/27	78 (59–89)	57/69	83 (72–90)

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- WHY
  - Practice-changing
- IMPLICATIONS
  - One dose of BPG should be standard for early syphilis, including where HIV+ve
    - Note 80% of HIV +ve people had CD4 count>350. Results were same if <200.
  - Most guidelines already recommend this, but these data should help change ongoing routine use of 3 doses in those with HIV
  - Current ongoing syphilis epidemics and BPG shortages increase the importance of these findings

N ENGL J MED 393;9 NEJM.ORG SEPTEMBER 4, 2025

ORIGINAL ARTICLE

Noninferiority of One HPV Vaccine Dose to Two Doses

A.R. Kreimer,[1] C. Porras,[2] D. Liu,[1] A. Hildesheim,[1] L.J. Carvajal,[2] R. Ocampo,[2] B. Romero,[2] M.H. Gail,[1] B. Cortes,[2] M.S. Sierra,[1] K. Coronado,[2] J. Sampson,[1] C. Coto,[2] C.L. Dagnall,[3] D. Mora,[2] T.J. Kemp,[4] M. Zuniga,[2] L.A. Pinto,[4] G. Barrientos,[2] J. Schussler,[5] Y. Estrada,[2] C. Montero,[2] C. Avila,[2] D. Ruggieri,[5] J.T. Cyr,[5] S. Chanock,[1] D.R. Lowy,[6] J.T. Schiller,[6] and R. Herrero[2,7]

- WHY
  - Practice-changing
- WHAT/HOW
- KEY FINDINGS

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- WHY
  - Practice-changing
- WHAT/HOW
  - Individually-randomised trial in 200 districts in Costa Rica
  - P – Girls aged 12-16 years, HPV vaccine naïve
  - I/C – Bivalent (16/18) or nonavalent HPV vaccine, two doses vs one plus DTP vaccine, 6/12 apart
  - O – New persistent vaginal HPV16 or 18 infection from 12-60/12 post rando

N ENGL J MED 393;24 NEJM.ORG DECEMBER 18/25, 2025

Table 1. Noninferiority Analysis.*

End Point	Bivalent HPV Vaccine				Nonavalent HPV Vaccine			
	No. of Participants	No. of Events	Cumulative Event Rate/100 Participants (95% CI)	Rate Difference (95% CI)†	No. of Participants	No. of Events	Cumulative Event Rate/100 Participants (95% CI)	Rate Difference (95% CI)†
Primary end point: infection with HPV type 16 or 18								
One dose	4880	14	0.29 (0.15 to 0.52)		4851	23	0.48 (0.28 to 0.75)	
Two doses	4880	21	0.42 (0.23 to 0.71)	–0.13 (–0.45 to 0.15)	4849	13	0.27 (0.12 to 0.51)	0.21 (–0.09 to 0.51)
P value‡				<0.001				<0.001
Secondary end point: infection with HPV type 16, 18, 31, 33, 45, 52, or 58								
One dose	4880	824	16.88 (15.71 to 18.11)		4851	79	1.64 (1.25 to 2.10)	
Two doses	4880	721	14.77 (13.63 to 15.96)	2.12 (0.46 to 3.76)	4849	52	1.08 (0.75 to 1.50)	0.56 (0.01 to 1.11)
P value‡				Not calculated				<0.001

* The noninferiority analysis was performed in the per-protocol population, which included all the participants who had received both assigned doses (the two assigned human papillomavirus [HPV] vaccine doses or one HPV vaccine dose and one dose of the control vaccine [tetanus, diphtheria, and pertussis vaccine]). The primary end point was new HPV16 or HPV18 infection that occurred during the period from month 12 to month 60 and persisted for at least 6 months. The secondary end point was new infection with the HPV types shown that occurred during the period from month 12 to month 60 and persisted for at least 6 months. Missing data have been imputed. The event numbers have been rounded to the nearest integer. Details regarding the methods for handling missing data are provided in the Supplementary Methods section in the Supplementary Appendix.

† The rate difference is the event rate in the one-dose group minus that in the two-dose group.

‡ The P value is for the noninferiority of one dose to two doses. A one-sided P value of less than 0.025 was considered to indicate statistical significance (i.e., the observed rate difference was significantly lower than the prespecified noninferiority margin). The prespecified noninferiority margin was 1.25 infections per 100 participants for the primary end point. The noninferiority test for the secondary end point was performed only for the nonavalent vaccine (prespecified noninferiority margin, 2.55 infections per 100 participants) and was not performed for the bivalent vaccine because the HPV types included in the secondary end point are not in the bivalent vaccine formulation.

Table 2. Analysis of Vaccine Effectiveness.*

End Point	Bivalent HPV Vaccine				Nonavalent HPV Vaccine			
	No. of Participants	No. of Events	Event Rate/100 Participants (95% CI)	Vaccine Effectiveness (95% CI)†	No. of Participants	No. of Events	Event Rate/100 Participants (95% CI)	Vaccine Effectiveness (95% CI)†
Primary end point: infection with HPV type 16 or 18								
Survey	2990	160	5.37 (4.55–6.17)		2990	159	5.32 (4.49–6.17)	
One dose	4068	4	0.10 (0.02–0.21)	98.2 (96.1–99.6)	4109	7	0.16 (0.05–0.30)	97.0 (94.3–99.1)
P value‡				<0.001				<0.001
Survey	2990	162	5.43 (4.56–6.24)		2990	160	5.35 (4.54–6.22)	
Two doses	4040	5	0.12 (0.03–0.23)	97.8 (95.6–99.3)	4083	3	0.08 (0.01–0.16)	98.5 (96.7–99.7)
P value‡				<0.001				<0.001
Secondary end point: infection with HPV type 16, 18, 31, 33, 45, 52, or 58								
Survey	2990	390	13.03 (11.88–14.24)		2990	389	13.01 (11.61–14.29)	
One dose	4068	363	8.93 (8.01–9.79)	31.5 (21.5–40.1)	4109	29	0.72 (0.45–0.99)	94.5 (92.3–96.6)
Survey	2990	385	12.89 (11.59–14.18)		2990	393	13.16 (11.91–14.50)	
Two doses	4040	311	7.69 (6.93–8.56)	40.3 (31.3 to 48.8)	4083	22	0.55 (0.31–0.81)	95.8 (93.8–97.6)

* Vaccine effectiveness was assessed in the per-protocol population. Shown are infections that were observed at the visits at month 54 and month 60 among the trial participants and at month 0 (the enrollment visit) and month 6 (the second visit) among the survey participants. Missing data have been imputed. The estimated numbers of events among the survey participants have been adjusted for prevalent infections, and propensity-score adjustment was used to adjust for different distributions in age, geographic region, and sexual activity between the trial participants and the survey participants (the adjusted number of events in the survey population is considered to be the standardized number of events in the same population as the trial group in the comparison). The event numbers have been rounded to the nearest integer. Details regarding the methods for estimating the vaccine effectiveness are provided in the Supplementary Methods section in the Supplementary Appendix.

† The vaccine effectiveness values are expressed as percentages.

‡ A one-sided P value of less than 0.025 was considered to indicate statistical significance (i.e., the vaccine effectiveness was higher than 80%).

ORIGINAL ARTICLE

Noninferiority of One HPV Vaccine Dose to Two Doses

A.R. Kreimer,[1] C. Porras,[2] D. Liu,[1] A. Hildesheim,[1] L.J. Carvajal,[2] R. Ocampo,[2] B. Romero,[2] M.H. Gail,[1] B. Cortes,[2] M.S. Sierra,[1] K. Coronado,[2] J. Sampson,[1] C. Coto,[2] C.L. Dagnall,[3] D. Mora,[2] T.J. Kemp,[4] M. Zuniga,[2] L.A. Pinto,[4] G. Barrientos,[2] J. Schussler,[5] Y. Estrada,[2] C. Montero,[2] C. Avila,[2] D. Ruggieri,[5] J.T. Cyr,[5] S. Chanock,[1] D.R. Lowy,[6] J.T. Schiller,[6] and R. Herrero[2,7]

- WHY
  - Practice-changing
- WHAT/HOW
- IMPLICATIONS
  - One dose of HPV vaccine (whether 2 or 9 valent) is sufficient as a cervical cancer prevention strategy
  - WHO's current recommendation of "one or two doses" should change to one
  - This will decrease costs, and increase uptake, especially in lower income countries

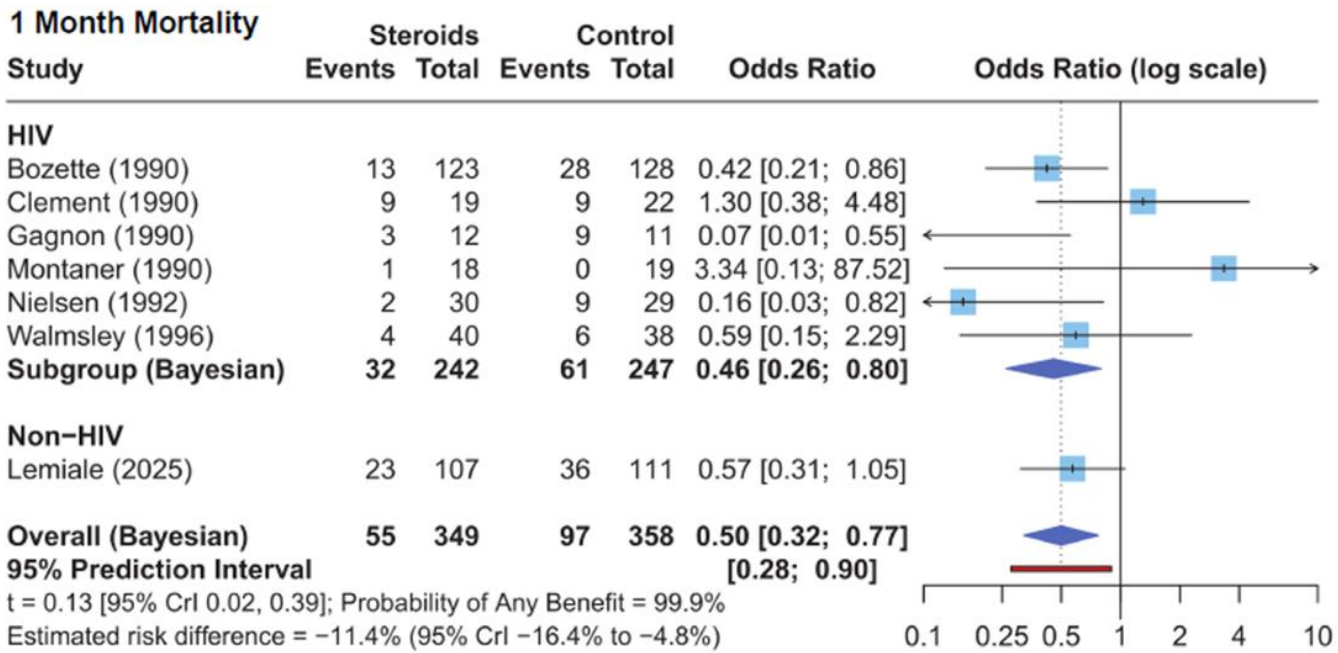
Lemiale et al – Lancet Resp Med – PIC trial

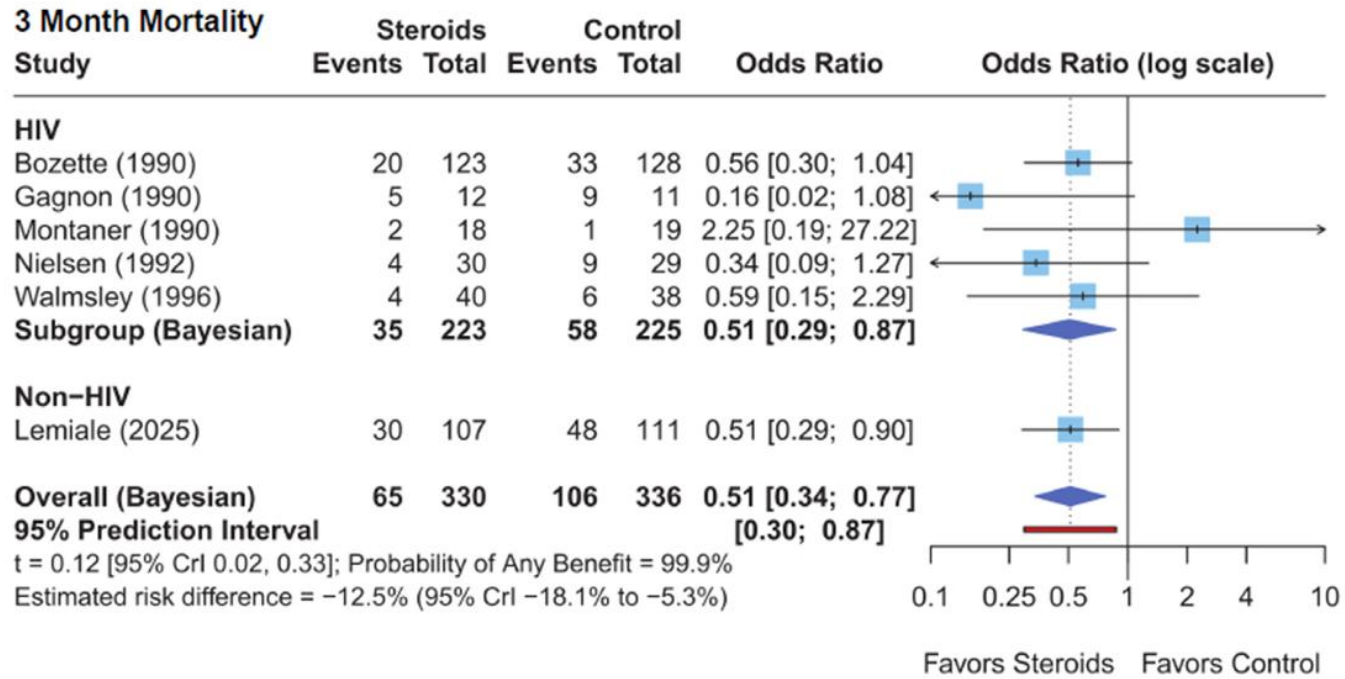
- WHY
  - Practice-changing (probably!)
- WHAT/HOW
- KEY FINDINGS

Lemiale et al – Lancet Resp Med – PIC trial

- WHY
  - Practice-changing (probably!)
- WHAT/HOW
  - Double blind RCT at 27 hospitals in France
  - P – HIV-ve adults with proven PJP with severe hypoxaemia (n=226)
  - I – Methylprednisolone IV 30mg BD for 5 days then tapered to day 21
  - C – Identical placebo
  - O – All cause 28-day mortality

Primary outcome Outcome (ITT)	Placebo	Corticosteroid	Absolute difference (placebo − steroid)	p value
28-day all-cause mortality	36/111 (32.4%)	23/107 (21.5%)	**10.9%** (95% CI −0.9 to 22.5)	0.069





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Concise communication

Contextualizing the use of corticosteroids in severe *Pneumocystis jirovecii* pneumonia through a Bayesian lens

Todd C. Lee[1], Arthur M. Albuquerque[2], Emily G. McDonald[3,*]

[1] *Division of Infectious Diseases, Department of Medicine, McGill University, Montréal, Canada*
[2] *Department of Medicine, School of Medicine, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil*
[3] *Division of General Internal Medicine, Department of Medicine, McGill University, Montreal, Canada*

Lemiale et al – Lancet Resp Med – PIC trial

- WHY
  - Practice-changing (probably!)
- IMPLICATIONS
  - Mortality “significantly” lower at 90 days but not 28 days; in meta-analysis, 99.1% posterior probability that steroids decrease mortality in PJP (HIV +ve and –ve combined)
  - Unless/until a repeat larger RCT is done showing no benefit, adjunctive corticosteroids should be recommended for hypoxaemic PJP

- WHY
  - Practice-changing, dogma challenging
- WHAT/HOW
- KEY FINDINGS

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trial of High-Dose Oral Rifampin in Adults with Tuberculous Meningitis

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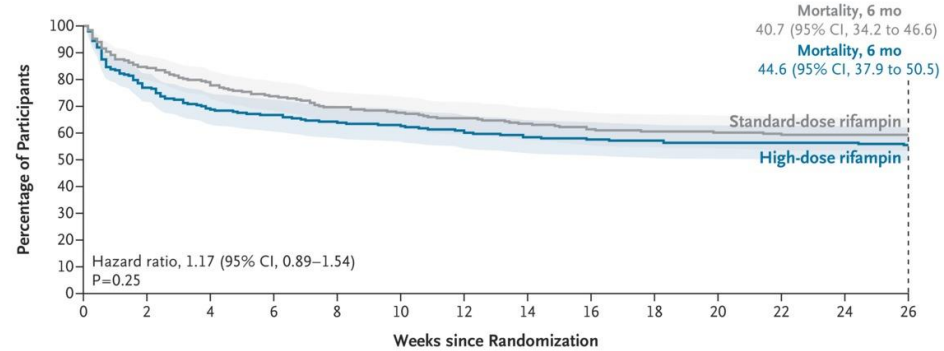
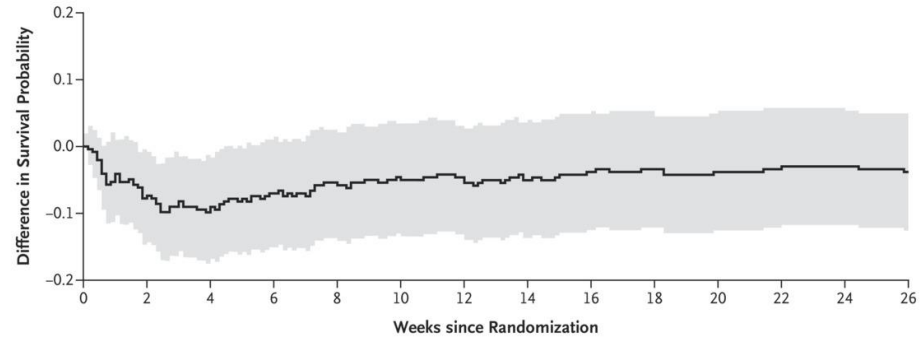
- WHY
  - Practice-changing, dogma challenging
- WHAT/HOW
  - Double-blind RCT in Indonesia, Sth Africa and Uganda
  - P – Adults with TB meningitis (n=499)
  - I – Rif 10mg/kg/day, plus standard INH, PYZ, ETH PLUS Rif 25mg/kg/day
  - C - Rif 10mg/kg/day, plus standard INH, PYZ, ETH PLUS Placebo
  - O – All-cause 6-month mortality

A Overall Survival at 6 Months



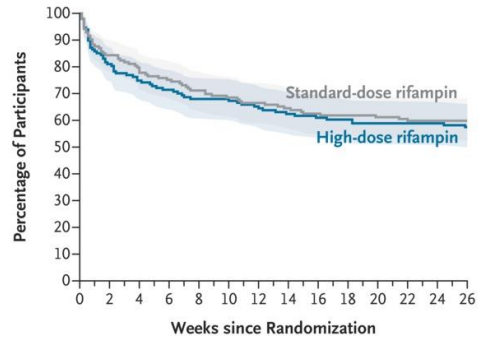
No. at Risk														
Standard-dose rifampin	250	209	194	180	170	164	159	153	148	146	144	143	142	142
High-dose rifampin	249	189	169	162	156	151	146	140	138	137	135	135	135	133

B Differences in Survival over Time



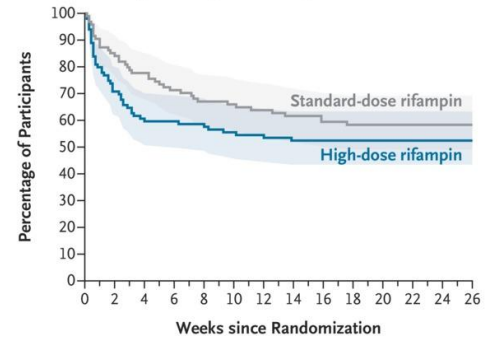
No. at Risk														
Standard-dose rifampin	250	209	194	180	170	164	159	153	148	146	144	143	142	142
High-dose rifampin	249	189	169	162	156	151	146	140	138	137	135	135	135	133

C Overall Survival among Participants Living with HIV



No. at Risk														
Standard-dose rifampin	155	129	121	113	107	103	100	97	94	93	91	90	89	89
High-dose rifampin	149	119	109	104	99	97	93	89	87	86	84	84	84	82

D Overall Survival among HIV-Negative Participants



No. at Risk														
Standard-dose rifampin	95	80	73	67	63	61	59	56	54	53	53	53	53	53
High-dose rifampin	100	70	60	58	57	54	53	51	51	51	51	51	51	51

The NEW ENGLAND JOURNAL of MEDICINE

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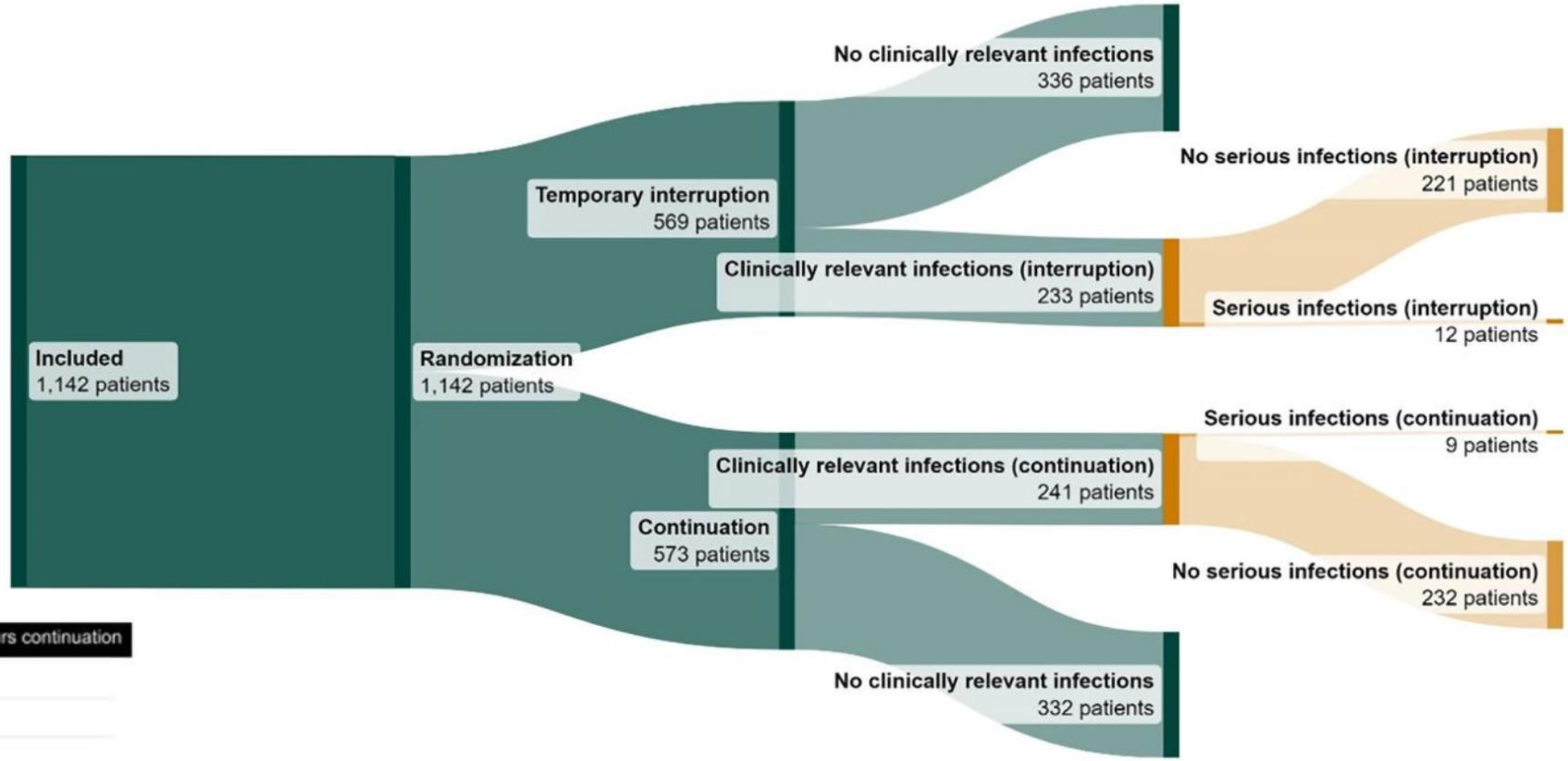
- WHY
  - Practice-changing, dogma challenging
- IMPLICATIONS
  - High dose rifampicin should not be used for TB meningitis
  - Don’t change practice based on mouse studies, phase 2 trials, observational data and/or PK rationale (e.g. CSF Rif levels ~0 in most patients)

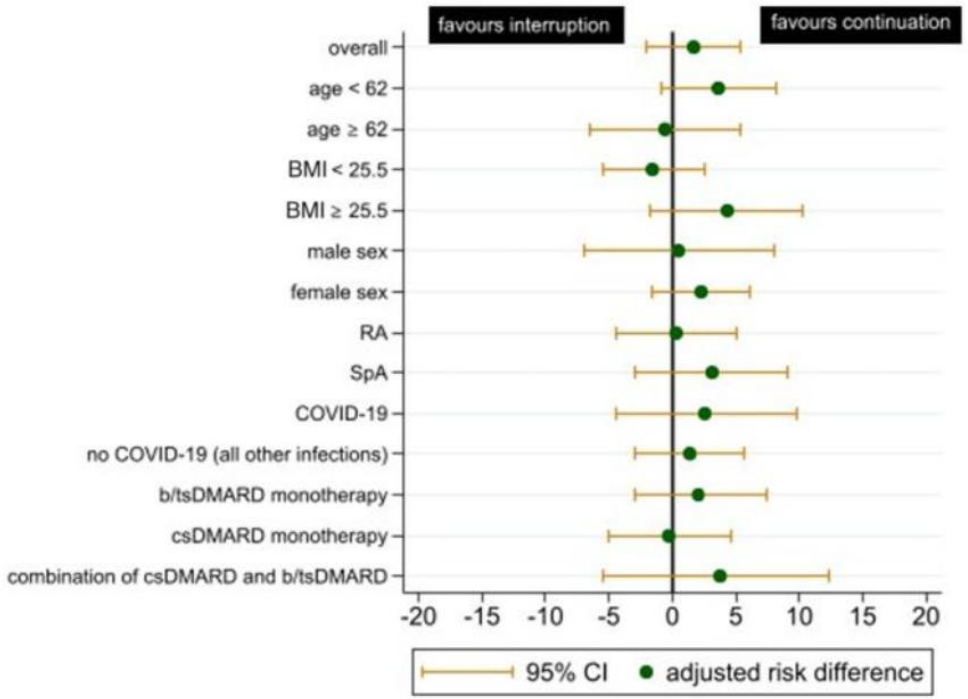
Continuation Versus Temporary Interruption of Immunomodulatory Agents During Infections in Patients With Inflammatory Rheumatic Diseases: A Randomized Controlled Trial

Merel A. A. Opdam,[1] Nathan den Broeder,[1] Reinout van Crevel,[2] Lisa Schapink,[1] Léon Raymakers,[1] Jasper Broen,[3] Lise M. Verhoef,[1] and Alfons A. den Broeder[1,4]

- WHY
  - Practice-changing, dogma challenging
- WHAT/HOW
  - Open-label, academically sponsored RCT at 5 Dutch sites
  - P – 1,142 adults with rheumatic diseases (RA, PsA, SpA) on immunosuppression
  - I – Continuation of immunosuppression if an infection occurs
  - C – Interruption of immunosuppression if an infection (>=grade 2) occurs
  - O – Proportion experiencing >=1 “serious” infection (>=grade 3)

Opdam, 2025. CID





Severity	Explanation
Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate; minimal, local or non-invasive intervention indicated; limiting age-appropriate instrumental ADL[a]
Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL[b]
Grade 4	Life-threatening consequences, urgent intervention indicated
Grade 5	Death related to AE

Table 4. Infection Types

Infection Type	Frequency (n, %)
Respiratory infections (excluding COVID-19)	781 (40.0%)
Infections caused by SARS-CoV-2	489 (25.1%)
Skin infections	211 (10.8)
Urogenital infections	208 (10.7)
Ear, nose, throat, teeth, jaw and maxillofacial infections	103 (5.3)
Abdominal infections	85 (4.4)
Eye infections	40 (2.1)
Other[a]	26 (1.1)
Musculoskeletal infections	9 (0.5)

Disease Activity

The first patient-reported disease activity after the first clinically relevant infection was similar between both treatment groups. Median disease activity was 3.5 (IQR 2.0–7.0) for temporary interruption and 4.0 (IQR 2.0– 6.0) for continuation ($P = .96$).

Continuation Versus Temporary Interruption of Immunomodulatory Agents During Infections in Patients With Inflammatory Rheumatic Diseases: A Randomized Controlled Trial

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- WHY
  - Practice-changing, dogma challenging
- IMPLICATIONS
  - Largely applies to patients with RA (and similar) who get URTIs
  - Such patients should continue their usual treatment unless the infection is severe (i.e. requires hospital admission)

Opdam, 2025. CID

Oral gepotidacin for the treatment of uncomplicated urogenital gonorrhoea (EAGLE-1): a phase 3 randomised, open-label, non-inferiority, multicentre study

Jonathan D C Ross, Janet Wilson, Kimberly A Workowski, Stephanie N Taylor, David A Lewis, Sally Gatsi, William Flight, Nicole E Scangarella-Oman, Charles Jakielaszek, Dan Lythgoe, Marcy Powell, Salim Janmohamed, Judith Absalon, Caroline Perry

- WHY
  - Practice-changing, paradigm-shifting

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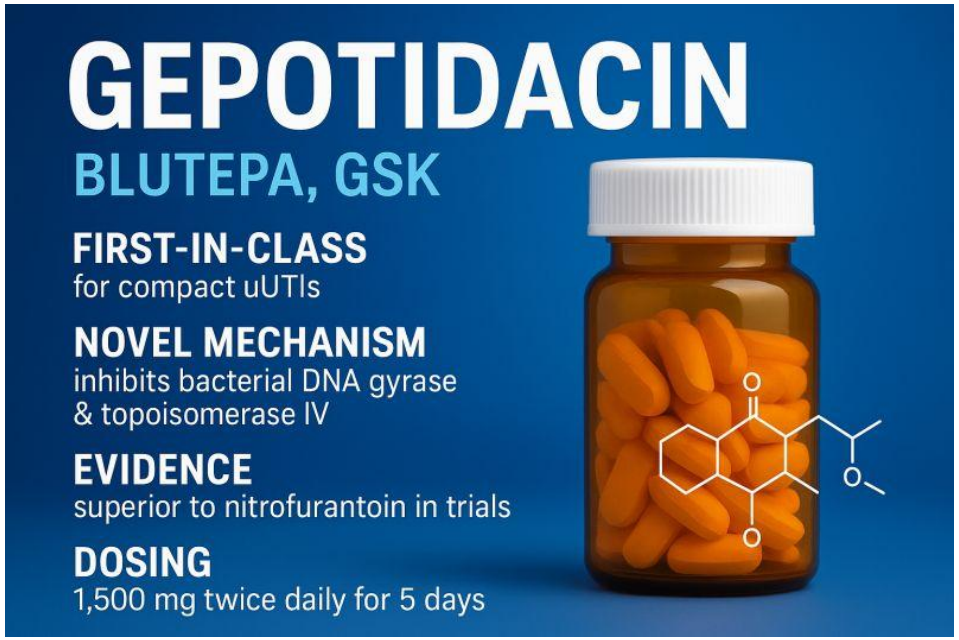
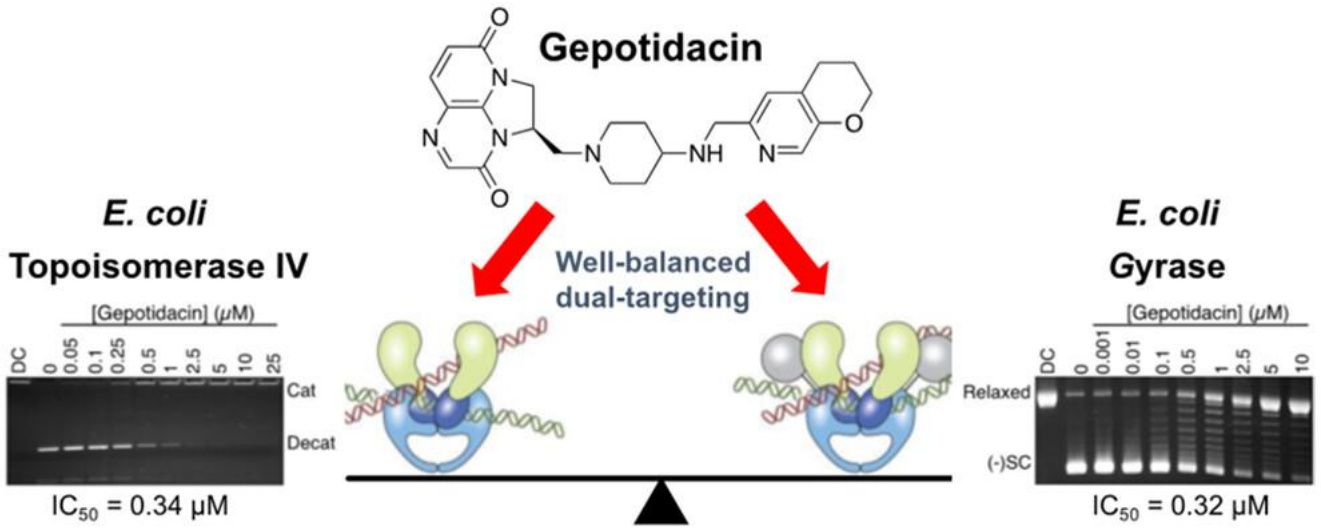
- WHY
  - Practice-changing, paradigm-shifting
- WHAT/HOW
  - Pharma-sponsored open-label non-inferiority phase 3 RCT
  - P – 629 people >=12yo with urogenital gonorrhoea
  - I – Gepotidacin 3g PO x 2 doses 12h apart
  - C – Ceftriaxone 500mg IMI plus Azithromycin 1g PO, both single dose
  - O – “Microbiological success” (eradication of urogenital N.gono at day 4-8)

	Micro-ITT population		Microbiologically evaluable population	
	2 × 3000 mg gepotidacin (N=202)	500 mg ceftriaxone plus 1 g azithromycin (N=204)	2 × 3000 mg gepotidacin (N=187)	500 mg ceftriaxone plus 1 g azithromycin (N=186)
Microbiological success, n (% [95% CI])	187 (92·6% [88·0 to 95·8])	186 (91·2% [86·4 to 94·7])	187 (100% [98·0 to 100])	186 (100% [98·0 to 100])
Treatment difference, % (95% CI)*	–0·1% (–5·6 to 5·5)	..	0·0% (–2·6 to 2·7)	..
One-sided p value for superiority	0·5072	..	..	..
Microbiological failure	15 (7·4%)	18 (8·8%)	0	0
Bacterial persistence	0	0	0	0
Unable to determine†	15 (7·4%)	18 (8·8%)	NA	NA
Use of other systemic antimicrobials‡	0	2 (1·0%)	NA	NA

AESI	208 (67%)	49 (16%)
CDAD	0	0
Cardiovascular‡	1 (<1%)	1 (<1%)
Gastrointestinal	206 (67%)	49 (16%)
Potential acetylcholinesterase inhibition§	197 (64%)	34 (11%)





Oral gepotidacin for the treatment of uncomplicated urogenital gonorrhoea (EAGLE-1): a phase 3 randomised, open-label, non-inferiority, multicentre study

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- WHY
  - Practice-changing, paradigm-shifting
- IMPLICATIONS
  - Note 92% of participants were male and 72% MSM.
  - First new drug class for gonorrhoea in decades
  - MDR gonorrhoea is now (potentially) treatable
  - Gonorrhoea can be treated without injections – BUT expensive ++
  - Zoliflodacin another new oral drug class FDA approved recently
  - Will the use of Gepo for UTI waste this opportunity to improve MDR Gono Rx?

JAMA | Original Investigation

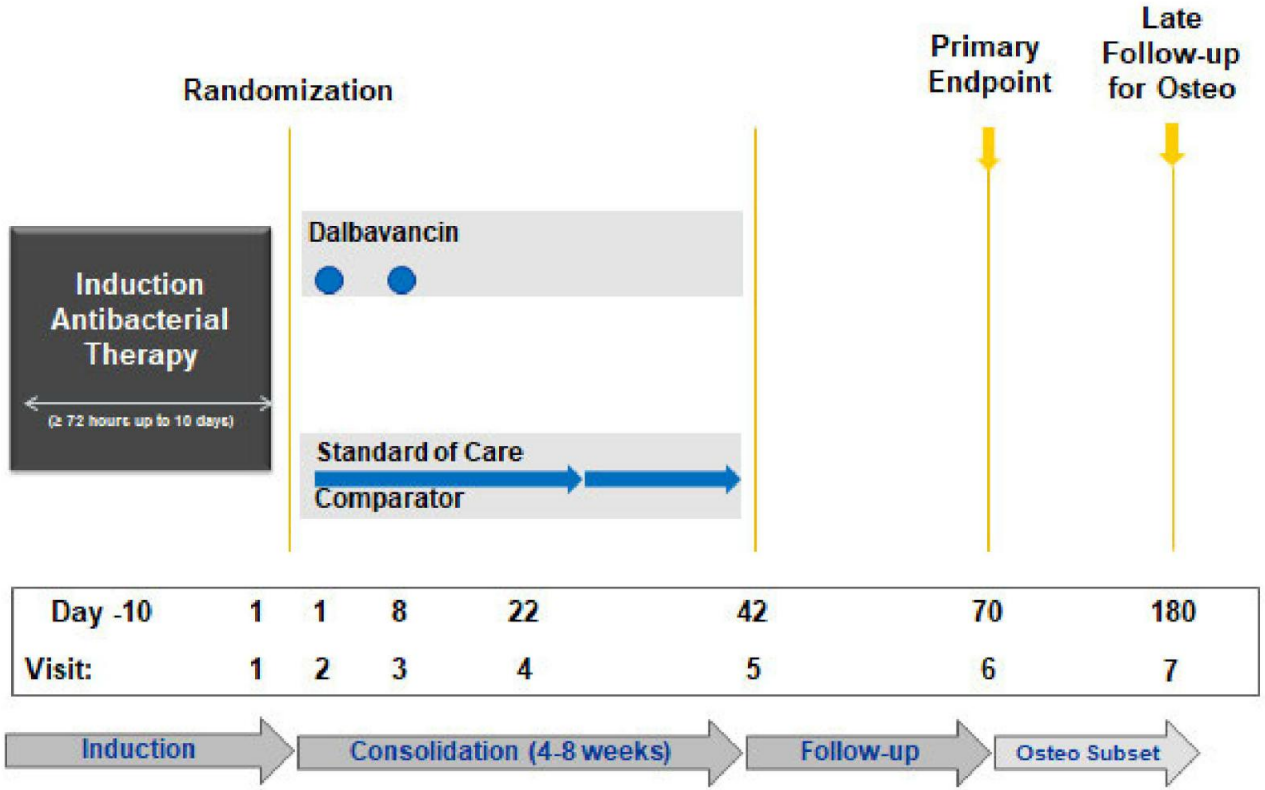
Dalbavancin for Treatment of *Staphylococcus aureus* Bacteremia
The DOTS Randomized Clinical Trial

- WHY
  - Paradigm-shifting

JAMA | Original Investigation

Dalbavancin for Treatment of *Staphylococcus aureus* Bacteremia
The DOTS Randomized Clinical Trial

- WHY
  - Paradigm-shifting
- WHAT/HOW
  - Open-label, NIAID funded, superiority RCT at 23 hospitals in USA and Canada
  - P – 200 adults w/ “complicated” SAB, cleared BC, resolution of fever, 3-10/7 Rx
  - I – Dalbavancin 1500mg IVI on days 1 and 8
  - C – “Standard of care” (4-8 weeks cefazolin, nafcillin, vanco or dapto)
  - O – DOOR at day 70



Rank	Alive	How many of: 1) Clinical Failure 2) Infectious Complication 3) SAE, or AE leading to study drug discontinuation	QoL
1	Yes	0 of 3	Tiebreaker based on QoL score
2	Yes	1 of 3	
3	Yes	2 of 3	
4	Yes	3 of 3	
5	No (Death)	Any	

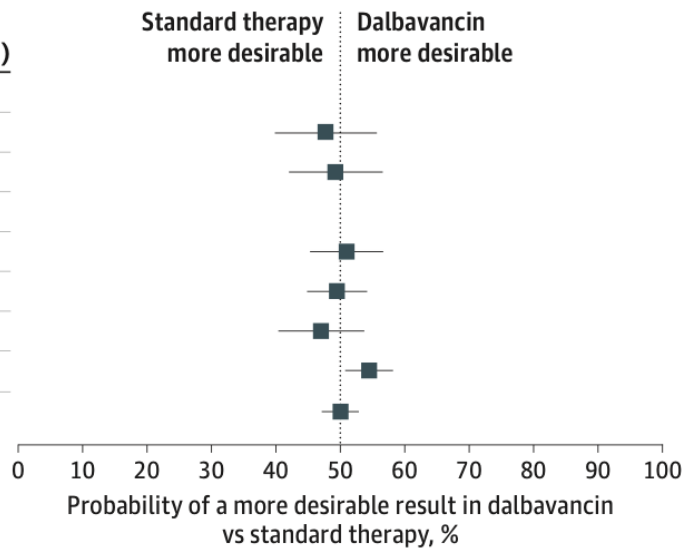
Anatomic site of infection, No. (%)[d]		
Soft tissue infection	40 (40)	30 (30)
Osteomyelitis, nonvertebral	17 (17)	19 (19)
Septic arthritis	12 (12)	14 (14)
Septic thrombophlebitis	10 (10)	14 (14)
Pneumonia/empyema	11 (11)	5 (5)
Septic pulmonary emboli	8 (8)	7 (7)
Right-sided endocarditis	6 (6)	4 (4)
Vascular graft infection/ mycotic aneurysm	4 (4)	6 (6)
Vertebral osteomyelitis	5 (5)	2 (2)
Cardiac device infection	4 (4)	2 (2)
Prosthetic joint infection	1 (1)	1 (1)
Visceral abscess	1 (1)	1 (1)
Deep-seated infection, No. (%)[e]	54 (54)	51 (51)
Days of bacteremia, No. (%)		
<2	77 (77)	64 (64)
2-4	21 (21)	26 (26)
>4	2 (2)	10 (10)
Transthoracic echocardiography performed, No. (%)	73 (73)	71 (71)
Transesophageal echocardiography performed, No. (%)	27 (27)	29 (29)
Duration of prerandomization therapy, median (IQR), d	8 (6-9)	7 (6-9)

Dalbavancin for Treatment of *Staphylococcus aureus* Bacteremia
The DOTS Randomized Clinical Trial

Figure 2. Primary Outcome (As-Randomized Population)

A Desirability of outcome ranking and components by treatment group

Source	Participants, No. (%)		Desirability of outcome ranking probability, % (95% CI)
	Dalbavancin (n = 100)	Standard therapy (n = 100)	
Desirability of outcome ranking			
With quality-of-life tiebreak (primary)			47.7 (39.8-55.7)
Without quality-of-life tiebreak			49.3 (42.0-56.6)
Desirability of outcome ranking components			
Clinical failure	20 (20.0)	22 (22.0)	51.0 (45.3-56.7)
Infectious complications	13 (13.0)	12 (12.0)	49.5 (44.8-54.2)
Nonfatal serious adverse events	40 (40.0)	34 (34.0)	47.0 (40.4-53.7)
Adverse events leading to discontinuation	3 (3.0)	12 (12.0)	54.5 (50.8-58.2)
Death	4 (4.0)	4 (4.0)	50.0 (47.1-52.9)

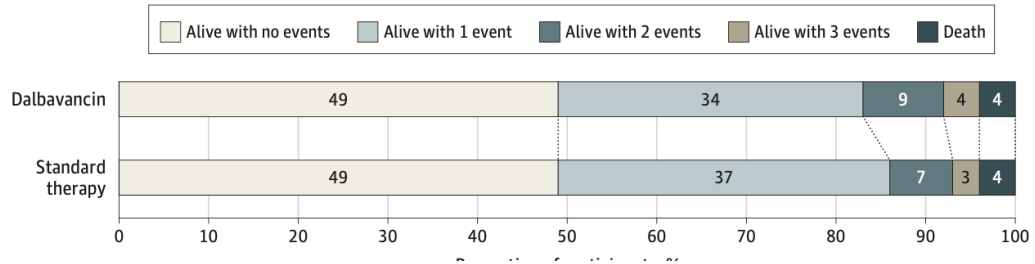


Dalbavancin for Treatment of *Staphylococcus aureus* Bacteremia
The DOTS Randomized Clinical Trial

B Desirability of outcome ranking and components by event status

DOOR component					Participants, No. (%)	
DOOR	Clinical failure	Infectious complications	Nonfatal SAE or AE leading to study drug discontinuation	Death	Dalbavancin (n = 100)	Standard therapy (n = 100)
Alive with no events	No	No	No	-	49 (49)	49 (49)
Alive with 1 event	No	No	Yes	-	24 (24)	23 (23)
	No	Yes	No	-	2 (2)	3 (3)
	Missing	No	No	-	8 (8)	11 (11)
Alive with 2 events	No	Yes	Yes	-	5 (5)	3 (3)
	Yes	Yes	No	-	1 (1)	2 (2)
	Missing	No	Yes	-	3 (3)	2 (2)
Alive with 3 events	Yes	Yes	Yes	-	4 (4)	2 (2)
	Missing	Yes	Yes	-	0	1 (1)
Death	-	-	-	Yes	4 (4)	4 (4)

C Distribution of desirability of outcome ranking by treatment group



JAMA | Original Investigation

Dalbavancin for Treatment of *Staphylococcus aureus* Bacteremia
The DOTS Randomized Clinical Trial

- WHY
  - Paradigm-shifting
- IMPLICATIONS
  - First RCT of a long-acting antibiotic for SAB
  - Note stable population, excluded L sided endocarditis . . . also small sample size
  - DOOR and clinical success the same – would probably have been better if dalbavancin's advantages measured (less lines, faster D/C home vs HITH etc.)
  - Oritavancin longer $T_{1/2}$ (~390h versus ~220h) likely would allow 1 dose
  - LGPs another option in stable SAB rather than EOS or D/C to HITH (but $$$)

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- WHY
  - Paradigm-shifting, practice changing

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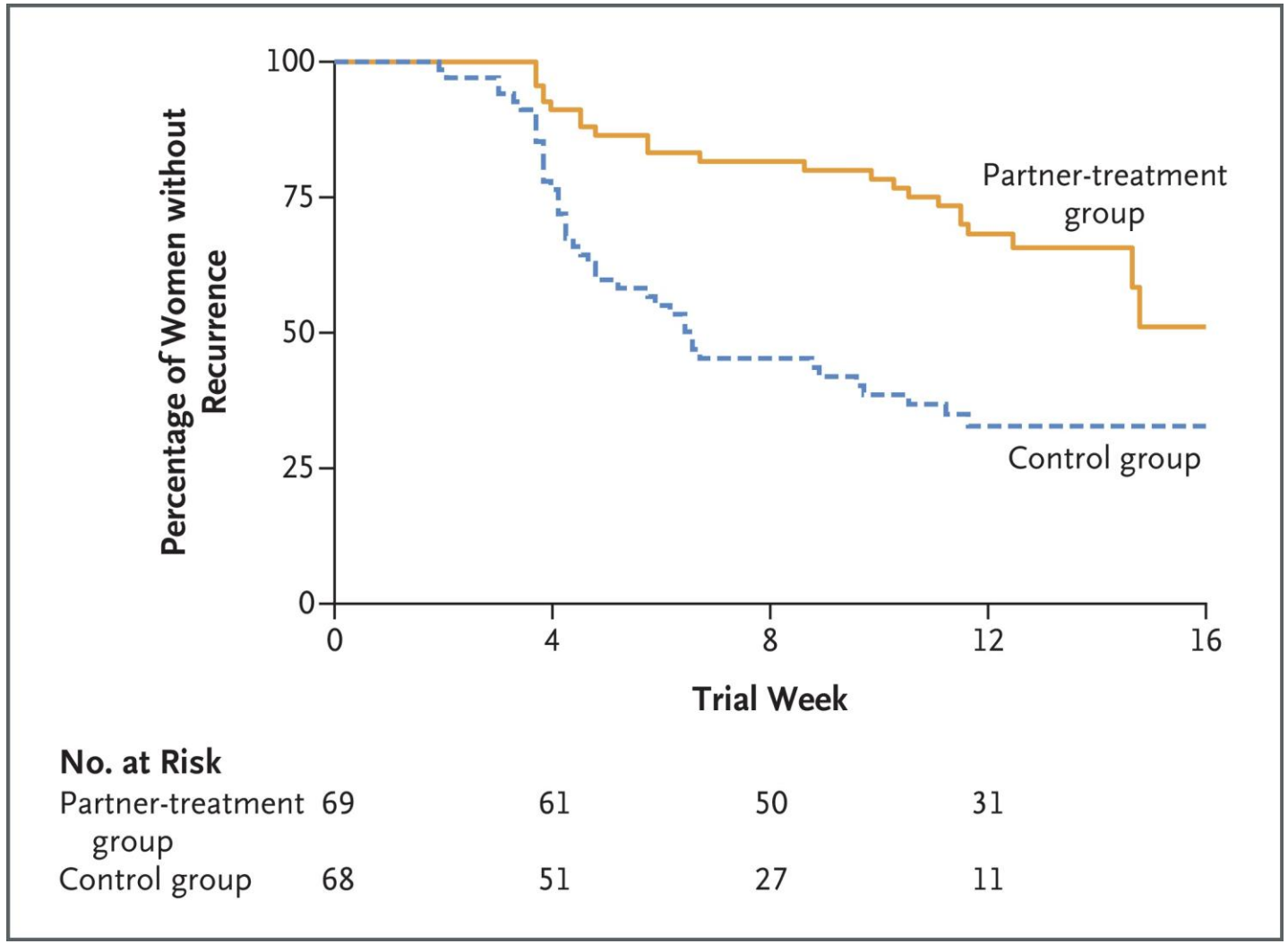
- WHAT/HOW
  - Open-label RCT at 5 sexual health or family planning clinics in Australia
  - P – Women Dx with BV in a monogamous relationship with a man+partners
  - I – Standard care+male partner Rx (PO MTZ +topical penile clinda BDx7 days)
  - C – Standard care (female partner PO MTZ BD for 7 days)
  - O – Recurrence of symptomatic BV within 12 weeks



No. at Risk

Partner-treatment group	69	61	50	31
Control group	68	51	27	11

Table 2. Primary and Secondary Analyses of Recurrence of Bacterial Vaginosis (Primary Outcome).*

Analysis and Population	Partner-Treatment Group				Control Group				Absolute Risk Difference (95% CI)	Hazard Ratio (95% CI)†	Difference in RMST (95% CI)‡
	No. with Recurrence/ Total No. (%)	Person-Yr	Recurrence Rate per Person-Yr (95% CI)	RMST	No. with Recurrence/ Total No. (%)	Person-Yr	Recurrence Rate per Person-Yr (95% CI)	RMST			
				days				*days*			*days*
Primary analysis											
Modified intention-to-treat population§	24/69 (35)	14.7	1.6 (1.1 to 2.4)	73.9	43/68 (63)	10.1	4.2 (3.2 to 5.7)	54.5	−2.6 (−4.0 to −1.2)	0.37 (0.22 to 0.61)	19.3 (11.5 to 27.1)¶
Secondary analyses‖											
Intention-to-treat population											
Missing data imputed as cure**	24/80 (30)	20.6	1.2 (0.8 to 1.7)	75.7	44/79 (56)	14.3	3.1 (2.3 to 4.1)	58.8	−2.0 (−3.0 to −0.9)	0.39 (0.24 to 0.64)	17.0 (10.0 to 23.9)
Missing data imputed as treatment failure**	44/80 (55)	20.4	2.2 (1.6 to 2.9)	75.0	59/79 (75)	14.2	4.1 (3.2 to 5.4)	58.1	−2.0 (−3.2 to −0.8)	0.45 (0.30 to 0.67)	16.9 (9.9 to 23.9)
Per-protocol population††	15/47 (32)	10.0	1.5 (0.9 to 2.5)	72.9	42/67 (63)	10.0	4.2 (3.1 to 5.7)	54.7	−2.7 (−4.2 to −1.2)	0.35 (0.19 to 0.64)	18.2 (9.4 to 27.0)

* Recurrence of bacterial vaginosis was defined by both the presence of at least three of four Amsel criteria and a Nugent score of 4 to 10 within 12 weeks. The four Amsel criteria are a characteristic homogeneous vaginal discharge, a vaginal pH of more than 4.5, a positive amine test (fishy odor), and the presence of clue cells on microscopic examination. During the coronavirus disease 2019 (Covid-19) pandemic, the Australian state of Victoria enacted strict government-enforced lockdown measures and isolation rules, which limited nonessential movement and reduced clinical capacity at clinical services. These measures commenced in March 2020 and extended for prolonged periods to the end of 2022. During this time, the protocol was revised to allow seven female participants who were unable to attend a clinical assessment of bacterial vaginosis to be included in the primary outcome. Four returned a vaginal smear for microscopy that had a Nugent score of 0 to 3, and two had an intermediate Nugent score (4 to 6). None of these six had clue cells present, so their trial end point was defined as no recurrence of bacterial vaginosis for the primary outcome. One person had a Nugent score of 7 and clue cells were present under microscopy, so the participant's trial end point was defined as recurrence of bacterial vaginosis. A sensitivity analysis that excluded persons whose participation was affected by the Covid-19 pandemic did not affect the primary outcome (hazard ratio, 0.37; 95% CI, 0.22 to 0.62).

† The hazard ratios were calculated with the use of Cox regression models.

‡ Shown is the between-group difference in days until recurrence, as calculated by the restricted mean survival time (RMST) method.

§ The primary analysis was a modified intention-to-treat analysis, excluding women who did not return for a post-treatment assessment for bacterial vaginosis. This population included all the women who had undergone randomization, were not deemed to have screening failure, received at least one dose of treatment, and underwent testing for clinical cure. If a participant attended the week 4 visit without bacterial vaginosis but was subsequently lost to follow-up, the week 4 data constituted the participant's trial end point and result (i.e., censored at this point).

¶ $P<0.001$.

‖ The widths of the confidence intervals for secondary analyses are not adjusted for multiplicity and should not be used for hypothesis testing.

** Two intention-to-treat analyses included all the participants who had undergone randomization. For those who were lost to follow-up, data missing at week 12 were imputed as cure or treatment failure.

†† The per-protocol analysis excluded nonadherent couples, defined as those taking less than 70% of all prescribed doses. If a participant attended the week 4 visit without bacterial vaginosis but was subsequently lost to follow-up, the week 4 data constituted the participant's trial end point and result (i.e., censored at this point).

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- IMPLICATIONS
  - BV is an STI (not a female only problem)
  - Male partners of women with BV should be offered treatment
  - But – small trial, one country – needs to be repeated
  - Recurrence rates are still very high, so better treatments are needed

Top 10 ID papers 2025+implications - less is more

1. Arundel – *Don't use NPWT for slow-healing post-op foot ulcers*
2. Chaccour – *Ivermectin mass Rx likely will reduce malaria transmission (as well as oncho)*
3. Hook – *One dose of Ben-penicillin is enough in early syphilis, regardless of HIV status*
4. Kreimer – *One dose of HPV vaccine is enough to prevent HPV and cervical cancer*
5. Lemiale – *Steroids should be used in hypoxic PJP, regardless of HIV status*
6. Meya – *Don't use high-dose rifampicin in TB meningitis*
7. Opdam – *Don't interrupt immunosuppression in RA patient with mild infections*
8. Ross – *Gonorrhoea – even MDR – can be treated with new oral agents*
9. Turner – *LGPs are a viable alternative to HITH for stable SAB*
10. Vodstricil– *BV is an STI and male partners should be treated*

Prof Josh Davis, February 2026 @gurujosh.bsky.social joshua.davis@health.nsw.gov.au

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