

## Antimicrobial Stewardship ECCMID 2023: une sélection

Johan Courjon CHU de Nice, SMIT













#### SY153

Antimicrobial stewardship in special populations



#### Hall J

08:30 - 10:30

#### SY002

Antibiotic stewardship for urinary tract infections: challenges and opportunities



#### 16:15 - 18:15

#### 05070

Late-breaking novel clinical trial results

#### 16:15 - 18:15

#### 08068

What is going on in the world of AMS: from admission to discharge and beyond

#### 13:30 - 14:30

#### EF048

Antibiotic stewardship: anything you always wanted of now

#### EW156

All for one and one for all! Physicition, diagnostic and antibiotic stewardship to reduce the burden of AMR: guidance in

#### 16:15 - 18:15

#### IS50

Disruptive innovations in the sepsis patient pathway and the impact of untibiotic stewardship

#### IS19

The value of diagnostic information for antimic obtains stewardship

#### **IS53**

Rapid AST on positive blood cut we: efficient as in clinical routine laboratories

#### 16:15 - 18:15

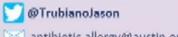
#### 05070

Late-breaking novel clinical trial results

## The use of a Penicillin Allergy cLinicAl deCision rulE to enable direct oral penicillin challenge – A multicenter non-inferiority randomized controlled trial

## PALACE Study

ECCMID 2023 Late Breaker Session 13th April 2023; Hall M 1615 - 1815



≤ antibiotic.allergy@austin.org.au

Ana M Copaescu, Sara Vogrin, Fiona James, Kyra YL Chua, Morgan T Rose, Joseph De Luca, Jamie Waldron, Andrew Awad, Jack Godsell, Elise Mitri, Belinda Lambros, Abby Douglas, Rabea Youcef Khoudja, Ghislaine A C Isabwe, Genevieve Genest, Michael Fein, Cristine Radojicic, Ann Collier, Patricia Lugar, Cosby Stone, Moshe Ben-Shoshan, Nicholas A. Turner, Natasha E Holmes, Elizabeth J Phillips, Jason A Trubiano\*











#### Development and Validation of a Penicillin Allergy Clinical Decision Rule

Jason A. Trubiano, MBBS, PhD; Sara Vogrin, MBBS, MBiostat; Kyra Y. L. Chua, MBBS, PhD; Jack Bourke, MBBS; James Yun, MBBS, PhD; Abby Douglas, MBBS; Cosby A. Stone, MD; Roger Yu, MD; Lauren Groenendijk, MD; Natasha E. Holmes, MBBS, PhD; Elizabeth J. Phillips, MD

2020

local and international cohorts. PEN-FAST was found to be a practical tool with a high negative predictive value of 96.3% that uses penicillin allergy history to identify low-risk allergies.

Figure. PEN-FAST Penicillin Allergy Clinical Decision Rule					
PEN	Penicillin allergy reported by patient	!]	If yes, proceed with assessment		
F	Five years or less since reaction <sup>a</sup>		2 points		
S	Anaphylaxis or angioedema OR Severe cutaneous adverse reaction <sup>b</sup>		2 points		
T	Treatment required for reaction <sup>a</sup>		1 point		
			Total points		
	Interpretation				
Points					
0 Very low risk of positive penicillin allergy test <1% (<1 in 100 patients reporting penicillin allergy)					
1-2 Low risk of positive penicillin allergy test 5% (1 in 20 patients)					
3 Moderate risk of positive penicillin allergy test 20% (1 in 5 patients)					
4-5 High risk of positive penicillin allergy test 50% (1 in 2 patients)					

1567 patients

## Background - Penicillin Allergy Impacts



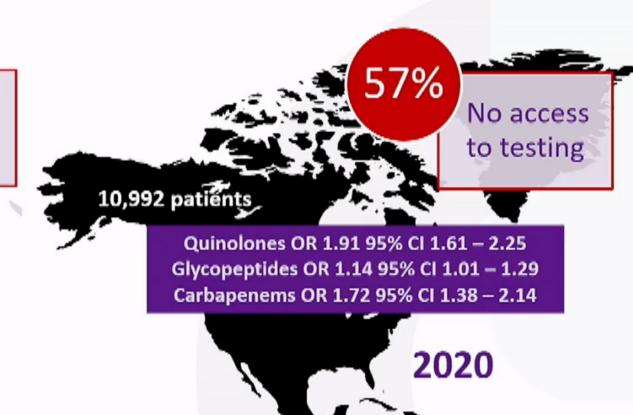
42% No access to testing

21,031 patients

Quinolones OR 2.07 95% CI 1.83-2.34 Glycopeptides OR 1.59 95% CI 1.38-1.83 Carbapenems OR 1.74 95% CI 1.43-2.13

2016

Trubiano et al. JAC 2016; 71(6): 1715 Trubiano et al. Intern Med J 2016; 46 (11): 1311



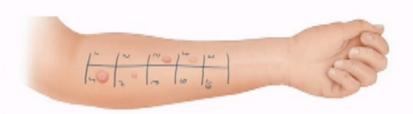
Blumenthal et al. JAMA Intern Med 2020; 180(8): 1120 Trubiano et al. Open Fourn Infect Dis 2016; 3(3):ofw153







## Background - Penicillin Allergy Solutions



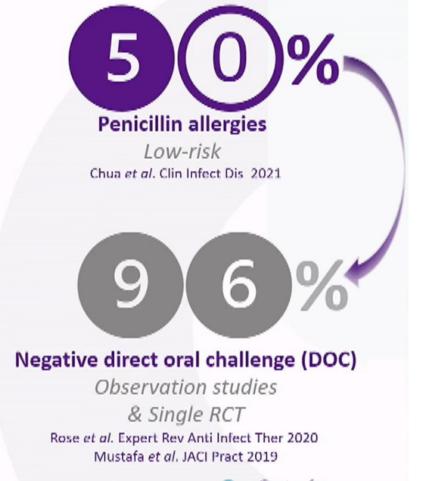
Traditional approaches

Skin prick & intradermal testing



Modern approaches

Direct oral challenge (DOC)





Centre for
Antibiotic Allergy
and Research
Optimizing antibiotic therapy

## **Study Objectives**

#### Study **Question**

▶ Is skin testing required for low risk penicillin allergies with a PEN-FAST score of <3?

#### Study Objective

► Evaluate the non-inferiority of direct oral challenge without prior skin testing to standard care (skin testing followed by oral challenge if negative) in low risk patients (determined as PEN-FAST < 3).</p>

#### Primary Outcome

 Physician-verified positive immune-mediated oral penicillin challenge within one-hour postintervention in the intention-to-treat population







## Study Design

- P Patients with a reported penicillin allergy PEN-FAST < 3
- Direct oral penicillin challenge
- C Skin testing followed by oral challenge
- O Positive immune mediated oral challenge

#### Study **Design**

- International multi-center non-inferiority randomized clinical trial
- Patients randomised 1:1
- Randomisation: permuted block design, stratified by clinical site
- Sample size: N = 380
  - ▶ 80% power; 4% event rate control; 5% non-inferiority margin







Patient with reported penicillin allergy referred to outpatient clinic Study information provided to patient prior to outpatient visit Enrollment Excluded Patient recruitment/ Consent form discussed and signed Penicillin allergy assessment with PEN-FAST tool PEN-FAST ≥ 3 Excluded Allocation PEN-FAST < 3 1:1 Randomisation Drug Hypersensitivity Quality of Life Questionnaire Intervention Control Skin testing<sup>△</sup> Direct oral drug Outcome Oral drug challenge challenge (if negative) penicillin unspecified, penicillin VK/G, amoxicillin, amoxicillin/clavulanate, ampicillin, anti-staphylococcal penicillins

#### **Exclusion** criteria

- 1) Patient age is < 18 years
- 2) Patients with a PEN-FAST score >3
- 3) Pregnancy
- Any other illness that, in the investigator's judgement, will substantially increase the risk associated with subject's participation in this study;
- 5) Patients with history of type A adverse drug reaction, drugassociated anaphylaxis, idiopathic urticaria/anaphylaxis, mastocytosis, serum sickness, blistering skin eruption or acute interstitial nephritis;
- 6) Patients where the allergy history was not able to be confirmed with patient;
- Patients on concurrent antihistamine therapy;
- Patients receiving more than stress dose steroids (i.e. > 50mg QID hydrocortisone [or steroid equivalent]).



A Skin prick testing followed by intradermal testing using standard beta-lactam panel

## Results – Phenotypic characteristics

	Pati	ents, No. (%)
	Intervention group (n=187)	Control group (n=190)
PEN-FAST score		
0	79 (42)	73 (38)
1	97 (52)	112 (59)
2	11 (6)	5 (3)
Reported allergy label		
Penicillin unspecified	146 (78)	156 (82)
Penicillin VK	3 (2)	2 (1)
Penicillin G	2 (1)	6 (3)
Amoxicillin/Ampicillin	34 (19)	20 (11)
Amoxicillin/clavulanate	1 (1)	6 (3)
Flucloxacillin	1(1)	0 (0)
Description of penicillin allergy label		
Childhood reaction	112 (60)	117 (62)
Immediate reaction (< 2 hours)	25 (13)	14 (7)
Timing of the index reaction		
10 to 15 years	23 (12)	14 (7)
More than 15 years	147 (79)	159 (84)



170 (91%)
intervention
vs. 163 (91%)
control allergy
> 10 years
previous





All data presented as n (%)



## Results – Primary Outcome

A positive immune-mediated penicillin oral challenge occurred in 1/187 (0.5%) of the **intervention group** and 1/190 (0.5%) of the **control group**, with a **risk difference** of 0.01 (90% CI 1.22, 1.24), below the non-inferiority margin of 5%







## Results – Adverse Events (AE)

	Intervention	Control	Risk difference (95% CI), percentage points	Risk ratio (95% CI)
	Cum	ulative within 48 hours of ch	allenge (2 days)	
All adverse events	18/187 (10%) (20 events)	17/190 (9%) (20 events)	0.68 (-5.18, 6.54)	1.08 (0.57, 2.02)
Immune mediated adverse event	8/187 (4%) (9 events)	6/190 (3%) (6 events)	1.12 (-2.70, 4.94)	1.35 (0.48, 3.83)
Antibiotic related immune mediated <sup>a</sup>	7/187 (4%) (8 events)	5/190 (3%) (5 events)	1.11 (-2.44, 4.66)	1.42 (0.46, 4.40)
Non-immune mediated adverse event	10/187 (5%) (11 events)	12/190 (6%) (14 events)	-0.97 (-5.70, 3.76)	0.85 (0.37, 1.91)
		lative within 120 hours of cl	nallenge (5 days)	
All adverse events	20/187 (11%) (22 events)	21/190 (11%) (24 events)	-0.36 (-6.64, 5.93)	0.97 (0.54, 1.73)
Immune mediated adverse event	9/187 (5%) (10 events)	10/190 (5%) (10 events)	-0.45 (-4.87, 3.96)	0.91 (0.38, 2.20)
Non-immune mediated adverse event	11/187 (6%) (12 events)	12/190 (6%) (14 events)	-0.43 (-5.26, 4.40)	0.93 (0.42, 2.06)
		Other safety outcom	ies	
Serious adverse event at any time	0/187 (0%)	0/190 (0%)	N/A	N/A
Protocol compliance <sup>b,c</sup>	175/190 (92%)	176/192 (92%)	0.44 (-5.04, 5.91)	1.01 (0.95, 1.07)

Median time to ADR: Intervention 4 hrs (0.67, 16.67); Control 6 hrs (0.54, 1.73)

## Results – Adverse Events (AE)

	Adverse events, No. (%)	
	Intervention group (n=22)	Control group (n=24)
Type of Adverse Event		
An antibiotic-associated adverse event - any non-immune mediated reaction	6 (27)	2 (8)
Nausea/ Vomiting/ Diarrhea	2 (9)	0 (0)
Immediate diffuse rash/ Urticaria	2 (9)	1 (4)
Delayed diffuse rash/ Urticaria (>1 hour)	6 (27)	3 (12)
Other non-severe adverse events	6 (27)	18 (75)
Angioedema/ Laryngeal involvement/ Respiratory compromise	0 (0)	0 (0)
Anaphylaxis (or unexplained collapse)	0 (0)	0 (0)
Death	0 (0)	0 (0)
Penicillin administered during the oral challeng	e	
Amoxicillin 250 mg	9 (40)	15 (63)
Amoxicillin 500 mg	12 (55)	8 (33)
Amoxicillin 400 mg	1 (5)	0 (0)
Severity Grading <sup>®</sup>		
Grade 1	17 (77)	16 (67)
Grade 2	5 (23)	8 (33)
Management		
None	13 (59) or mild symptoms - clinical or diagnostic observation	16 (67)





\*Grade 1: Asymptomatic or mild symptoms - clinical or diagnostic observations only; no intervention; Grade 2: Moderate - minimal, local or non-invasive intervention indicated, limiting age-appropriate instrumental activities of daily living

Centre for Antibiotic Allergy & Research

Department of Infectious Diseases (Austin Health)



## Limitations

- Predominance of PEN-FAST scores 0-1 (94%)
- Observed rate of primary outcome
- Open label design
- Outpatient study
- Penicillin (oral) only





#### Hall J

08:30 - 10:30

#### SY002

Antibiotic stewardship for urinary tract infections: challenges and opportunities

#### Urologists are frequent prescribers



Urologists are the

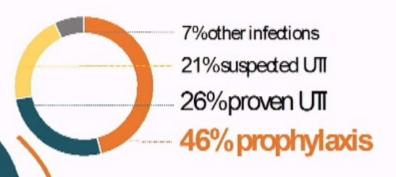
8th

top prescribers for outpatient antibiotics

2018 JAWANet Open, Khaw; 2016 Pathogens, Wagenlehner

The framework for AMS in Urology

#### Antibiotics not only for infections



2016 Pathogens, Wagenlehner

#### Ahigh burden of AMR

#### Common prescription routines



- Urology admission is a risk factor for MDR 2005 CMI Lepelletier
- Complications after urologic procedures are increasing due to impaired prophylaxis efficacy. 2021 World J Urol, Alidjanov
- Urologists are more aware than other specialties of the AMR crisis. 2017 Eur Urol, Lepelletier

# **Prophylaxis**

## Discordances across guidelines:

When is prophylaxis indicated?

	EAU Guidelines (2022)	AUA Statement (2020)	
Urodynamics	No prophylaxis (1b, Strong)	Recommended in high-risk patients	
Cystoscopy	No prophylaxis (1a, Strong)	Recommended in high-risk patients	
Extracorporeal shockwave lithotripsy	No prophylaxis (1a, Strong)	Recommended if positive urine culture	
Ureteroscopy	Recommended (1a, Weak)	Recommended	
Percutaneous nephrolithotomy	Recommended (1b, Strong)	Recommended	
Transurethral bladder resection	Recommended in high-risk patients (1b, Weak)	Recommended	
Transurethral prostate resection	Recommended (1b, Strong)	Recommended	
Transrectal prostate biopsy	Recommended (1a, Strong)	Recommended	
Other procedures	?	?	

2022 EAU Guidelines (available at www.uroweb.org) 2020 AUA Best Practice Statement. J Urol, Lightner

https://online.eccmid.org/media-2384-what-is-going-on-in-the-world-of-ams-from-admission-to-discharge-and-beyond

#### 16:15 - 18:15

#### 0S068

What is going on in the world of AMS: from admission to discharge and beyond

#### Session detail

Chairs - E. TACCONELLI

Chairs - T. TÄNGDÉN

What is going on in the world of AMS: from admission to discharge and beyond

☐ 2-hour Oral Session

☐ 5. New antibacterial agents, PK/PD & Stewardship



# Factors related to inappropriate antibiotic therapy in the Emergency Department: results from a prospective observational study in a large university hospital

F. Giovannenze, M. Covino, F. Sangiorgi, F. Catania, P. Del Vecchio, E. Rando, S. Guerriero, F. Frondizi, D. A. Della Polla, F. Franceschi, M. Fantoni, R. Murri

#### Francesca Giovannenze

Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome
UOC Malattie Infettive



## Methods

#### Study design

Prospective observational phase of a pre-post quasi-experimental study

#### Setting

- Fondazione Policlinico Universitario A. Gemelli, IRCCS
- Large tertiary ED in Rome
- ~ 65.000 ED attendances per year, only adults (admission rate 23%)

#### Population

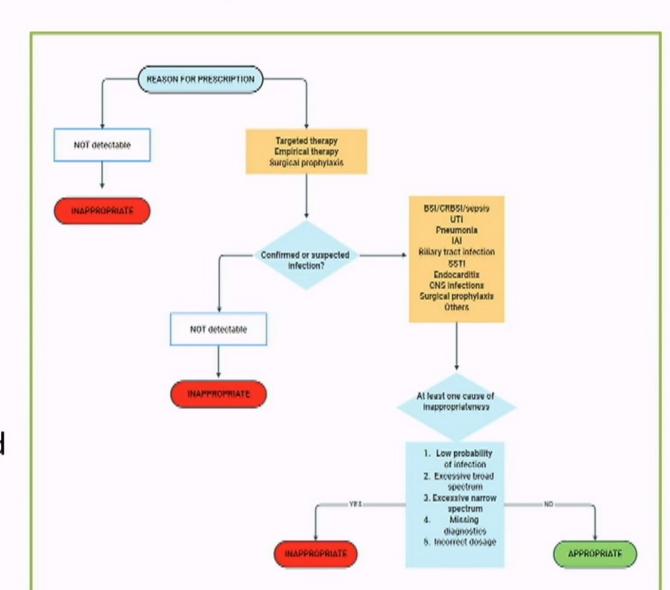
- All patients in temporary observation or waiting for hospital admission, prescribed with at least one antibiotic
- From February 2022 to August 2022
- Two randomly selected days per week

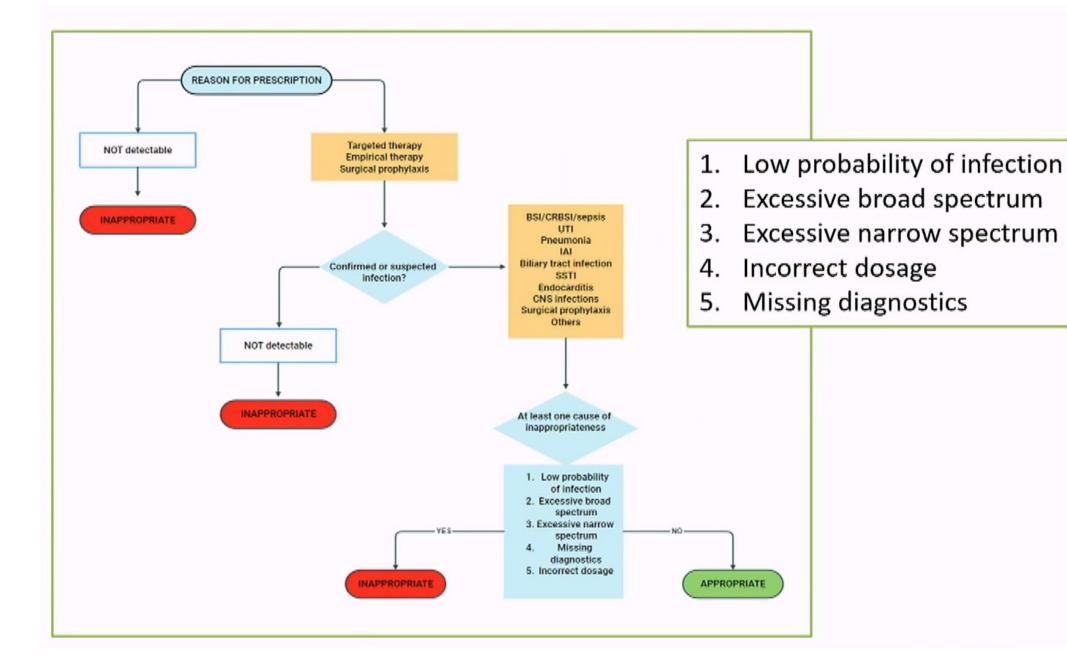
#### Outcome

Rate of inappropriate antibiotic therapies

## Assessment of antibiotic appropriateness

- A computer-based algorithm
- Local hospital procedures and international guidelines
- Each antibiotic therapy was evaluated independently by an ID specialist and an ID trainee (if no agreement, discussion with a third ID physician)
- Only data available to the ED-based prescriber at the time of antibiotic decision-making





## Results

Table 1. Characteristics of appropriate vs. inappropriate antibiotic therapies

APP 247 (48.6%) INAPP 261 (51.4%)

#### Antibiotictherapy

Characteristic	Overall, N = 508 <sup>1</sup>	Appropriate <sup>1</sup>	Inappropriate <sup>1</sup>	p-value <sup>z</sup>	
General characteristics					
Age, years	73 (60,82)	71 (58, 80)	75 (62, 83)	0.019	
Sex, male	279/506(55)	129/246(52)	150/260(58)	0.24	
Fever	240/508(47)	152/247 (62)	88/261(34)	<0.001	
Respiratory signs/symptoms	115/508(23)	55/247(22)	60/261(23)	0.85	
Urinary signs/symptoms	36/508(7.1)	23/247(9.3)	13/261(5.0)	0.057	
Abdominal signs/symptoms	145/508(29)	75/247(30)	70/261(27)	0.38	
Skin and soft tissue manifestations	29/508(5.7)	17/247(6.9)	12/261(4.6)	0.27	
CRP, mg/L	88 (27, 168)	116 (45, 192)	62 (18, 140)	<0.001	
PCT, ng/mL	0.3 (0.1, 1.1)	0.5 (0.1, 1.4)	0.2 (0.1, 0.6)	<0.001	
SOFA score	1.00 (0.00, 3.00)	2.00 (0.00, 3.00)	1.00 (0.00, 2.00)	0.10	
Charlson comorbidity index	5.0 (3.0, 6.0)	5.0 (2.0, 6.0)	5.0 (3.0, 7.0)	0.11	
In-hospital death	48/508 (9.4)	25/247(10)	23/261(8.8)	0.61	
Lenght of hospital stay	9 (5, 17)	10 (5, 18)	9 (4, 15)	0.23	

Table 1. Characteristics of appropriate vs. inappropriate antibiotic therapies

			Antibiotictherapy			
	Characteristic	Overall, N = 508 <sup>3</sup>		Appropriate <sup>1</sup>	Inappropriate <sup>1</sup>	p-value <sup>2</sup>
_	Prescriber					
	Emergency physician	381/508(75)		160/247(65)	221/261(85)	<0.001
	ID physician	65/508(13)		60/247 (24)	5/261 (1.9)	<0.001
	Suspected infection					
	Pneumonia	120/508(24)		52/247(21)	68/261(26)	0.18
	BSIs/Sepsis	84/508(17)	<b>→</b>	61/247(25)	23/261(8.8)	<0.001
	UTI	98/508(19)		40/247(16)	58/261(22)	0.085
	Adbominal infection	50/508(9.8)		25/247(10)	25/261(9.6)	0.84
	Biliary tract infection	52/508(10)		27/247(11)	25/261(9.6)	0.62
	SSTIs	46/508(9.1)		25/247(10)	21/261(8.0)	0.42
	Other	58/508(11)		17/247(6.9)	41/261(16)	0.002
	<sup>3</sup> Median (IQR) or Frequency (%)					
	<sup>2</sup> Wilcoxon rank sum test; Pearson's Chi-squared to	est; Fisher's exact test				



Ramzy Helou, MD – PhD student
Department of Medical Microbiology & Infectious Diseases
Erasmus MC, Rotterdam, The Netherlands
15 April 2023



### Time

Disease onset

Time from disease onset to antimicrobial order Time from antimicrobial order to administration Initial antimicrobial administration

#### **Antimicrobial lead time**



- Antimicrobial lead time (ALT):
  - Time from antimicrobial order to antimicrobial administration
- Patients with sepsis ↑ mortality if ALT >1h (Kashiouris et al. 2019).
- But what about other infections?



- Primary outcome
  - ALT per infectious disease
- Secondary outcome
  - Difference in ALT between
    - Sepsis and other infectious diseases
    - Patients with positive blood cultures and no blood cultures
    - Emergency room and ward
    - Recently admitted patients and patients whom were already admitted
    - Medical and surgical departments
  - Impact of ALT on length of stay (LoS)
- Establish value of ALT as potential new quality or process indicator.

#### **Methods**



- Retrospective study conducted in the Erasmus University Medical Center,
   Rotterdam, the Netherlands
  - Academic, tertiary care hospital.
  - 20-month period.
- Study population
  - Adult hospitalized patients receiving systemic antimicrobial therapy on medical and surgical wards.

#### Antimicrobial lead time - Definition

- Definition
  - The time (h) from antimicrobial order to antimicrobial administration initiation of the first dose.
- ALT was automatically calculated: Drug administration date and time \_\_\_\_\_
   Drug order date & time
- Shortest possible ALT: 0.00 hours.
- ALT was calculated for the first therapeutic antimicrobial order.
  - If >1 antimicrobial was prescribed at the same time the shortest ALT was used in the analysis.

#### Results



- 1000 patients included
  - After exclusion of 37 patients.
  - 561 men and 439 women.
  - Median age: 61 years (interquartile range (IQR) 47 71).
- 15 different specialties
  - 6 medical, 9 surgical departments.

#### **Results - ALT varies per indication**

. . . . . . . .



- Median ALT for all patients was 1.05 hours (IQR 0.32 3.02)
  - Min. ALT: 0.00 h Max. ALT: 24.05 h.

Indication	Patients	ALT median (IQR) (hours)
Cholangitis	51	0.37 (0.15 - 1.38)
Community-acquired pneumonia - organism unspecified	61	0.98 (0.25 - 3.6)
Cystitis	72	1.96 (0.56 - 3.7)
Endocarditis	10	1.67 (0.83 - 2.32)
Hospital acquired pneumonia	104	1.68 (0.73 - 3.45)
Infected joint prosthesis	18	2.63 (0.88 - 5.12)
Intravascular line infection	13	0.63 (0.5 - 2.37)
Meningitis – Bacterial	30	1.18 (0.46 - 2.85)
Osteomyelitis	30	1.89 (0.62 - 3.94)
Sepsis	65	0.27 (0.07 - 0.67)
Wound infection	46	2.17 (0.33 - 3.86)

#### Results



- Blood cultures obtained (659 patients) vs. No blood cultures (341 patients)
  - Median ALT 0.85h (IQR 0.28 2.42) vs. 1.77h (IQR 0.43 3.65); p<0.001.

- Positive blood culture (126 pts) vs. Negative blood cultures (533 pts)
  - Median ALT 0.66h (IQR 0.28 1.73) vs. 0.92h (IQR 0.28 2.57); p = 0.04.

#### Results - ALT varies per medical specialty and admission



- Antimicrobials ordered at emergency room (331 pts) vs. Ordered at medical wards (669 pts)
  - Median ALT 0.43h (IQR 0.17 1.43) vs. 1.57h (IQR 0.57 3.43); p<0.001.</p>
- Antimicrobials ordered <=24 hours of admission (597 pts) vs. Antimicrobials ordered >24h of admission (403 pts)
  - Median ALT 0.77h (IQR 0.23 2.45) vs. 1.67h (IQR 0.61 3.42); p<0.001.</p>
- Difference of ALT between individual wards.
- No difference in median ALT for patients at medical and surgical wards (p=0.70).

### Results - ALT and length of stay



- Median length of stay (LoS) was 7.7 days (IQR 4.5 13.9) for all patients.
- No relation between ALT and LoS (p=0.33)
  - After correcting for confounder 'indication'.

### Conclusion

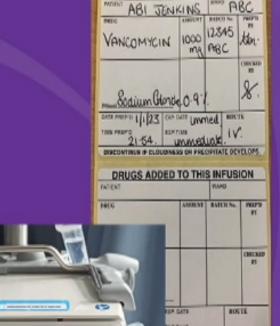


- ALT seems an informative and easy to measure quality indicator (QI) for sepsis
  - ALT may be feasible as QI for meningitis and community-acquired pneumonia.
  - More studies needed to establish an optimial ALT.
- For all infections, ALT can be used as process indicator
  - Identification of potential targets of antimicrobial drug administration optimization.

Time the Whole Process of Medicines Preparation and Administration

DANG MARK	Roote	Dise	Link	BLeius	Time BALA
Management	219	17	106	Your	34:00-24.05 91
vitamine 5 ASS P	141-	Organia	795	Pers.	14:00 24:09:23
Vitamino 9 and o	tvi-	Ahmoute	100	74.95	33,00 74 05 15
Vaccometts	PII+	1200mg	-	Pana	
	IVI+	1210my	716	Pers	28.00.00.03.23
co.amminler	TAB	rename .	TOS	2748	14100 24.07.17
o Li Crokemporkin	PVI.	Allowy	959	-	12:00 24:07:01
r)usimmetlis	rwa	2000mg	648		12:00 24:03:23
Paracetado)	IVI	18	9079	Pres	10:00 34.07.11









### Intravenous and Oral Administrations

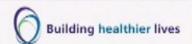
- Timed:
  - 140 oral administrations
  - 87 intravenous administrations
- Mean time to administer:
  - Oral formulations 80 seconds
  - Intravenous injections/ infusions 22 minutes 5 seconds
- One appropriate IVOS of a medication given tds could release one hour of nursing time each day.





# **Organisational Impact**

- University Hospitals Birmingham has approximately 2,500 beds on the Electronic Management System.
- Assessed the number of intravenous antibiotics given in a 24 hour period on a different day over 7 weeks.
- Mean number of administrations was 2400 over 24 hours.
- This has been repeated at two other local Trusts.





### Potential for IVOS

Generally considered between 10-50%

- On UHB data:
  - 2400 daily administrations taking 800 hours of nursing time
  - Potential for 10% to be switched to oral therapy
  - Implementing an effective IVOS scheme could release at least 80 hours of nursing time across the organisation.



# Nurses' contribution to Antimicrobial Stewardship: finding integration in daily practice

Maria Bos RN <sup>1,2</sup> C. de Bot RN, PhD <sup>1</sup> Prof. H. Vermeulen <sup>2,3</sup> Prof. M. Hulscher <sup>2</sup> J. Schouten MD, PhD <sup>2,4</sup>

1 Avans University of Applied Sciences, Breda, the Netherlands

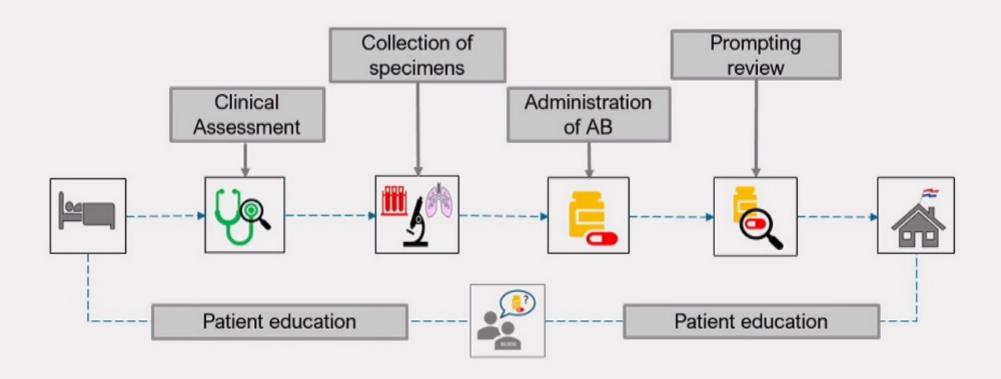
Department of Intensive Care Medicine, Radboud University Medical Center, Nijmegen, the Netherlands



<sup>&</sup>lt;sup>2</sup> Scientific Center for Quality of Healthcare (IQ Healthcare), Radboud University Medical Center, Nijmegen, the Netherlands

<sup>&</sup>lt;sup>3</sup> School of Health, HAN University of Applied Sciences, Nijmegen, the Netherlands

### **ANTIBIOTIC PATHWAY- NURSE CONTRIBUTION**





### **RESEARCH QUESTION**

What are the

perceptions, views and opinions

of

Dutch bedside nurses on their role

regarding

appropriate antimicrobial use?



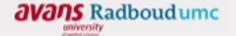
### METHOD: Qualitative exploratory design

### <u>Participants</u>

- Purposeful sampling (variation in participants)
- Invitation through nursing networks
- Bedside nurses ("direct care")
- Registered nurse (RN/LPN)
- Surgical ward or internal medicine ward (or equivalent of those)
- Min. 28 hrs/week contract
- Academic, non-academic (teaching) and general hospitals

### Datacollection

- Semi-structured interviews, using topic list
- Digital platform (ZOOM)
- Audiorecording
- Verbatim transcription



### "this is what we do...."

#### Continuous factor

Alerting prescriber

.....we have a signaling function; when are the labs done again, what do we do with the antibiotics?....

Prompting review e.g. i.v. to oral switch

...when we see that someone is clinically stable, we evaluate with the doctor if the antibiotic can be stopped or can be switched to oral.... Critical reflection and anticipation

**Explanation of treatment** 



### "this is what can help us....."

**Awareness** 

I think you should start with creating more awareness, this is very important and I don't think that this awareness is present right now...

Education

- Checklist during ward rounds
- "antibiotic champions"

Tools

...some sort of guideline for antibiotic use and the role of nurses. I think that will help to get a more complete overview..

Clarification of role and responsibilities



### CONCLUSION

Nurses feel that they are already contributing in ensuring appropriate antimicrobial use

Nurses envision their future role as an enhanced, elaborated and empowered version of their current daily practice

Clarification of (shared) responsibilities between prescriber and nurses may support further development of nurses' roles

Formal acknowledgement and increased awareness of the role nurses have, will encourage the contribution of the bedside nurse to AMS





# A COMPUTER-BASED ALGORITHM TO IDENTIFY INAPPROPRIATENESS OF CARBAPENEM THERAPY IN A LARGE ITALIAN UNIVERSITARY HOSPITAL

P. Del Vecchio, F. Sangiorgi, E. Rando, F. Giovannenze, M. Fantoni, R. Murri

### Pierluigi Del Vecchio

Università Cattolica del Sacro Cuore Rome, Italy



## **METHODS**

### Study design

- Pre-intervention observational phase of a pre-post quasi-experimental study
- Intervantion (ongoing)
- Post-intervention phase

### Setting

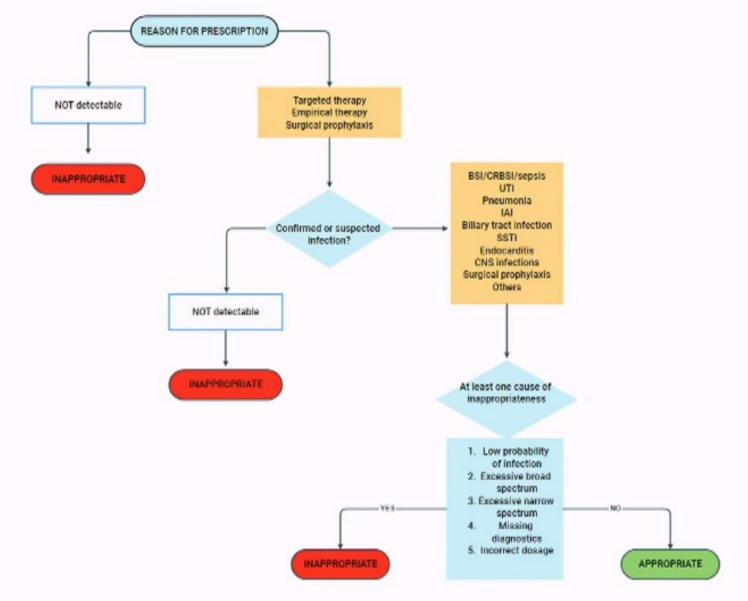
- Policlinico Universitario A. Gemelli, IRCCS, Rome, Italy
- University Hospital, 1500 hospital beds

### Study Population

 Weekly data (april 2018-february 2023) was collected from patients admitted to the hospital units (except for Hematology, Intensive Care and Pediatric units) who had received at least one carbapenem prescription

#### Outcome

- Appropriateness of carbapenem prescriptions



# **RESULTS**

VARIABLES		Carb. Appropriate	Carb. Inappropriate	P value	тот.	
		228 (66%)	117 (34%)		345	
Pres	cribers n (%)					
1.	Ward physician	77 (33.9)	80 (68.4)	<0.001	157 (45.6)	
1.	ID specialist	89 (80.2)	22 (19.8)	<0.001	111 (32.3)	
1.	AMS team ID specialist	32 (100)	0 (0)	<0.001	32 (9.3)	
1.	ED physician	17 (68)	8 (32)	1.000	25 (7.2)	
	ected or confirmed tion n (%)					
•	BSI	137 (78.7)	37 (21.3)	<0.001	174 (50.6)	
•	IAI	22 (53.7)	19 (46.3)	0.081	41 (11.9)	
•	SSTI	8 (50)	8 (50)	0.183	16 (4.7)	
•	UTI	22 (55)	18 (45)	0.155	40 (11.6)	
•	Pneumonia	27 (69.2)	12 (30.8)	0.722	39 (11.3)	
•	Biliary tract infection	3 (60)	2 (40)	1.000	5 (1.5)	
•	Surgical prophylaxis	1 (33.3)	2 (66.7)	0.268	3 (0.9)	
•	Osteoarticular infection	3 (50)	3 (50)	0.413	6 (1.7)	
•	Undetectable	4 (20)	16 (80)	< 0.001	20 (5.8)	

# Antimicrobial Therapeutic Drug Monitoring in critically ill adult patients –

An international perspective on access, utilisation, barriers and clinical value

Paul Williams. Menino Osbert Cotta, Alexis Tabah, Indy Sandaradura, Salmaan Kanji, Marc II. Scheetz, Sahand Imani, Muhammed Elhadi, Sonia Luque Pardos, Natalie Schellack, Cristina Sanches, Jean Francois Timsit, Jiao Xie, Andras Farkas, Kathryn Wilks and Jason A. Roberts on behalf of the European Society of Intensive Care Medicine (ESICM) and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Study Group for Infections in Critically III Patients [ESGCIP]

<sup>1</sup>University of Queensland Centre for Clinical Research (UQCCR), The University of Queensland, Brisbane, Queensland, Australia











# Methods

- Online cross-sectional survey
  - Developed by international panel
  - MCQ and 5-point Likert scale
  - Describe access to MIC results, drug assay availability,
     TDM utilisation, and clinical value of dose optimisation strategies
  - Distributed via professional societies and networks











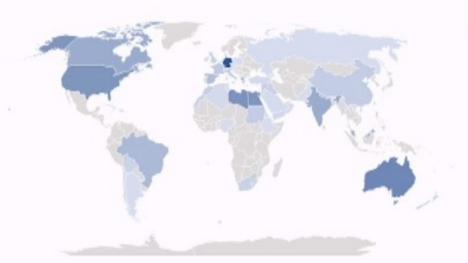
# Results

538 respondents, 409 hospitals, 292 cities, 45 countries

54% HIC, 23% UMIC, 23% LMIC or LIC

30% Europe and Central Asia

71% Physicians, 29% Pharmacists













# MIC access

- 25% of LMICs and LICs had no access to MIC results or susceptibility reports
  - Critical for ensuring appropriate AB use
  - Prevent AMR
- Disparity in MIC access on a global level, broader access must be a priority

Characteristic	Total	HIC	UMIC	LMIC	LIC
MIC reported?	n = 534	n = 288	n = 122	n = 100	n = 24
Yes	308 (58)	193 (67)	55 (45)	48 (48)	12 (50)
Yes, for all ICU susceptibilities	174 (33)	120 (42)	21 (17)	31 (31)	2 (8)
Yes, only when requested by ICU or ID	118 (22)	64 (22)	27 (22)	17 (17)	10 (42)
Yes, only for specific pathogen/antibiotics	16 (3)	9 (3)	7 (6)	0 (0)	0 (0)
No	221 (41)	91 (32)	66 (54)	52 (52)	12 (50)
No MIC or susceptibilities reported	71 (13)	14 (5)	26 (21)	25 (25)	6 (25)
No, however specific antibiotics are reported as susceptible or resistant	150 (28)	77 (27)	40 (33)	27 (27)	6 (25)
Unsure	1 (0.2)	0 (0)	1 (1)	0 (0)	0 (0)
Other	4 (0.7)	4 (1)	0 (0)	0 (0)	0 (0)



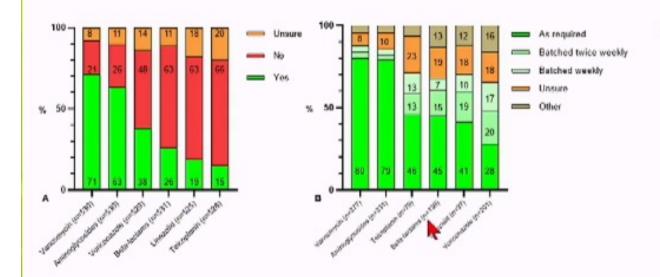








# **TDM** availability



According to A: drug assay access & B: assay results

- Most respondents had timely access to vancomycin and aminoglycoside assays
  - HICs had greater access
  - TDM approach well established
  - 21% and 26% had no vancomycin or AG assay access
  - >38% and >50% in LMIC and LIC

- Evidence and guidelines supporting TDM is slow to translate into clinical practice
- Equitable access remains a challenge







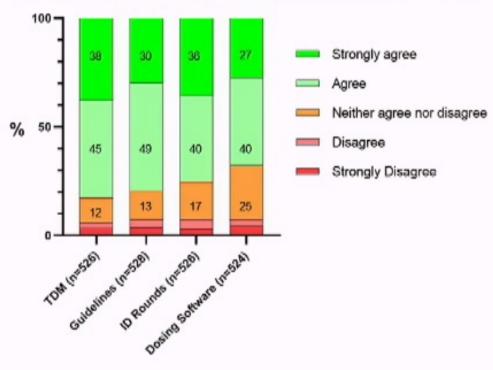






# Improve patient outcomes?

The following antibiotic dosing strategies improve patient outcomes when treating critically ill patients with infection?



- TDM ranked highest (38% SA)
  - more common belief in HICs
    - TDM more readily available?
    - ↑ familiarity with TDM principles and literature?
    - First-hand experience of benefits?











# Conclusions

- Geographical disparity in clinician access to timely drug assay results and MIC and susceptibility reports
- Dosing software rarely used in clinical practice and predominantly the role of a Pharmacist
- Respondents believe TDM improves patient outcomes, although, significant TDM barriers identified.





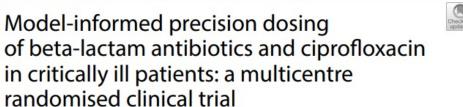






### TDM et réanimation Pour information: RCT, 2022-2023

#### ORIGINAL





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RESEARCH Open Access

Right dose, right now: bedside, real-time, data-driven, and personalised antibiotic dosing in critically ill patients with sepsis or septic shock—a two-centre randomised clinical trial

Luca F. Roggeveen<sup>1\*†</sup>, Tingjie Guo<sup>1,2,3†</sup>, Lucas M. Fleuren<sup>1†</sup>, Ronald Driessen<sup>1</sup>, Patrick Thoral<sup>1</sup>, Reinier M. van Hest<sup>2</sup>, Ron A. A. Mathot<sup>2</sup>, Eleonora L. Swart<sup>2</sup>, Harm-Jan de Grooth<sup>1</sup>, Bas van den Bogaard<sup>4</sup>, Armand R. J. Girbes<sup>1</sup>, Rob J. Bosman<sup>4</sup> and Paul W. G. Elbers<sup>1</sup>

**Conclusions:** In critically ill patients, personalised dosing was feasible, safe and significantly improved target attainment for ciprofloxacin.

Clinical outcomes: NS

#### ORIGINAL

Effect of therapeutic drug monitoring-based dose optimization of piperacillin/tazobactam on sepsis-related organ dysfunction in patients with sepsis: a randomized controlled trial

Stefan Hagel<sup>1,2\*</sup>O, Friedhelm Bach<sup>3</sup>, Thorsten Brenner<sup>4,5</sup>, Hendrik Bracht<sup>6</sup>, Alexander Brinkmann<sup>7</sup>, Thorsten Annecke<sup>8,9</sup>, Andreas Hohn<sup>8,10</sup>, Markus Weigand<sup>5</sup>, Guido Michels<sup>11</sup>, Stefan Kluge<sup>12</sup>, Axel Nierhaus<sup>12</sup>, Dominik Jarczak<sup>12</sup>, Christina König<sup>12</sup>, Dirk Weismann<sup>13</sup>, Otto Frey<sup>14</sup>, Dominic Witzke<sup>3</sup>, Carsten Müller<sup>15</sup>, Michael Bauer<sup>16</sup>, Michael Kiehntopf<sup>17</sup>, Sophie Neugebauer<sup>2,17</sup>, Thomas Lehmann<sup>18</sup>, Jason A. Roberts<sup>19,20,21</sup> and Mathias W. Pletz<sup>1,2</sup> on behalf of the TARGET Trial Investigators

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SOFA score: NS Tendance à un impact clinique



The impact on the CO<sub>2</sub> footprint when inappropriate intravenous antibiotic therapy is used instead of an earlier, clinically appropriate switch to an oral formulation or stopping the therapy entirely at UHCW, UK.

**April 2023** 

Dr Steven Laird BSc (hons) MBChB MPH DTM&H MRCP FRCPath
Consultant Physician in Medical Microbiology

# The United Kingdom's Pledge for Net Zero Healthcare

The Government issued its vision for a net zero health service in October 2020, delivering a net zero National Health Service which sets mandatory targets for NHS Trusts:

- For emissions we control directly net zero by 2040, with 80% reduction by 2028-2032.
- For emissions we can influence net zero by 2045, with 80% reduction by 2036 – 2039.

Official documentation was published with statutory guidance in July 2022 (1). The UHCW Green Plan aims to meet these targets in advance to the mandatory dates given by the UK government.



# What part have we played in reducing our carbon footprint?

This studies' objective...

Calculate the carbon footprint of inappropriately prescribed intravenous amoxicillin and co-amoxiclav in a UK based tertiary hospital



### Our Study: Methodology

- Retrospective descriptive study.
- Performed by two medical consultants who independently reviewed every prescription of IV amoxicillin and co-amoxiclav.
- Based on a respiratory and infectious disease ward from 1<sup>st</sup> of September 2022 to 31<sup>st</sup> September 2022.
- Each prescription was deemed to be either appropriate or inappropriate based on clinical criteria.
- Inappropriate prescriptions were then further categorised into prescriptions that should have been terminated earlier or converted into an oral formulation of the same antibiotic.





# Our Study: Methodology and figures

The difference in the mass of the oral and intravenous therapy was calculated and then converted into the carbon footprint

#### Every dose of;

- IV amoxicillin had a weight 49.84g and carbon footprint of 0.0441kgCO<sub>2</sub>e
- IV co-amoxiclav has a weight 32.5g and a carbon footprint of 0.0687 kgCO<sub>2</sub>e
- PO amoxicillin has a weight of 1.43g carbon footprint of 0.00129kgCO<sub>2</sub>e
- PO co-amoxiclav has a weight of 2.076g and carbon footprint of 0.0018kgCO<sub>2</sub>e

The conversion factor was from the latest metrics for carbon foot printing from NHSEI. Each tonne of medicinal waste is 901.1 KgCO₂e





### Results:

- 431 doses of co-amoxiclav (423 doses of 1200mg) and amoxicillin (8 doses were 500mg or 1000mg (5 doses and 3 respectively)) were selected.
- From 93 patients.
- IV amoxicillin was considered inappropriate in 6 out of 8 doses (75%)
- IV co-amoxiclav was considered inappropriate in 105 out of 423 (24.8%).



Table 1: The weight of the packaging of a single dose of antibiotic (glass vial or blister packing) and the water ampule packaging plus the needle and syringe with its associated carbon footprint.

Weight (g)	Carbon foot prir (kgCO₂e) per dose	doses which should not	doses which should have	Total additional carbon foot print (kgCO <sub>2</sub> e) per antibiotic
49.84	0.0449	0	6	0.2646
76.35	0.0687	24	81	7.1090
1.43	0.0013	0	NA	NA
2.076	0.0018	0	NA	NA
	49.84 76.35	(kgCO <sub>2</sub> e) per dose  49.84 0.0449  76.35 0.0687	(kgCO <sub>2</sub> e) per dose doses which should not have been prescribed  49.84 0.0449 0  76.35 0.0687 24	(kgCO <sub>2</sub> e) per dose doses which should not have been prescribed to an oral route  49.84 0.0449 0 6  76.35 0.0687 24 81



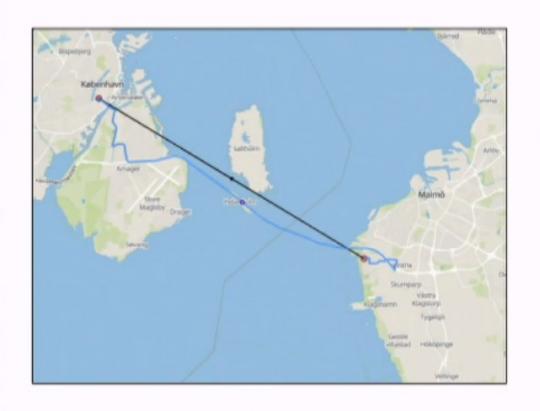


### Conclusion:

This study shows that an appropriate early IV to PO switch of antibiotic therapy can reduce the carbon footprint of antibiotic use just by factoring in clinical wastage alone.

Average fuel car produces 170.5grCO2e/km

Inappropriate use of IV antibiotics was equivalent to 43.25km driven average petrol car. This is close to the equivalent of Copenhagen Denmark) to Malmo (Sweden)







# Antibiotic prescribing in remote versus face-to-face consultations for acute respiratory infections in English primary care: An observational study using TMLE

Emma Vestesson<sup>1,2\*</sup>, Kaat De Corte<sup>1</sup>, Paul Chappell<sup>3</sup>, Elizabeth Crellin<sup>1</sup>, Geraldine M. Clarke<sup>1</sup>

1.The Health Foundation, London, UK 2. UCL Great Ormond Street Institute of Child Health, London, UK, 3. NHS England, London, UK

preprint: shorturl.at/aHJLM



# Antibiotic prescribing in the UK

- GPs prescribed 71.4% of the total consumption of antibiotics in 2019
- Antibiotic prescribing in primary care declined between 2014 –2019
- 20% of antibiotic prescribing is estimated to be inappropriate
- Acute respiratory infections (ARI) most common reason for antibiotic prescription
- Limited evidence on the impact of remote consultations on antibiotic prescribing
- Recent survey found that 67% of GPs in the UK think that the use of telehealth has increased their antibiotic prescribing



# Research question

Are patients that are seen remotely for an ARI more likely to be prescribed antibiotics compared to those seen faceto-face?

preprint: shorturl.at/aHJLM



# Study population and data

- Nationally representative patient level data (CPRD Aurum)
- Patients with a GP consultation for acute respiratory infections (ARI) between 1
   April 2021 22 March 2022 at ~400 GP practices
- Code list based on previous studies can be subset into URTI, LRTI, sinusitis, otitis media, otitis externa and COVID
- Antibiotics in BNF section 5.1 (excluding antileprotic and TB drugs)
- Grouped GP ARI consultations happening in a 7-day period included (if a mix of consultation modes then face-to-face)
- Analysis was carried out separately for adults and children



# Targeted maximum likelihood estimation (TMLE)

A causal inference method that uses machine learning to estimate the effects of treatments in observational studies

- Propensity score model (remote consultation)
- Outcome model (antibiotics prescribed)

Combine two models to estimate the average treatment effect and the odds ratio

It is doubly robust so if you get either of the two models right then your estimate is consistent

preprint: shorturl.at/aHJLM



## Variables included in model

#### **Patient**

Age

Sex

Deprivation

Infection type

Comorbidities
Previous consultation

Previous antibiotic use

#### Clinician

GP role (eg locum, partner)

#### **Practice**

Patient list size Rural/urban Previous antibiotic prescribing level

Previous consultation rates

## Regional

Covid infection rates in regions

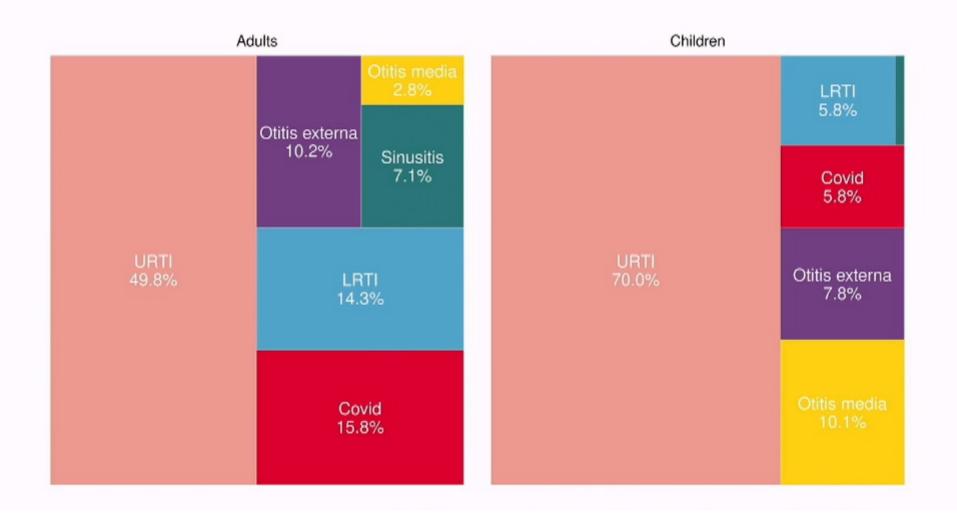
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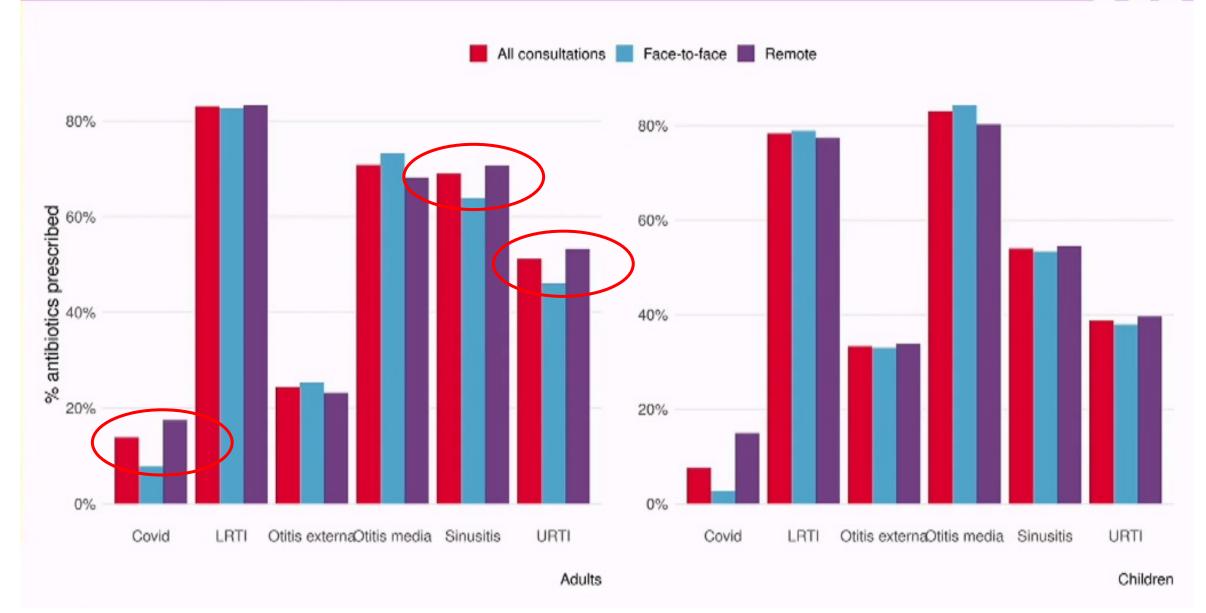
## Summary statistics

- There were 45,997 consultations for ARIs (34,555 unique patients),
   of which 61% (28,127) were remote and 39% (17,870) face-to-face
- Adults had a higher proportion of remote consultations (66% compared to 48%)
- Antibiotics were prescribed in 48% of all consultations for adults, and the proportion was higher in remote compared to face-to-face (52% vs 42%)
- For children, 43% of all consultations led to antibiotic prescriptions and similar proportion in remote and face-to-face consultations (42% vs 43%)











# Adjusted results - TMLE

- Being seen remotely was associated with a 23% increase in the odds (odds ratio 1.23; 95% CI: 1.18, 1.29) of antibiotics being prescribed for adults
- For children there was a 4% increase but this was not a statistically significant, meaning that we cannot be confident that there is any effect (1.04; 95% CI: 0.98, 1.11).



# **Implications**

- The results for adults are concerning
- There are implications for both antibiotic prescribing rates and the use of remote consultations.
- Increased prescribing in adults could have a substantial impact on the UK's commitment to reduce antibiotic prescribing by 15% by 2024
- Raises questions about when remote consultations are safe and appropriate
- Guidelines and clinical risk scores used to guide antibiotic prescribing need to be adapted for remote consultations



## Possible explanations

- The factors affecting antibiotic prescribing for ARIs, and the interaction with consultation mode are complex
- Patient and GP behaviour might differ between remote and face-toface consultations
- Clinical examinations such as listening to a chest or looking in an ear are not possible in a remote consultation
- Total triage should ensure that patients have the right type of consultation but this system is not perfect, especially when there is high demand for appointments.

#### SY153

Antimicrobial stewardship in special populations

 $\blacksquare$  AMS in dental practice: are interventions needed? ( *L. TEOH* )



# Dentistry and antibiotics – dental treatment, not drugs!













Antibiotics are not required for localised infections



## Dental antibiotic prescribing choices

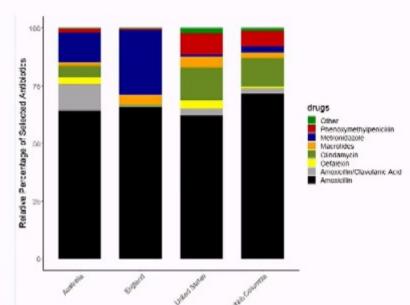


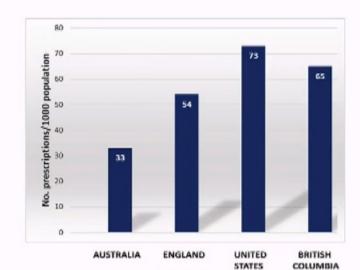
Patterns of dental antibiotic prescribing in 2017: Australia, England, United States, and British Columbia (Canada)

Published online by Cambridge University Press: 05 April 2021

Wendy Thompson (I). Leanne Teoh, Colin C. Hubbard, Fawziah Marra, David M. Patrick, Abdullah Mamun, Allen Campbell and Katie J. Suda

Show author details >>















### Why is antibiotic stewardship needed in dentistry?

- Dental antibiotic prescribing accounts for 10% of all prescribed antibiotics
- Up to 80% of dental antibiotics are overprescribed in Australia, UK and the US



55% overprescribing for therapeutic indications hisputhini.org/10.1136/s12408-014-0882-6

BMC Oral Health

#### RESEARCH ARTICLE

Open Access

A survey of prescribing practices by general dentists in Australia



L. Tech 17 to R. J. Marino 1, K. Stewart 2 and M. J. McCullough 1



80% overprescribing for therapeutic indications



Original Article

Antibiotic prescribing in UK general dental practice: a crosssectional study

Anwen L. Cope & Nick A. Francis, Fiona Wood, Ivor G. Chestnutt

First published: 27 October 2016 | https://doi.org/10.1111/cdoe.12199 | Citations: 90



80% overprescribing for prophylaxis Assessment of the Appropriateness of Antibiotic Prescriptions for Infection Prophylaxis Before Dental Procedures, 2011 to 2015

Natio J. Suda, Pharmill,  $MS^{1,2}$ ; Gregory S. Calip, Pharmill, MH1,  $PhD^{1}_{1}$ , Afang Zhou, <math>MD,  $MH^{1}_{2}$  or M

Predict Alleuten, | Adelir Internation

AMM Netwidgen, 2019-3(3)-499909. doi:10.1001/januariwarkigen.2019.3909



#### Non-clinical reasons for antibiotic prescription



Australian dentists would prescribe antibiotics routinely or occasionally due to:



77% Limited clinical time



82% Patient expectations



67% Unsure of a diagnosis





#### **FDI World Dental Federation**





#### International Dental Journal

Available online 12 April 2023 In Press, Corrected Proof ① What's this? >>



Scientific Research Report

#### International Consensus on a Dental Antibiotic Stewardship Core Outcome Set

Wendy Thompson.\* A. 185. Learning Teach.\*, Colinic Pulcini.\*, Susic Sanderson.\*,
David Williams.\*, Vanessa Carter.\*, Carole Pitkeathley.\*, Tanya Walsh.\*





### Our intervention: Drugs4dent®

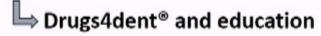
During 2018 to 2020, we:

Awareness raixing

Tackling antibiotic

Determined what dentists prescribe

- Determined factors that influenced inappropriate prescribing in Australia
  - Developed an intervention to address those factors





ORIGINAL ARTICLE

Improvement of dental prescribing practices using education and a prescribing tool: A pilot intervention study

Leanne Teoh . Kay Slewart, Rodrigo J Marino, Michael J McCullough

First published: 20 May 2020 | https://doi.org/10.1111/bcp.14373

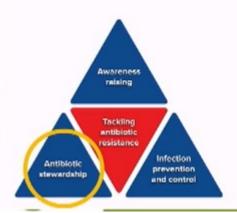


#### **Our intervention: Drugs4dent®**

#### Drugs4Dent

Medication and Prescribing Guidelines for Dentists

- Dental clinical decision tool
- Provides dentally relevant information
- Provides patient education
- Assists with prescribing to guidelines (Australian dental guidelines)





ORIGINAL ARTICLE

Improvement of dental prescribing practices using education and a prescribing tool: A pilot intervention study

Leanne Teoh . Kay Stewart, Rodrigo J Marino, Michael J McCollough

First published: 20 May 2020 | https://doi.org/10.1111/bcp.14373



# Access to dental care is important to reduce antibiotic use



Awareness raising

Tackling antibiotic resistance

Antibiotic stewardship

Infection prevention and control

Thompson, W, Williams D, Pulcini C, et al. The essential role of the dental team in reducing antibiotic resistance. Geneva: FDI World Dental Federation; 2020.