Recurrent UTIs (rUTI)

Dr Meghan Perry

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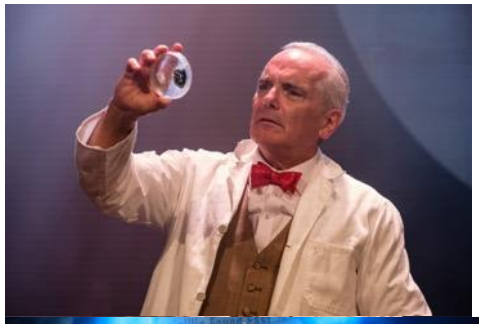
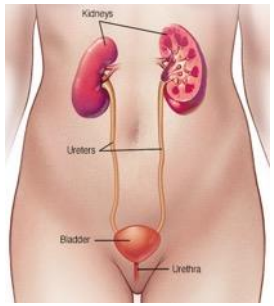
Antimony resistance in visceral leishmaniasis

Antimicrobial resistance gene abundance in hospital sewage



Antibiotics musical: The Mould that Changed the World

ANTIMICROBIAL RESISTANCE (AMR)



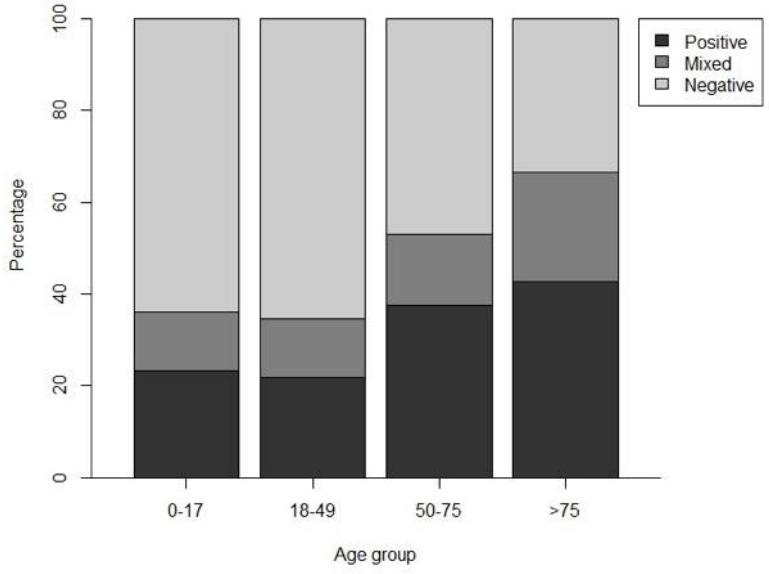
Resistance in uropathogens

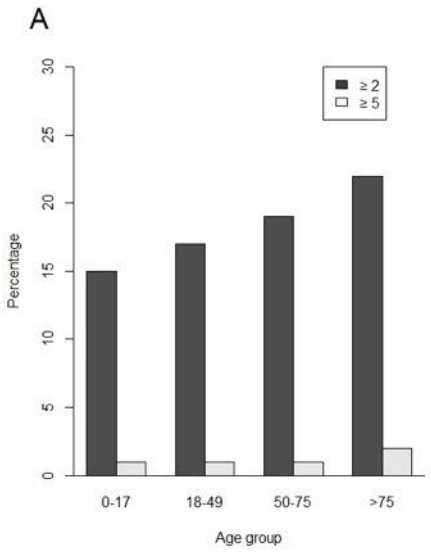
Urine culture Auth

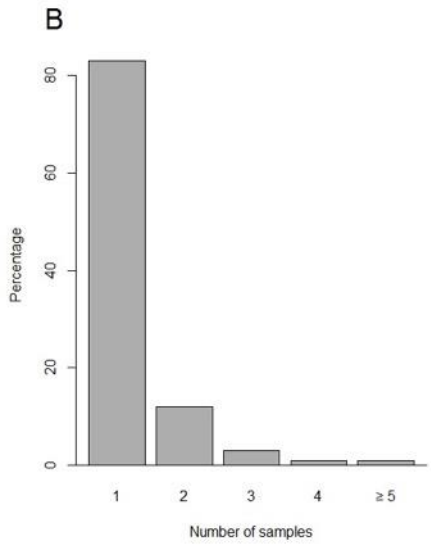
Klebsiella pneumoniae greater than 100,000 cfu/ml

Amoxicillin R	Ertapenem S
Amp/Amoxicillin r	Fosfomycin R
Cefalexin R	Gentamicin R
Cefotaxime r	
Cefoxitin r	Meropenem s
Ceftazidime r	Nitrofurantoin R
Ceftriaxone R	Piperacillin/Tazobactam R
Cefuroxime r	Pivmecillinam S
Ciprofloxacin R	Temocillin S
Co-amoxiclav R	Tetracycline r
Doxycycline R	Trimethoprim R

NHS Lothian MSU data from primary care 2016-2017 n=101704

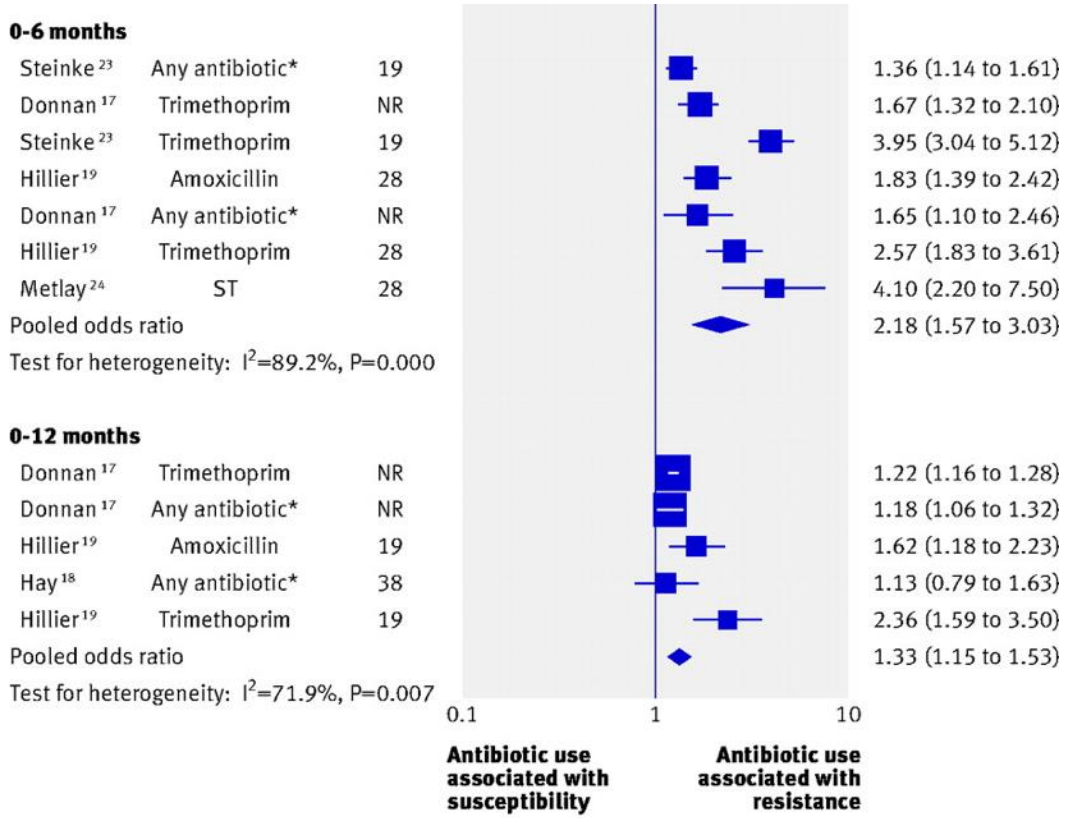






Costelloe *et al*
BMJ 2010

Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis



* Any antibiotic other than trimethoprim. ST=sulfamethoxazole-trimethoprim. NR=not reported

40,984 isolates

- 28% fully susceptible
- 45% resistant
- **27% MDR**

73% *E. coli*

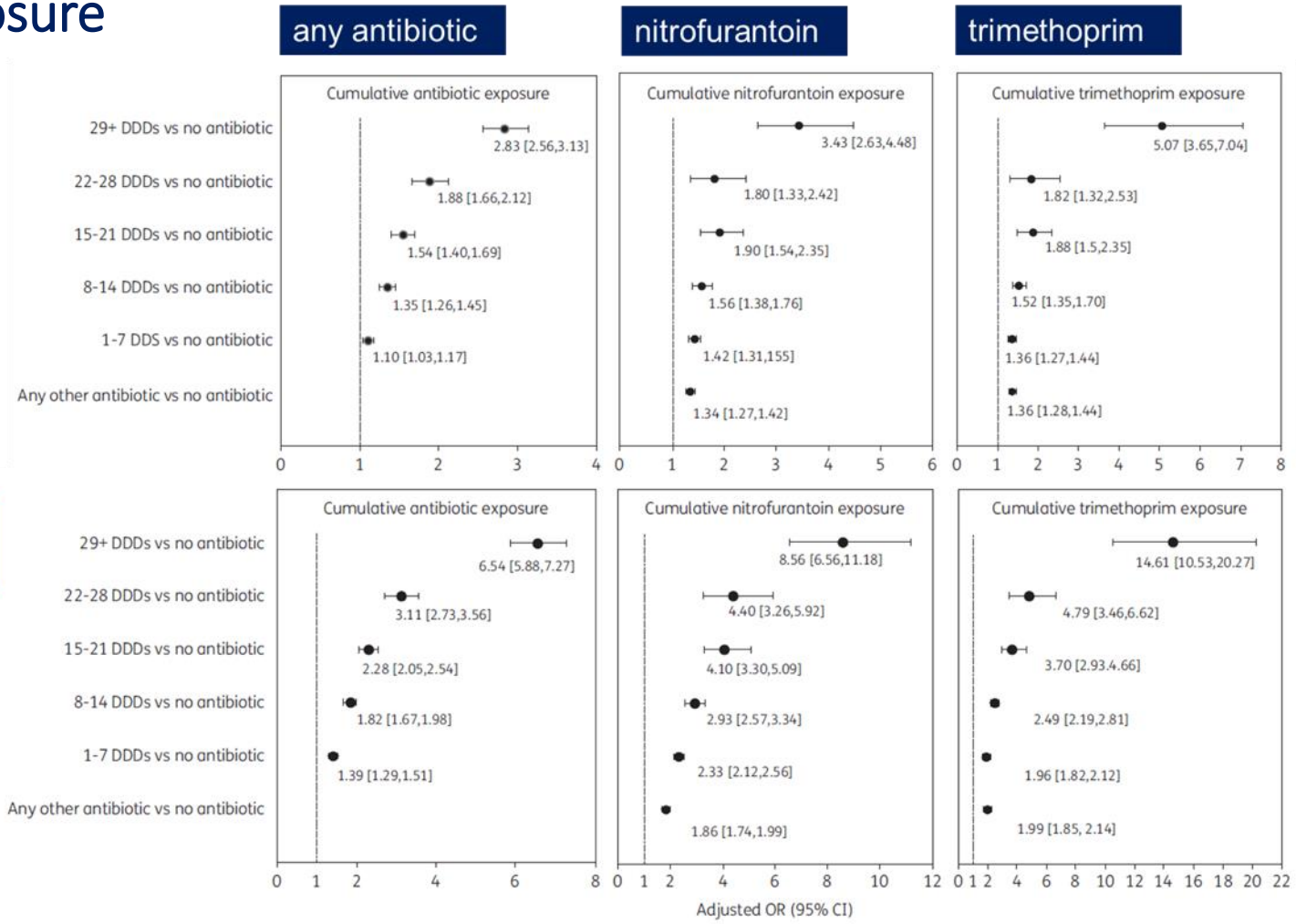
Risk factor	Resistant OR (95%CI)	Multidrug Resistant OR (95%CI)
Male vs female gender	1.36 (1.27–1.44)	1.17 (1.09–1.26)
85+ vs 16-24 years old	1.21 (1.07–1.37)	1.81 (1.56–2.10)
Charlson comorbidity index 5+ vs 0	1.36 (1.16–1.59)	1.31 (1.11–1.56)
4+ hospital admissions vs none	1.25 (1.08–1.45)	1.82 (1.56–2.13)
Care home residence vs not	2.16 (1.90–2.45)	3.36 (2.95–3.83)
4+ different antibiotics vs none	2.79 (2.36–3.31)	6.81 (5.73–8.11)

J Antimicrob Chemother
doi:10.1093/jac/dkx363

Cumulative exposure

Resistant vs. susceptible

MDR vs. susceptible



J Antimicrob Chemother
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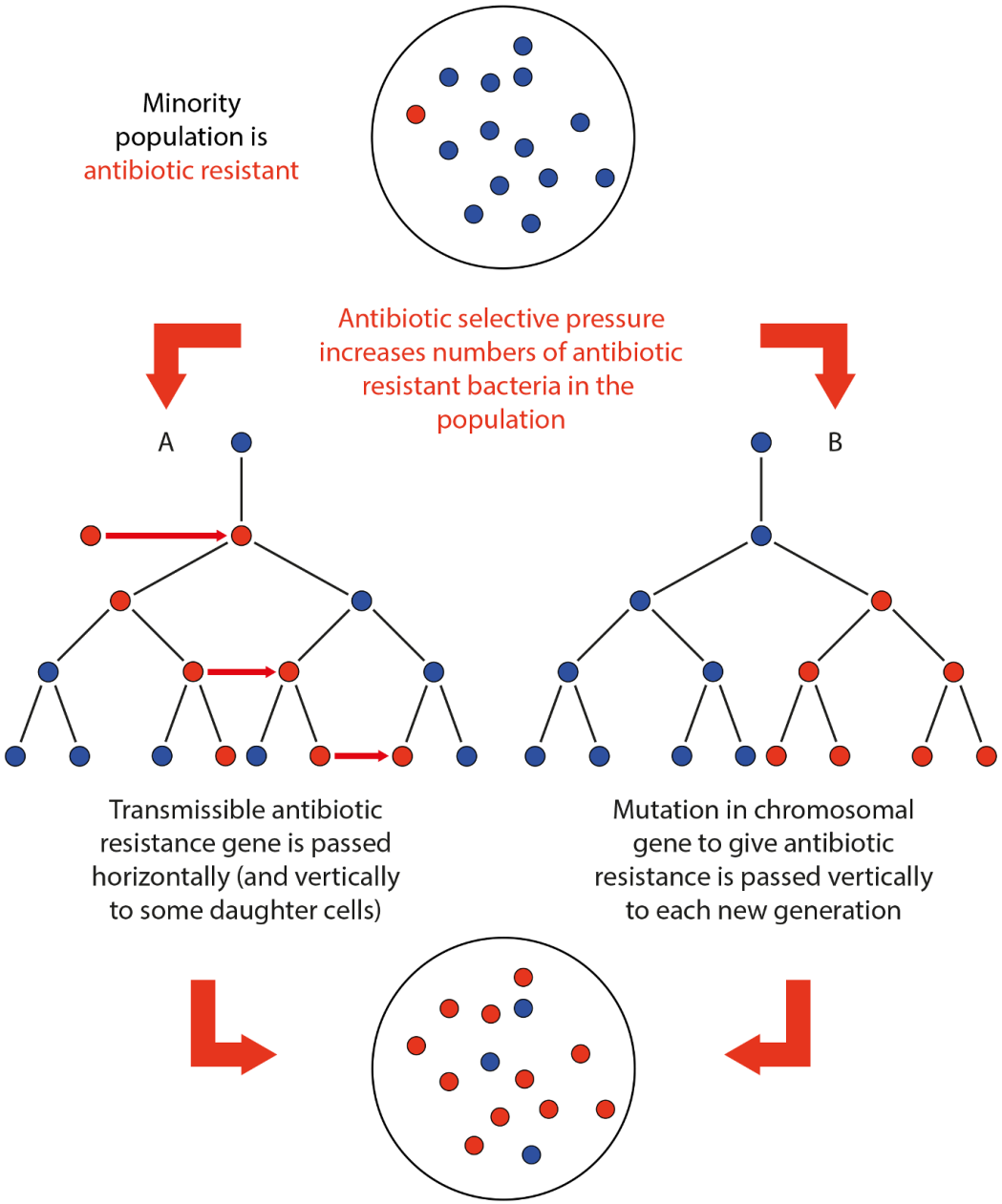

Minority population is antibiotic resistant
Antibiotic selective pressure increases numbers of antibiotic resistant bacteria in the population
A
B
Transmissible antibiotic resistance gene is passed horizontally (and vertically to some daughter cells)
Mutation in chromosomal gene to give antibiotic resistance is passed vertically to each new generation

Urine culture Auth

Klebsiella pneumoniae greater than 100,000 cfu/ml

Amoxicillin R	Ertapenem S
Amp/Amoxicillin r	Fosfomycin R
Cefalexin R	Gentamicin R
Cefotaxime r	
Cefoxitin r	Meropenem s
Ceftazidime r	Nitrofurantoin R
Ceftriaxone R	Piperacillin/Tazobactam R
Cefuroxime r	Pivmecillinam S
Ciprofloxacin R	Temocillin S
Co-amoxiclav R	Tetracycline r
Doxycycline R	Trimethoprim R

RECURRENT UTI CLINIC

AIM – to improve urinary health and minimise (unnecessary) antimicrobial use

Holistic assessment

- Urologist
- Infectious Diseases physician
- Antimicrobial pharmacist

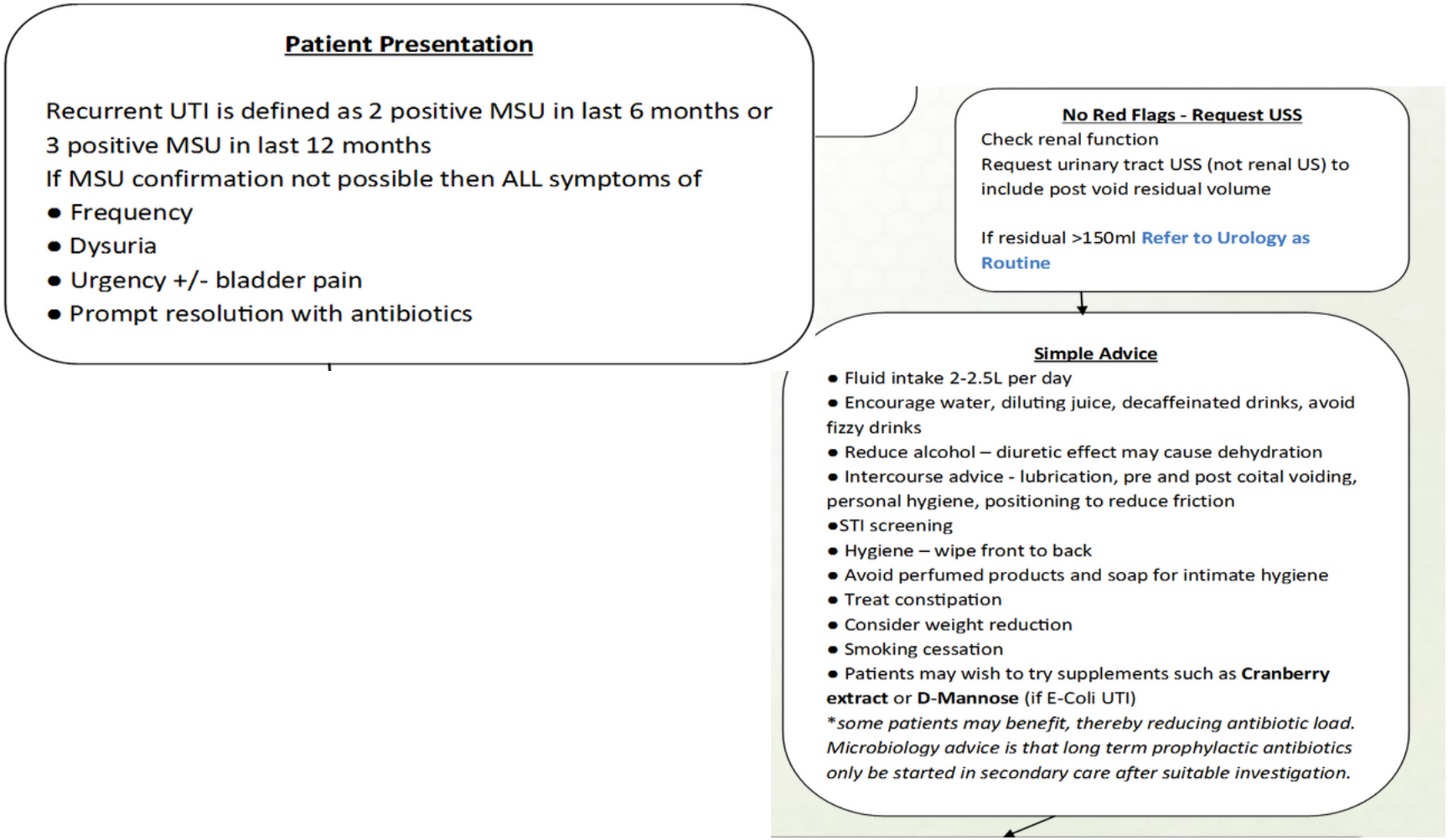
****IS IT *REALLY* A UTI****

- Symptoms of UTI
  - Upper or lower
  - Fever
  - Improvement with antibiotics?
- Microbiology history
- Antimicrobial history

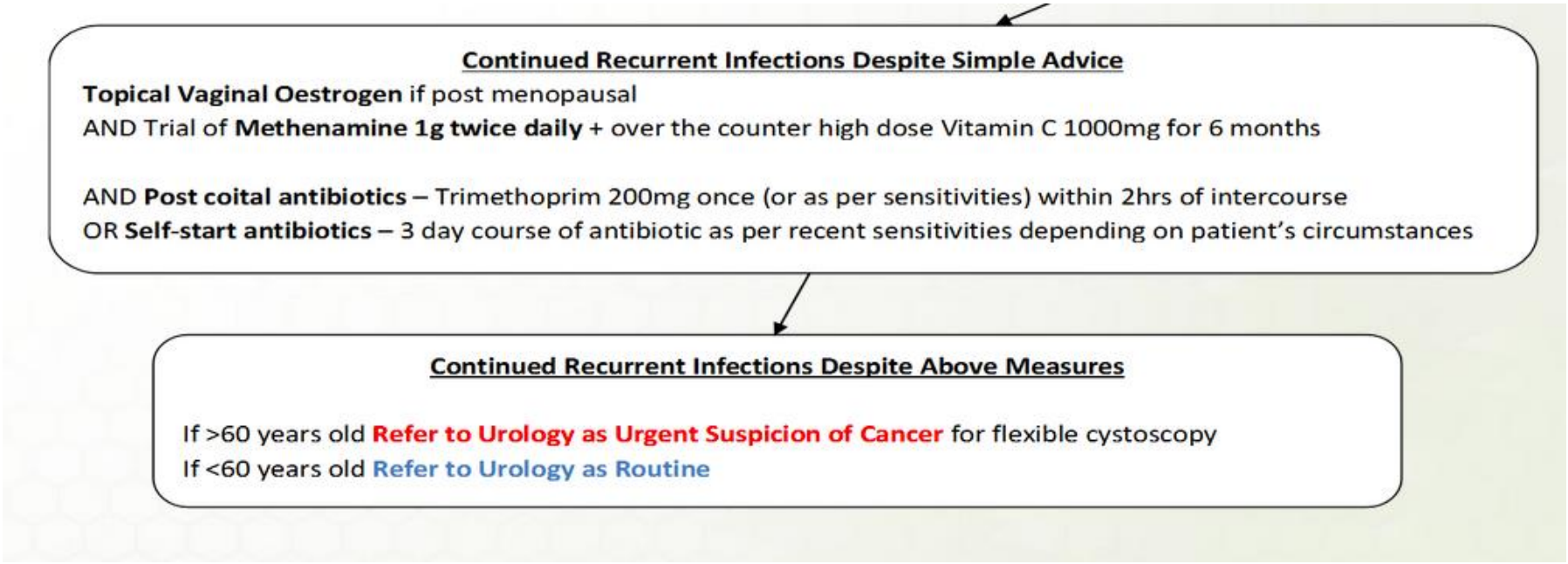
- Function
  - Symptoms
  - Bladder scan
- Factors which affect risk of UTI
  - Diabetes
  - Immunosuppression
  - Menopause
  - Sexual history
  - Medications with urinary side-effects
  - Bowels

How can a patient get to this clinic?

https://apps.nhslothian.scot/refhelp/guidelines/recurrentutisfemale/



https://apps.nhslothian.scot/refhelp/guidelines/recurrentutisfemale/



rUTI clinic recommendations

- Non antimicrobial prophylactic regime
  - Methenamine hippurate
  - Topical vaginal oestrogen
  - D-mannose
  - Iauril instillations
  - Gentamicin instillations
  - Vaccines
  - Faecal microbiota transplant
- Urology physiotherapy
- Further investigation/procedure

Topical oestrogen

ORIGINAL ARTICLE

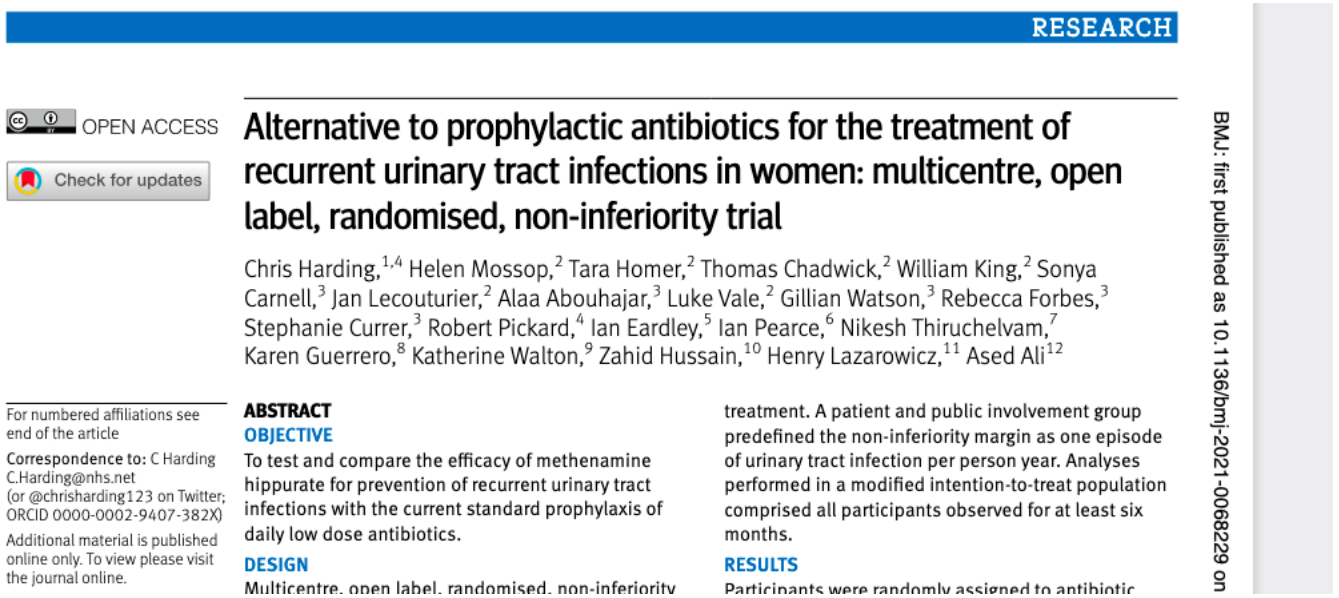
A Controlled Trial of Intravaginal Estriol in Postmenopausal Women with Recurrent Urinary Tract Infections

Raul Raz, and Walter E. Stamm

September 9, 1993
N Engl J Med 1993; 329:753-756
DOI: 10.1056/NEJM199309093291102

93 women, oestrogen vs placebo, 8 mths follow up
0.5 vs. 5.9 episodes per patient-year, P<0.001
Growth of lactobacilli in 61% of oestrogen treated females
Reduction in *Enterobactericeae* vaginal colonisation from 67 – 31%

Methenamine hippurate



RESEARCH

OPEN ACCESS

Check for updates

Alternative to prophylactic antibiotics for the treatment of recurrent urinary tract infections in women: multicentre, open label, randomised, non-inferiority trial

Chris Harding,[1,4] Helen Mossop,[2] Tara Homer,[2] Thomas Chadwick,[2] William King,[2] Sonya Carnell,[3] Jan Lecouturier,[2] Alaa Abouhajar,[3] Luke Vale,[2] Gillian Watson,[3] Rebecca Forbes,[3] Stephanie Currer,[3] Robert Pickard,[4] Ian Eardley,[5] Ian Pearce,[6] Nikesh Thiruchelvam,[7] Karen Guerrero,[8] Katherine Walton,[9] Zahid Hussain,[10] Henry Lazarowicz,[11] Ased Ali[12]

For numbered affiliations see end of the article

Correspondence to: C Harding C.Harding@nhs.net (or @chrisharding123 on Twitter; ORCID 0000-0002-9407-382X)

Additional material is published online only. To view please visit the journal online.

ABSTRACT

OBJECTIVE

To test and compare the efficacy of methenamine hippurate for prevention of recurrent urinary tract infections with the current standard prophylaxis of daily low dose antibiotics.

DESIGN

Multicentre, open label, randomised, non-inferiority

treatment. A patient and public involvement group predefined the non-inferiority margin as one episode of urinary tract infection per person year. Analyses performed in a modified intention-to-treat population comprised all participants observed for at least six months.

RESULTS

Participants were randomly assigned to antibiotic

BMJ: first published as 10.1136/bmj-2021-0068229 on

240 women – methenamine vs Abx prophylaxis

Methenamine non-inferior to antimicrobial prophylaxis at preventing rUTI

D-mannose

Springer Link

Original Article | Published: 30 April 2013

D-mannose powder for prophylaxis of recurrent urinary tract infections in women: a randomized clinical trial

Bojana Kranjčec, Dino Papeš & Silvio Altarac

World Journal of Urology **32**, 79–84 (2014) | Cite this article

11k Accesses | **219** Citations | **148** Altmetric | Metrics

Only for E.coli UTI

308 women – D-mannose vs nitrofurantoin vs placebo
- D-mannose non-inferior to nitrofurantoin

lauril instillations

Randomized Controlled Trial > Eur Urol. 2011 Apr;59(4):645-51.
doi: 10.1016/j.eururo.2010.12.039. Epub 2011 Jan 18.

Prevention of recurrent urinary tract infections by intravesical administration of hyaluronic acid and chondroitin sulphate: a placebo-controlled randomised trial

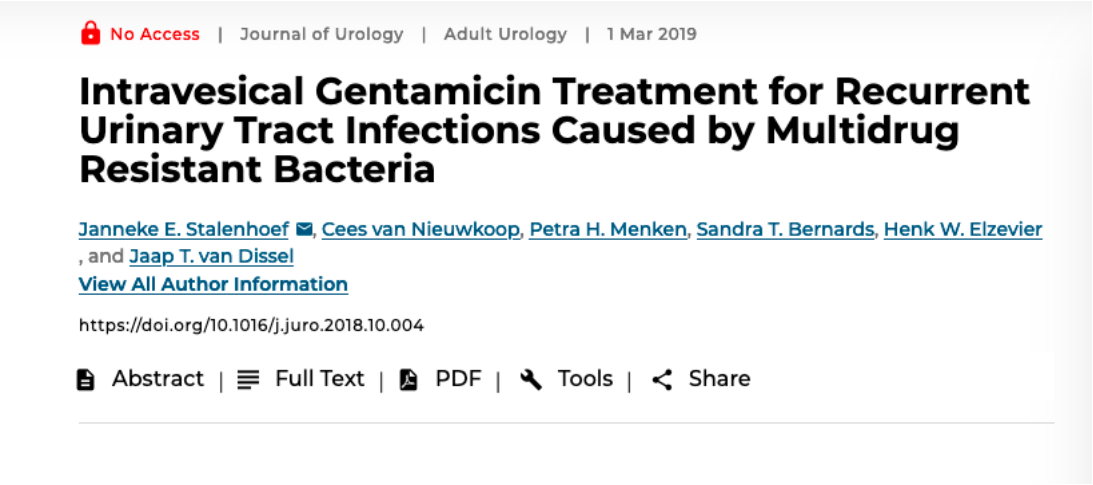
Rocco Damiano [1], Giuseppe Quarto, Ilaria Bava, Giuseppe Ucciero, Renato De Domenico, Michele I Palumbo, Riccardo Autorino

Affiliations + expand

PMID: 21272992 DOI: 10.1016/j.eururo.2010.12.039

57 women,
Reduction in UTI rate
Increased QoL

Gentamicin instillations



No Access | Journal of Urology | Adult Urology | 1 Mar 2019

Intravesical Gentamicin Treatment for Recurrent Urinary Tract Infections Caused by Multidrug Resistant Bacteria

Janneke E. Stalenhoef, Cees van Nieuwkoop, Petra H. Menken, Sandra T. Bernards, Henk W. Elzevier, and Jaap T. van Dissel

View All Author Information

https://doi.org/10.1016/j.juro.2018.10.004

Abstract | Full Text | PDF | Tools | Share

- mean number of urinary tract infections was reduced from 4.8 to 1.0 during intravesical treatment
- resistance rate of the uropathogens decreased from 78% to 23%
- no systemic side-effects

Vaccines

- Uro-vaxom
  - *E.coli only*
- Uromune
  - *E.coli, Klebsiella,Enterococcus, Proteus,*

> BJU Int. 2018 Feb;121(2):289-292. doi: 10.1111/bju.14067. Epub 2017 Nov 23.

First experience in the UK of treating women with recurrent urinary tract infections with the bacterial vaccine Uromune®

Bob Yang [1], Stephen Foley [1 2]

Affiliations + expand

PMID: 29171130 DOI: 10.1111/bju.14067

Observational data – 77 women, 59 no recurrence in 1 year

Faecal microbiota transplant

Clinical Infectious Diseases

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Volume 65, Issue 10
15 November 2017

Article Contents

Abstract

JOURNAL ARTICLE

Fecal Microbiota Transplantation for Recurrent *Clostridium difficile* Infection Reduces Recurrent Urinary Tract Infection Frequency FREE

Raseen Tariq, Darrell S Pardi, Pritish K Tosh, Randall C Walker, Raymund R Razonable, Sahil Khanna

Clinical Infectious Diseases, Volume 65, Issue 10, 15 November 2017, Pages 1745–1747,
https://doi.org/10.1093/cid/cix618
Published: 18 July 2017 **Article history** ▾

PDF | Split View | Cite | Permissions | Share ▾

Antimicrobial prophylaxis

- Avoided (except in very specific circumstances)

Non-Abx Mx of acute symptoms

- Education re Abx's role in Rx of cystitis

- Increase fluid intake
- Increase methenamine dose to tds for 5 days

Asymptomatic bacteriuria

Clinical Trial > Clin Infect Dis. 2012 Sep;55(6):771-7. doi: 10.1093/cid/cis534.
Epub 2012 Jun 7.

The role of asymptomatic bacteriuria in young women with recurrent urinary tract infections: to treat or not to treat?

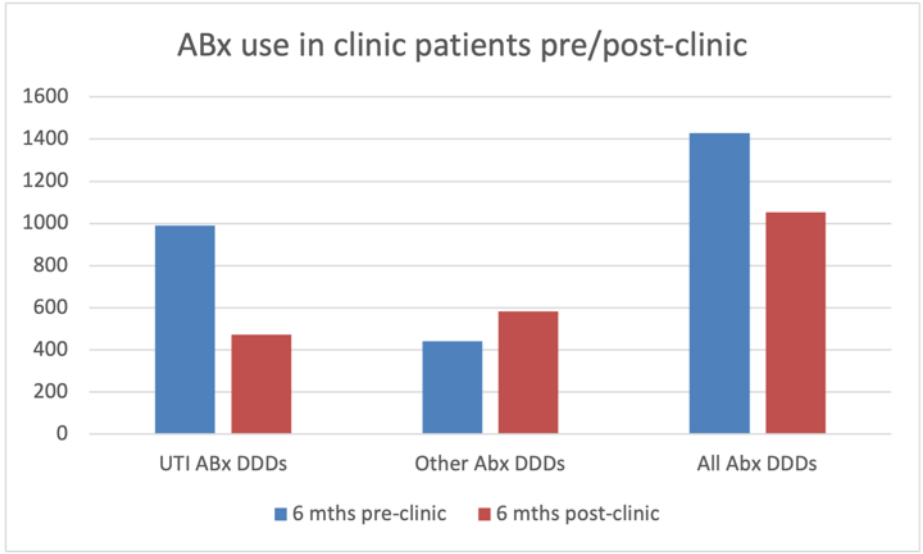
Tommaso Cai [1], Sandra Mazzoli, Nicola Mondaini, Francesca Meacci, Gabriella Nesi, Carolina D'Elia, Gianni Malossini, Vieri Boddi, Riccardo Bartoletti

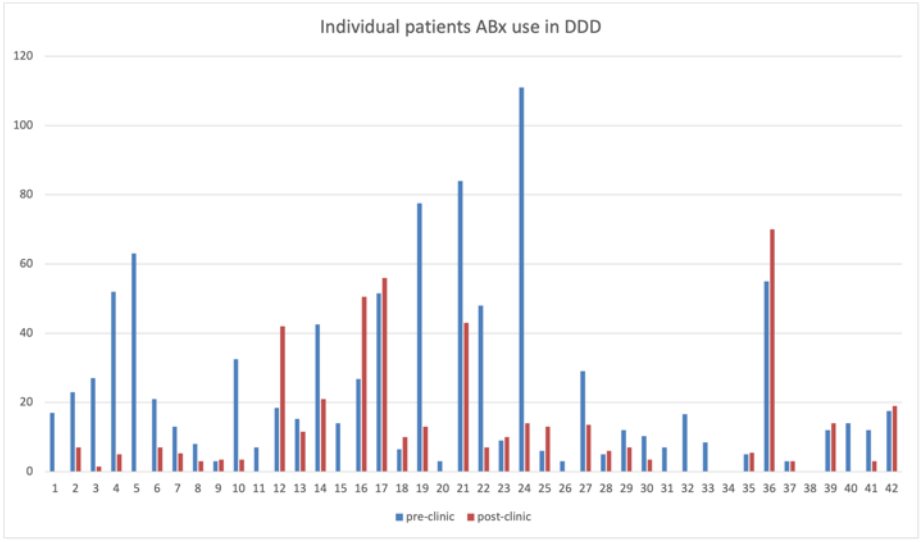
Affiliations + expand

PMID: 22677710 DOI: 10.1093/cid/cis534

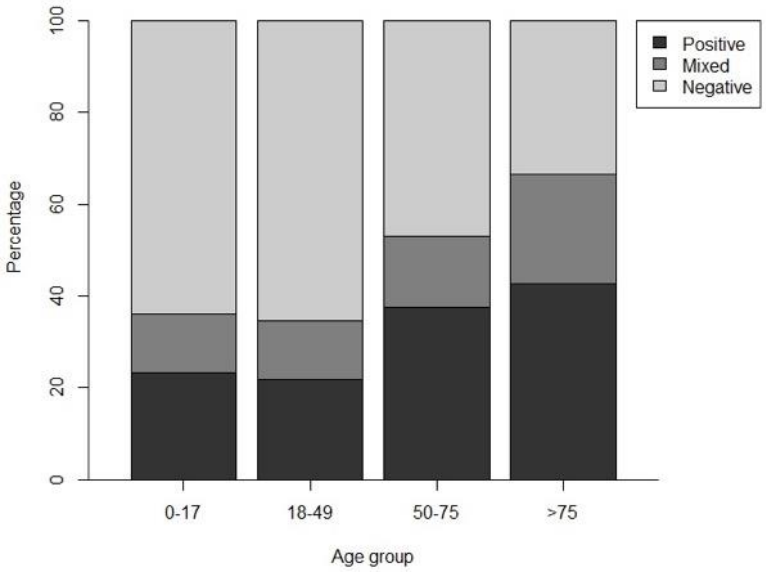
673 women. No Rx vs Rx
Follow- up 3,6,12 months
No difference at 3 mths
At 6 and 12 months higher rates of recurrence in treated group - (RR, 3.17; 95% CI, 2.55-3.90; P < .0001)

Impact of rUTI clinic





Future challenges – changing perspectives



Urgent need for improved diagnostics

- Acknowledgements:
  - Voula Granitsiotis
  - Carol Philip

Clinical Infection Research Group Edinburgh