

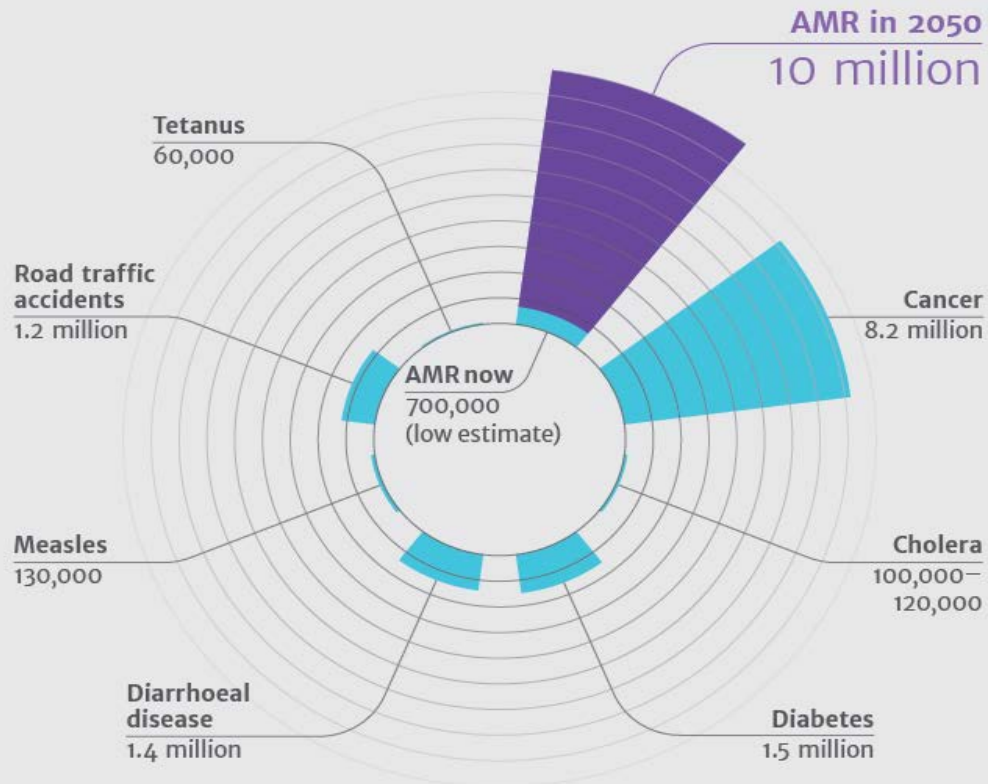
“Supermobile Superbugs”

International travel and antibiotic resistance

Patrick Harris

Microbiologist, Pathology Queensland; ID Physician PA Hospital

**Deaths attributable
to AMR every year**
compared to other
major causes of death



Review on Antimicrobial Resistance

Tackling drug-resistant infections globally

Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations

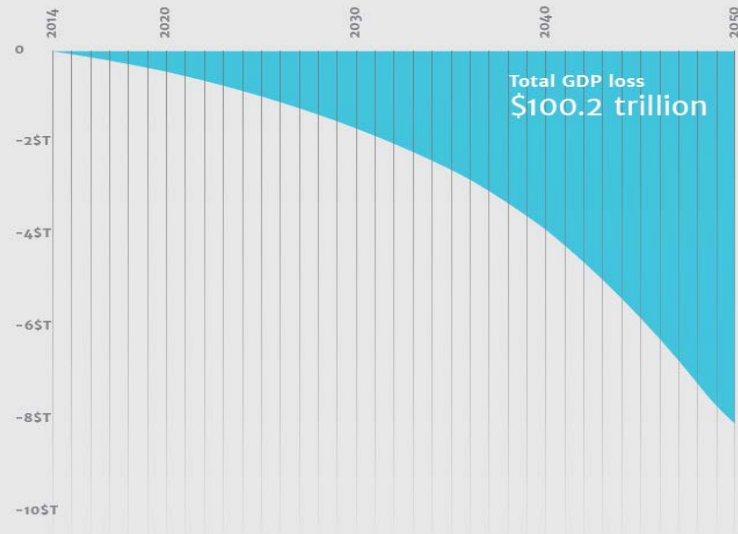
The Review on Antimicrobial Resistance
Chaired by Jim O'Neill
December 2014



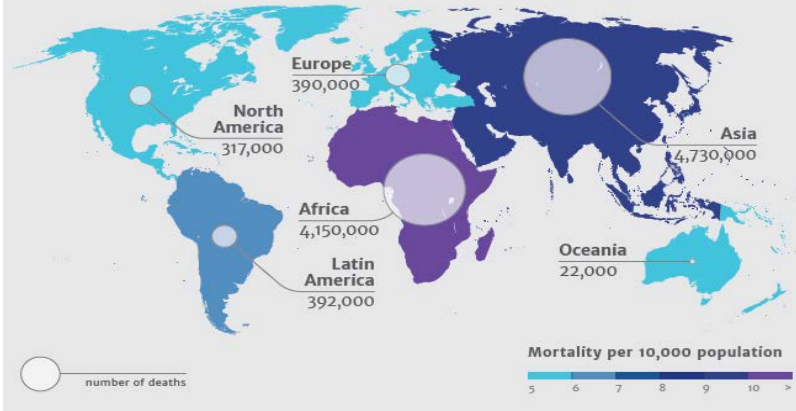
HM Government

wellcometrust

AMR's impact on World GDP in trillions of USD



Deaths attributable to AMR every year by 2050



**Review on
Antimicrobial
Resistance**

Tackling drug-resistant infections globally

More than 2 billion people travel long distances each year



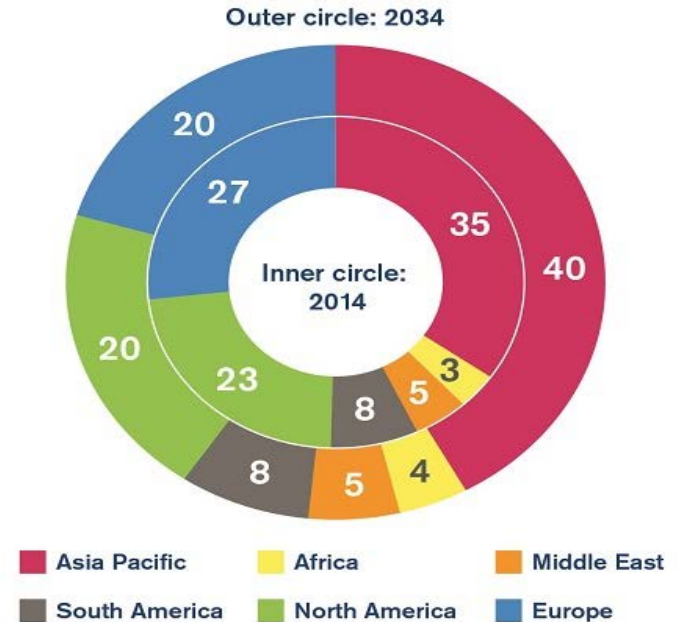
~300 million / year travel to areas highly endemic for antibiotic resistance



Global movement of people

- **IATA:** ~1.45 billion international air travel passengers estimated for 2016
 - ~35% of all international air travel in Asia-Pacific region, set to expand rapidly
- **UN Tourism:** 348 million international tourists Jan-April 2016
 - ~18 million more than the same period in 2015 (+5.3%)
 - 2016: will be the 7th consecutive year of above-average growth in tourism

Global air passengers by region
(% of total flows)



<http://www.iata.org>; <http://www2.unwto.org>



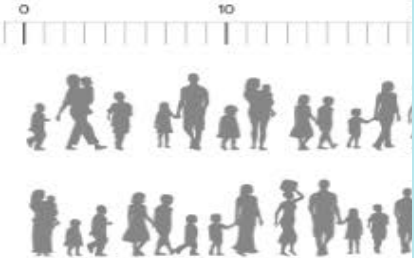
World
at war

Global Refugee Trends



Countries of Origin

Countries of Destination



www.unhcr.org

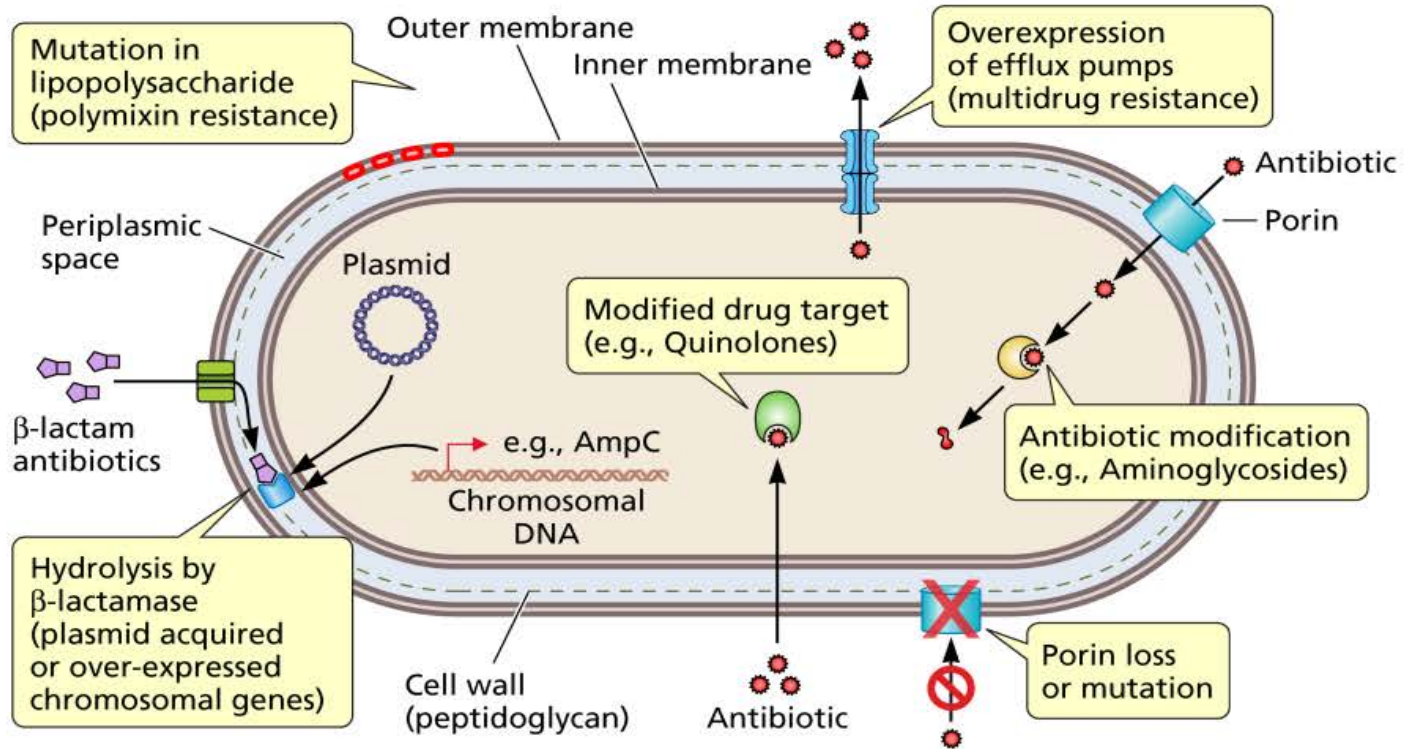


Data Source: UNHCR Global Trends 2014 Report (2015)

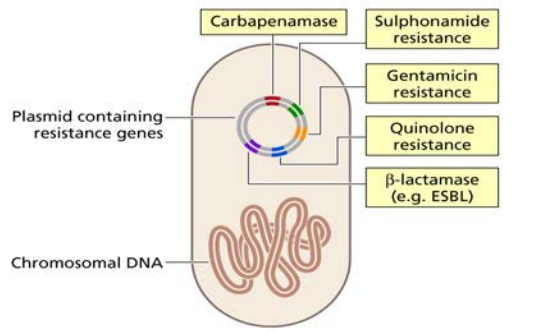
Map created by Tina Gotthardt & Benjamin Hennig

www.viewsoftheworld.net

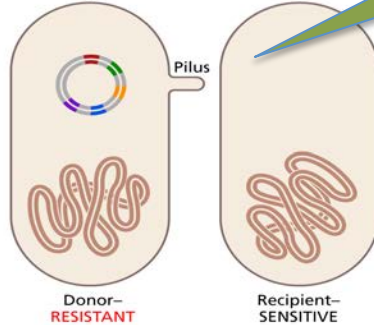
Gram-negatives possess multiple mechanisms to resist antibiotics



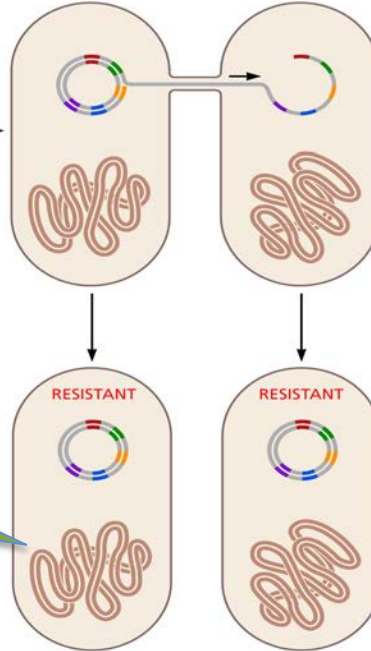
Plasmids and resistance



Plasmid transfer via conjugation
—horizontal gene transfer



Plasmid copied and transferred



Lateral (Horizontal)
Gene Transfer

Daughter cells inherit
resistance genes

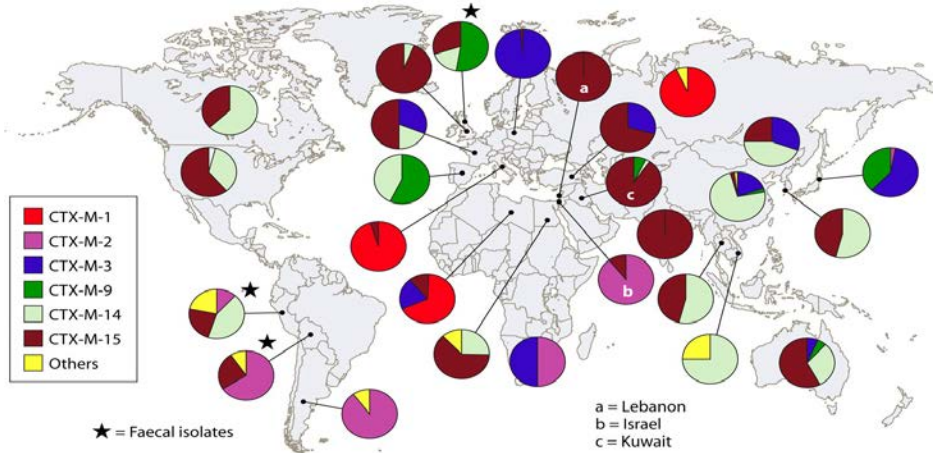
- ~25% of bacterial genome acquired by Lateral Gene Transfer
- Allows phenomenal diversity and rapid adaptation
- >18,000 potential genes in the *E. coli* “pan-genome” despite there being only ~2000 genes in each cell

“Lateral gene transfer potentially makes ***all genes in the microbial biosphere a single, common and shared resource***. In the same way that wars can be won by nations with the greatest industrial capacity, so it is that bacteria can draw on a global resource that can rapidly mobilize and transfer useful genes across physical and phylogenetic distances.”

Stokes & Gillings FEMS Microbiol Rev **35** (2011): 790–819

CTX-M: A true global traveller

The Trade Routes of the CTX-M Enzymes



- Once CTX-M penetrates a specific geographic area it tends to displace TEM / SHV ESBLs
- Frequently seen in successful pandemic clones e.g. ST131 uropathogenic *E. coli*

- “Cefotaximase-Munich” ESBL
- Origins from chromosomal *klu* beta-lactamase of *Kluyvera*
 - plasmid uptake in common pathogens e.g. *E. coli*, *Salmonella* spp
 - ***May have occurred multiple times***
- During 1990s, different reports at the same time of the same enzymes in very distant countries

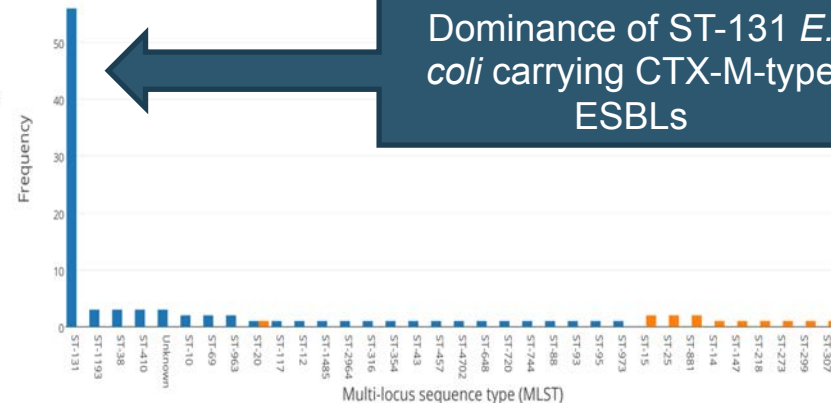
A map of Australia and New Zealand with pie charts indicating land cover types at various locations. The pie charts are color-coded: green for forest, brown for agriculture, blue for water, orange for urban, and purple for other. The numbers on the pie charts represent the percentage of each land cover type.

Australia:

- Top Left:** Forest (22%), Agriculture (9%), Water (21%), Urban (4%), Other (1%).
- Bottom Left:** Forest (22%), Agriculture (9%), Water (21%), Urban (4%), Other (1%).
- Bottom Right:** Forest (6%), Agriculture (9%), Water (5%), Urban (3%), Other (1%).
- Bottom Center:** Forest (3%), Agriculture (7%), Water (2%), Urban (3%), Other (1%).

New Zealand:

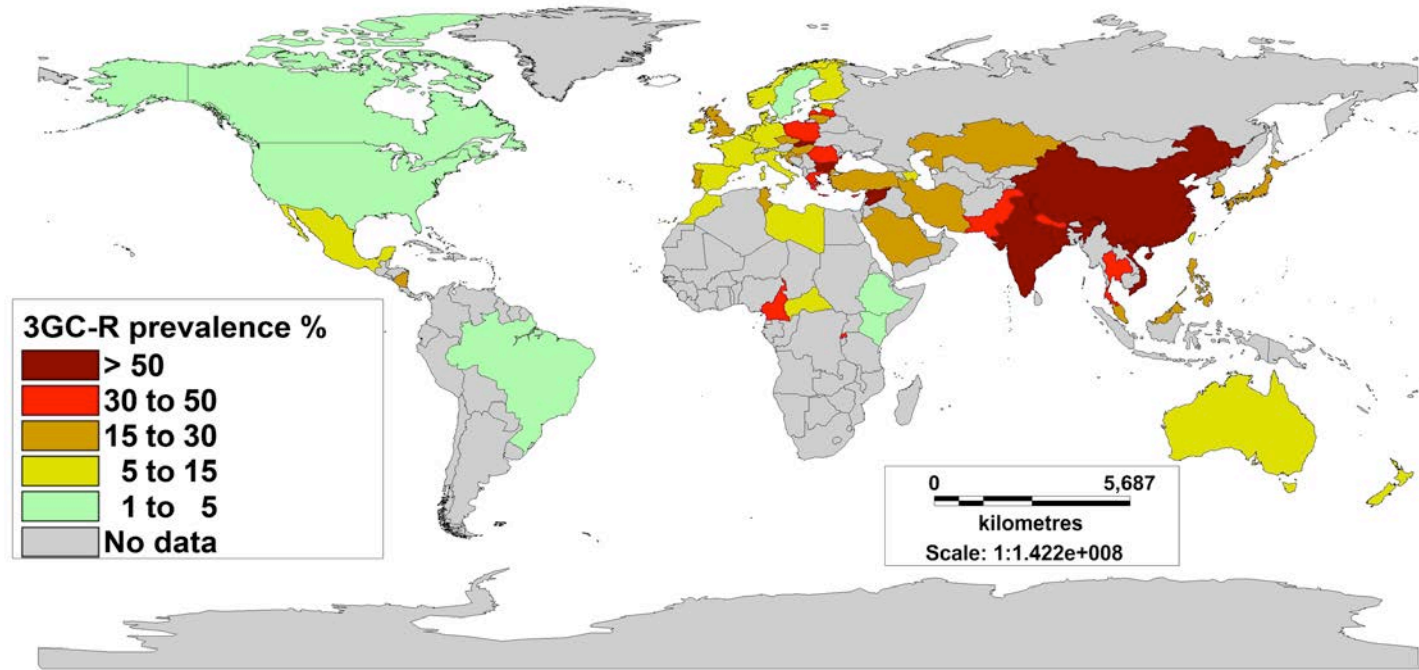
- Bottom Right:** Forest (6%), Agriculture (1%), Water (2%), Urban (2%), Other (1%).



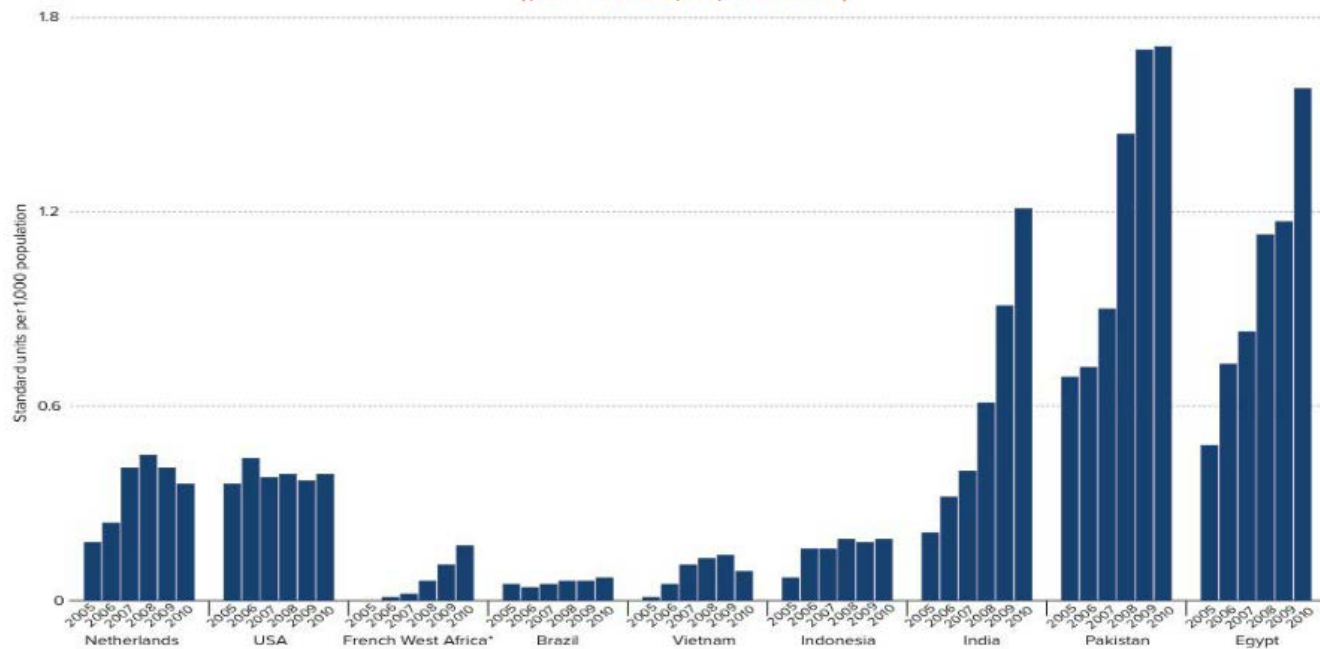
Dominance of ST-131 *E. coli* carrying CTX-M-type ESBLs

33% *bla*_{CTX-M-15}
23% *bla*_{CTX-M-27}
9% *bla*_{CTX-M-14}
 (all belong to
 CTX-M-9 lineage)

3rd generation cephalosporin resistant Enterobacteriaceae – urinary isolates



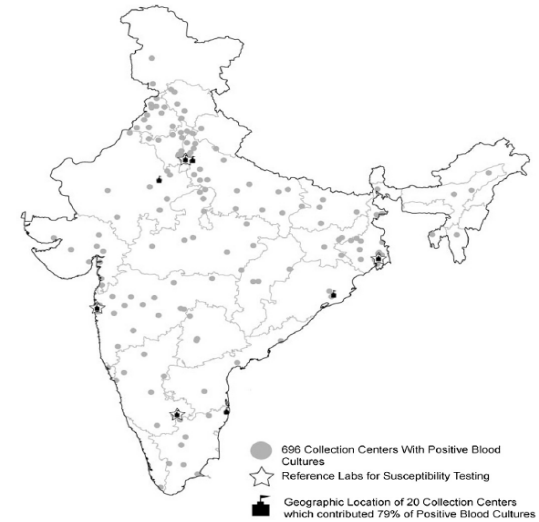
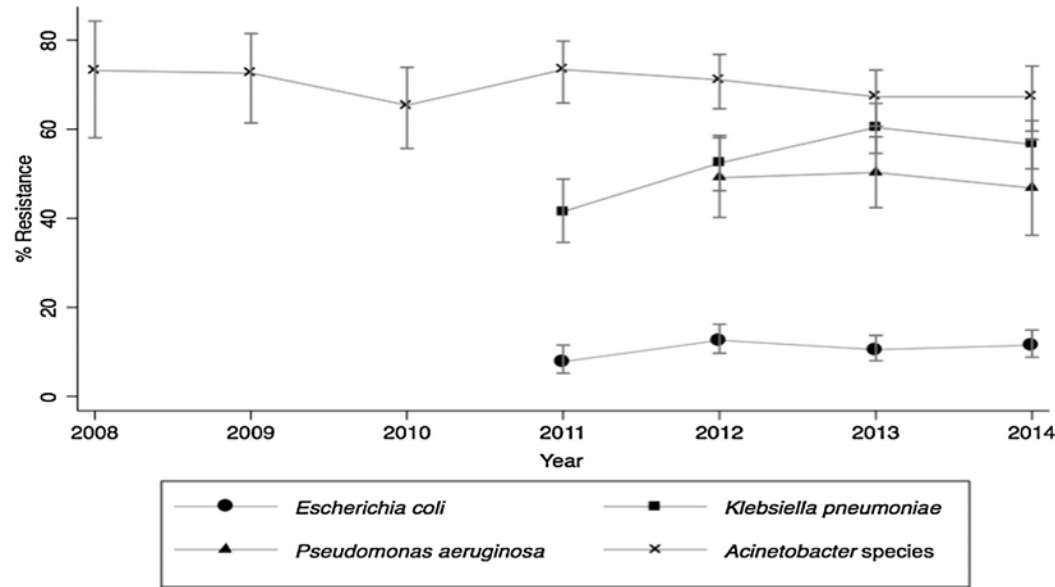
Carbapenem retail sales in selected countries, 2005–2010 (per 1,000 population)



Source: Laxminarayan et al. 2013 (based on IMS MIDAS)

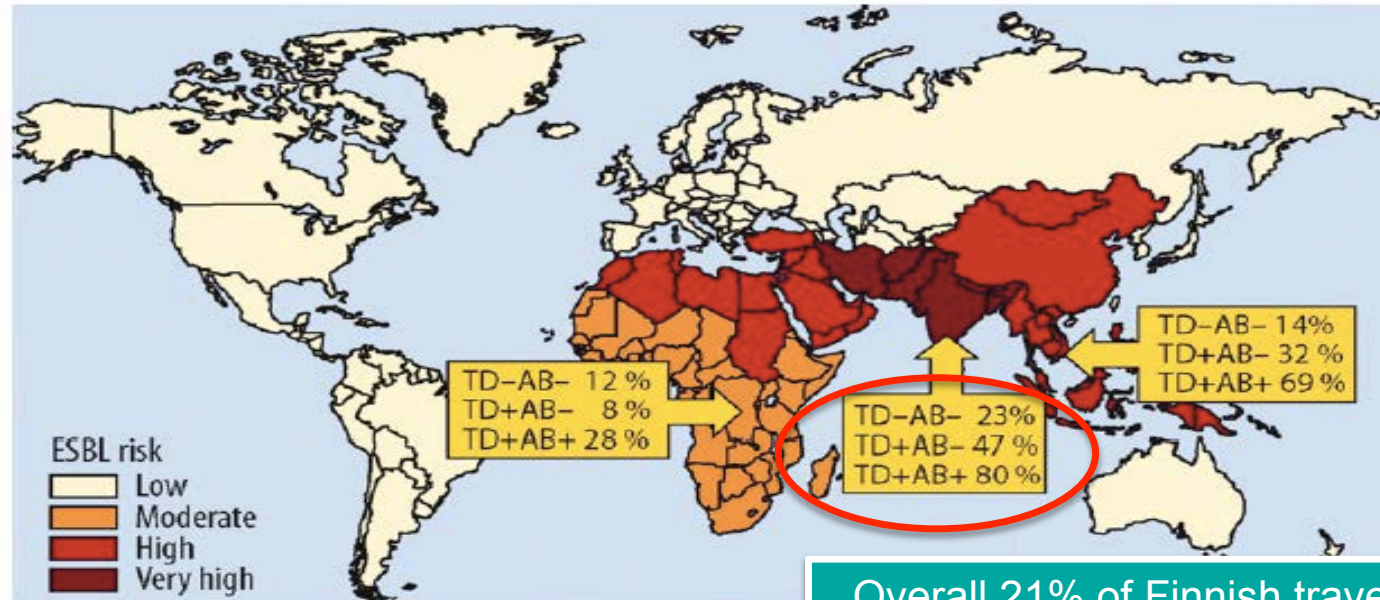
*An IMS grouping of Benin, Burkina Faso, Cameroon, Côte d'Ivoire, Gabon, Guinea, Mali, Republic of the Congo, Senegal, and Togo

Trends in antibiotic resistance among major bacterial pathogens isolated from blood cultures tested at a large private laboratory network in India, 2008–2014[☆]



18,695 isolates, 47.5% Gram-negative bacilli
~60% of *K. pneumoniae* resistant to carbapenems!

Antimicrobials Increase Travelers' Risk of Colonization by Extended-Spectrum Betalactamase-Producing *Enterobacteriaceae*



Overall 21% of Finnish travellers acquired ESBLs; 37% if had diarrhoea and antibiotics

THE RESISTANCE MOVEMENT

Carbapenem-resistant Enterobacteriaceae have been on the move since at least 1996.



1 **2000:** Analysis of a 1996 sample from a North Carolinian hospital finds infectious *Klebsiella pneumoniae* carrying a gene called KPC that confers resistance to carbapenems.

2 **2003:** KPC-positive bacteria are found spreading rapidly through hospitals across New York City. By 2007, 21% of *Klebsiella* in the city carry the resistance gene.

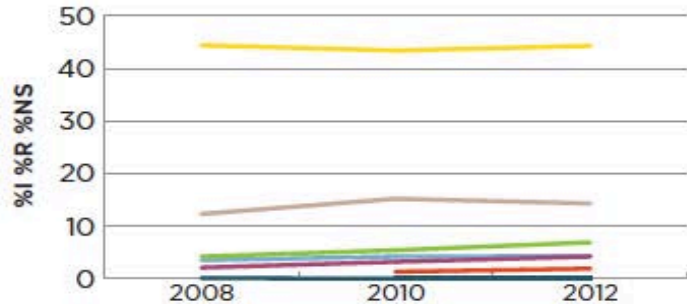
3 **2005:** KPC-positive bacteria make their way from New York to several other countries, including Israel. From Israel, the bacteria travel to Italy, Colombia, the United Kingdom and Sweden.

4 **2008:** Doctors in Sweden find a new carbapenem-resistance gene, NDM. Traced back to India, NDM-positive bacteria have moved quickly.

What is happening in Australia?

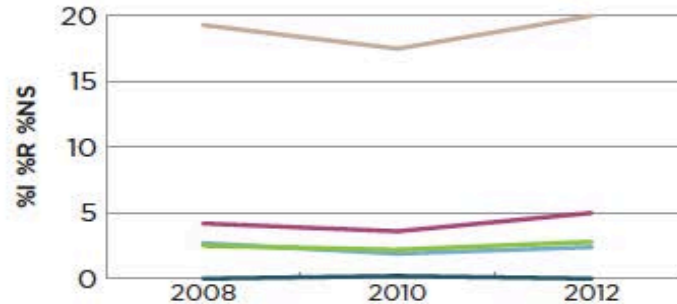
Resistance in community-onset infections

Escherichia coli



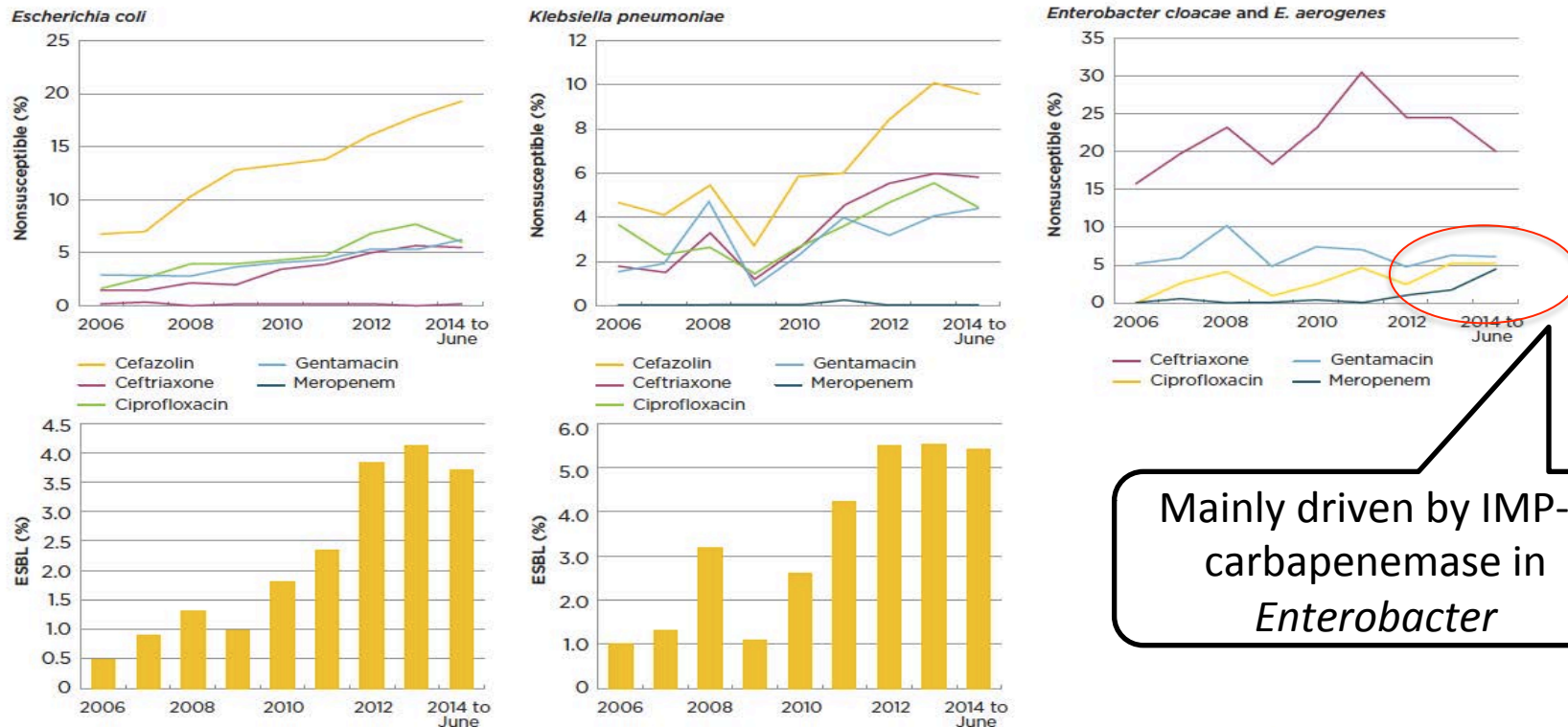
	Year		
	2008	2010	2012
Ampicillin %I	-	1.3	1.9
Ampicillin %R	44.4	43.4	44.3
Cefazolin %R	12.3	15.2	14.3
Ceftriaxone %NS	2.1	3.2	4.2
Ciprofloxacin %NS	4.2	5.4	6.9
Gentamycin %R	3.5	4.2	4.3
Meropenem %NS	0.1	0.0	0.0

Klebsiella species



	Year		
	2008	2010	2012
Cefazolin %R	19.3	17.5	20.0
Ceftriaxone %NS	4.2	3.6	5.0
Ciprofloxacin %NS	2.5	2.2	2.8
Gentamycin %R	2.7	1.9	2.4
Meropenem %NS	0.0	0.2	0.0

Figure 3 Resistance patterns in the Queensland public hospital sector for bacterial isolates from blood culture for species from the family *Enterobacteriaceae*, 2006 to June 2014



Note: Isolates were the first isolate per specimen per person per year. The upper panels show the percentage of nonsusceptible isolates for each antimicrobial. The lower panels show resistance to ceftriaxone, which is mostly attributable to production of extended-spectrum β -lactamase (ESBL). ESBL was not determined for *Enterobacter* species.

Source: OrgTRx, Queensland Health²

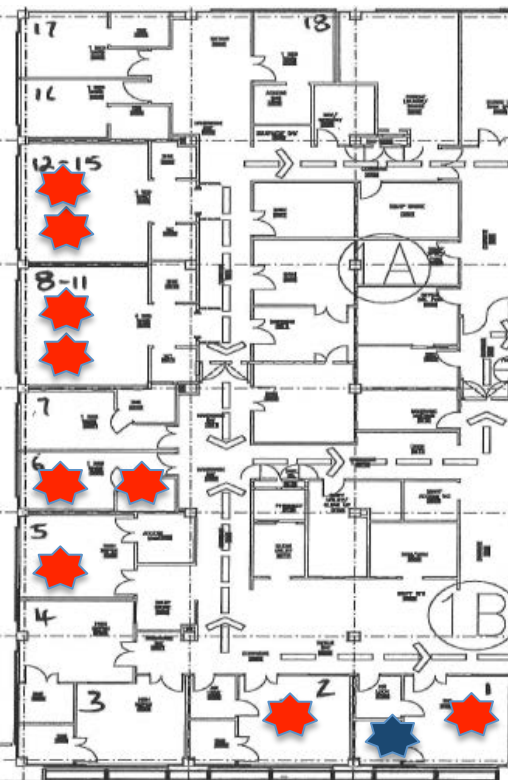
May 2016: retrieval from an overseas hospital

- Severe burns – day 4 of admission (under contact precautions from admission)

SENSITIVITIES: Blood

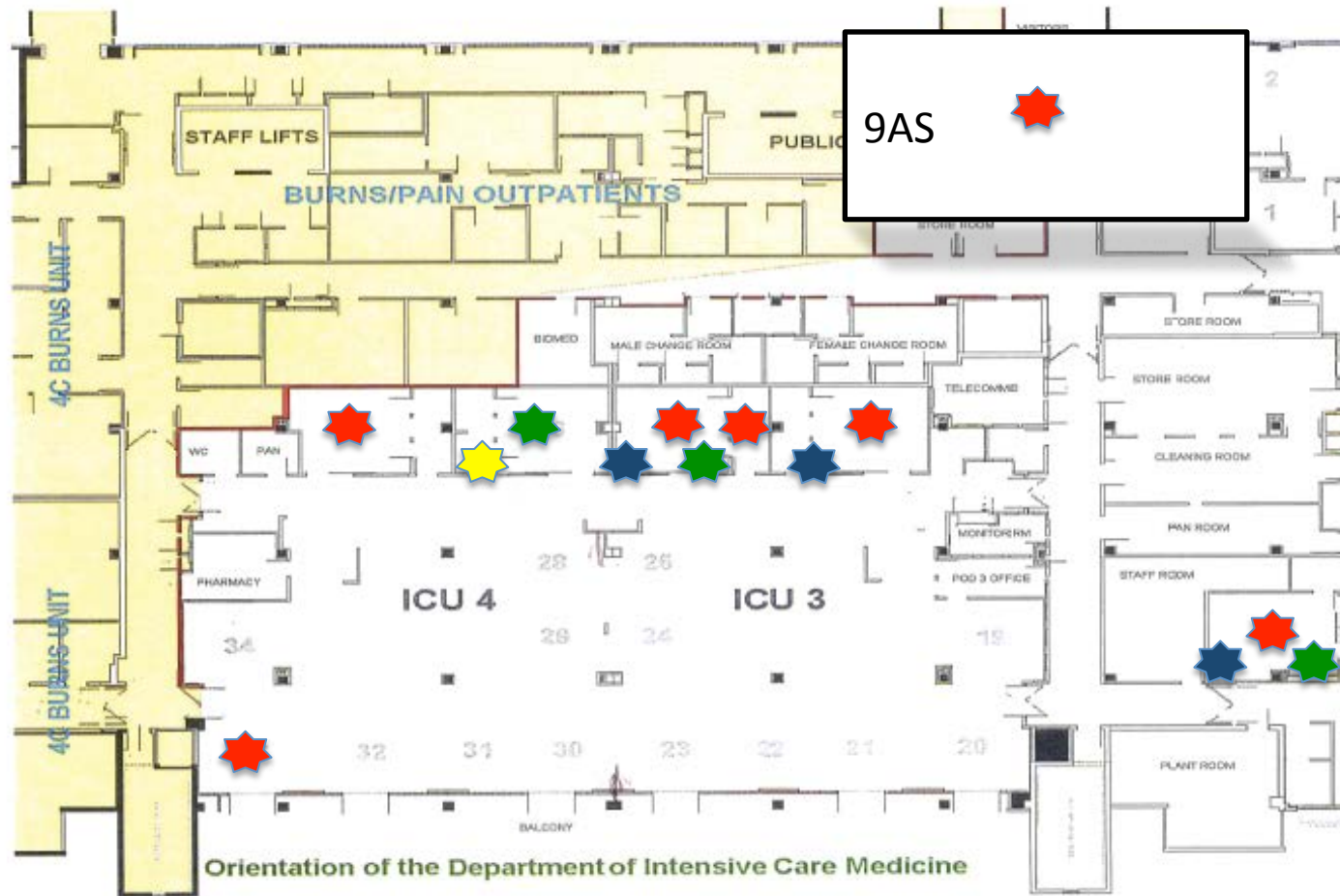
	TAZ	CIP	NOR	ATM	MER	COL
<i>S. pneumoniae</i> (ESBL producer)	R	R			S	
<i>Pseudomonas aeruginosa</i>	S	S			S	
<i>Acinetobacter baumannii</i> complex	R	R	R		R	S

Polymicrobial bloodstream infection, including carbapenem-resistant *A. baumannii* (CRAB): susceptible only to colistin (MIC 0.125), tigecycline (MIC=2) and doxycycline (MIC=2)



CRAB

ESBL-*K. pneumoniae*

Mero-R *Pseudomonas*IMP-4 +ve *Enterobacter cloacae*

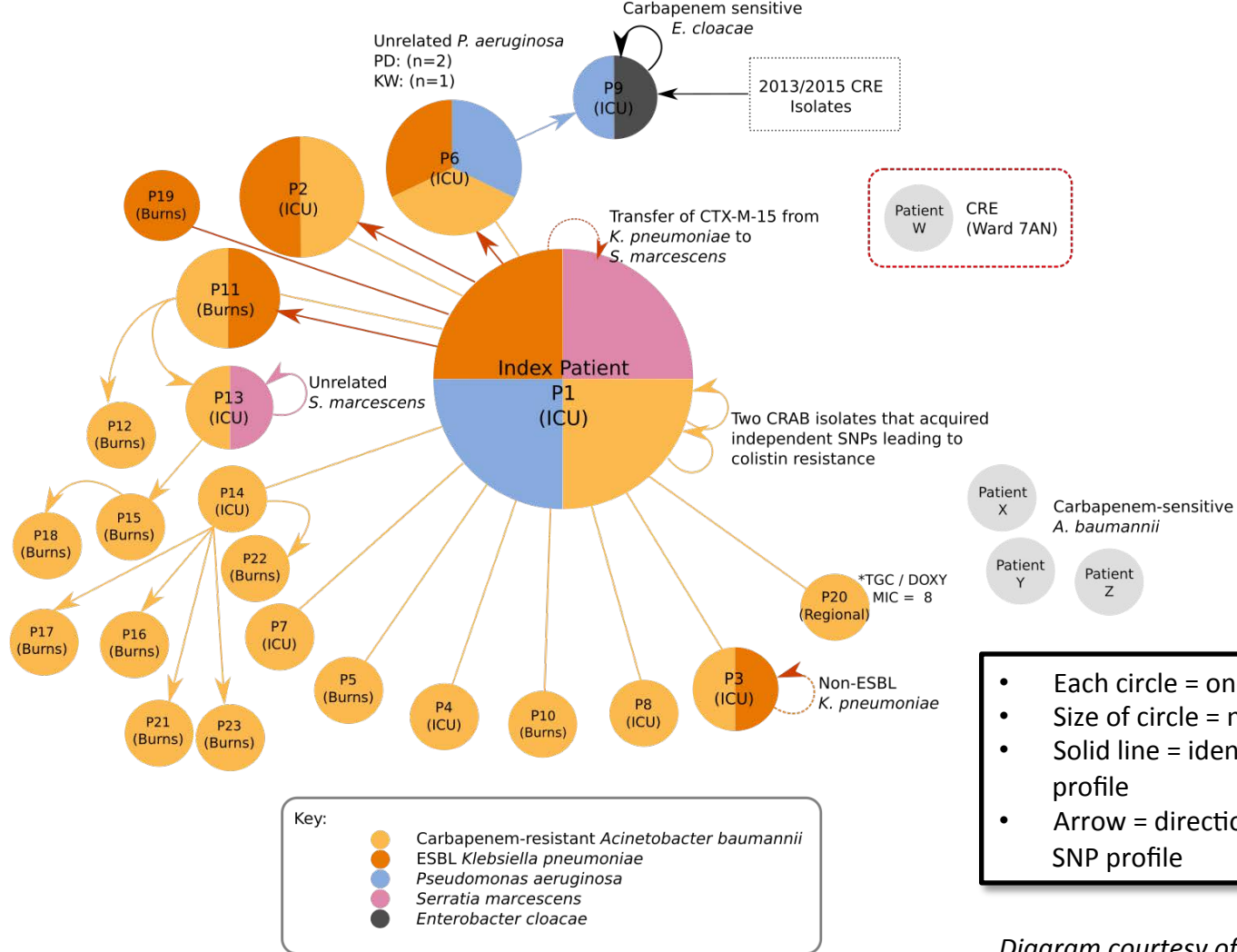


Diagram courtesy of Leah Roberts

Acknowledgements



p.harris@uq.edu.au

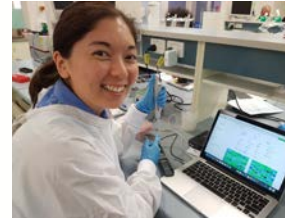
@padstamundo



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