Antimicrobial Resistance in Gram-negative bacteria from Urinary Specimens (ARGUS)
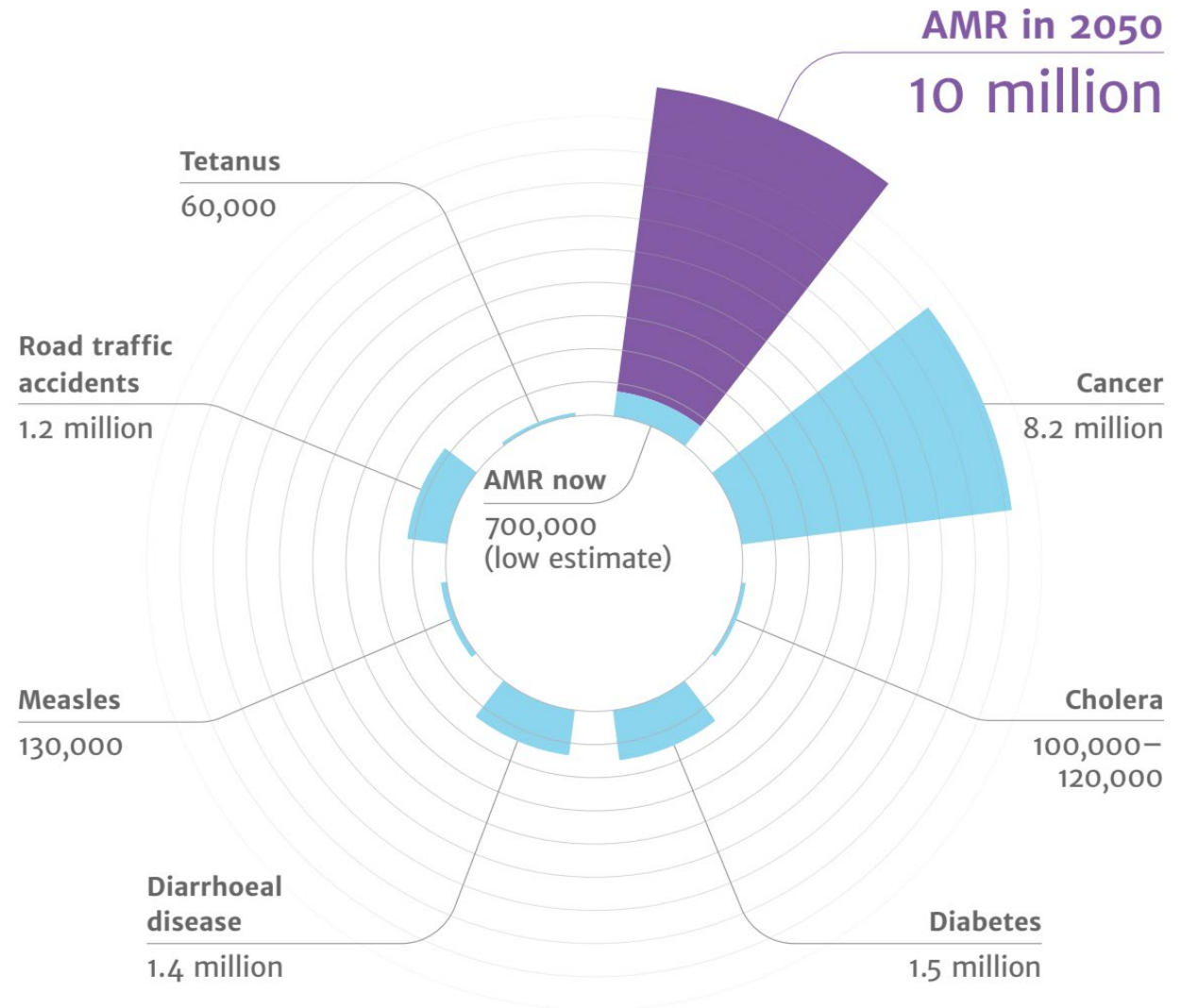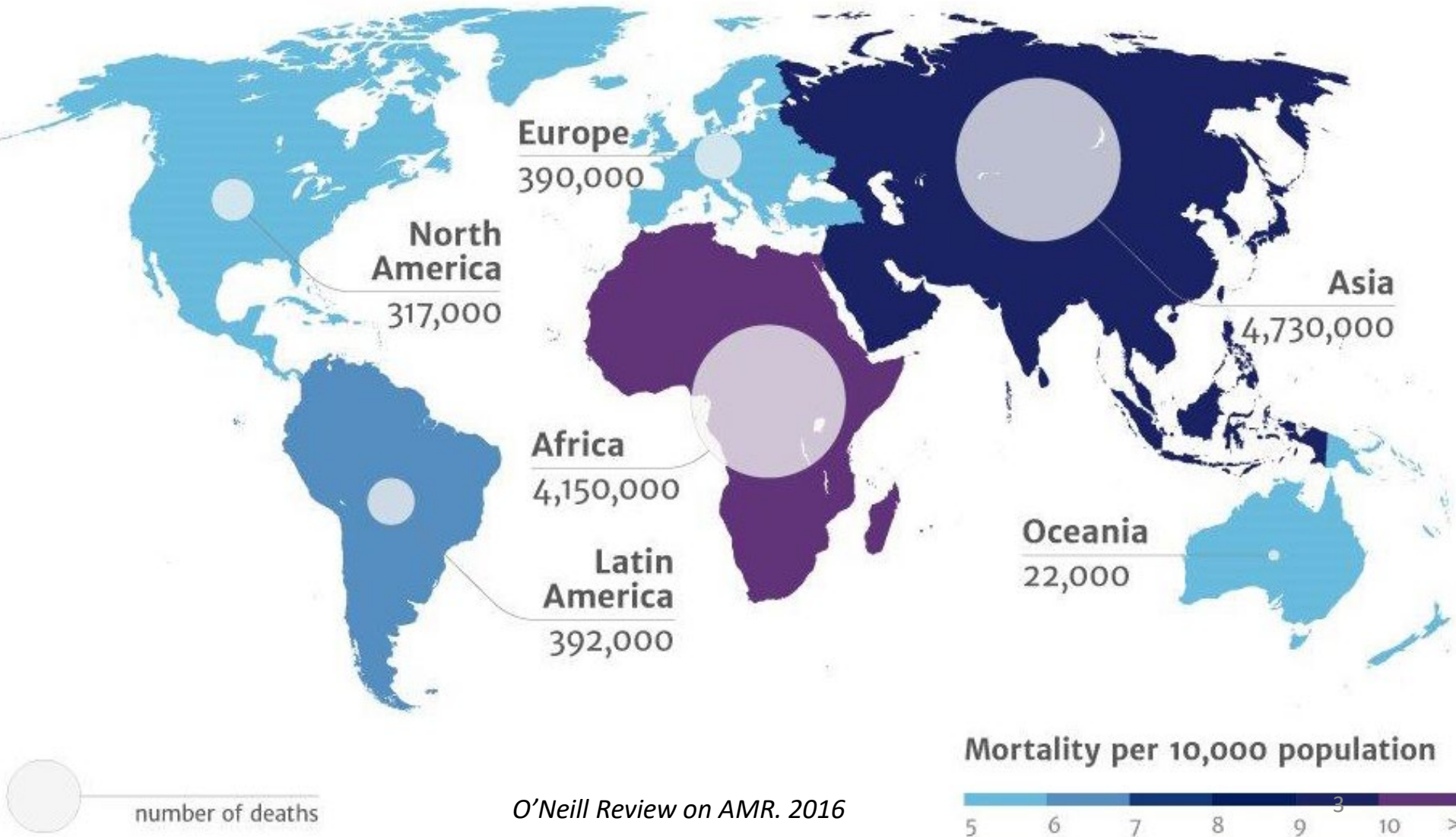
Dr. Ioana D Olaru

Mortality due to AMR in 2050

AMR in 2050
10 million

Tetanus
60,000

Road traffic accidents
1.2 million

Cancer
8.2 million

AMR now
700,000
(low estimate)

Measles
130,000

Cholera
100,000–120,000

Diarrhoeal disease
1.4 million

Diabetes
1.5 million

O'Neill Review on AMR. 2016

AMR-related deaths in 2050

Europe
390,000

North America
317,000

Asia
4,730,000

Africa
4,150,000

Latin America
392,000

Oceania
22,000

Mortality per 10,000 population

number of deaths

O'Neill Review on AMR. 2016

5 6 7 8 9 10 >

United Nations high-level meeting on antimicrobial resistance

Antimicrobial resistance summit to shape the international agenda

"…acknowledge that, due to antimicrobial resistance, many achievements of the twentieth century are being gravely challenged…"

Date: 21 September 2016
Place: New York, USA

Global Action Plan for AMR

GAP-AMR OBJECTIVES

1. to improve awareness of AMR;

2. to strengthen knowledge through surveillance and research;

3. to reduce the incidence of infection;

4. to optimize the use of antimicrobial agents;

5. develop sustainable investment for new medicines, diagnostic tools, vaccines and other interventions.

WHO Global Action Plan on AMR 2015

AMR prevalence studies in *E. coli* and *Klebsiella pneumoniae*
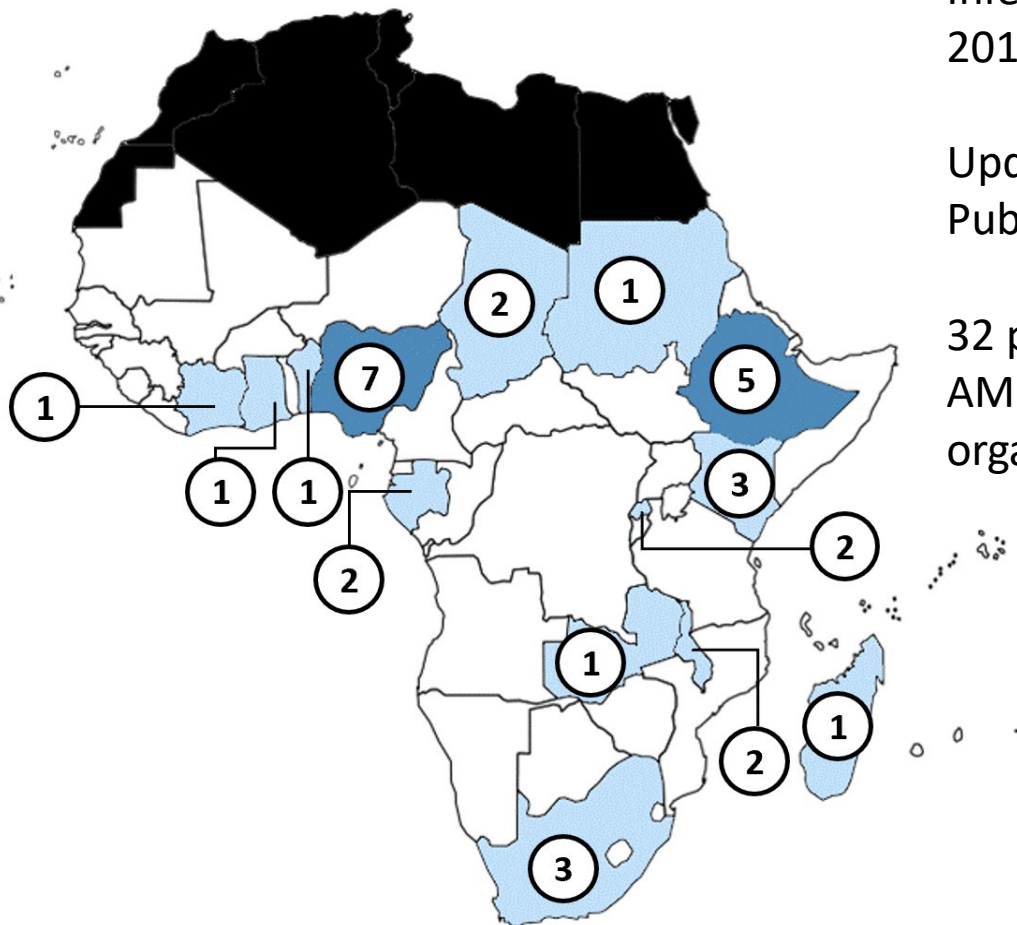
Systematic review by Tadesse et al. (BMC Infect Dis 2017) on AMR in Africa 2013-2016
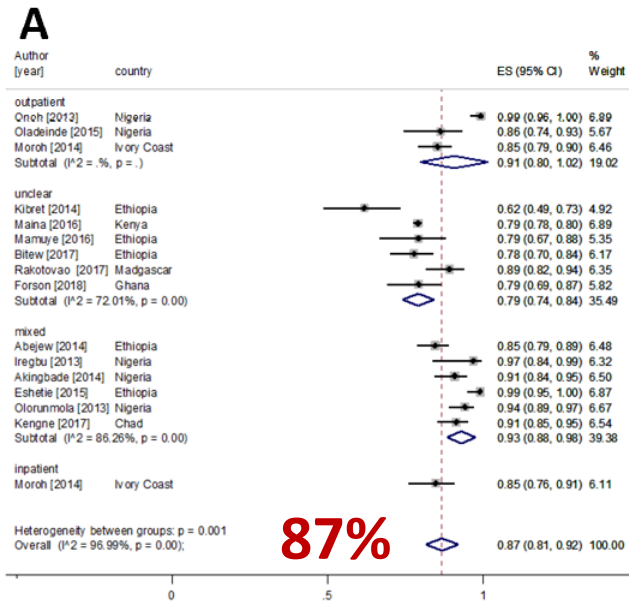
Updated search to July 2019 (MEDLINE and PubMed)

32 publications reporting on prevalence of AMR in *E. coli* and *K. pneumoniae* (priority organisms)
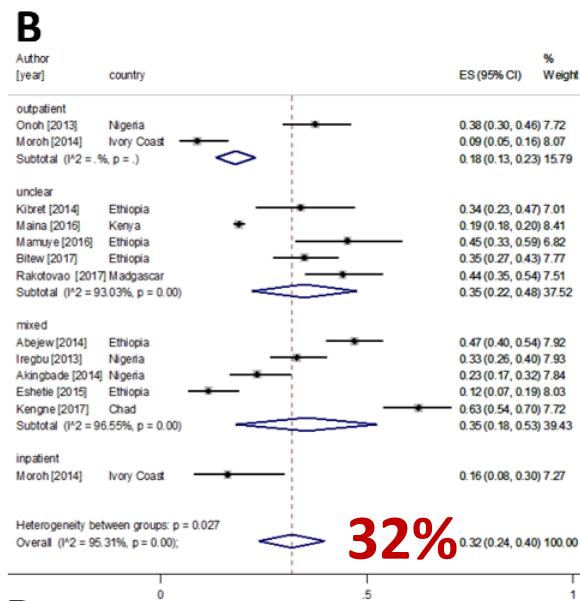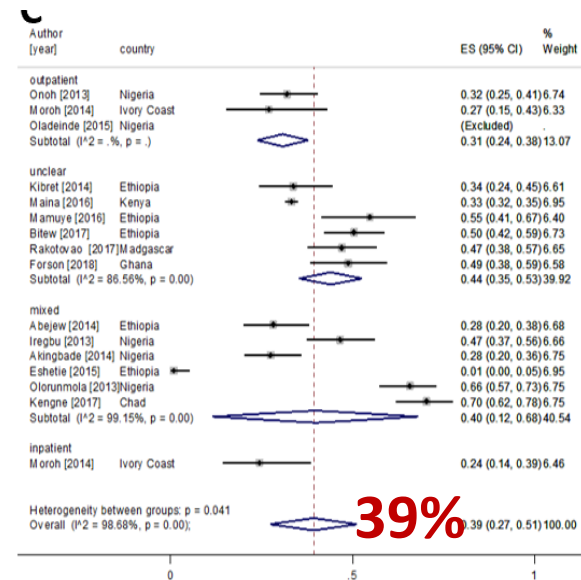
Prevalence of resistance in *E. coli*

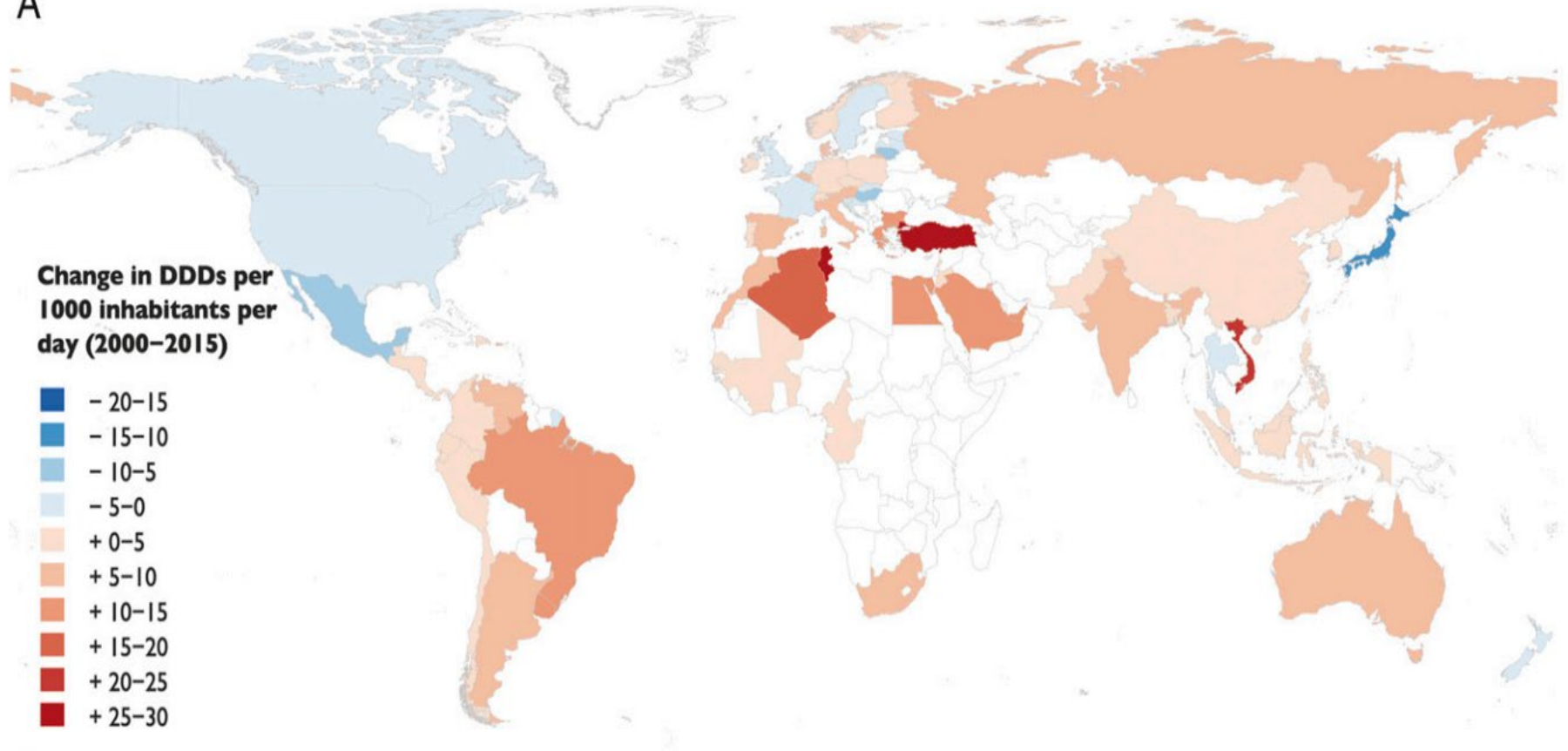**Amoxicillin**   **Cephalosporins**   **Fluoroquinolones**

Most data from large hospitals/ laboratories
Few studies in outpatients
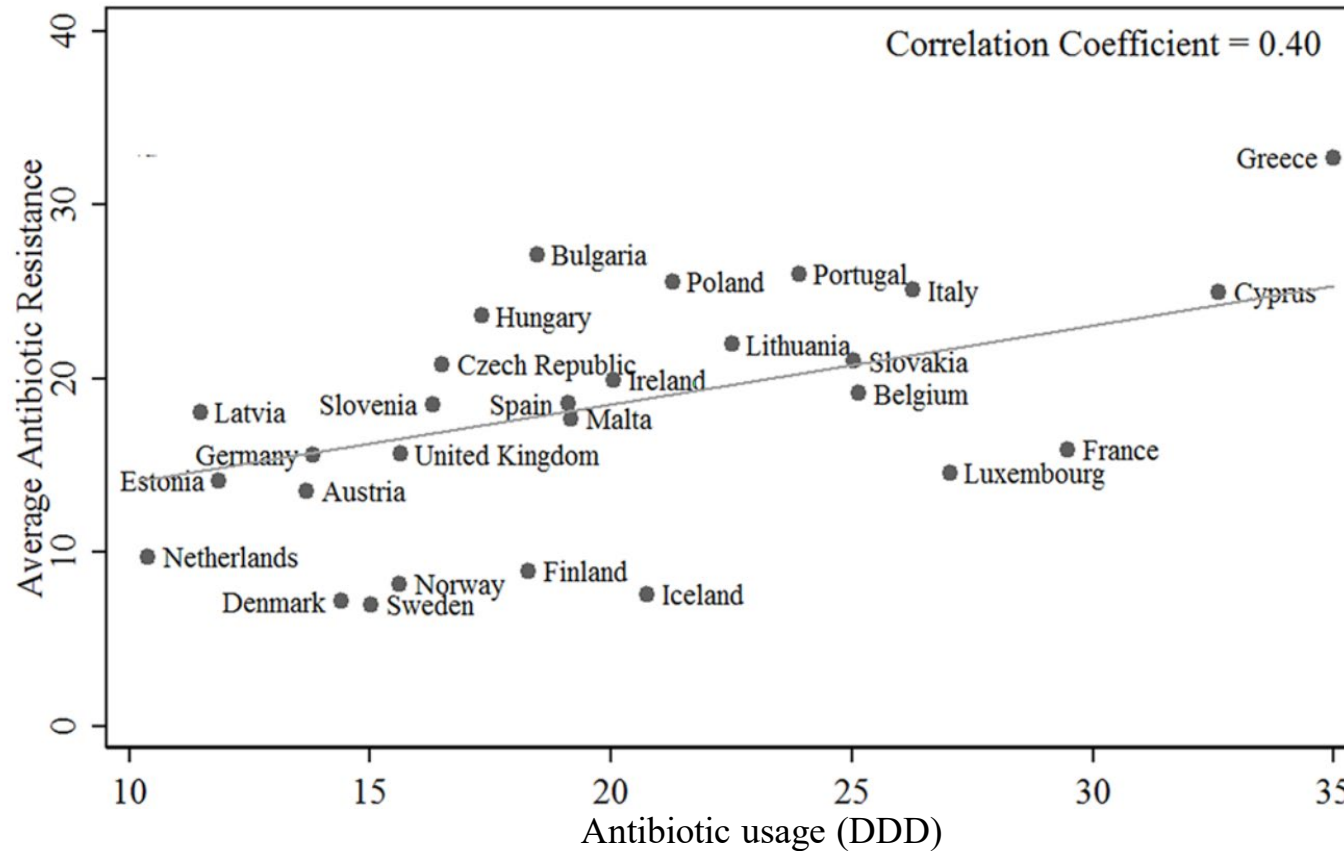
7

Global trends in antimicrobial use

A

Change in DDDs per 1000 inhabitants per day (2000–2015)

- ■ – 20–15
- ■ – 15–10
- ■ – 10–5
- ■ – 5–0
- ■ + 0–5
- ■ + 5–10
- ■ + 10–15
- ■ + 15–20
- ■ + 20–25
- ■ + 25–30

Little data on antimicrobial usage from sub-Saharan Africa

Klein et al. PNAS 2018

Antimicrobial consumption and AMR

Collington et al. PLoS One 2015

Strategies to combat AMR

Global action plan on antimicrobial resistance (World Health Assembly)

Current needs to achieve objectives

Strengthen surveillance	**Understand prevalence of resistance**
Optimize antibiotic use	**Evaluate antibiotic prescribing**
Improve awareness and knowledge of AMR	**Improve prescriber knowledge of AMR**

Study overview

**ARGUS Study
3 components**

**Patients presenting
to PHC with
suspected UTI**

**Antimicrobial usage
at PHC-level**

**Perceptions
of AMR**

**Questionnaire and
urine samples from
1500 patients**

**Collection of data
from registers**

**Survey in nurses
from polyclinics**

Prevalence of resistance
Risk factors for AMR
AMR and outcomes
Whole genome sequencing

Drug consumption (DDD)
Guideline adherence

Knowledge, attitudes and
practice relating to
diagnosis of AMR and
antibiotic prescribing

DDD: defined daily doses measured per 1000 population

Prevalence of resistance

Eligibility criteria

Inclusion criteria:

- age ≥18 years
- symptoms of UTI
    - ≥2 of the following: dysuria, urgency, frequency, suprapubic pain and/or flank pain
- onset of symptoms within two weeks prior to presentation
- presence of symptoms within the last 24 hours
- provision of written informed consent.

Exclusion criteria:

- discharge from hospital within the previous 72 hours
- having a urinary catheter in-situ

ARGUS clinic sites
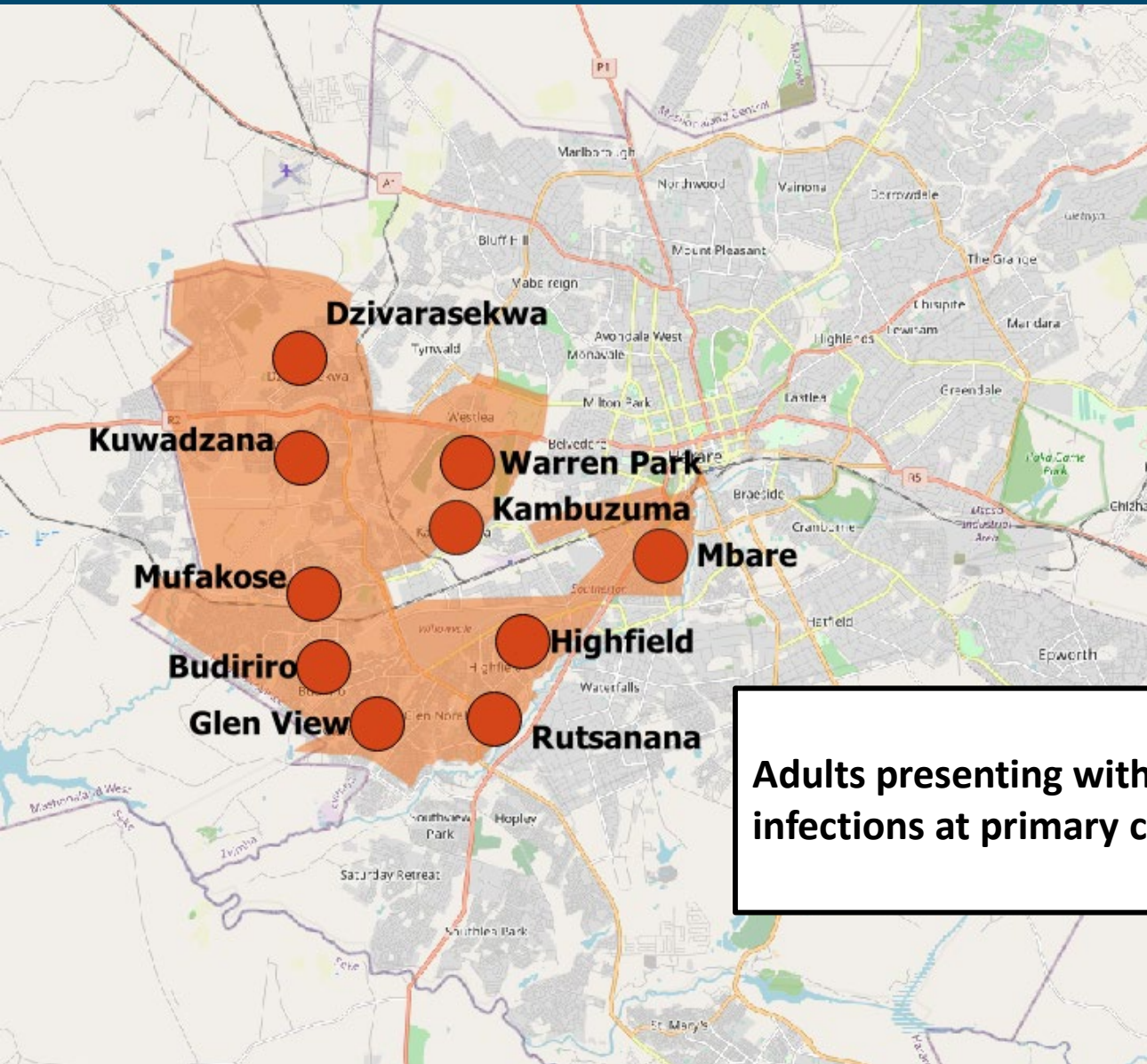
Adults presenting with symptoms of urinary tract infections at primary clinics in Harare

Prevalence of AMR

1164 participants recruited

64% female

15% pregnant women

36% HIV+

Pie chart legend:
- *E. coli*
- Other coliforms
- *Enterococcus spp.*
- *S. saprophyticus*
- *S. aureus*

Bar chart: Percent resistant by antibiotic — Cotrimoxazole, Amoxicillin, Ceftriaxone, Ciprofloxacin, Gentamicin, Fosfomycin, Nitrofurantoin
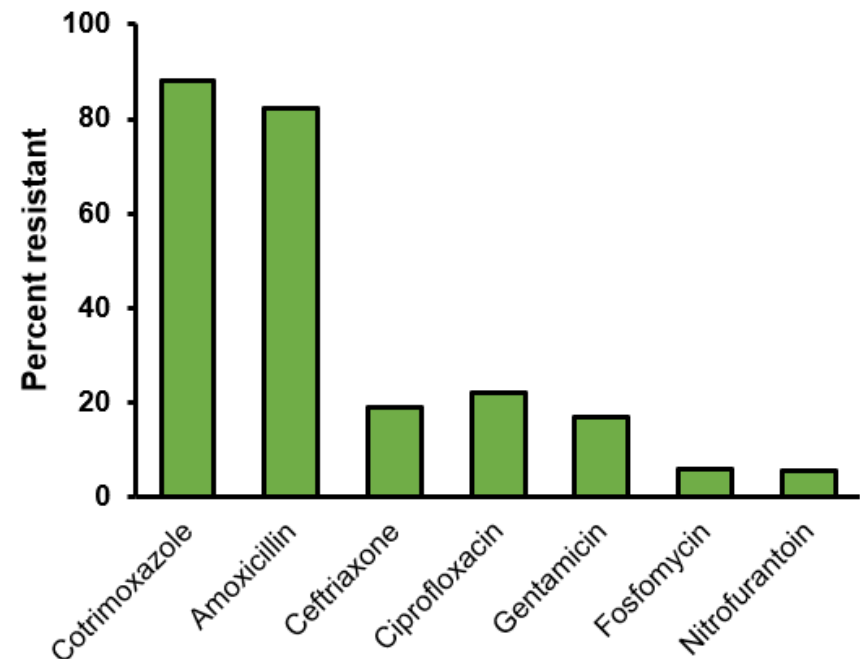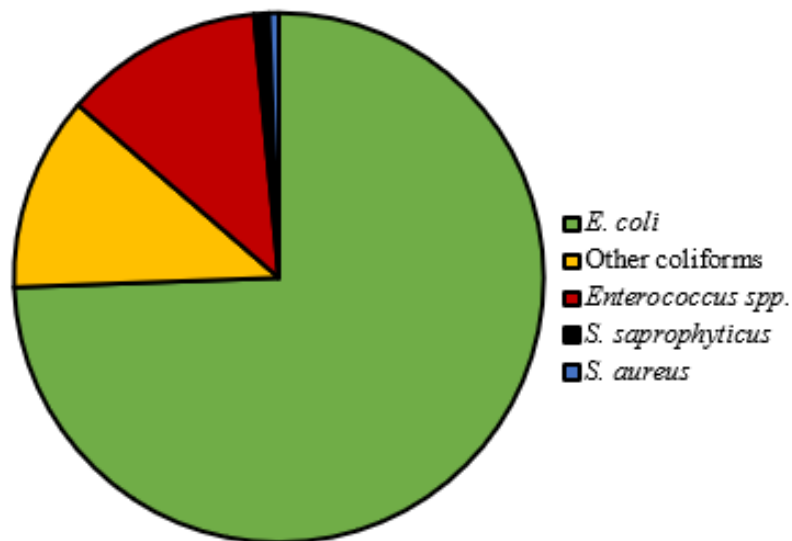
Resistance accoding to HIV status in *E. coli*

E. coli	HIV+ N=81	HIV- N=142	OR (95% CI)
Ceftriaxone resistance	21 (26%)	18 (13%)	2.41 (1.2-4.9)
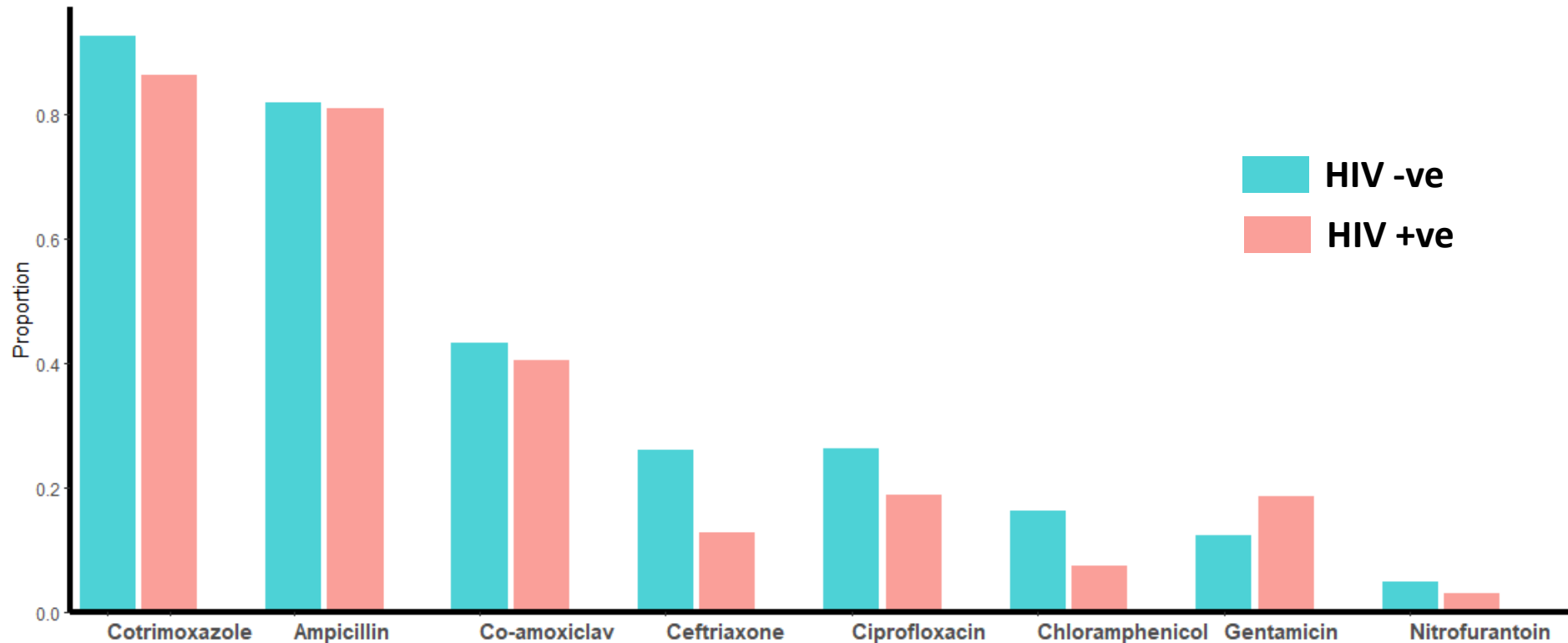
Evaluation of new culture systems

Brilliance UTI agar (reference)

Urine samples from 414 participants tested in parallel with the 3 systems
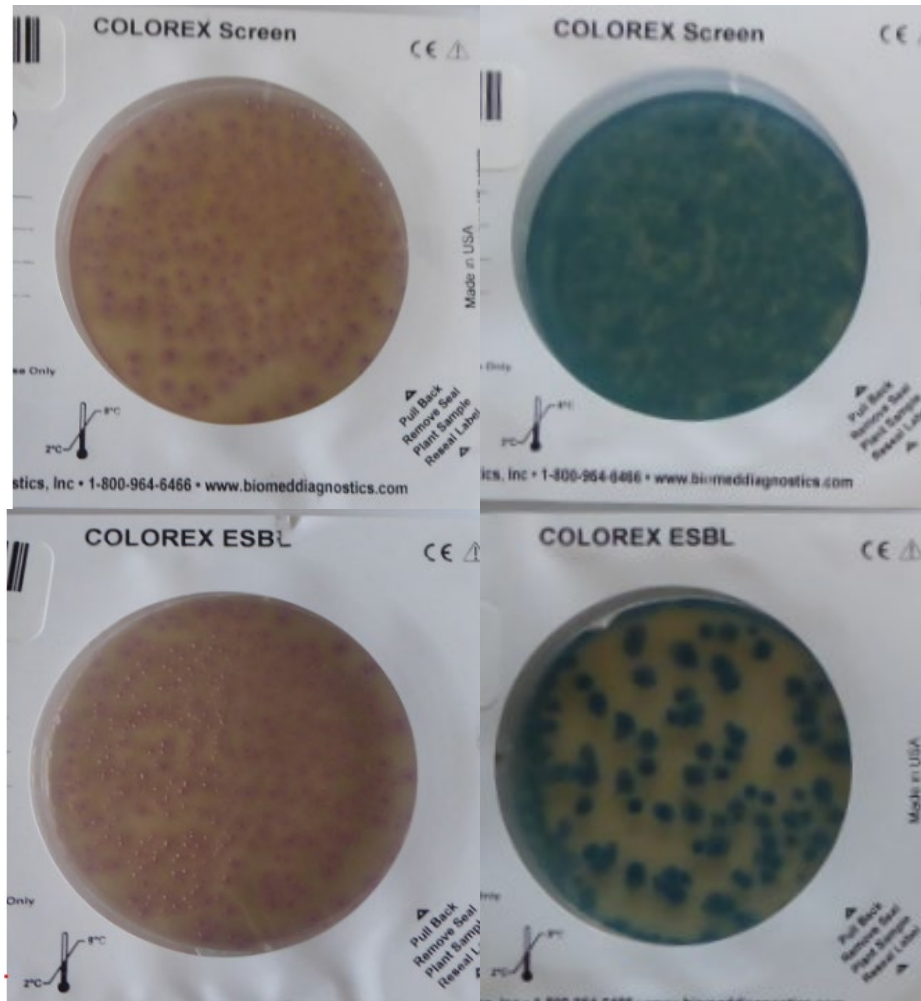
InTray COLOREX Screen
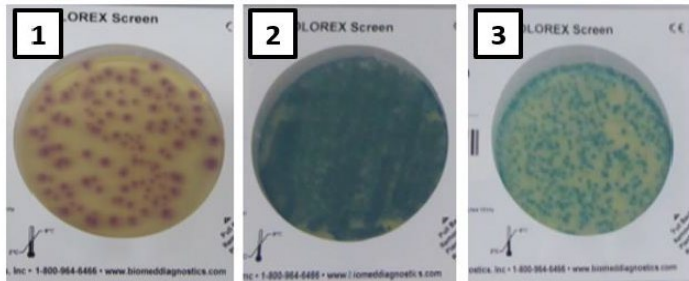
	Sensitivity (95% CI)	Specificity (95% CI)
InTray Screen	89 (82-96)	98 (97-100)
Compact Dry	95 (91-100)	100 (99-100)

Compact Dry EC

Rapid ESBL detection

Reduced time to resistance detection to 1 day (or less)

Sensitivity 96%
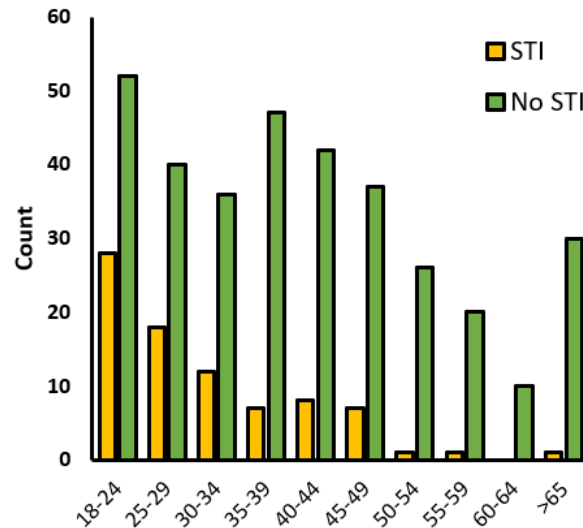**Specificity 100%**

Negative urine cultures

35% of urine cultures are positive

- Prior antimicrobials? → Antibiotic bioassay
- Symptoms due to an STI? → Xpert CT/NG/TV
- Low bacterial load/ dilution? → CompactDry
- Delayed culture inoculation → InTray
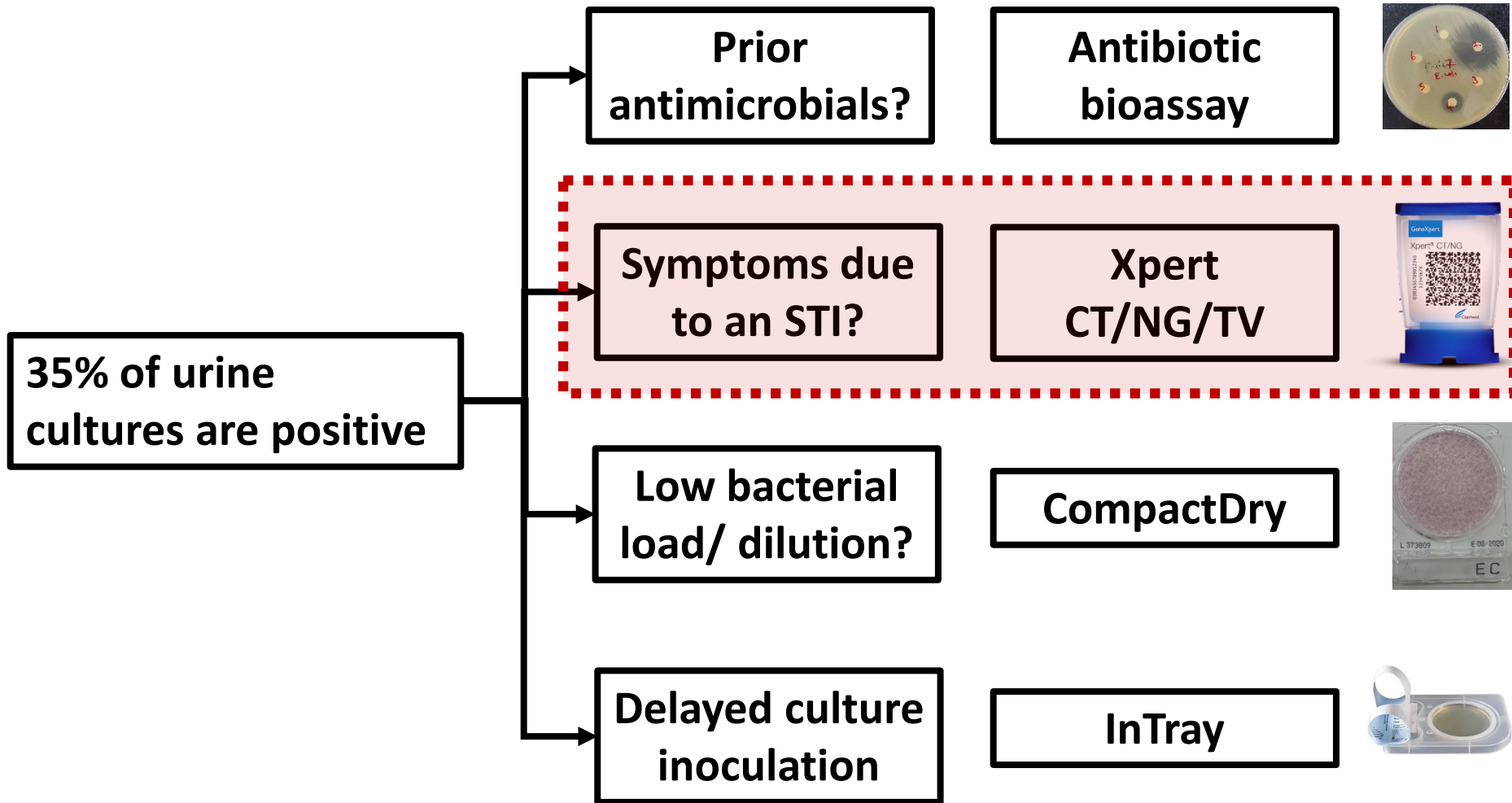
STI prevalence

	Number tested	Number positive	Prevalence (95%CI)
Chlamydia trachomatis	425	43	10.1 (7.4-13.4)
Neisseria gonorrhoeae	425	37	8.7 (6.2-11.8)
Trichomonas vaginalis	175*	14	8.0 (4.4-13.1)
Any STI	425	83	19.5 (15.8-23.6)

For TV - a subset of consecutively enrolled women were included
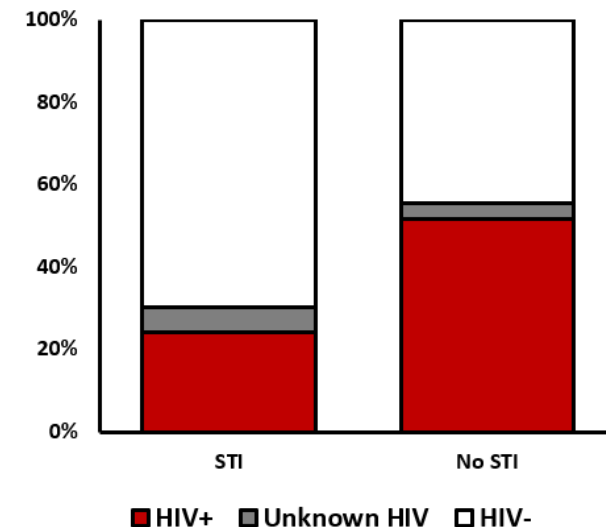
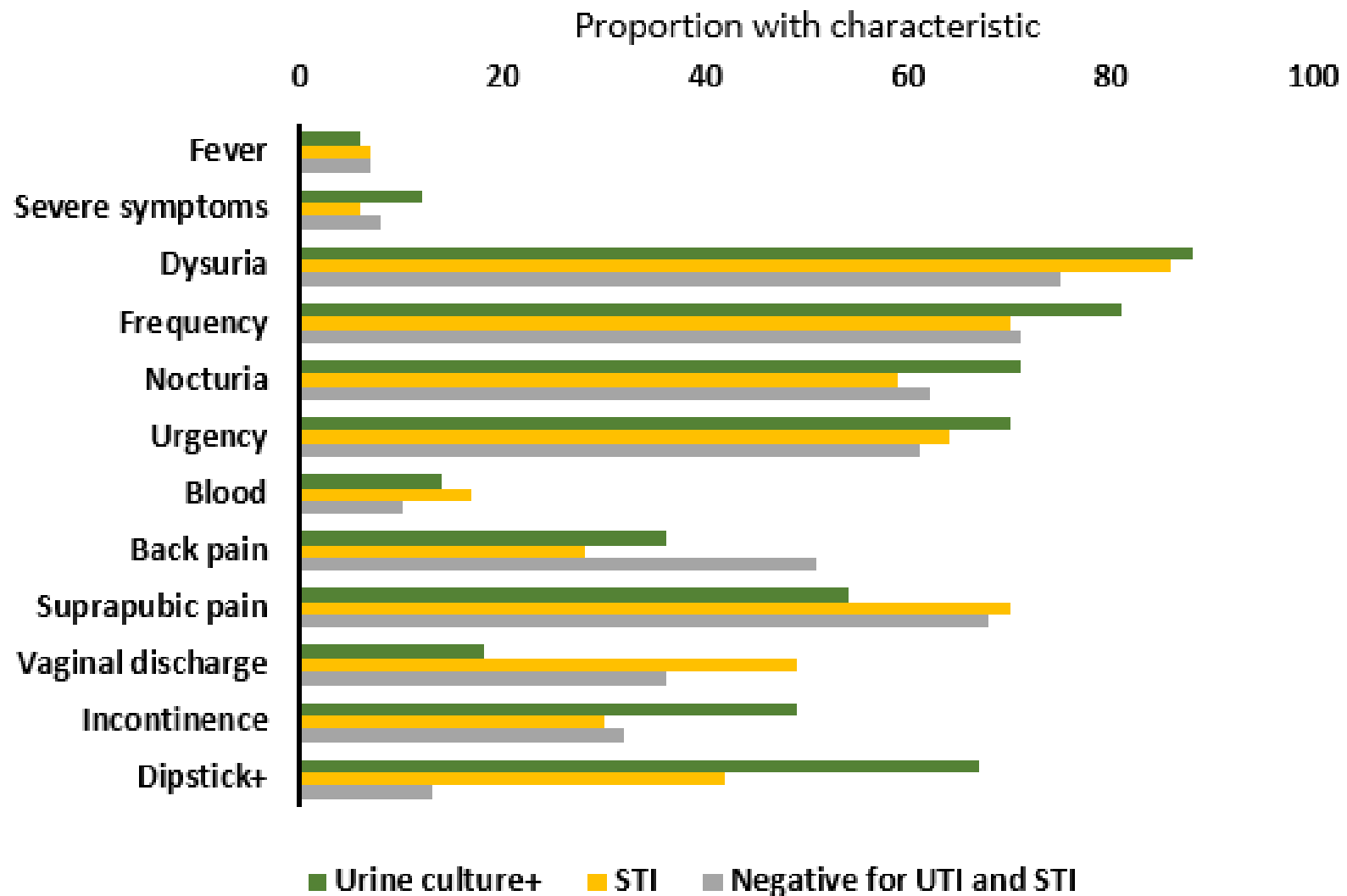# Characteristics of participants tested for STIs

Presenting symptoms

Proportion with characteristic

Categories (top to bottom): Fever, Severe symptoms, Dysuria, Frequency, Nocturia, Urgency, Blood, Back pain, Suprapubic pain, Vaginal discharge, Incontinence, Dipstick+
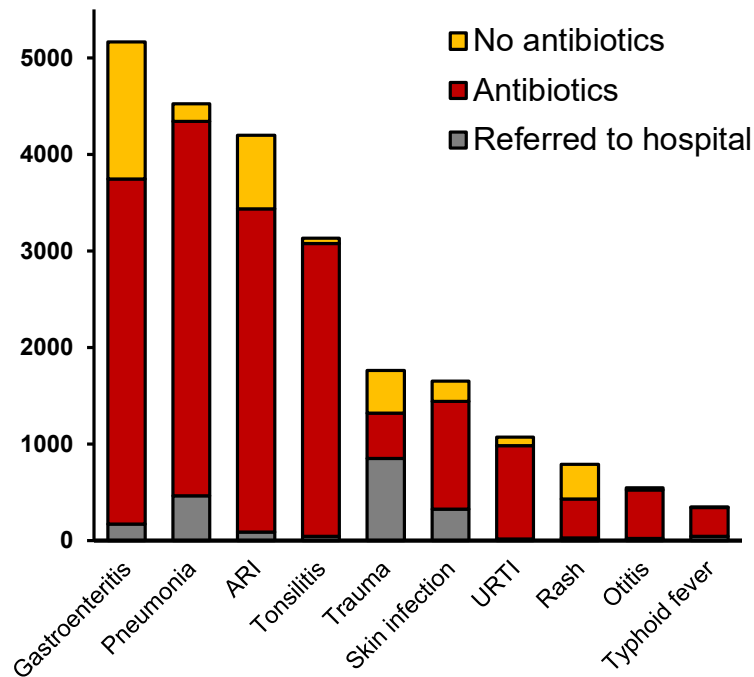
Legend: ■ Urine culture+ ■ STI ■ Negative for UTI and STI
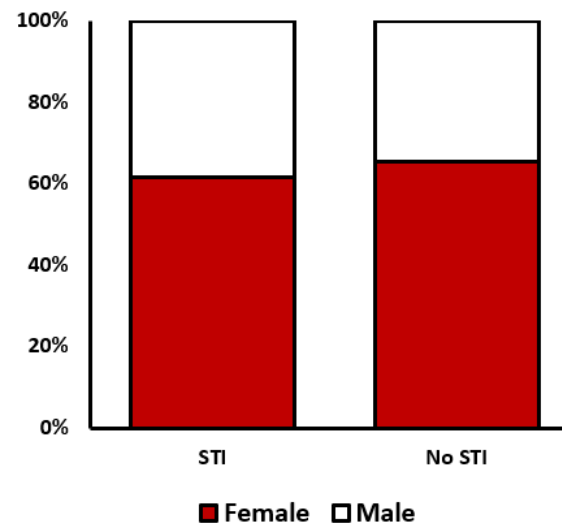
Antimicrobial prescriptions

Diagnoses and prescribed antibiotics

Data from clinic registries 2016-2020 (ongoing data collection)
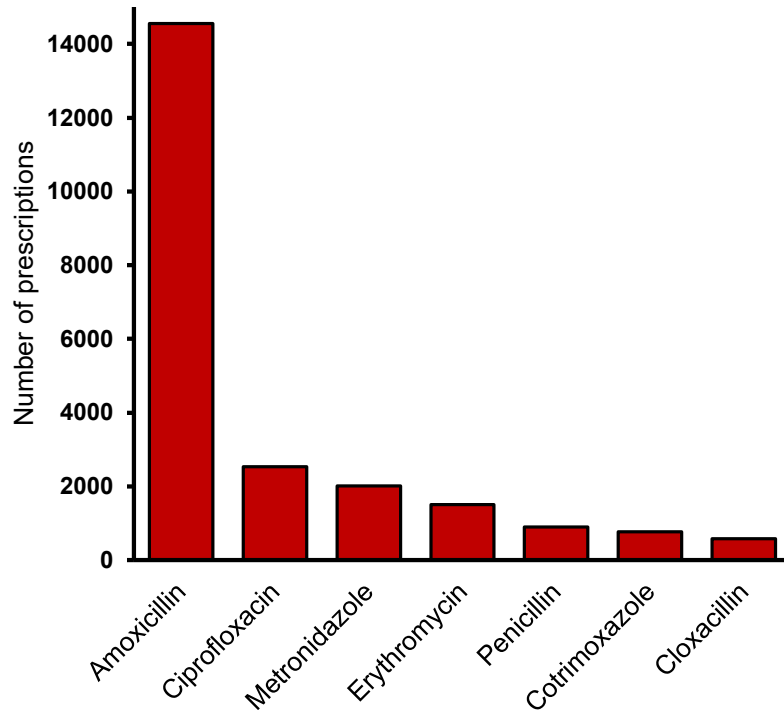

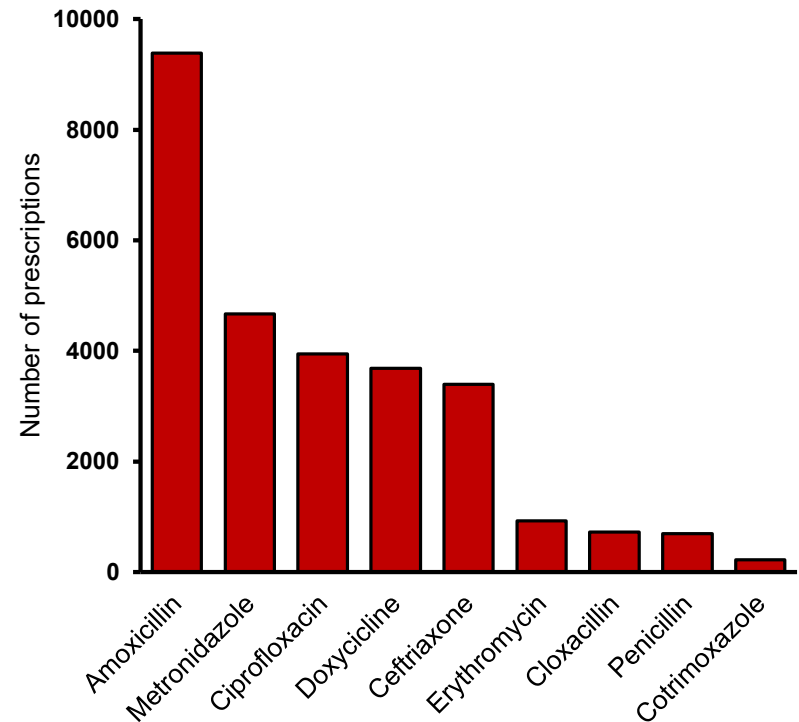Children: 68% received antibiotics

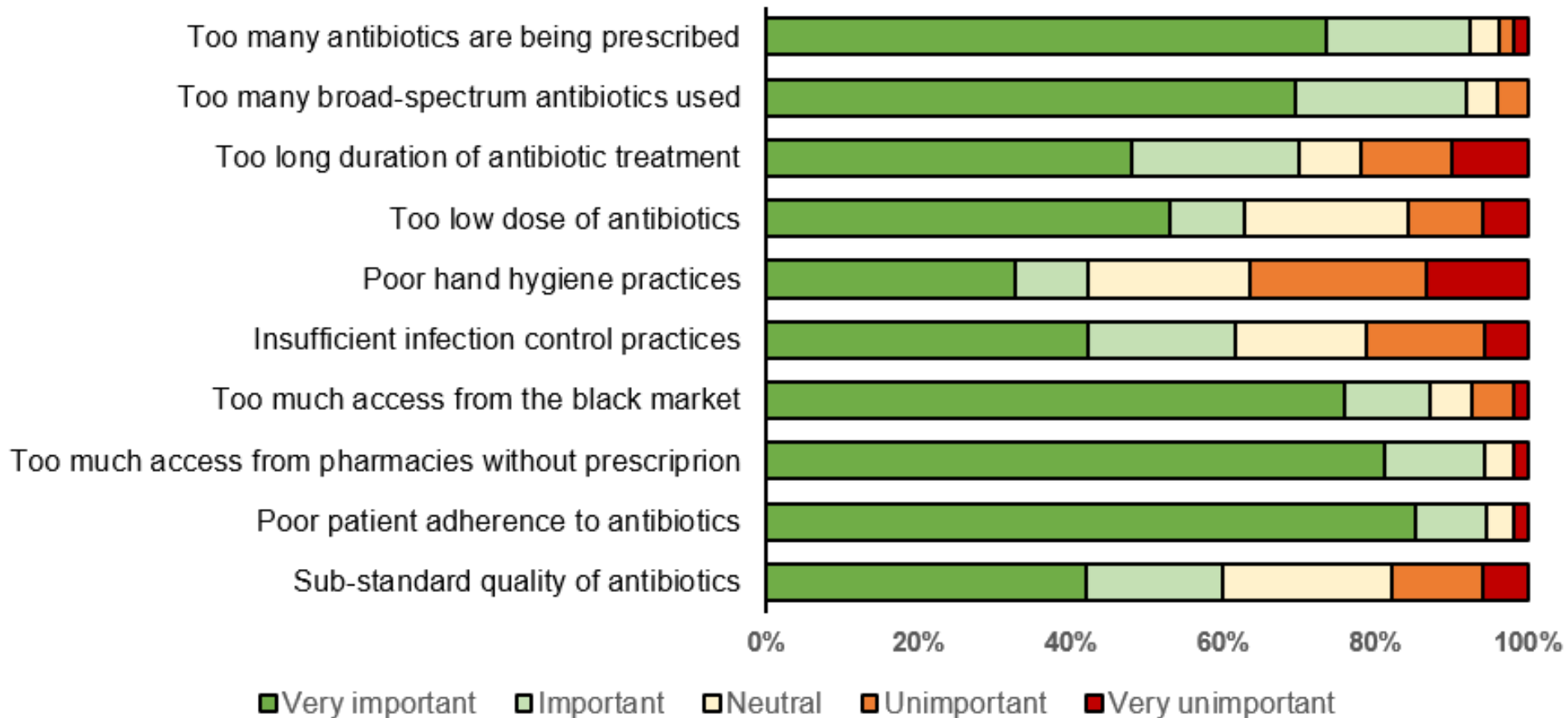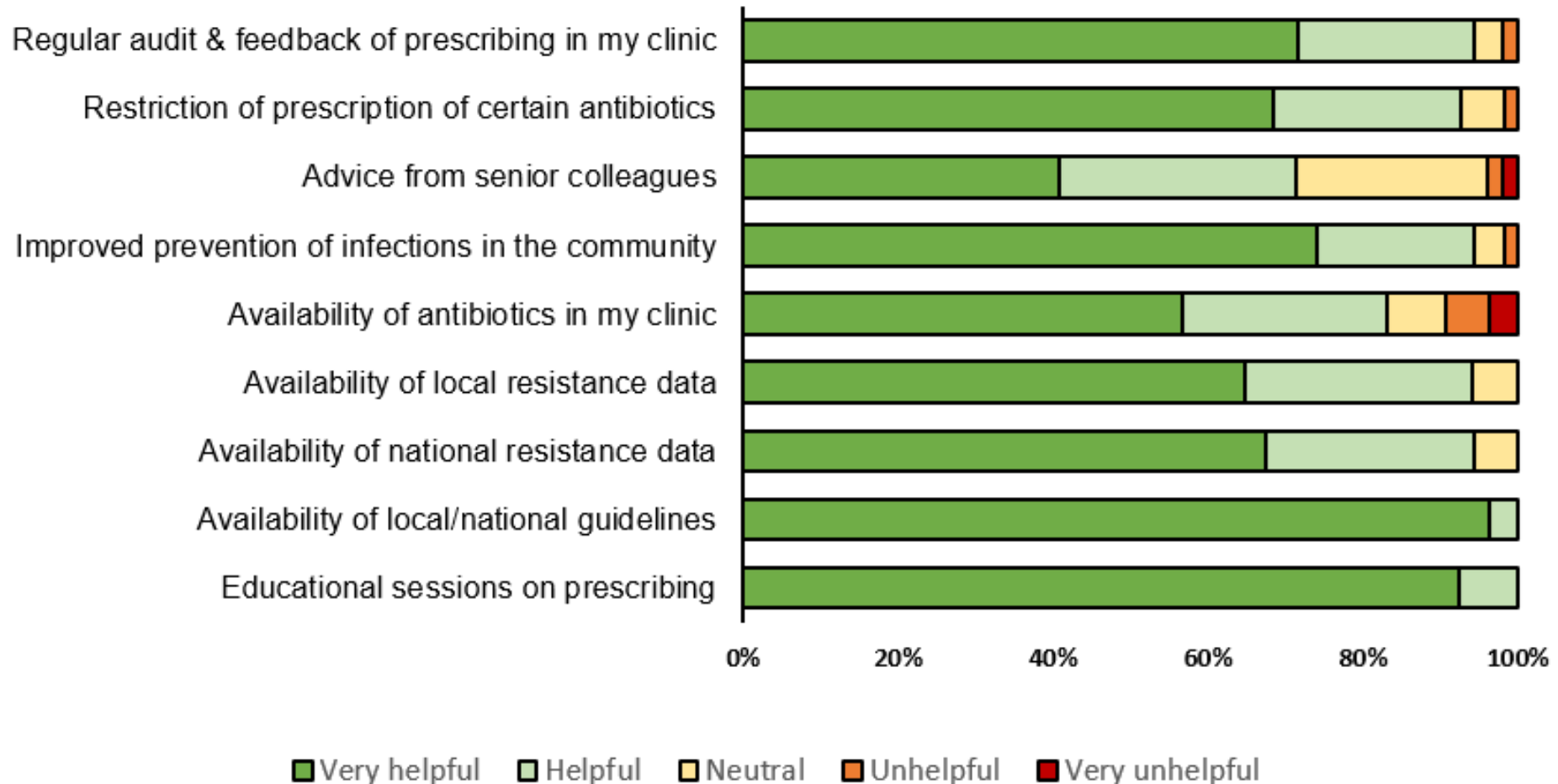Adults: 54% received antibiotics
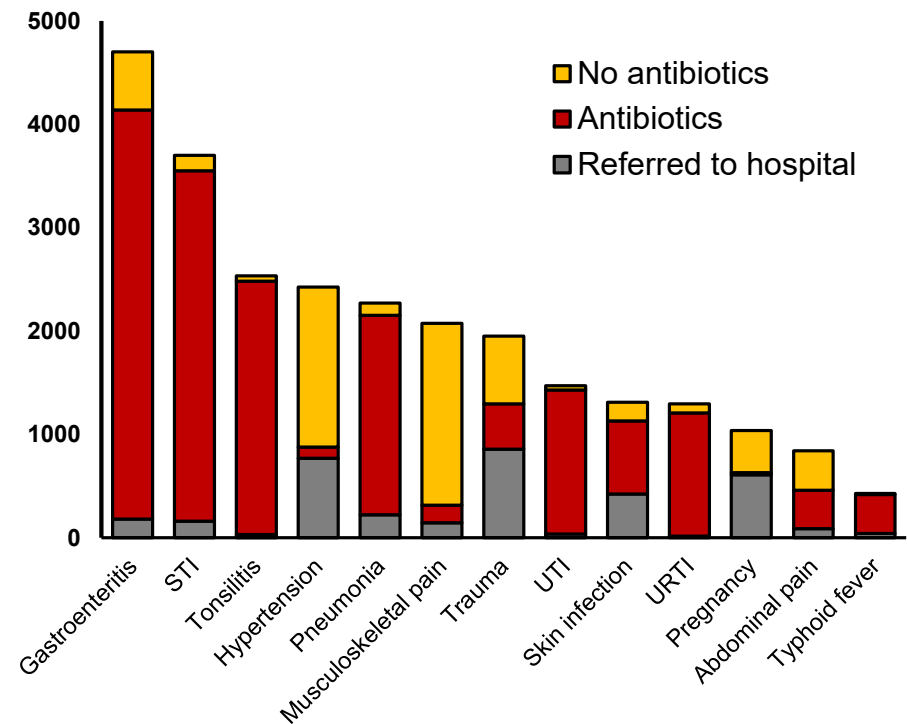
Antibiotic prescriptions
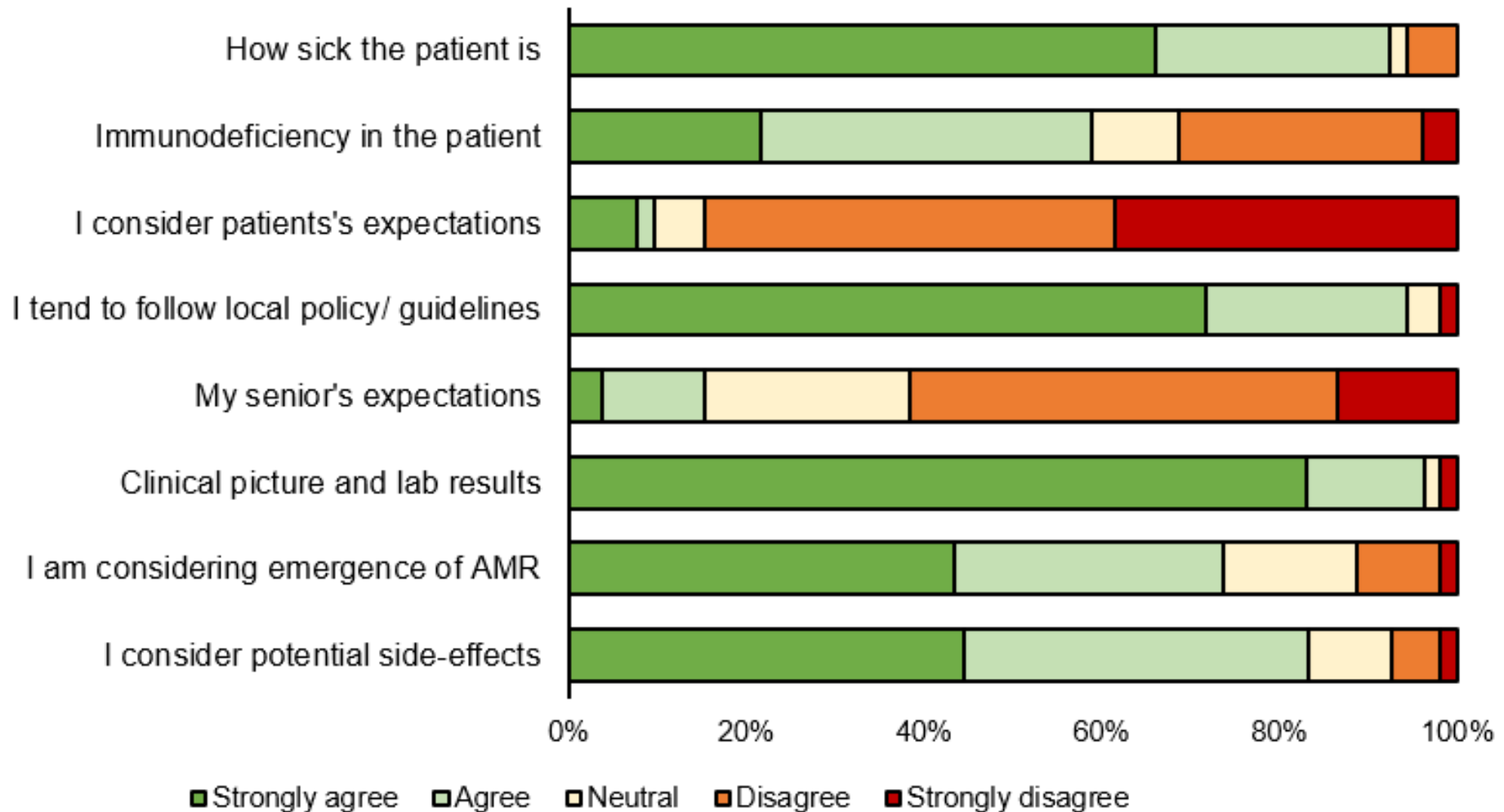
Prescriber survey

Causes of AMR

Measures to improve antibiotic prescribing

Decision to start antibiotics

Conclusions

- Urinary tract infections
  - High prevalence of resistance to first-line antibiotics (amoxicillin in particular)
  - Ceftriaxone resistance higher in patients with HIV
  - Resistance to nitrofurantoin and Fosfomycin very low

- Sexually transmitted infections
  - ~20% STI prevalence
  - STIs are also the 2nd most common diagnosis in adults presenting to polyclinics (registry data)

- Clinic registers
  - 54% of adults and 68% of children received antibiotic prescriptions

Acknowledgements

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Thank you!

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