



Recurrent UTIs (rUTI)

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Antimony resistance in visceral leishmaniasis

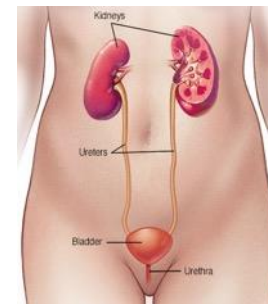


Antimicrobial resistance gene abundance in hospital sewage

**ANTIMICROBIAL RESISTANCE
(AMR)**



Antibiotics musical: The Mould that Changed the World



Resistance in uropathogens

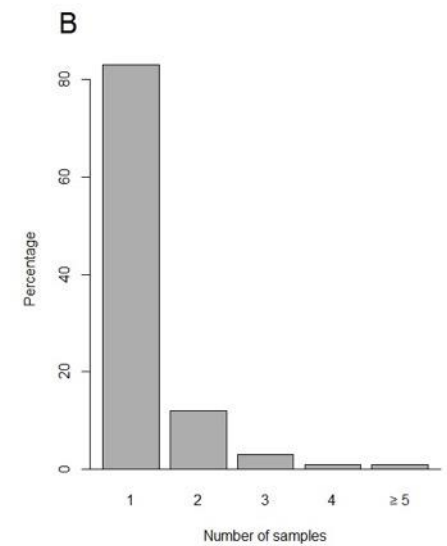
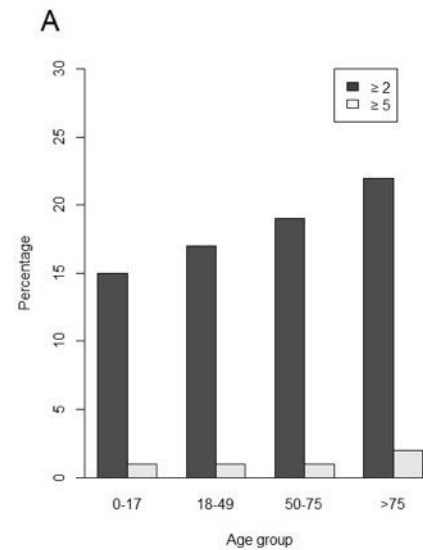
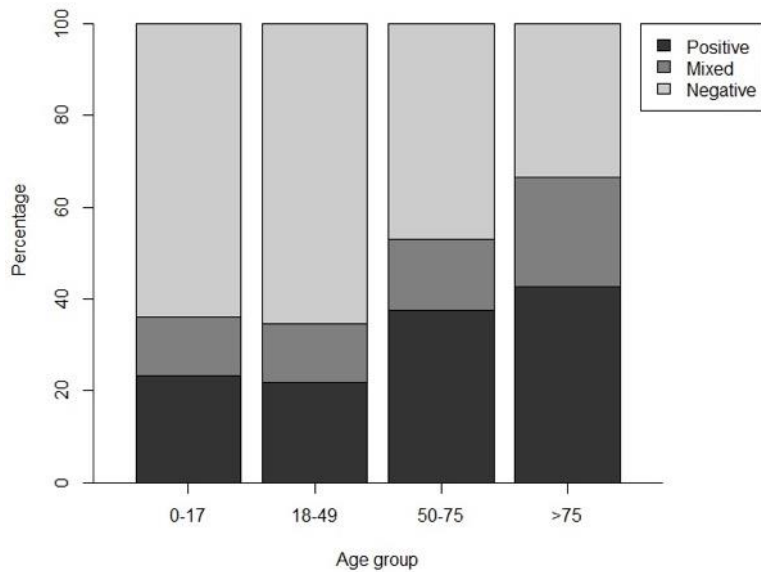
Urine culture

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



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

Costelloe *et al*
BMJ 2010

0-6 months

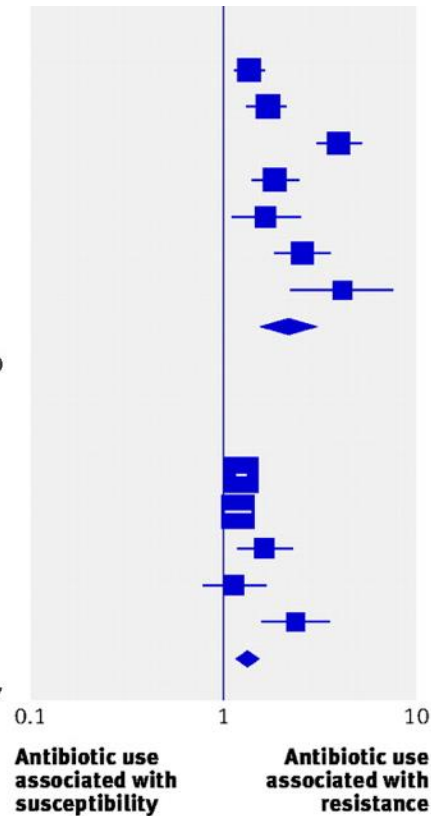
Steinke ²³	Any antibiotic*	19	1.36 (1.14 to 1.61)
Donnan ¹⁷	Trimethoprim	NR	1.67 (1.32 to 2.10)
Steinke ²³	Trimethoprim	19	3.95 (3.04 to 5.12)
Hillier ¹⁹	Amoxicillin	28	1.83 (1.39 to 2.42)
Donnan ¹⁷	Any antibiotic*	NR	1.65 (1.10 to 2.46)
Hillier ¹⁹	Trimethoprim	28	2.57 (1.83 to 3.61)
Metlay ²⁴	ST	28	4.10 (2.20 to 7.50)
Pooled odds ratio			2.18 (1.57 to 3.03)

Test for heterogeneity: $I^2=89.2\%$, $P=0.000$

0-12 months

Donnan ¹⁷	Trimethoprim	NR	1.22 (1.16 to 1.28)
Donnan ¹⁷	Any antibiotic*	NR	1.18 (1.06 to 1.32)
Hillier ¹⁹	Amoxicillin	19	1.62 (1.18 to 2.23)
Hay ¹⁸	Any antibiotic*	38	1.13 (0.79 to 1.63)
Hillier ¹⁹	Trimethoprim	19	2.36 (1.59 to 3.50)
Pooled odds ratio			1.33 (1.15 to 1.53)

Test for heterogeneity: $I^2=71.9\%$, $P=0.007$



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

40,984 isolates

- 28% fully susceptible

- 45% resistant

- **27% MDR**

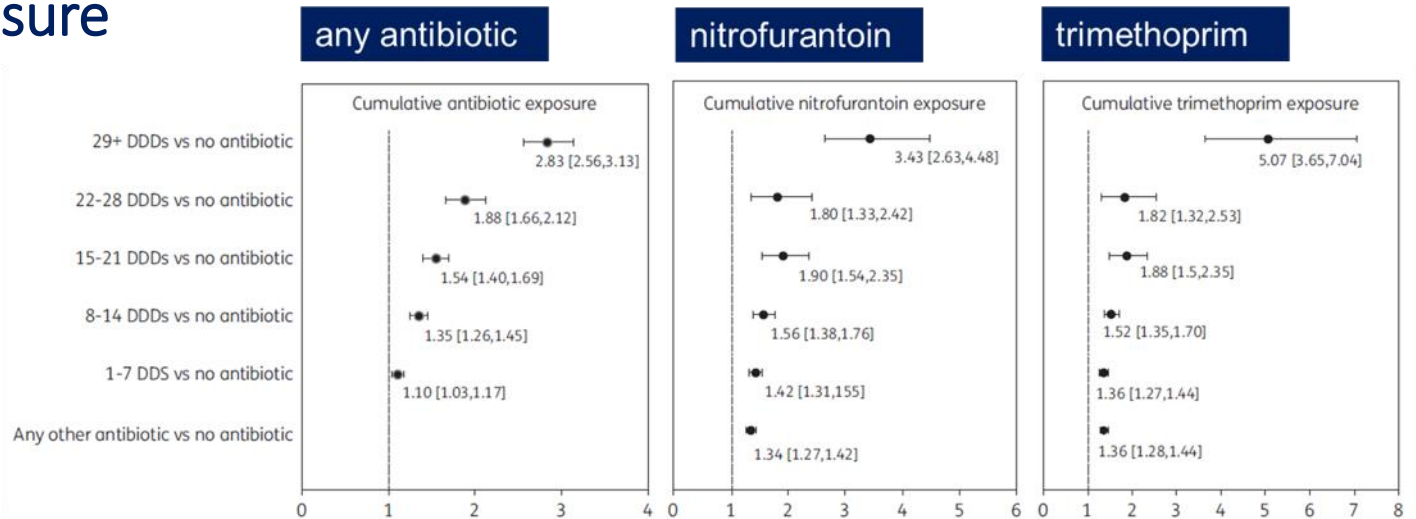
73% *E. coli*

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)

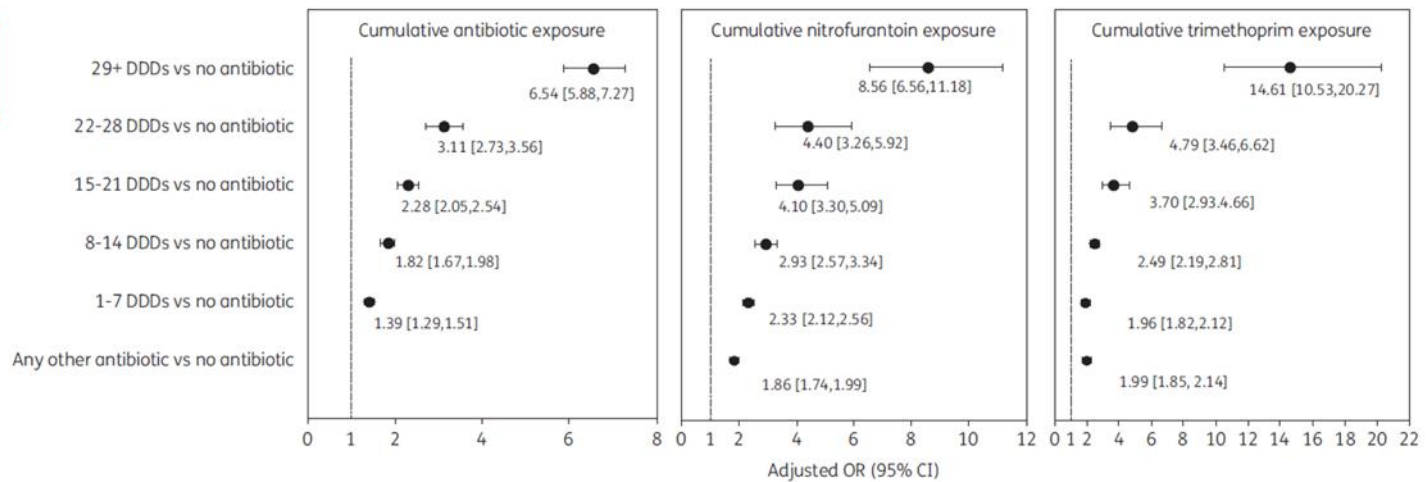
J Antimicrob Chemother
doi:10.1093/jac/dkx363

Cumulative exposure

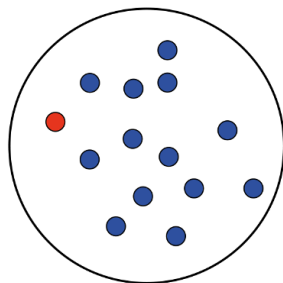
Resistant vs. susceptible



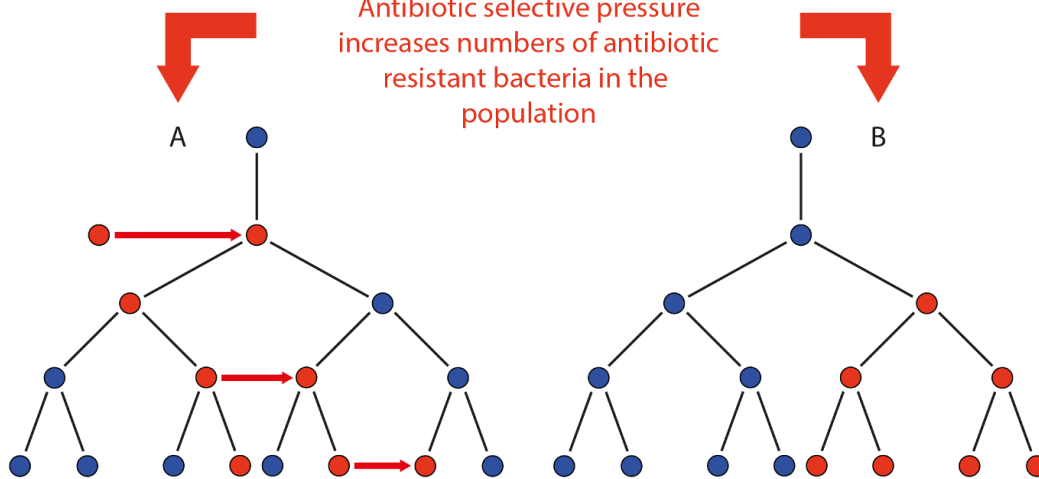
MDR vs. susceptible



Minority population is antibiotic resistant

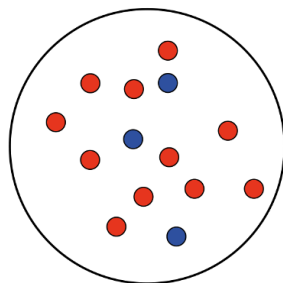


Antibiotic selective pressure increases numbers of antibiotic resistant bacteria in the population



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/>

Patient Presentation

Recurrent UTI is defined as 2 positive MSU in last 6 months or 3 positive MSU in last 12 months

If MSU confirmation not possible then ALL symptoms of

- Frequency
- Dysuria
- Urgency +/- bladder pain
- Prompt resolution with antibiotics

No Red Flags - Request USS

Check renal function
Request urinary tract USS (not renal US) to include post void residual volume

If residual >150ml **Refer to Urology as Routine**

Simple Advice

- Fluid intake 2-2.5L per day
- Encourage water, diluting juice, decaffeinated drinks, avoid fizzy drinks
- Reduce alcohol – diuretic effect may cause dehydration
- Intercourse advice - lubrication, pre and post coital voiding, personal hygiene, positioning to reduce friction
- STI screening
- Hygiene – wipe front to back
- Avoid perfumed products and soap for intimate hygiene
- Treat constipation
- Consider weight reduction
- Smoking cessation
- Patients may wish to try supplements such as **Cranberry extract** or **D-Mannose** (if E-Coli UTI)

**some patients may benefit, thereby reducing antibiotic load. Microbiology advice is that long term prophylactic antibiotics only be started in secondary care after suitable investigation.*

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

Continued Recurrent Infections Despite Simple Advice

Topical Vaginal Oestrogen if post menopausal

AND Trial of **Methenamine 1g twice daily** + over the counter high dose Vitamin C 1000mg for 6 months

AND **Post coital antibiotics** – Trimethoprim 200mg once (or as per sensitivities) within 2hrs of intercourse

OR **Self-start antibiotics** – 3 day course of antibiotic as per recent sensitivities depending on patient's circumstances

Continued Recurrent Infections Despite Above Measures

If >60 years old **Refer to Urology as Urgent Suspicion of Cancer** for flexible cystoscopy

If <60 years old **Refer to Urology as Routine**

rUTI clinic recommendations

- Non antimicrobial prophylactic regime
 - Methenamine hippurate
 - Topical vaginal oestrogen
 - D-mannose
 - lauril 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

[Article](#) [Figures/Media](#)

[September 9, 1993](#)

[N Engl J Med 1993; 329:753-756](#)

[DOI: 10.1056/NEJM199309093291102](#)

[23 References](#) [596 Citing Articles](#)

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 *Enterobacteriaceae* 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 Ali¹²

For numbered affiliations see end of the article

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(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



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](#)

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PAGE NAVIGATION

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 Disse!](#)

[View All Author Information](#)

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

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- 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 ▾](#)



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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 Cai¹, 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](https://doi.org/10.1093/cid/cis534)

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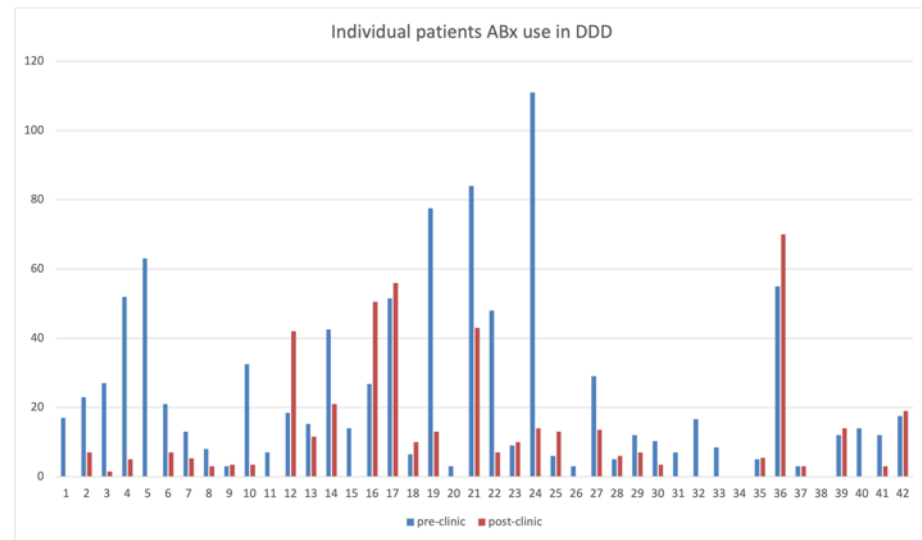
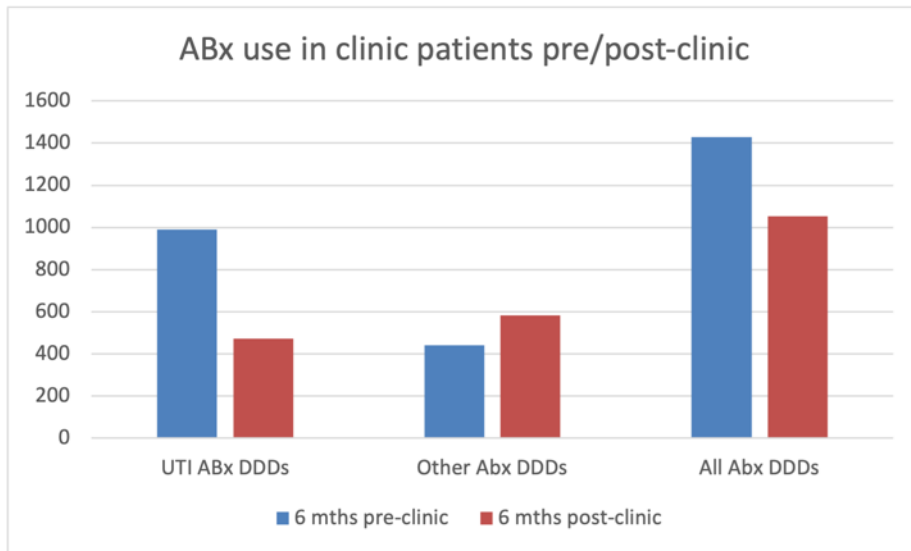
673 women. No Rx vs Rx

Follow- up 3,6,12 months

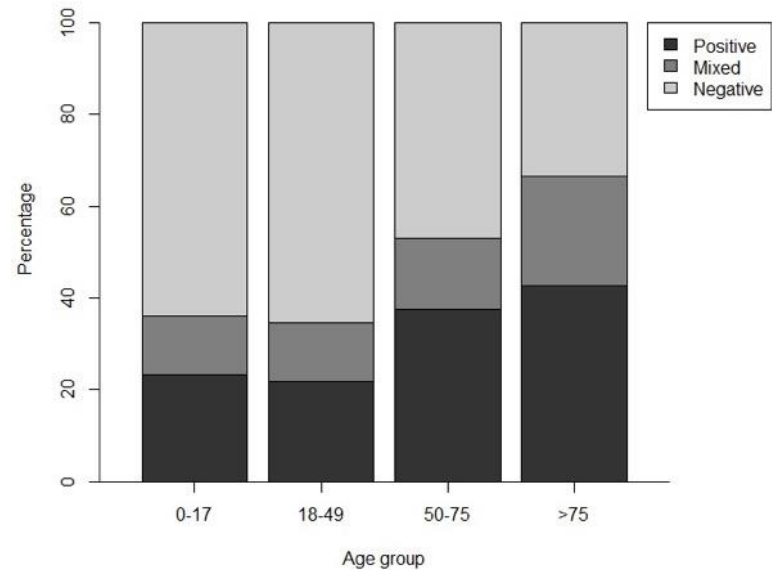
No difference at 3 mths

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

