

# Community study on the effect of antibiotic use for urinary tract infections on the emergence and spread of resistance

<b>Submission date</b> 14/10/2010	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered
<b>Registration date</b> 24/11/2010	<b>Overall study status</b> Completed	<input type="checkbox"/> Protocol
<b>Last Edited</b> 18/01/2019	<b>Condition category</b> Urological and Genital Diseases	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Prof Stephan Harbarth

**Contact details**  
Infection Control Program  
University of Geneva Hospitals and Medical Faculty  
4 Rue Gabrielle Perret-Gentil  
Geneva 14  
Switzerland  
1211  
+41 (0)22 372 9828  
[stephan.harbarth@hcuge.ch](mailto:stephan.harbarth@hcuge.ch)

## Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**

## Study information

### Scientific Title

A multicentre, prospective, observational cohort study on the effect of antibiotic use for urinary tract infections on the emergence and spread of antimicrobial resistance in gastrointestinal and oral commensal flora

### Acronym

SATURN Workpackage 3

### Study objectives

Background:

Antimicrobial resistance (AMR) is rampant among bacteria that cause healthcare- and community-acquired infections, generating additional costs and increasing the difficulty of therapeutic management. To gain a handle on the factors that are propelling the problem of AMR, molecular and patient-level investigations are necessary to better elucidate the time-varying and heterogeneous role of antibiotic selection pressure on emergence and selection of AMR.

For AMR to develop, a genetic mutation must occur or the organism must take up a resistance-conferring plasmid or DNA fragment. These mutations occur in nature, but not at a rate such that every case of AMR could be explained by a new mutation. Selective pressure exerted by antibiotics plays a central role on the acquisition, selection, persistence and transmission of resistant pathogens.

Hypothesis:

The main hypothesis to be investigated in this observational clinical cohort study is that short antibiotic treatment duration decreases the risk of carriage and transmission of antibiotic-resistant bacteria in patients treated for community-acquired urinary tract infection. More specifically, this study hypothesises that the longitudinal data provided in this cohort study and the inclusion of household members will allow to determine the effects of antibiotic treatment duration and choice of antibiotic agents (e.g. fluoroquinolones) on carriage of resistant *E. coli* and other clinically relevant bacteria (e.g. viridans streptococci) at the individual and household level. It is hypothesised that individuals taking longer antibiotic courses will experience a decrease of carriage of susceptible *E. coli* and respiratory tract commensal bacteria while on treatment, possibly increasing their subsequent risk for acquisition and selection of antibiotic-resistant bacteria. Finally, we expect differences in resistance development and impact on the commensal flora according to the initial treatment regimen.

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

1. Bioethics Committee, Medical University of Lodz approved on the 13th of July 2010 (ref: RNN /127/10/KE)
2. Medical Ethics Committee, University of Antwerp Hospital approved on the 26th of July 2010 (ref: B30020109056)
3. Internal and Community Medicine Ethics Committee, University of Geneva Hospitals approved on the 18th of August (ref: Protocole 10-123)

**Study design**

Prospective observational multicentre cohort study

**Primary study design**

Observational

**Secondary study design**

Cohort study

**Study setting(s)**

Hospital

**Study type(s)**

Prevention

**Participant information sheet**

Not available in web format, please use contact details below to request a patient information sheet

**Health condition(s) or problem(s) studied**

Urinary tract infection (UTI); antimicrobial resistance (AMR)

**Interventions**

Once a subject has agreed to participate and has signed the consent he/she will be asked to fill out the study questionnaire. An oral swab will be taken while the patient and, if the patient agrees, a rectal swab will be performed. The patient will be instructed on how to take a stool sample at the first defecation after the visit. These swabs will establish the subjects baseline intestinal resistance prior to the introduction of antibiotics. The household members of the subject (maximum 3) will be asked to participate in the study as well. Consenting household members will be asked to complete a survey and provide baseline stool samples and oral swabs.

All participants (index participants and household members) will be asked to provide a stool sample and oral swab:

1. on the last day of antibiotic therapy, but earliest on day five and latest on day 14 of therapy
2. twenty-eight days after the end of antibiotic treatment (28 to 43 days after initial subject entry into the study)

Antimicrobial susceptibility testing will be performed on each phenotypically distinct *E. coli* colony isolated. A central laboratory will perform primary cultures and susceptibility testing for stool samples, and confirmatory identification and susceptibility testing for clinical isolates. Putative *E. coli* colonies from stool samples will be confirmed using standard methods. Antimicrobial susceptibility to 12 antimicrobial agents will be assessed by semi-automated systems (Vitek 2, Biomerieux). Screening for ESBL-producing strains will be done on chromogenic media and using standard methodology as described in current EUCAST guidelines.

From the oral swabs, mutations in the topoisomerase genes of oral viridans group streptococci will be analyzed by sequencing the fluoroquinolone-resistant determining region (QRDR) of topoisomerase IV and DNA gyrase. Resistance mediated by efflux pumps will be detected by determination of the minimum inhibitory concentration of indicator fluoroquinolones in the absence/presence of reserpine, an efflux pump inhibitor. If new mechanisms of resistance are

found in the viridans group streptococci, they will be analyzed in detail and their ability to be transferred in *S. pneumoniae* after transformation will be assessed.

**Intervention Type**

Other

**Phase**

Not Applicable

**Primary outcome measure**

Carriage of antibiotic-resistant *E. coli* on follow-up cultures (at the end of antibiotic therapy and four weeks after the end of antibiotic therapy), stratified by duration of exposure and choice of antibiotic treatment (including also the causative pathogen of the initial episode of urinary tract infection), as well the baseline resistance prevalence of the index patient and his household members.

**Secondary outcome measures**

1. The impact of antibiotic therapy duration on carriage of resistant streptococci in the oropharyngeal flora
2. The proportion of susceptible bacteria on follow-up cultures

**Overall study start date**

01/01/2011

**Completion date**

31/12/2013

**Eligibility****Key inclusion criteria**

1. Adult patients  $\geq 18$  years old
2. Presenting with an acute lower or upper, uncomplicated or complicated UTI to the Emergency Room or Outpatient Clinic of the participating GP practices, clinics and hospitals
3. Requiring an antibiotic treatment of at least one dose
4. No antibiotics taken within the last 30 days
5. At least one other person living in the patient's household, defined as a person who spends at least three nights per week in the same house or apartment
6. Informed consent to the study participation

Household members (maximum 3) of the index patients will also be invited to participate. Control patients will be recruited from patients (and their household contacts) presenting either with minor trauma or for a gynaecologic exam to the GPs / outpatient clinics.

**Participant type(s)**

Patient

**Age group**

Other

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

450 households with 2-4 participants per household (ratio of antibiotic to control households will be 4:1)

**Key exclusion criteria**

1. Refusal to participate
2. Unable to give informed consent
3. Presence of indwelling urinary catheters or urethral pigtail catheters
4. Renal transplant recipients; acute or chronic renal failure requiring dialysis
5. Recent discharge from hospital (during the last 30 days)
6. Treatment with systemic antibiotics within the last 30 days
7. Patients with severe sepsis or septic shock requiring intensive care
8. Permanently institutionalized residents of nursing homes or long term care facilities
9. Follow-up not possible or unlikely to be successful

**Date of first enrolment**

01/01/2011

**Date of final enrolment**

31/12/2013

## **Locations**

**Countries of recruitment**

Belgium

Poland

Switzerland

**Study participating centre**

**Infection Control Program**

Geneva 14

Switzerland

1211

## **Sponsor information**

**Organisation**

University of Geneva Hospitals (Switzerland)

### Sponsor details

Rue Gabrielle-Perret-Gentil 4  
Geneva 14  
Switzerland  
1211

### Sponsor type

Hospital/treatment centre

### Website

<http://www.hug-ge.ch/>

### ROR

<https://ror.org/01m1pv723>

## Funder(s)

### Funder type

Government

### Funder Name

European Commission (Belgium) - DG Research (FP7-HEALTH-2009-SINGLE STAGE - N°241796)

## Results and Publications

### Publication and dissemination plan

Not provided at time of registration

### Intention to publish date

### Individual participant data (IPD) sharing plan

### IPD sharing plan summary

Not provided at time of registration

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/09/2018	18/01/2019	Yes	No