Oral is the new IV

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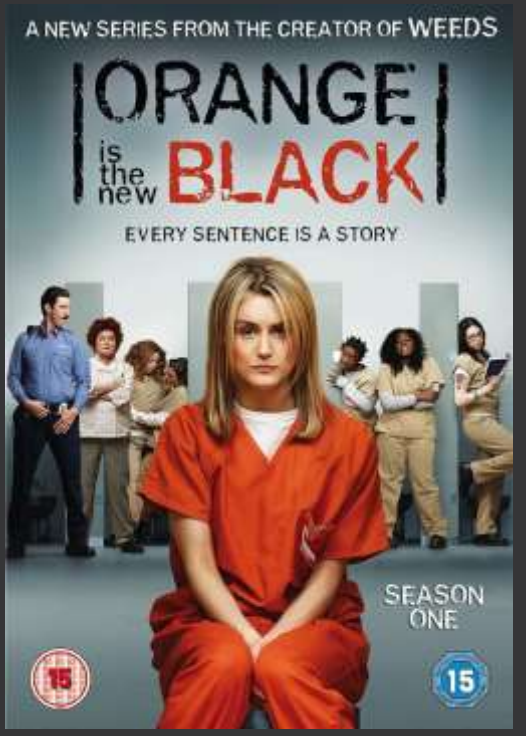

Why should we care?

- IV antibiotics
  - Risk of CRBSI
  - Risk of DVT (PICC/central lines)
  - Need for hospital or OPAT care
  - More expensive than oral

NHS England

Switching from intravenous to oral antibiotics as early as possible could save the NHS in England:

- Up to **5 million** bed days per year
- **1.7 million** hours of nursing time

#KeepAntibioticsWorking

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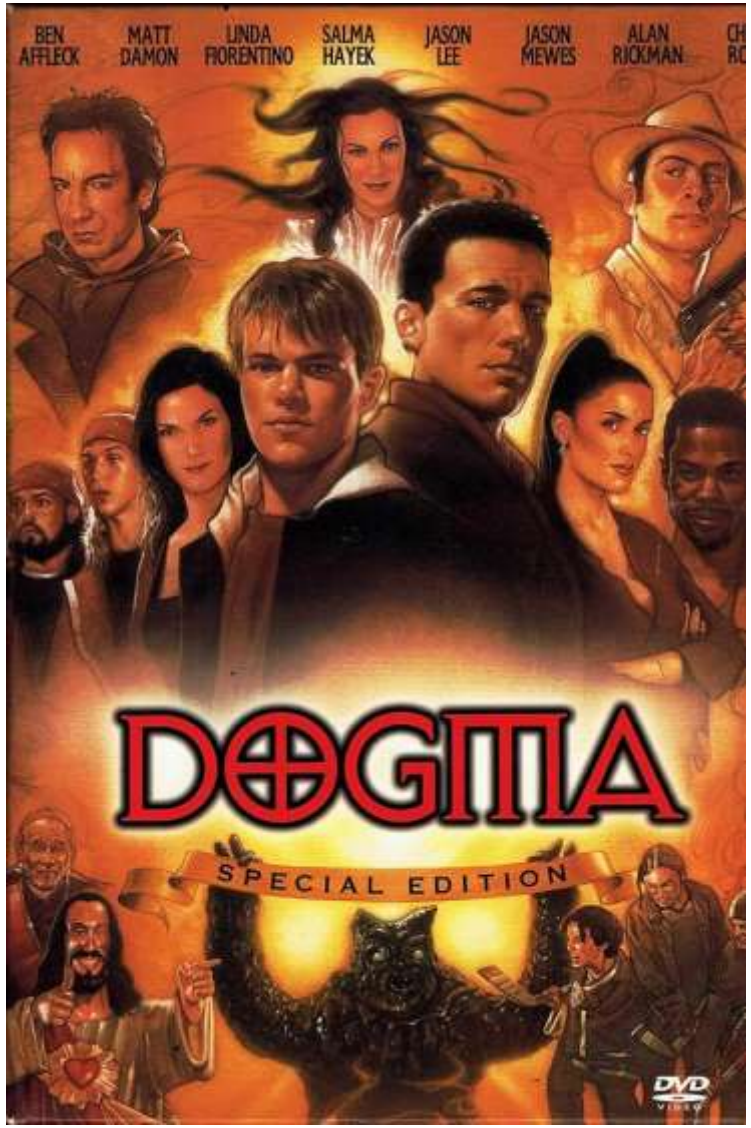
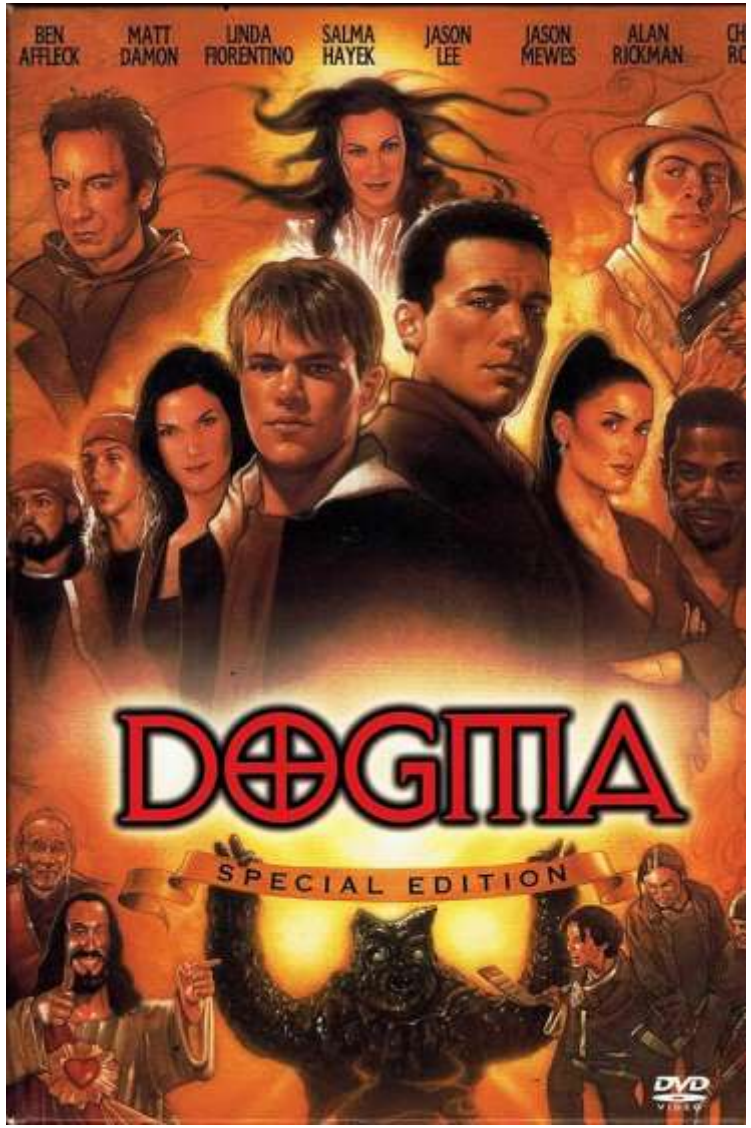
- “Serious infections” need IV antibiotics
- IV antibiotics are more powerful
- There is no role of oral antibiotics in severe infections



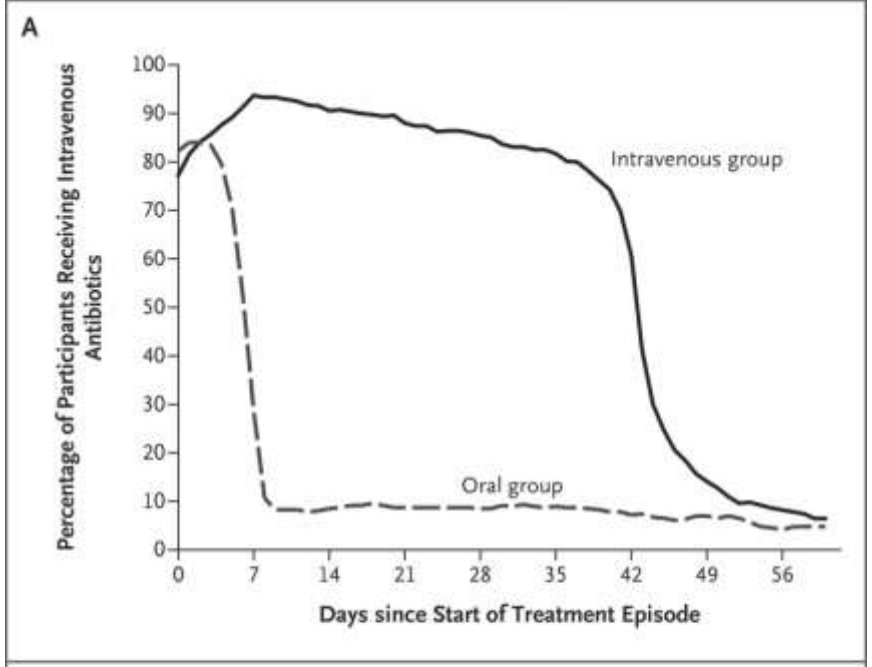
- “Serious infections” need IV antibiotics
- IV antibiotics are more powerful
- There is no role of oral antibiotics in severe infections

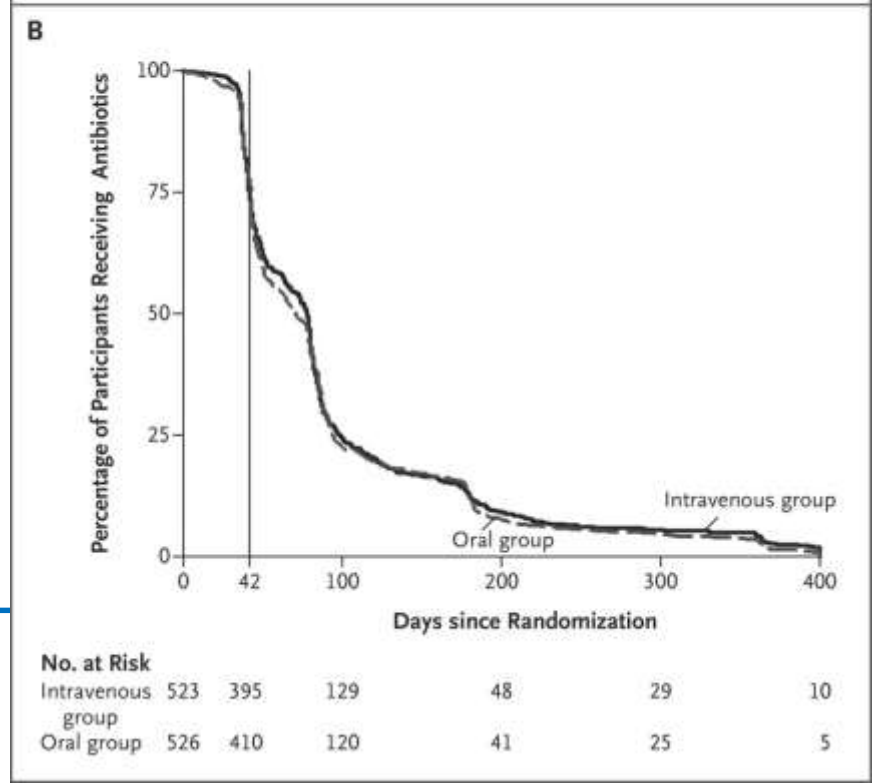
- The bacteria don’t care how the antibiotics got to them!
- High doses of highly bioavailable antibiotics provide similar PK/PD to IV antibiotics
- Multiple RCTs show that oral are as effective, safer and cheaper – in selected patients



OVIVA trial

- 1,054 adults with BJI
- Randomised 1:1 to “usual care” (6 weeks IV) or oral switch(after a mean of 7 days)
- 1ry outcome=Rx failure at 1 year





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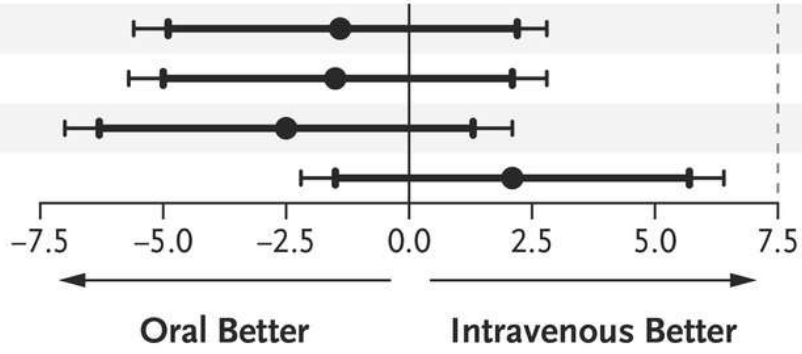
OVIVA trial

- Catheter complications 1.0% versus 9.4%
- Costs far less

Subgroup	Oral Group	Intravenous Group	Risk Difference (90% CI; 95% CI)
	patients with treatment failure/ total no. of participants		
Intention-to-treat population	70.0/527	77.3/527	−1.4 (−4.9 to 2.2; −5.6 to 2.9)
Modified intention-to-treat population	67/509	74/506	−1.5 (−5.0 to 2.1; −5.7 to 2.8)
Per-protocol population	61/466	69/443	−2.5 (−6.3 to 1.3; −7.0 to 2.1)
Worst-case sensitivity analysis	85/527	74/527	2.1 (−1.5 to 5.7; −2.2 to 6.4)



Stabilization criteria

POET

Median length of stay

Oral step-down = 24 days (IQR 17–36)

Intravenous = 43 days (IQR 32–51)

(p <0.001)

Composite primary outcome

i Symptomatic embolic event

ii Unplanned cardiac surgery

iii Relapse of bacteraemia

iv All-cause mortality

Left-sided IE with *S. aureus*, coagulase-negative staphylococci, *Streptococcus spp.* or *Enterococcus faecalis*

Yes / No

Intravenous antibiotics administered ≥10 days and ≥7 days after heart surgery

Yes / No

Stabilization of infection

i No fever (T <38°C) >2 days

ii CRP <25% of max or <20 mg/l

iii Leucocytes <15 x 10^9 per L

Yes / No

Other indication for continued intravenous antibiotic administration, BMI >40 kg/m^2 or reduced gastrointestinal uptake

Yes / No

No new surgical indication / New surgical indication

Perform TEE

Consider oral step-down antibiotic therapy

Continue intravenous antibiotic therapy

1017 Patients with IE

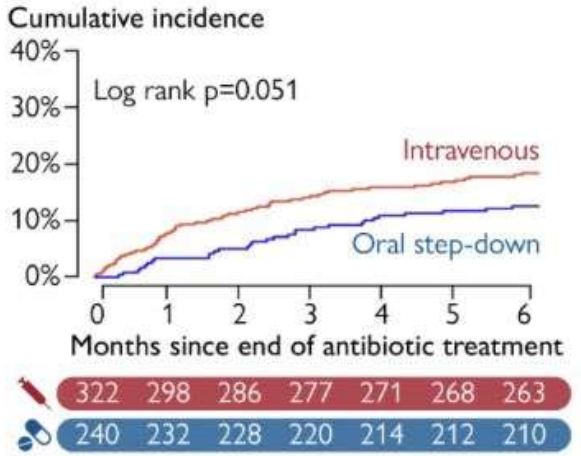
455 Patients excluded due to ineligibility or death

562 Patients considered possible candidates for POET-treatment

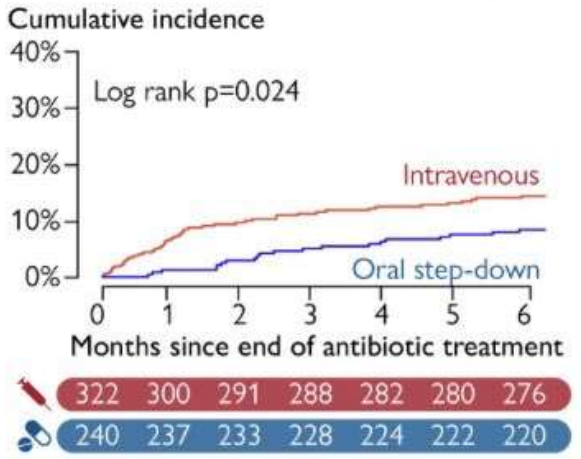
240 Patients received oral step-down antibiotic therapy

322 Patients received traditional intravenous antibiotic therapy

A Primary outcome



B All-cause mortality



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Examples of highly bioavailable ABs

Agent	Oral Bioavailability	Recommended dosing (80kg adult, normal renal function)
Amoxycillin	80%	1g TDS
Cefalexin	90%	1g QID
Ciprofloxacin	70%	750mg BD
Cotrimoxazole	70-90% (both components)	DS ii BD
Clindamycin	90%	450mg TDS
Doxycycline	90%	100mg BD
Fusidic acid	90%	500mg TDS
Linezolid	100%	600mg BD

Oral vs. IV Abx for Osteomyelitis

Author	Yr	N	Regimen (Oral vs. IV)	Success
Greenberg	'87	30	Ciprofloxacin vs. std IV	50% (7/14) v 65% (11/16)
Gentry	'90	59	Ciprofloxacin vs. βL+aminoglyc	77% (24/31) v 79% (22/28)
Mader	'90	26	Ciproflox vs. βL/clinda+aminoglyc	79% (11/14) v 83% (10/12)
Gentry	'91	33	Ofloxacin vs. cephalosporin	74% (14/19) v 86% (12/14)
Gomis	'99	32	Ofloxacin vs. imipenem	69% (11/16) v 50% (8/16)
Schrenzel	'04	39	Fleroxacin+rifampin v βL/vanco	82% (18/22) v 65% (11/17)
Euba	'09	48	TMP-SMX+rifampin vs. cloxacillin	81% (17/21) v 77% (21/27)
Li	'19	1054	Std oral vs. std IV	87% (457/527) v 85% (450/527)
Manning	'22	60	PJI/DAIR: IV/Oral vs. IV only	71% (22/31) v 76% (22/29)
Total (N=9 RCTs)		1,381		84% (581/695) v 83% (567/686)

Success = absence of osteo at long term follow up (most studies >1 year); std = standard of care, protocol specified; all RCTs comparing oral to IV-only are in adults, however there are also 9 other adult and 8 pediatric RCTs or quasi-experimental studies comparing mostly oral vs. mostly oral, with high cure rates; refs at https://www.bradspellberg.com/oral-antibiotics

Oral vs. IV Abx for Bacteremia

Author	Yr	N	Regimen (Oral vs. IV)	Success
Amodio-Groton	'96	50	Ciprofloxacin oral vs. IV—GNB	83% (20/24) v 77% (20/26)
San Pedro	'02	51	Linezolid vs. ceph—*S. pneumo*	93% (27/29) v 68% (15/22)
Deville	'03	36	Linezolid vs. vanco—GPC (peds)	80% (20/25) v 64% (7/11)
Jantausch	'03	103	Linezolid vs. vanco—GPC (peds)	72% (54/75) v 64% (18/28)
Kaplan	'03	80	Linezolid vs. vanco—GPC (peds)	82% (47/57) v 74% (17/23)
Schrenzel	'04	67	FQ + rif vs. βL/vanco—*Staph*	87% (34/39) v 89% (25/28)
Wilcox	'04	56	Linezolid vs. teicoplanin—GPC	89% (23/26) v 57% (17/30)
Wilcox	'09	166	Linezolid vs. vancomycin—GPC	75% (70/93) v 81% (59/73)
Monmaturopaj*	'12	17	Cefditoren vs. ceftriaxone—GNB	100% (6/6) v 91% (10/11)
Park	'14	59	Ciprofloxacin vs. std IV—GNB	93% (27/29) v 93% (28/30)
Omrani	'23	165	FQ/TMPSMX/BL vs. std IV—GNB	78% (65/83) v 74% (61/82)
Total (N=11 RCTs)		850		81% (393/486) v 76% (277/364)

*N = 82 pts with pyelonephritis of whom 17 were bacteremic with *E. coli*, patients were randomized to continue ceftriaxone or switch to oral ceftditoren at day 3. Refs at https://www.bradspellberg.com/oral-antibiotics

Oral vs. IV Abx for Endocarditis

Author	Yr	N	Regimen (Oral vs. IV)	Success
Stamboulian	'91	30	Amox 1 gm qid vs. CTX—*Strep*	100% (15/15) v 100% (15/15)
Heldman	'96	93	Cipro + Rif vs. std IV—*Staph*	95% (18/19) v 88% (22/25)
Iversen/ Bungaard‡	'19	400	Std oral vs. std IV—GPC	74% (146/199) v 62% (125/201)
*Tissot-Dupont**	*'19*	*341*	*TMP-SMX+clinda vs. std IV--Staph*	*81% (138/171) v 70% (119/170)*
Totals (N=3 RCTs)	523			77% (179/233) v 70% (162/241)
(+ 1 quasi expt)*	*(864)*			*78% (317/404) v 68% (281/411)*

*Quasi-experimental, pre-post study. Italicized totals include the quasi-experimental data.
‡Iversen reported early follow up, Bungaard 3 year follow up from the same study.
Refs at https://www.bradspellberg.com/oral-antibiotics

Oral vs. IV Abx for Intra-Abdominal

Author	Yr	N	Regimen (Oral vs. IV)	Success
			Liver Abscesses	
Chen	'02	31	Fleroxacin vs. cefazolin/gent	70% (14/20) v 82% (18/22)
Molton	'20	152	Ciprofloxacin vs. ceftriaxone	96% (71/74) v 93% (72/78)
Total (N=2)		183		90% (85/94) v 90% (90/100)
			cIAI*	
Solomkin	'96	671	Cipro/metro vs. Cipro/metro or Imipen	84% (183/219) v 82% (371/452)
Cohn	'00	250	Cipro/metro vs. pip-tazo	74% (99/134) v 63% (73/116)
Wacha	'06	475	Cipro/metro vs. CTX/metro	91% (213/235) v 88% (211/240)
Fraser	'10	102	Augmentin vs. CTX/metro (peds)**	60% (30/50) v 63% (33/52)
Arnold	`18	82	Augmentin vs. Ertapenem (peds)**	71% (27/38) v 73% (32/44)
Total (N=5)		1580		82% (552/676) v 80% (720/904)

*Patients stepped down to the oral option when tolerating POs
**Both peds studies of perforated appendicitis
Refs at https://www.bradspellberg.com/oral-antibiotics

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When should we use IV antibiotics?

- Sepsis
  - Poor gut perfusion, poor oral absorption
- Nil by mouth
  - Short gut, bowel obstruction, peri-operative
- Nausea, vomiting, diarrhoea
- No good oral option (e.g. Cipro R Pseudomonas)

When should we use IV antibiotics?

- The jury is still out on some deep-seated infections
  - Meningitis
  - *S.aureus* bacteraemia
  - Endocarditis
- Psychosocial reasons
  - Predicted poor adherence

Every ward round, every patient on IV ABs

- Do they still need antibiotics? (short is the new long)
  - If no, stop all antibiotics
- Check all of these criteria
  - Haemodynamically stable?
  - Gut working/absorbing food/medications?
  - Clinically improving?
  - Suitable oral agent available?
- **If yes to all, switch to PO antibiotics**

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