UTI in the age of multi drug resistance

Luke Moore

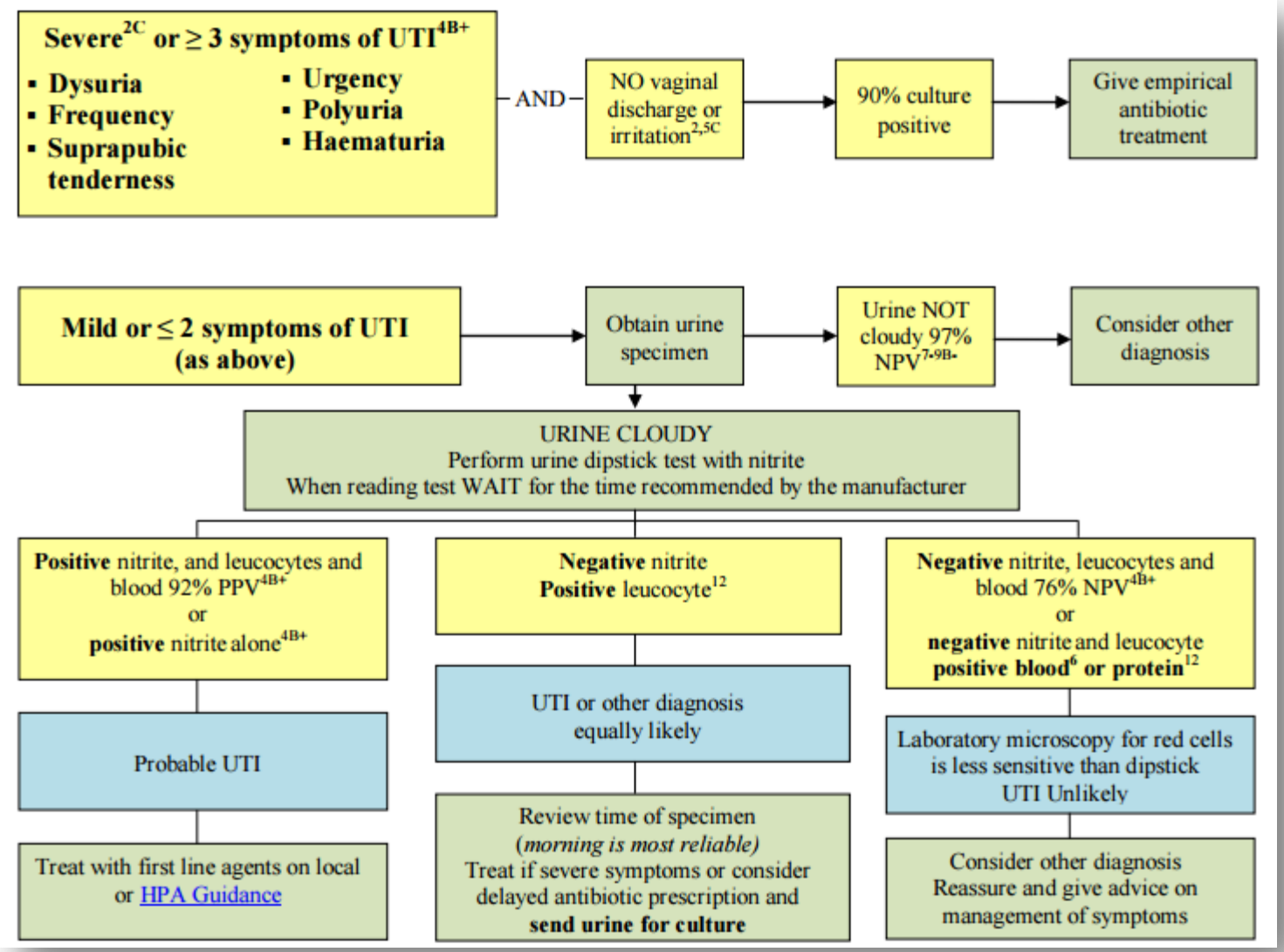
Consultant Infectious Diseases & Microbiology

FRCPath MRCP(Inf Dis) PhD MPH MSc DTM&H

Learning objectives

- Appraise the national guidelines for UTIs:
  - HPA/PHE
  - NICE
  - SIGN
- Understand the epidemiology of UTI pathogens in West London
- Revise the clinical utility of the less commonly used antimicrobials for UTIs
- Understand and implement pathways for expert help for multi-drug resistant UTIs in West London

HPA/BIA: diagnostic pathway



HPA 2011

NICE: Quality standards

Statement 1. Adults aged 65 years and over have a full clinical assessment before a diagnosis of urinary tract infection is made.

Statement 2. Healthcare professionals do not use dipstick testing to diagnose urinary tract infections in adults with urinary catheters.

Statement 3. Men who have symptoms of an upper urinary tract infection are referred for urological investigation.

Statement 4. Adults with a urinary tract infection not responding to initial antibiotic treatment have a urine culture.

Statement 5. Healthcare professionals do not prescribe antibiotics to treat asymptomatic bacteriuria in adults with catheters and non-pregnant women.

Statement 6. Healthcare professionals do not prescribe antibiotic prophylaxis to adults with long-term indwelling catheters to prevent urinary tract infection unless there is a history of recurrent or severe urinary tract infection.

Quality statement 7 (placeholder). Treatment of recurrent urinary tract infection.

NICE 2015

SIGN: Guidelines

MANAGEMENT OF BACTERIAL UTI IN ADULT WOMEN

D	**Consider the possibility of UUTI in patients presenting with symptoms or signs of UTI who have a history of fever or back pain**
B	**Use dipstick tests to guide treatment decisions in otherwise healthy women under 65 years of age presenting with mild or ≤2 symptoms of UTI.**
D	**Consider empirical treatment with an antibiotic for otherwise healthy women aged less than 65 years of age presenting with severe or ≥3 symptoms of UTI.**
B	**Treat non-pregnant women of any age with symptoms or signs of acute LUTI with a three day course of trimethoprim or nitrofurantoin.**
✓	Particular care should be taken when prescribing nitrofurantoin to elderly patients, who may be at increased risk of toxicity.
D	**Treat non-pregnant women with symptoms or signs of acute UUTI with a course of ciprofloxacin** (7 days) **or co-amoxiclav** (14 days).
A	**Do not treat non-pregnant women** *(of any age)* **with asymptomatic bacteriuria with an antibiotic.**

SIGN 2012

SIGN: Guidelines

MANAGEMENT OF BACTERIAL UTI IN ADULT MEN

B	Treat bacterial UTI empirically with a quinolone in men with symptoms suggestive of prostatitis.
D	Refer men for urological investigation if they have symptoms of upper urinary tract infection, fail to respond to appropriate antibiotics or have recurrent UTI.

MANAGEMENT OF BACTERIAL UTI IN PATIENTS WITH CATHETERS

D	Do not rely on classical clinical symptoms or signs for predicting the likelihood of symptomatic UTI in catheterised patients.
B	Do not use dipstick testing to diagnose UTI in catheterised patients.
A	Do not routinely prescribe antibiotic prophylaxis to prevent symptomatic UTI in patients with catheters.
B	Do not treat catheterised patients with asymptomatic bacteriuria with an antibiotic.

SIGN 2012

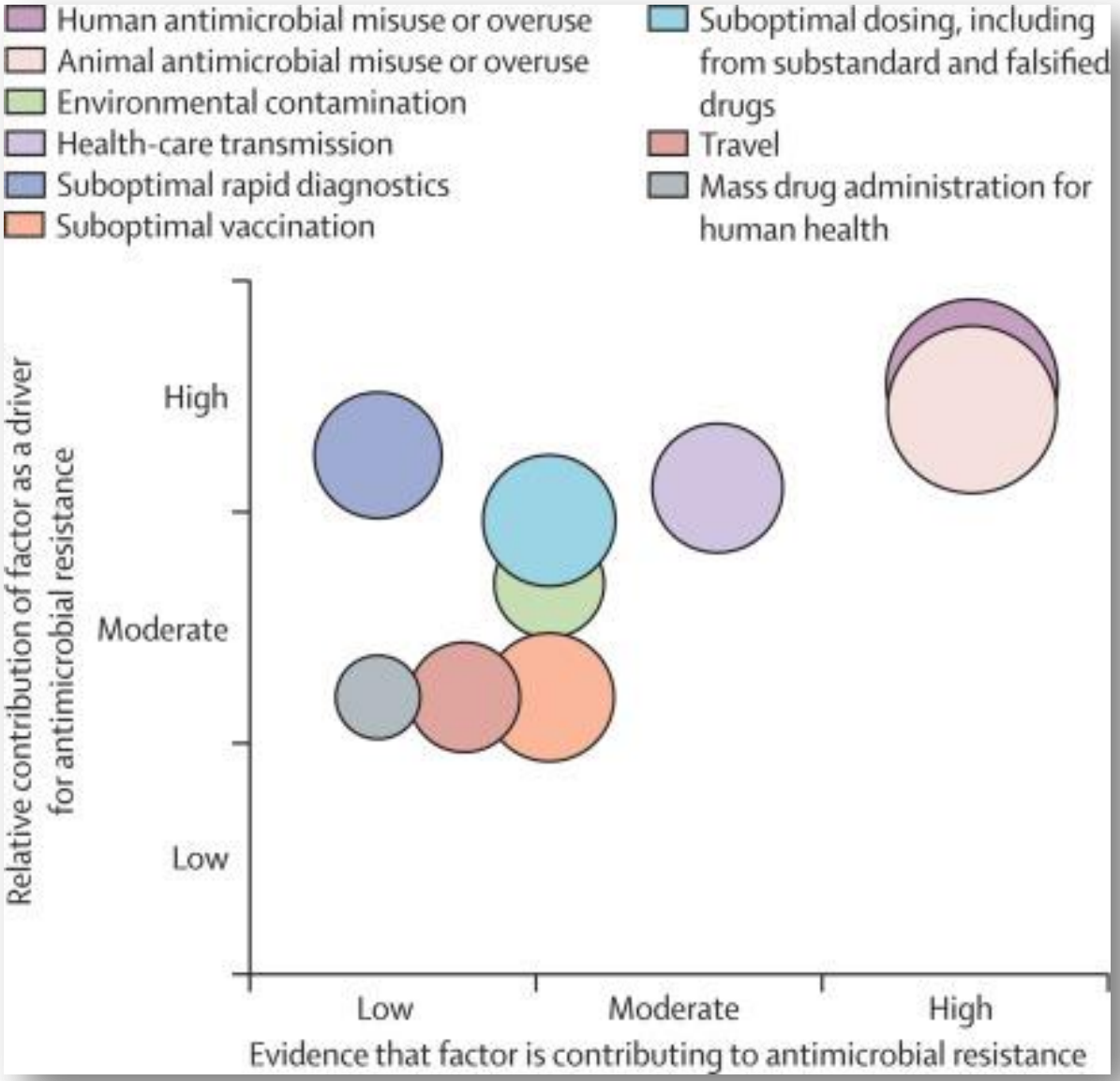
PHE: guidelines

UTI in adults (lower) PHE URINE SIGN CKS women CKS men RCGP UTI clinical module SAPG UTI	**Treat women** with severe/or ≥3 symptoms.[1A+,3D] **All patients first line antibiotic:** nitrofurantoin if GFR >45mls/min; if GFR30-45,[22B+,24B+] only use if resistance and no alternative. **Women (mild/≤ 2 symptoms):**[1A+] Pain relief,[42A-,43A-] and consider back-up/ delayed antibiotic.[19A+] If urine not cloudy, 97% NPV of no UTI.[4A-] If urine cloudy, use dipstick to guide treatment: nitrite, leucocytes, blood all negative 76% NPV; nitrite plus blood or leucocytes 92% PPV of UTI.[4A-] **Men:** Consider prostatitis and send MSU[1A+] OR if symptoms mild/non-specific, use negative dipstick to exclude UTI. **>65 years:** treat if fever ≥38°C or 1.5°C above base twice in 12h AND dysuria OR ≥2 other symptoms.[40] **If treatment failure:** always perform culture.[1A+]	***1st line:* nitrofurantoin** *If low risk of resistance:* trimethoprim ***If 1st line options unsuitable:*** *If GFR<45mls/min:* pivmecillinam[10A+,12A-,30A+] *If high risk of resistance:* fosfomycin[15B-,16B-,17A-] *If organism susceptible:* amoxicillin[30A+]	100mg m/r BD[7A-,9D,31D,32B-,33B+,35A-] 200mg BD[12A+,30A+] 400mg stat then 200mg TDS[12A+,36B+,37A+,38B+] 3g stat in women; men: 2nd 3g dose 3d later (unlicensed)[1A+,15B-,16B-,17A-] 500mg TDS	3 days Men: 7 days
		Low risk of resistance: younger women with acute UTI and no resistance risks. **Risk factors for increased resistance include:** care home resident,[41B-] recurrent UTI (2 in 6 months; ≥3 in 12 months), hospitalisation for >7d in the last 6 months, unresolving urinary symptoms, recent travel to a country with increased resistance, previous UTI resistant to trimethoprim, cephalosporins, or quinolones.[18B-] **If risk of resistance:** send urine for culture & susceptibilities, & always safety net.		
Catheter in situ: antibiotics will not eradicate asymptomatic bacteriuria. Only treat if systemically unwell or pyelonephritis likely;[1B+] do not use prophylaxis for catheter change unless history of catheter-change-associated UTI or trauma.[2D] Take sample if new onset of delirium, or two or more symptoms of UTI.[3B+]				

PHE 2017

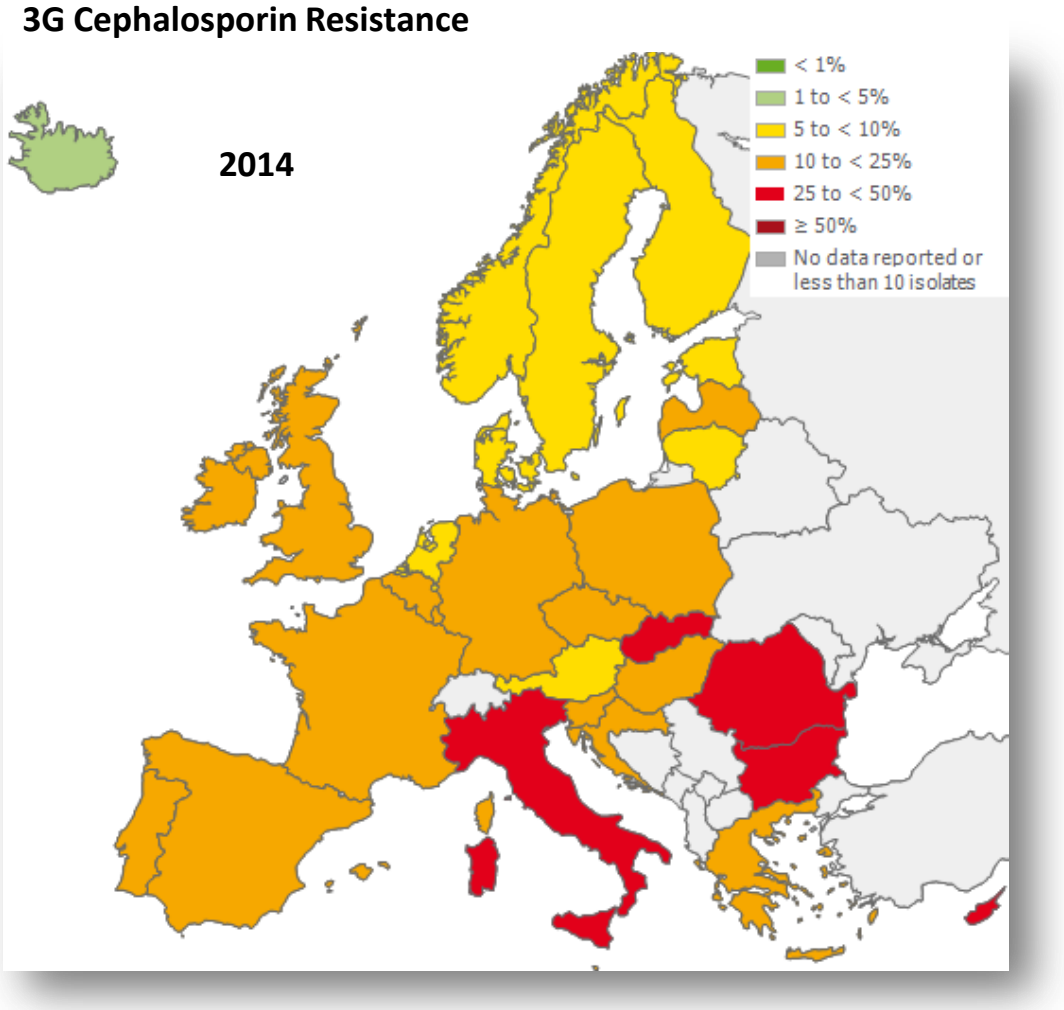
Susceptibility testing

Understanding the drivers of AMR

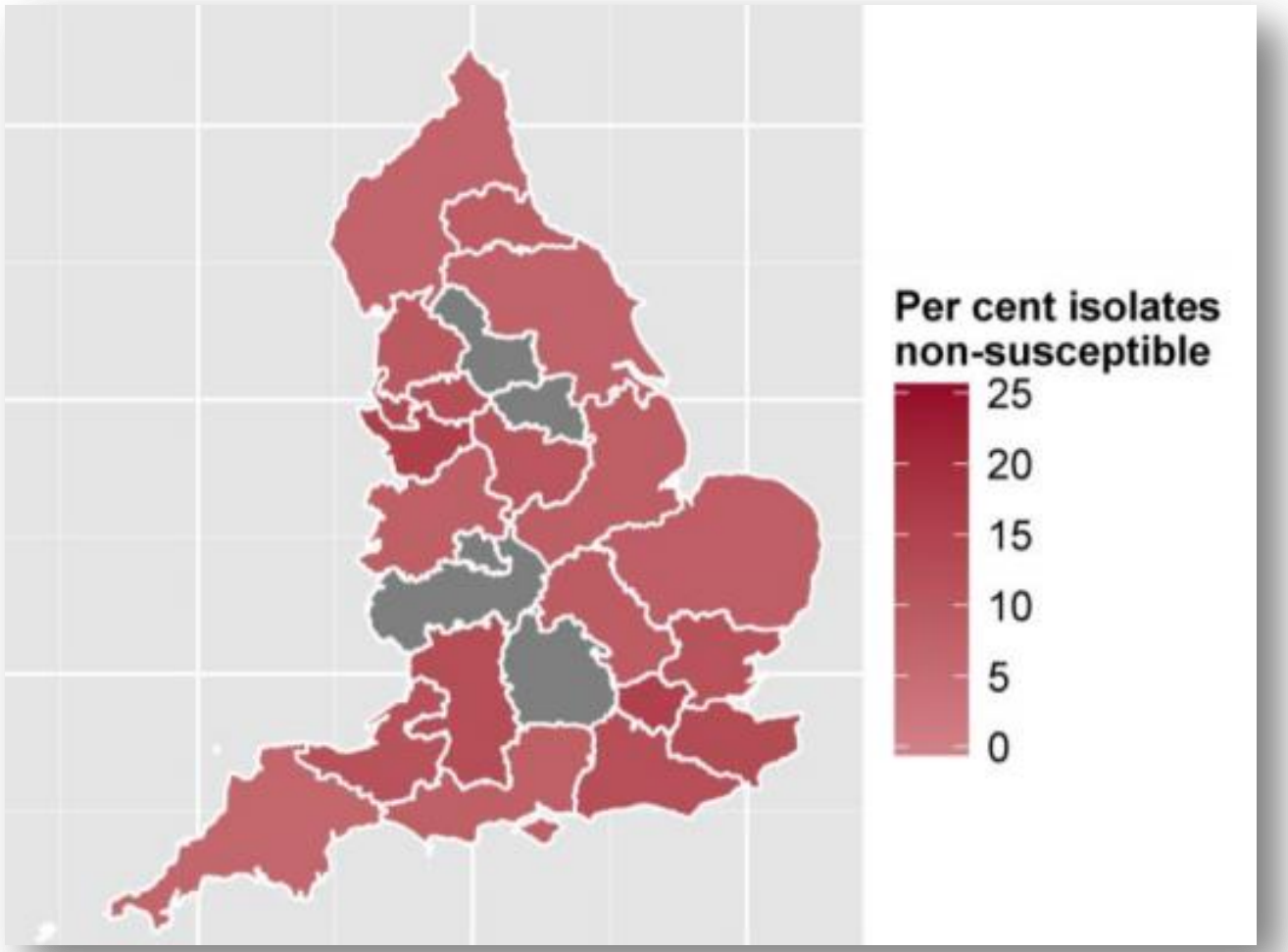


Holmes Lancet 2016

Enterobacteriaceae resistance to co-amoxiclav & cephalosporins

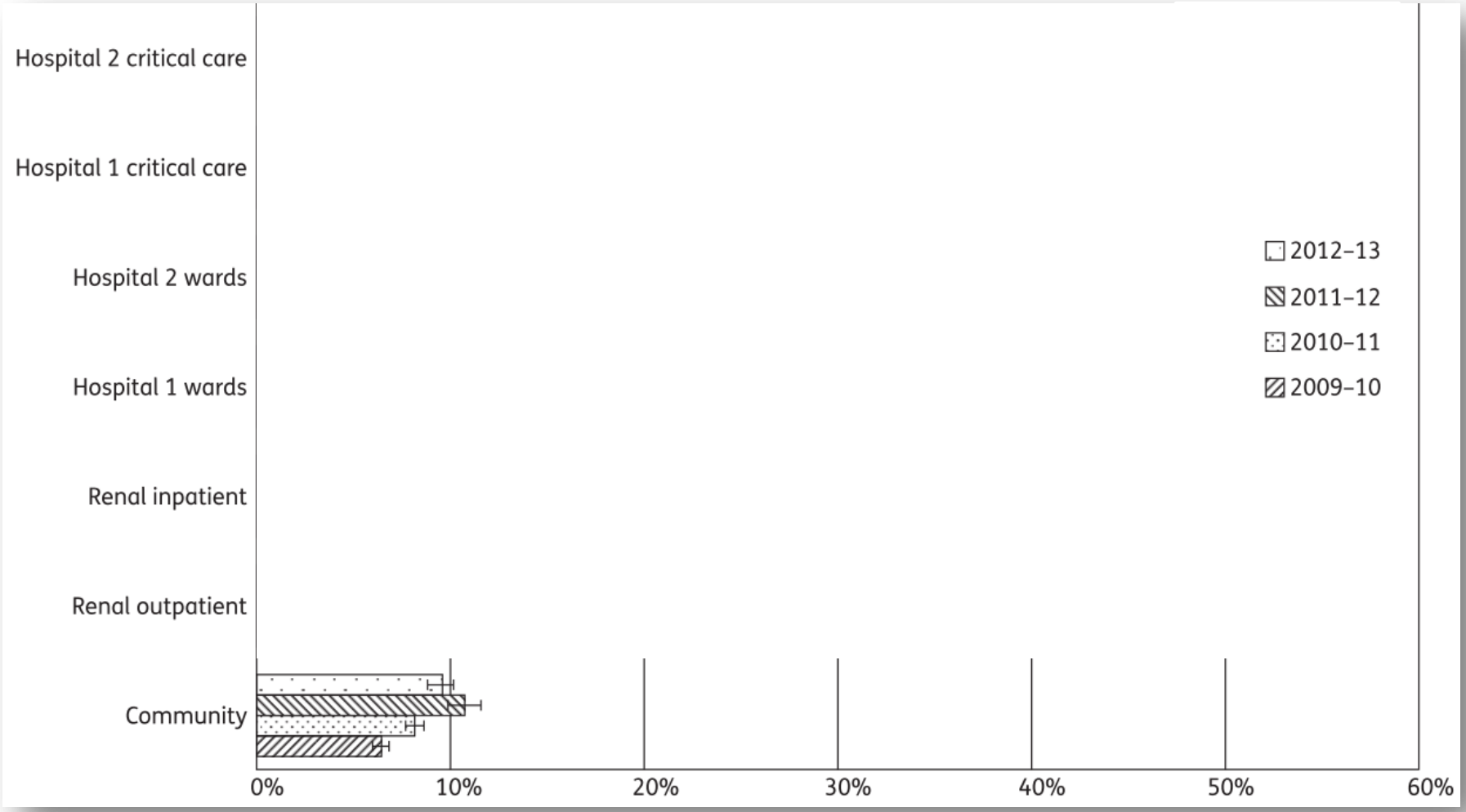


Enterobacteriaceae resistance to co-amoxiclav & cephalosporins



ESPAUR 2014

Enterobacteriaceae resistance to co-amoxiclav & cephalosporins



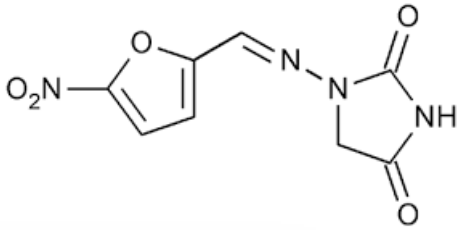
Moore JAC 2013

NWL susceptibility testing

Organism	Total number of isolates	Percentage resistance
Mecillinam	1931	2.7%
Co-amoxiclav	2128	7.9%
Cephalexin	2131	8.1%
Ciprofloxacin	1931	10.5%
Nitrofurantoin	2132	1.0%
Trimethoprim	2131	35.9%

Farah FIS 2016

Nitrofurantoin



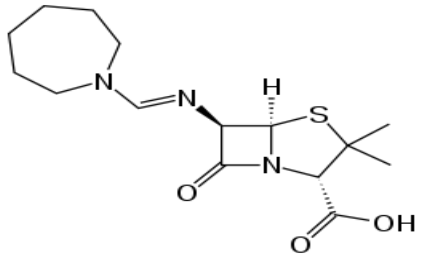
GOV.UK

Home > Drug Safety Update

Nitrofurantoin now contraindicated in most patients with an estimated glomerular filtration rate (eGFR) of less than 45 ml/min/1.73m2

From: Medicines and Healthcare products Regulatory Agency
Published: 25 September 2014

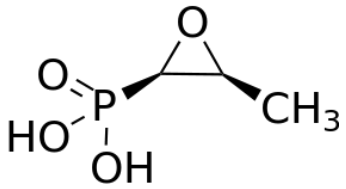
(Piv)mecillinam



Infections and infestations	
Common:	Vulvovaginal mycotic infection
Uncommon:	*Clostridium difficile* colitis
Blood and lymphatic system disorders	
Uncommon:	Thrombocytopenia
Immune system disorders	
Uncommon:	Anaphylactic reaction
Metabolism and nutrition disorders	
Uncommon:	Carnitine decreased
Nervous system disorders	
Uncommon:	Headache Dizziness
Ear and labyrinth disorders	
Uncommon:	Vertigo
Gastrointestinal disorders	
Common:	Diarrhoea Nausea

eMC 2015

Fosfomycin



Effectiveness

- No statistically significant difference between fosfomycin trometamol and carbapenems in clinical success rates (n=47; 77.8% compared with 95.0%).
- Clinical success rates were similar with fosfomycin trometamol and co-amoxiclav (n=65; 92.9% compared with 83.8%; significance not reported).
- Clinical success occurred in 94.2% of people in 1 case series (n=52).
- A second case series reported microbiological outcomes only (n=41).

Safety

- Adverse events were not reported in 2 studies; the other 2 studies stated that no adverse events were reported.
- The summary of product characteristics for fosfomycin trometamol states that it is 'generally well tolerated'.
- The most common adverse effects reported are GI disturbances and skin rashes.

Patient factors

- Fosfomycin trometamol is administered orally.
- The number of doses of fosfomycin trometamol is generally between 1 and 3, which may help some people to adhere to treatment.

Resource implications

- A single 3 g sachet of fosfomycin trometamol costs £62.10.

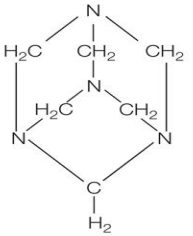
NICE 2013

PHE: guidelines

Recurrent UTI in non-pregnant women: 2 in 6mths or ≥ 3 UTIs/year	**First line:** Advise simple measures, incl. hydration & analgesia.[7D] Cranberry products work for some women, but good evidence is lacking.[4D,5A+,6A+] **Second line:** Standby or post-coital antibiotics.[1A,3B+] **Third line:** Antibiotic prophylaxis.[1A+,2A-] Consider methenamine if no renal or hepatic impairment.[8A,9A]	*First line:* nitrofurantoin *Second line:* pivmecillinam *If recent culture sensitive:* trimethoprim Methenamine hippurate[9A+]	100mg 200mg 200mg 1g BD[10D]	At night OR *post-coital* stat (off- label)[1A+,3B]	3-6 months; then review recurrence rate and need[3C] 6 months[9A+]

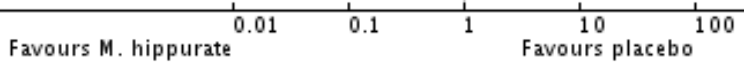
PHE 2017

Methenamine



Review: Methenamine hippurate for preventing urinary tract infections
Comparison: 1 Symptomatic UTI (confirmed by positive urine test)
Outcome: 2 Symptomatic bacteruria: Renal tract abnormalities

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 No renal tract abnormalities					
Furness 1975	14/70	17/67		34.8 %	0.79 [0.42, 1.47]
Knoff 1985	1/31	8/29		19.8 %	0.12 [0.02, 0.88]
Schiotz 2002	2/75	10/75		25.3 %	0.20 [0.05, 0.88]
Tyreman 1986	1/51	14/58		20.0 %	0.08 [0.01, 0.60]
Subtotal (95% CI)	**227**	**229**		**100.0 %**	**0.24 [0.07, 0.89]**
Total events: 18 (Treatment), 49 (Control)					
Heterogeneity: Tau² = 1.16; Chi² = 9.93, df = 3 (P = 0.02); I² =70%					
Test for overall effect: Z = 2.14 (P = 0.032)					
2 Renal tract abnormalities					
Lee 2007	53/150	55/155		72.4 %	1.00 [0.74, 1.35]
Pettersson 1989	5/47	1/45		27.6 %	4.79 [0.58, 39.40]
Subtotal (95% CI)	**197**	**200**		**100.0 %**	**1.54 [0.38, 6.20]**
Total events: 58 (Treatment), 56 (Control)					
Heterogeneity: Tau² = 0.68; Chi² = 2.15, df = 1 (P = 0.14); I² =53%					
Test for overall effect: Z = 0.60 (P = 0.55)					



Cochrane 2012

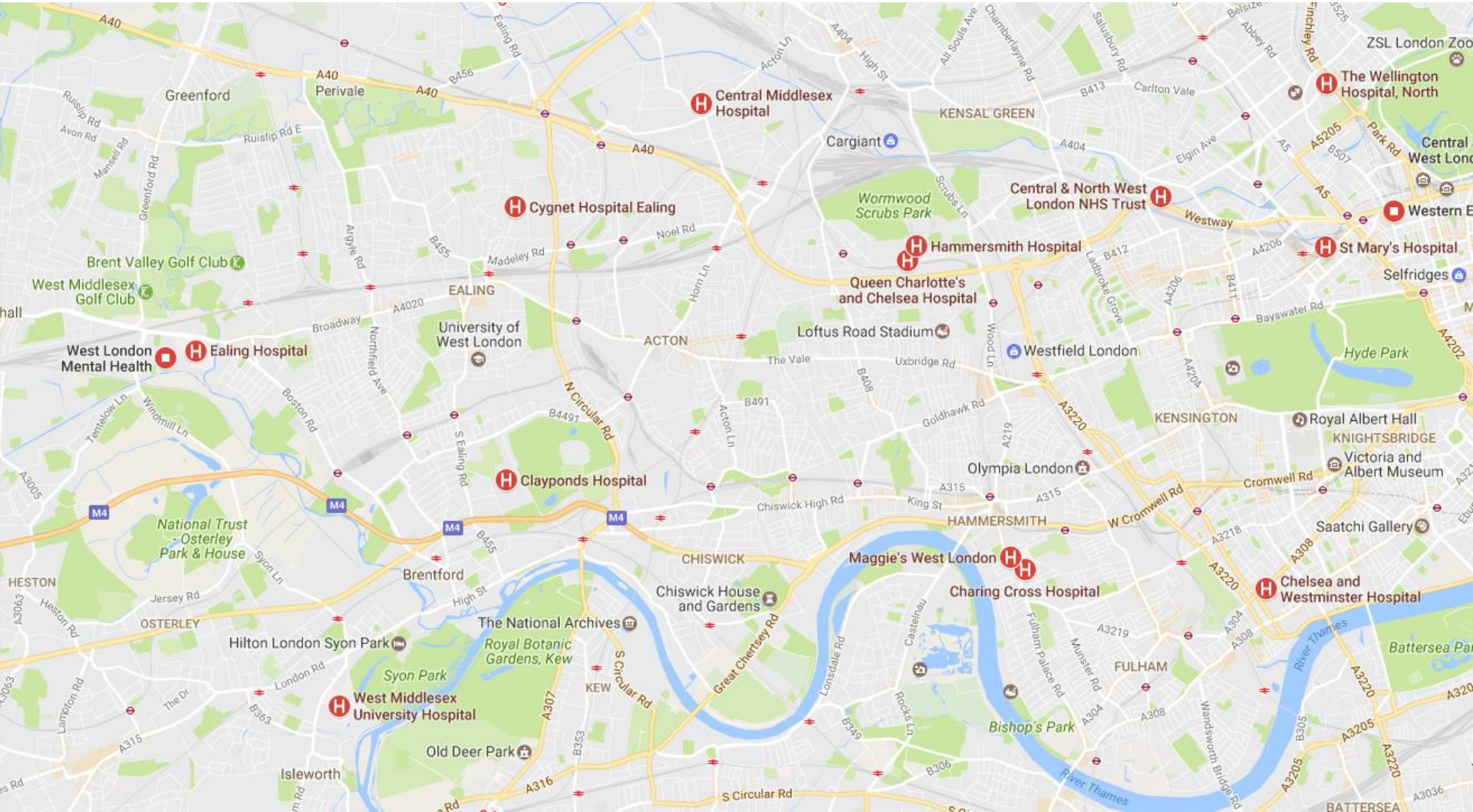
Ambulatory care

www.e-opat.com

Ambulatory care harmonisation

NWL STP 2016

Accessing ambulatory care



Accessing ambulatory care

Microbiology

Hammersmith/Ch. Cross/ St Mary's/Chelsea & Westminster/West Middlesex

07827 904038

OPAT

Hammersmith/Ch. Cross

020 3311 1234 bleep

St Mary's

020 3312 6666

Chelsea & Westminster

West Middlesex

020 8321 5966

Ambulatory care options