Surveillance to stewardship: antimicrobial resistance in the ICU

Luke Moore
FRCPath MRCP(Inf.Dis) PhD MPH MSc DTM&H
@dr_l_moore

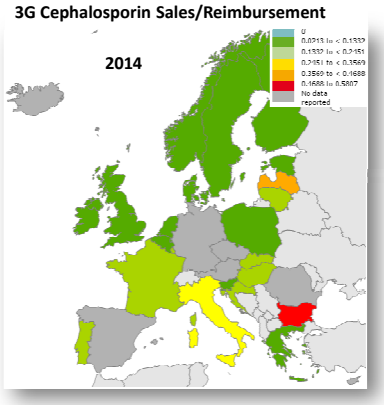
NHS National Institute for Health Research

Surveillance to stewardship: antimicrobial resistance in the ICU

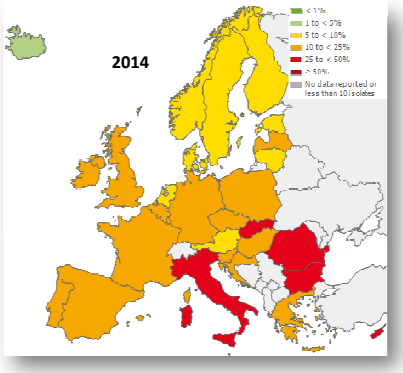
- Locating antimicrobial resistance: identifying the burden
- Drivers for antimicrobial resistance : understanding the complexity
- Retarding antimicrobial resistance : potential technological solutions

Enterobacteriaceae resistance to cephalosporins

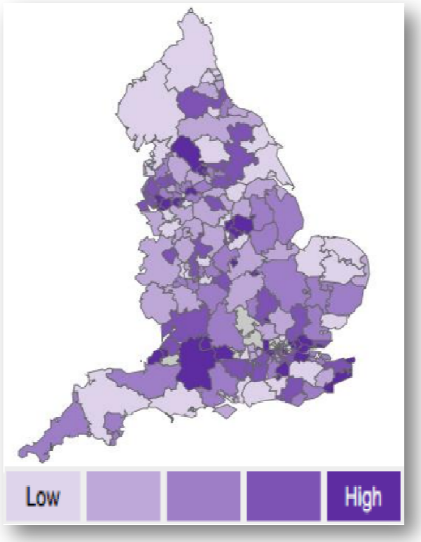
3G Cephalosporin Sales/Reimbursement



3G Cephalosporin Resistance

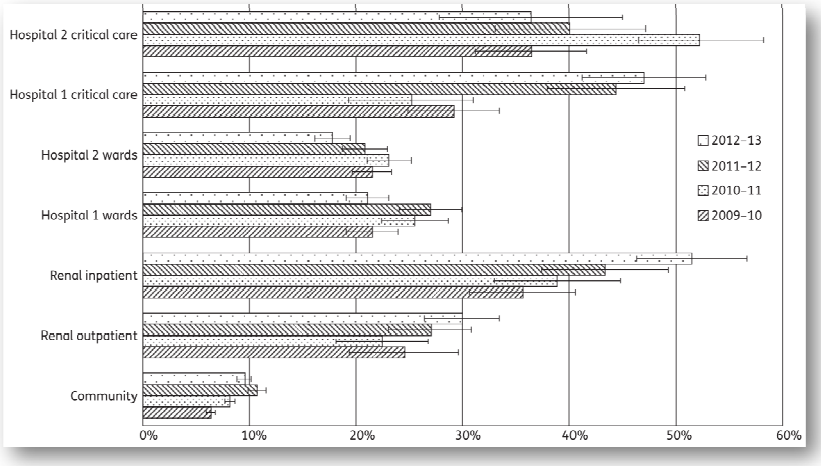


Enterobacteriaceae resistance to cephalosporins



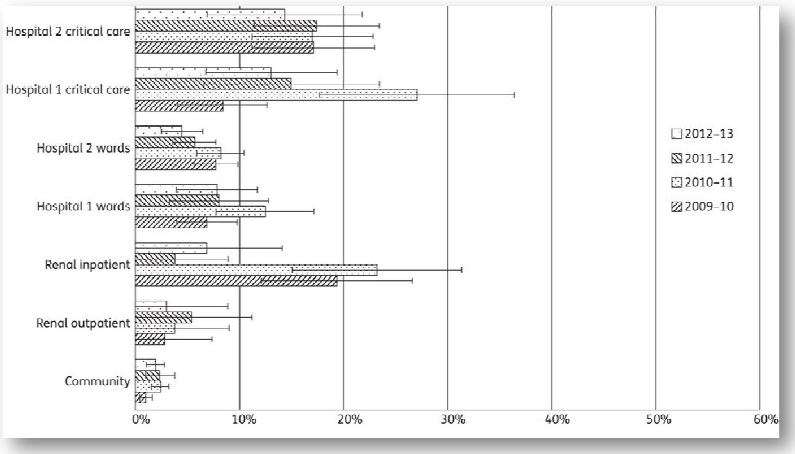
ESPAUR 2016

Enterobacteriaceae resistance to cephalosporins



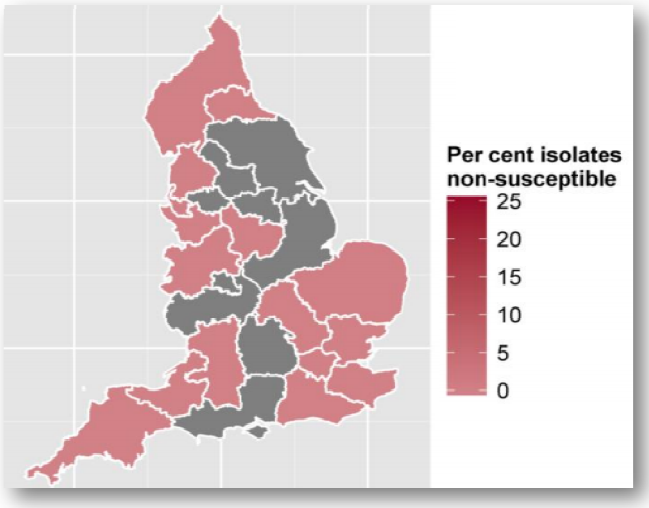
Moore, Freeman et al
J Antimicrob Chemo.
2014;69(12):3409-22
Funders: NIHR

Pseudomonas spp. resistance to ceftazidime/pip-taz



Moore, Freeman et al
J Antimicrob Chemo.
2014;69(12):3409-22
Funders: NIHR

Enterobacteriaceae resistance to carbapenems



ESPAUR 2014

Enterobacteriaceae resistance to carbapenems

Clinical specialty	Proportion of carbapenem-resistant isolates, %	
	E. coli	*Klebsiella* spp.
Medicine	0.2	3.6
Surgery and Cancer	0.5	1.7
Specialist Services	2.3	6.5
Circulation Sciences and Renal Medicine	0.8	9.3
Clinical and Investigative Sciences	5.8	0
Private patients	2.5	5.9
Unknown	0	0

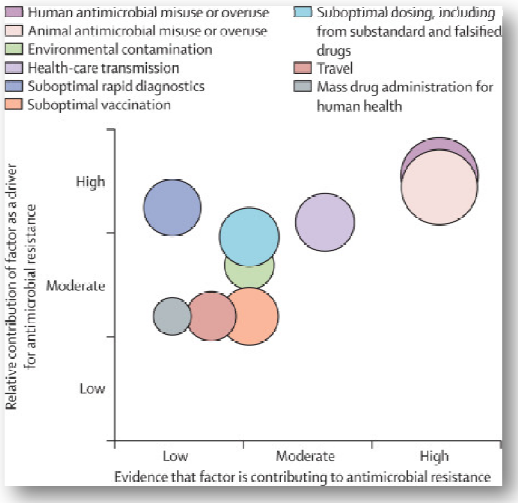
Freeman, Moore et al.
J Antimicrob Chemo.
2015;70(4):1212-8.
Funders: UKCRC

Carbapenem resistance & population movement

Holmes, Moore et al.
Lancet.
2016;387:176-187.
Funders: NIHR

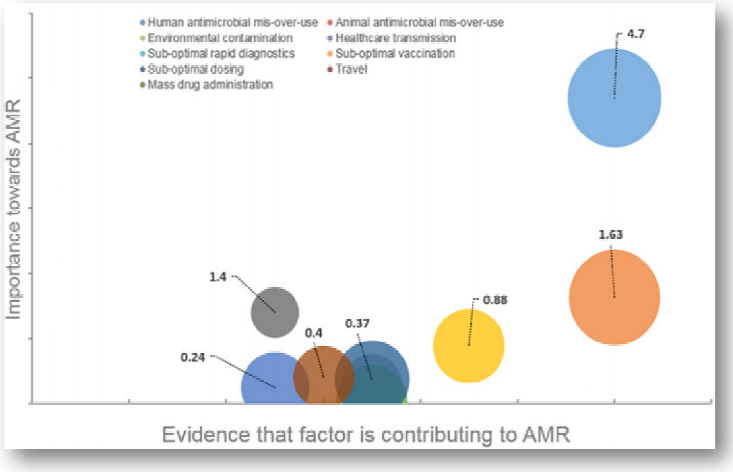
- Locating AMR:
  identifying the burden
- Drivers for AMR:
  understanding the complexity
- Retarding AMR:
  potential technological solutions

Understanding the drivers of AMR - Expert opinion



Holmes, Moore et al.
Lancet.
2016;387:176-187.
Funders: NIHR

Understanding the drivers of AMR - Public opinion



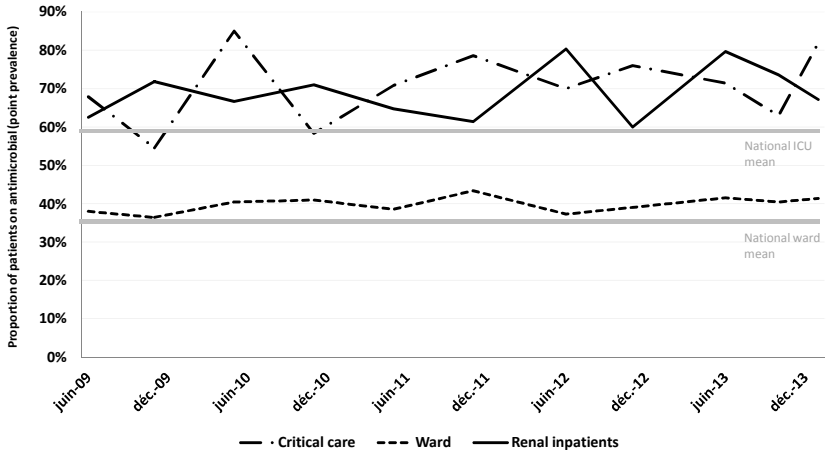
Castro-Sanchez,Moore et al
BMC Infect Dis.
2016;16:465.
Funders: NIHR

Increasing AMR:
Driven by antimicrobial use

	Hospital 1				Hospital 2			
	2009–10	2010–11	2011–12	2012–13	2009–10	2010–11	2011–12	2012–13
Ciprofloxacin	7.1%	7.3%	6.4%	4.9%	6.2%	5.9%	6.0%	5.2%
Amoxicillin/ clavulanate	20.4%	21.5%	23.2%	21.6%	21.5%	19.1%	21.1%	21.0%
Piperacillin/ tazobactam	5.8%	6.7%	6.1%	6.2%	4.2%	5.0%	5.2%	5.3%
Meropenem	5.2%	6.8%	5.9%	6.0%	3.5%	4.1%	3.8%	4.5%
Cumulative	38.5%	42.3%	41.6%	38.7%	35.2%	34.2%	36.2%	36.1%

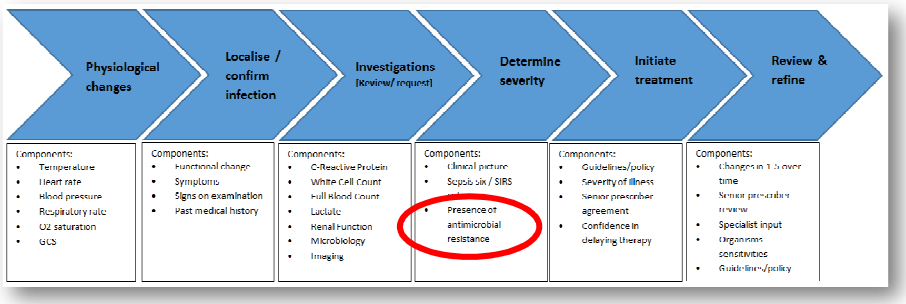
Moore et al.
J Antimicrob Chemo.
2014;69(12):3409-22
Funders: NIHR

Increasing AMR:
Driven by antimicrobial use



WIP

Increasing antimicrobial use: In turn…..driven by AMR?



Rawson, Charani et al.
BMC Medicine.
2016;[In Press]
Funders: NIHR

Increasing antimicrobial use: In turn…..driven by AMR?

Enterobacteriaceae resistance to carbapenems

Clinical specialty	Proportion of carbapenem-resistant isolates, %	
	E. coli	*Klebsiella* spp.
Medicine	0.2	3.6
Surgery and Cancer	0.5	1.7
Specialist Services	2.3	6.5
Circulation Sciences and Renal Medicine	0.8	9.3
Clinical and Investigative Sciences	5.8	0
Private patients	2.5	5.9
Unknown	0	0

Freeman, Moore et al.
J Antimicrob Chemo.
2015;70(4):1212-8.
Funders: UKCRC

Increasing AMR: Driven by outbreaks

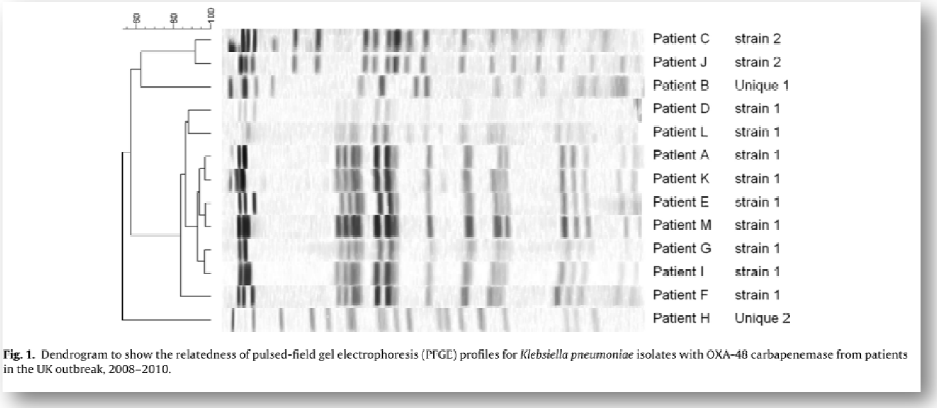
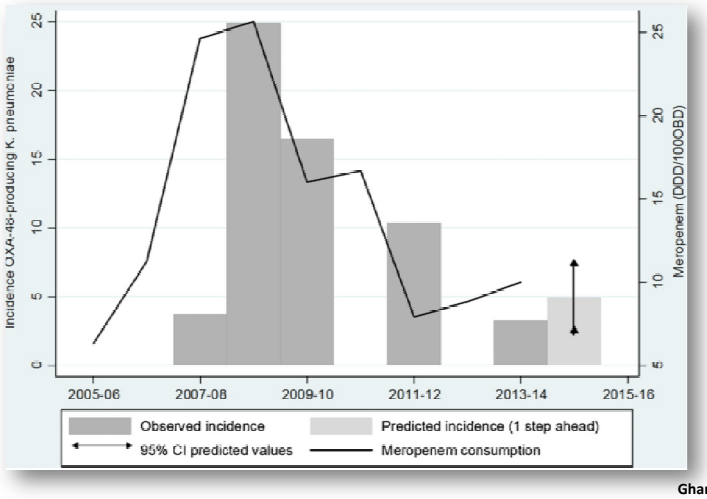


Fig. 1. Dendrogram to show the relatedness of pulsed-field gel electrophoresis (PFGE) profiles for *Klebsiella pneumoniae* isolates with OXA-48 carbapenemase from patients in the UK outbreak, 2008–2010.

Thomas, Moore et al.
I J Antimicrob Agents.
2013;42(6):531-6.
Funders: NIHR

AMR Outbreaks:
In turn….driven by antimicrobial use



Gharbi, Moore et al.
I J Antimicrob Agents.
2015;46(2):150-6.
Funders: NIHR

AMR Outbreaks:
financially costly

Carbapenemase-producing *Enterobacteriaceae*						
Episode 1: 1 month Episode 2: 2 months	Episode 1: 6 Episode 2: 10/463	Screening (n = 716): €31 665	—	Cost for ward closure: €520 503	Cost for 1663 h of nursing staff: €65 385	€617 553
Carbapenem-resistant *Acinetobacter baumannii*						
1 month	S/NR	—	Cleaning: €13 048 Destruction of supplies: €39 144	Ward closure: €235 467	—	€287 659
Unclear	Episode 1: 20/230 Episode 2: 7/34	Episode 1: screening (n = 230): €8 474 environmental samples (n = 500): €13 052 Episode 2: screening (n = 34): €1252 environmental samples (n = 200): €5221	Isolation supplies: Episode 1: €5187 Episode 2: €853	Ward closure: Episode 1: 560 days: €586 727 Episode 2: 220 days: €222 676	—	Episode 1: €613 440 Episode 2: €230 002

Birgand, Moore et al.
Clin Microb Infect.
2016;22(2):162e1-9.
Funders: NIHR

- Locating AMR:
  identifying the burden

- Drivers for AMR:
  understanding the complexity

- Retarding AMR:
  potential technological solutions

Retarding AMR: potential technological solutions

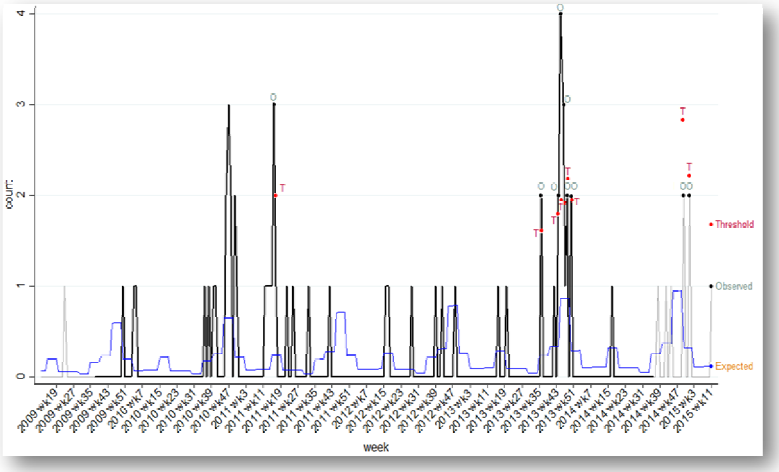
1) Improved surveillance

Automated surveillance for HCAIs

	Study	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	Clinical Specialties
Primary BSI Secondary BSI	Bouam *et al.*	92.0 (89.0–95.0) 80.0 (75.0–85.0)	96.0 (94.0–98.0) 97.0 (56.0–99.0)	85.0 (80.0–90.0) 80.0 (75.0–85.0)	95.0 (92.0–98.0) 97.0 (95.0–99.0)	Surgery, medicine, ICU
BSI CVC-related BSI	Bouzbid *et al.*	98.0 (93.9–100) 00.0	58.3 (55.8–60.9) 37.3 (33.9–40.7)	7.4 (5.4–9.4) 9.5 (7.1–12.2)	99.9 (99.6–100) 100.0	ICU
CAUTI	Choudhuri *et al.*	86.4	93.8	85.0	94.4	Whole hospital
CDI	Shaklee *et al.*	80.7 (72.1–87.7)	99.9 (99.8–99.9)	74.0 (65.1–81.6)	99.9 (99.9–100)	Paediatrics
VAP	Claridge *et al.*	97.0	100.0	–	–	ICU

Freeman, Moore et al.
J Hosp Infect.
2013;84(2):106-19.
Funders: UKCRC

Automated surveillance for AMR outbreaks



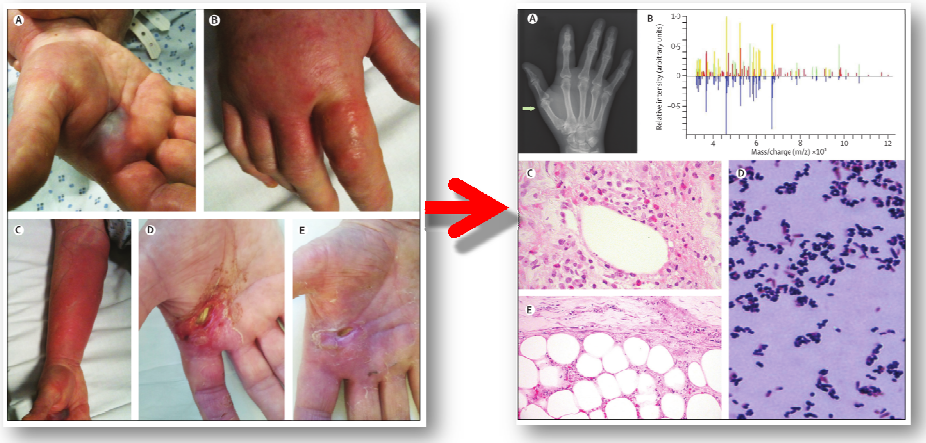
Moore, Freeman et al
I J Infect Dis.
2016;45(1):211
Funders: NIHR

Retarding AMR: potential technological solutions

2) Rapid diagnostics

Rapid diagnostics

Rapid bacterial identification

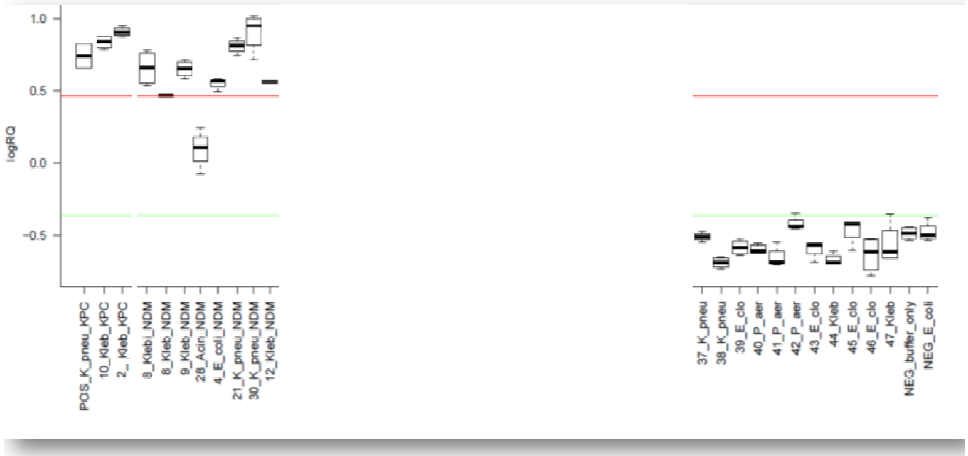


Moore et al.
Lancet Inf Dis
2015;15(9):1100-07.
Funders: NIHR

Rapid outbreak identification

Moore et al.
Emerg Inf Dis
2016;22(1):9-17.
Funders: NIHR

Rapid AMR determination



Pitty, Moore et al. *ECCMID.* 2015.
Funders: NIHR

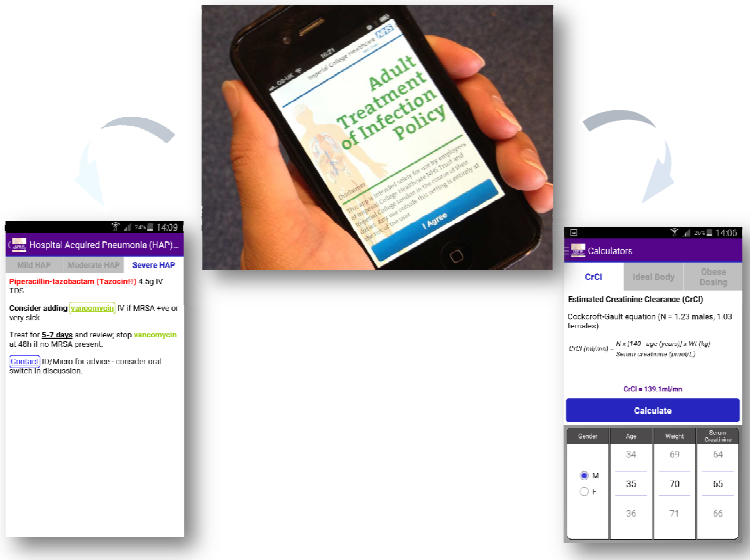
But…..

"Would it help us if we could get ID and sensitivities on the same day? …. if you know that if the results say that there is no infection, that was reliable, then you wouldn't prescribe antibiotics at all, but you'd want to be pretty damn sure about it, you'd need quite a lot of evidence both from extensive research and from one's own experience of it being reliable before you actually eased back on your prescribing." *ICU Cons, 51yoM*

Retarding AMR: potential technological solutions

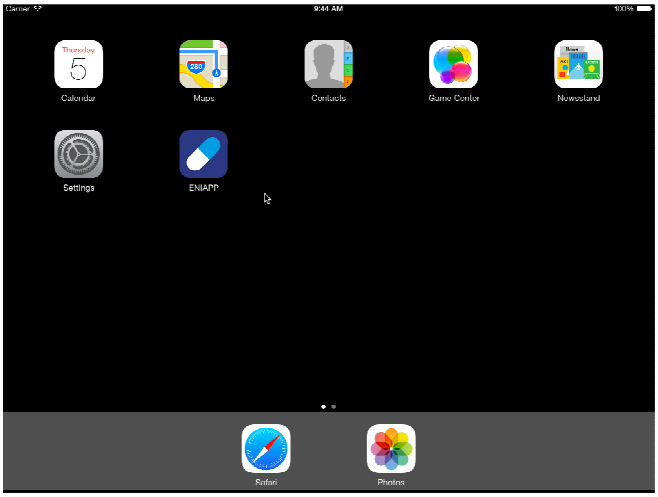
3) Decision support

Decision support for antimicrobial stewardship



Charani et al.
J Antimicrob Chemo.
2013;68(4):960-7.
Funders: UKCRC

Decision support for antimicrobial stewardship



Moore et al.
MEC Bio Eng.
2014.
978-0993039003.
Funders: UKCRC

Surveillance to stewardship: antimicrobial resistance in the ICU

- Locating AMR:
  identifying the burden
- Drivers for AMR:
  understanding the complexity
- Retarding AMR:
  potential technological solutions

Acknowledgements

NIHR Health Protection Research Unit
Healthcare Associated Infection
and Antimicrobial Resistance

Alison Holmes
Esmita Charani
Gabriel Birgand
Enrique Castro-Sanchez
Myriam Gharbi
Timothy Rawson
Venanzio Vella

Imperial College Healthcare NHS Trust

Hugo Donaldson
Lee Pitty
Eimear Brannigan
Mark Gilchrist
Anthony Gordon

NHS National Institute for Health Research

UK Clinical Research Collaboration

Centre for Bio-Inspired Technology

Christofer Toumazou
Pantelis Georgiou
Pau Herrero-Vinas
Bernard Hernandez-Perez

Public Health England

Rachel Freeman
Andre Charlett
David Livermore
Neil Woodford
Jane Turton

@dr_l_moore