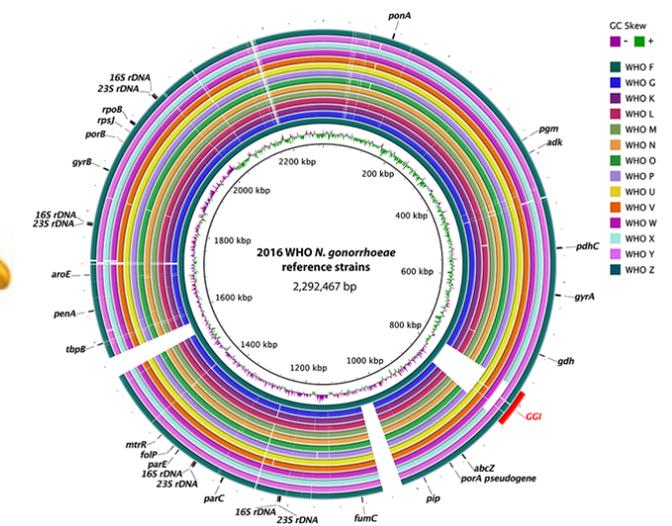




Sex Superbug



# Antibiotikaresistens hos *N. gonorrhoeae* (NG) – har vi förlorat kampen?

Magnus Unemo

WHO CC for Gonorrhoea and other STIs

Swedish Reference Laboratory for Pathogenic Neisseria

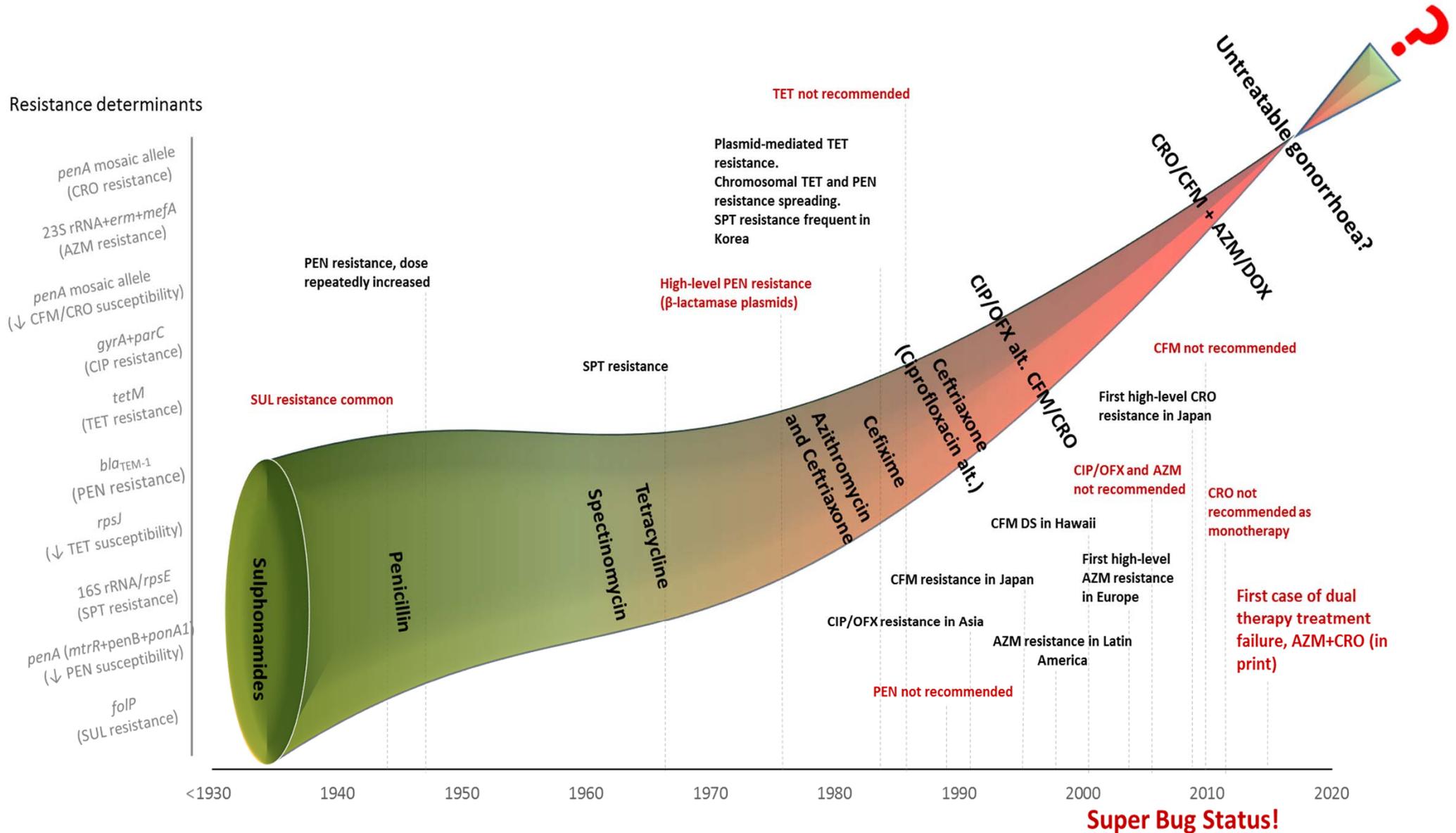
Department of Laboratory Medicine, Microbiology



WHO Collaborating Centre for  
Gonorrhoea and other Sexually  
Transmitted Infections

Örebro University Hospital, Sweden

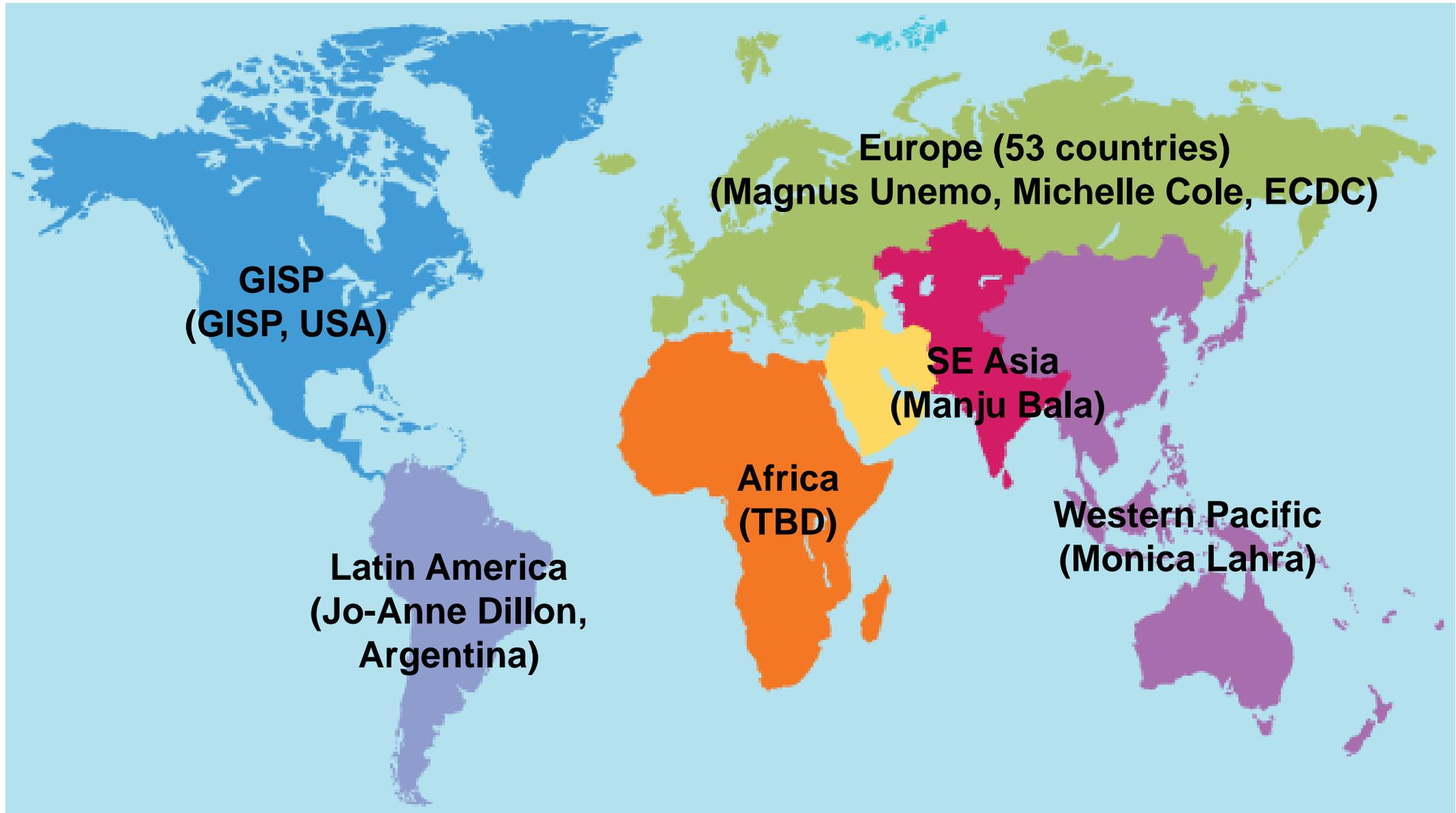
# Accumulation of antimicrobial resistance (AMR) determinants $\Rightarrow$ excluded treatments in 80 years



# WHO Global Gonococcal Antimicrobial Surveillance Programme (GASP)



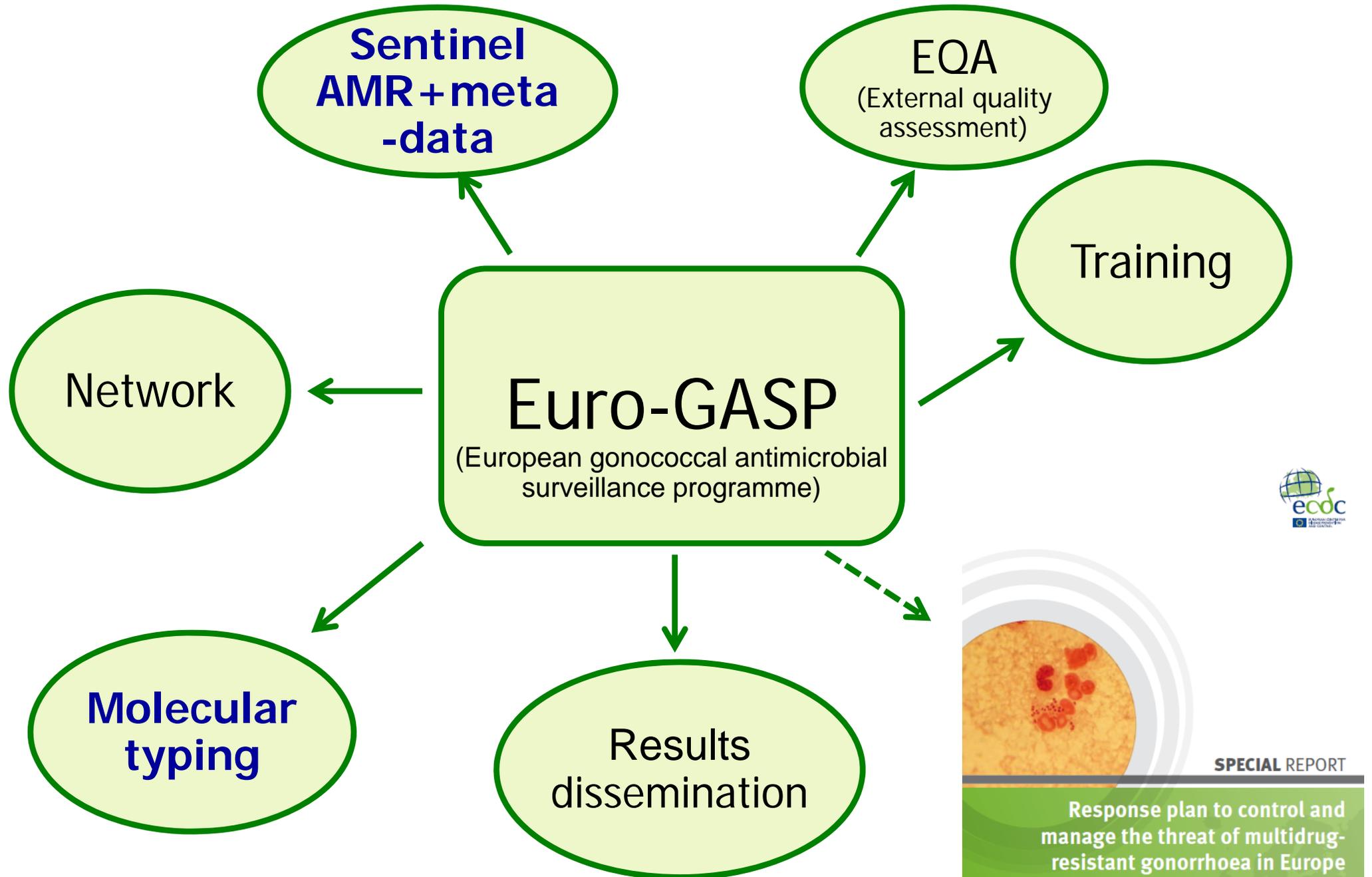
(Focal Centres at WHO HQ, and in each WHO region)



Antimicrobial resistance in *Neisseria gonorrhoeae*:  
Global surveillance and a call for international  
collaborative action **Results from 77 countries, 2009-2014**

Teodora Wi<sup>1\*</sup>, Monica M Lahra<sup>2,3</sup>, Francis Ndowa<sup>4</sup>, Manju Bala<sup>5</sup>, Jo-Anne R Dillon<sup>6</sup>, Pilar Ramon-  
Pardo<sup>7</sup>, Sergey R Eremin<sup>8</sup>, Gail Bolan<sup>9</sup>, Magnus Unemo<sup>10</sup> **PLoS Med. Accepted**

# ECDC (Gianfranco Spiteri) ⇒ contract to PHE (Michelle Cole) and ÖUH (Magnus Unemo) + EU/EEA STI Network



# Antimicrobial resistance in the EU/EEA, 2004-2015

(Euro-GASP: ~2100-2200 isolates per year)



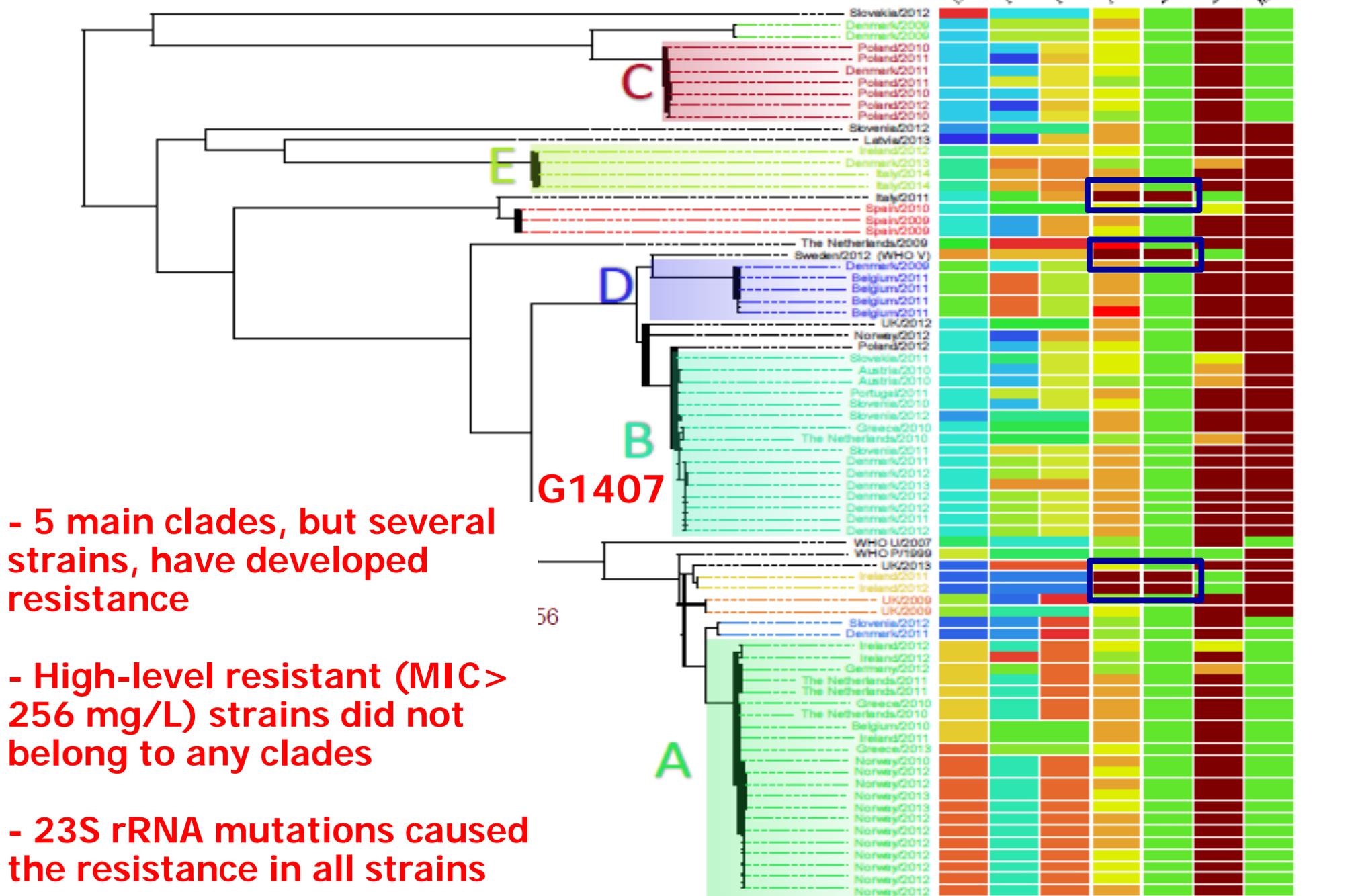
Ceftriaxone resistance (1 (0.05%) isolate in 2015, 5 (0.2%) in 2014, 7 (0.4%) in 2013)

# WGS analysis and molecular resistance mechanisms of azithromycin-resistant (MIC >2 mg/L) *Neisseria gonorrhoeae* isolates in Europe from 2009 to 2014

Susanne Jacobsson<sup>1</sup>, Daniel Golparian<sup>1</sup>, Michelle Cole<sup>2</sup>, Gianfranco Spiteri<sup>3</sup>, Irene Martin<sup>4</sup>, Thea Bergheim<sup>5</sup>, Maria José Borrego<sup>6</sup>, Brendan Crowley<sup>7</sup>, Tania Crucitti<sup>8</sup>, Alje P. Van Dam<sup>9</sup>, Steen Hoffmann<sup>10</sup>, Samo Jeverica<sup>11</sup>, Peter Kohl<sup>12</sup>, Beata Mlynarczyk-Bonikowska<sup>13</sup>, Gatis Pakarna<sup>14</sup>, Angelika Stary<sup>15</sup>, Paola Stefanelli<sup>16</sup>, Peter Pavlik<sup>17</sup>, Eva Tzelepi<sup>18</sup>, Raquel Abad<sup>19</sup>, Simon R. Harris<sup>20</sup> and Magnus Unemo<sup>1\*</sup>

**J Antimicrob Chemother. 2016**

# Azithromycin resistant Ng (MIC>2 mg/L) in EU/EEA, 2009-2014



- 5 main clades, but several strains, have developed resistance

- High-level resistant (MIC > 256 mg/L) strains did not belong to any clades

- 23S rRNA mutations caused the resistance in all strains

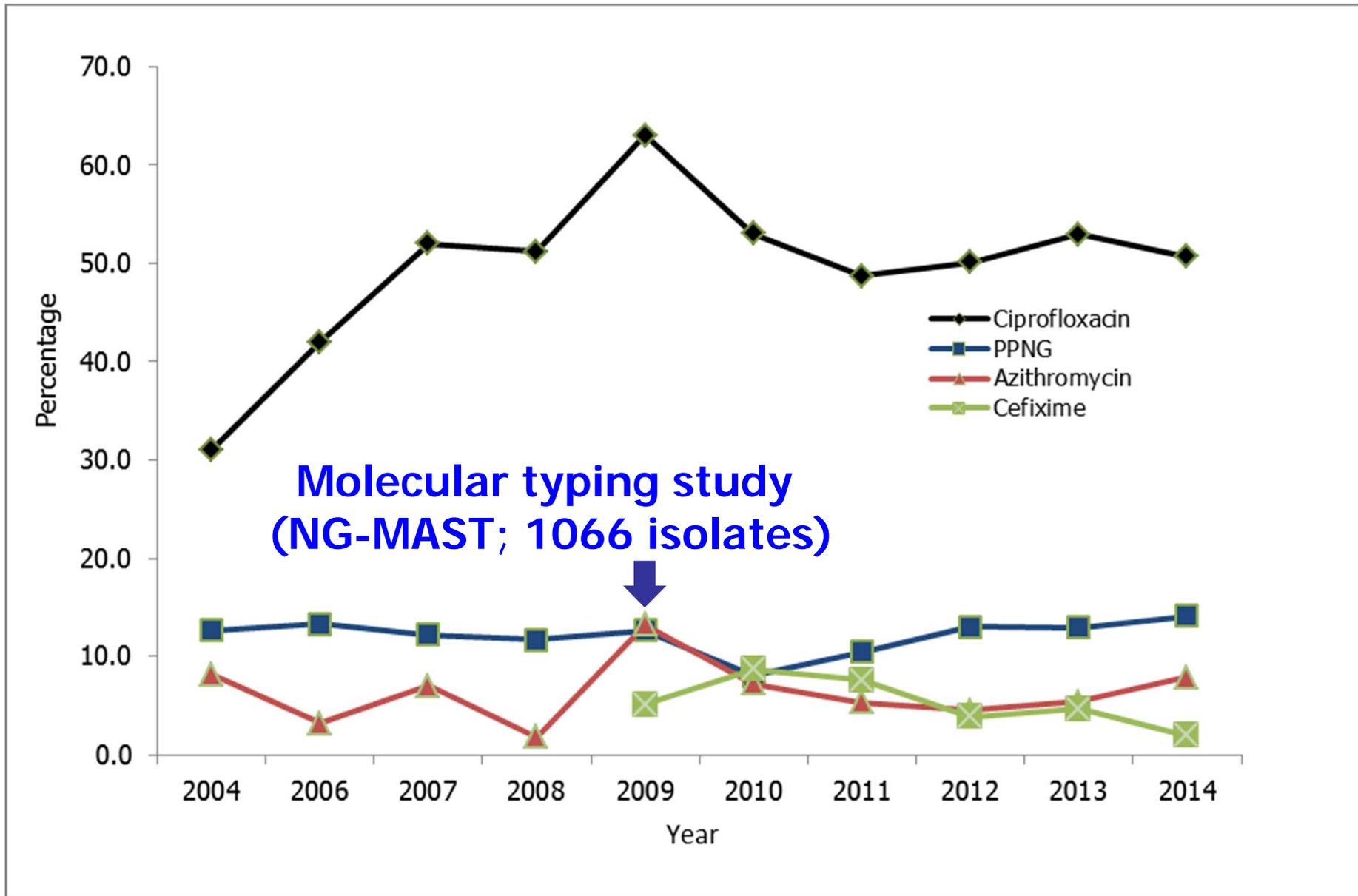
## Antimicrobial resistance in Sweden in 2008-2016

	2008 (n=447)	2009 (n=384)	2010 (n=618)	2011 (n=805)	2012 (n=877)	2013 (n=967)	2014 (n=384)*	2015 (n=462)*	2016 (n=601)*
<b>Cefixime</b>	1	5	6	8	10	4	2	2	1
<b>Ceftriaxone</b>	<1	0	2	2	1	<1 (0.3)	<1 (0.3)	0	0
<b>Azithromycin</b>	13	6	12	11	10	13	9	10	3
<b>Ciprofloxacin</b>	63	75	56	55	62	53	60	53	53
<b>Spectinomycin</b>	0	0	0	0	0	0	0	0	0

**Unemo M, Jacobsson S, Lindroth Y, Fredlund H. SWEDRES 2016**

**\*No data from Stockholm area in SWEDRES**

# Antimicrobial resistance in the EU/EEA, 2004-2014



**Ceftriaxone resistance (1 isolate in 2015, 5 in 2014, and 7 in 2013)**

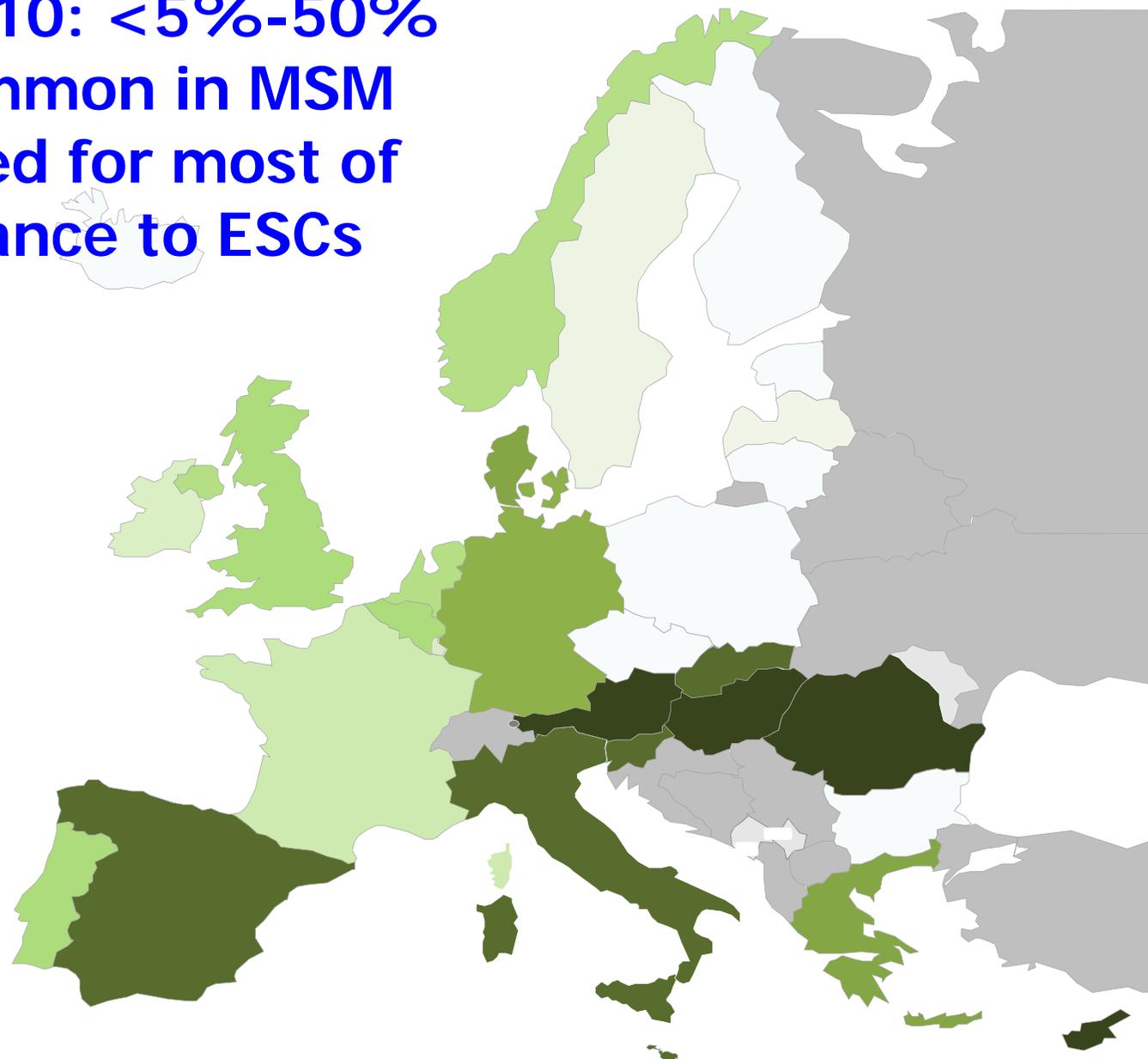
NG-MAST, *N. gonorrhoeae* multiantigen sequence type (*porB* and *tbpB*)

# NG-MAST G1407 in EU/EEA, 2009-2010



- 2009-2010: <5%-50%
- Most common in MSM
- Accounted for most of the resistance to ESCs

Non-participating countries



# NG-MAST G1407 in EU/EEA, 2009-2010

<5%

- 2009-2010: <5%-50%

5

## NG-MAST G1407:

1

- Spreading basically globally

2

- Multidrug-resistant and responsible for most resistance to ESCs

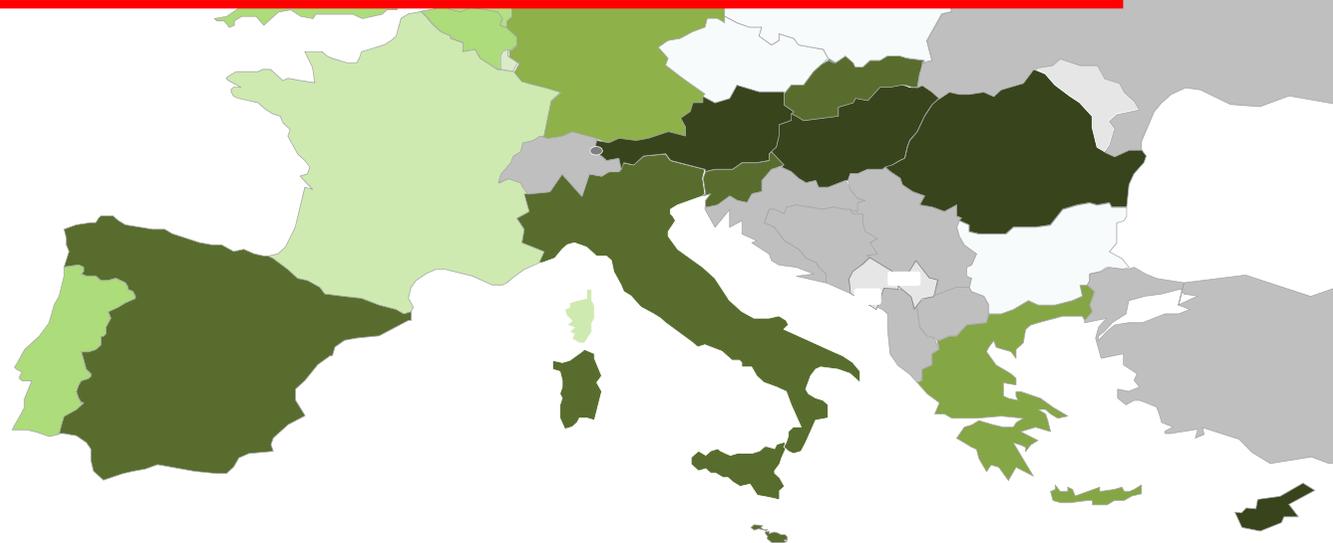
3

4

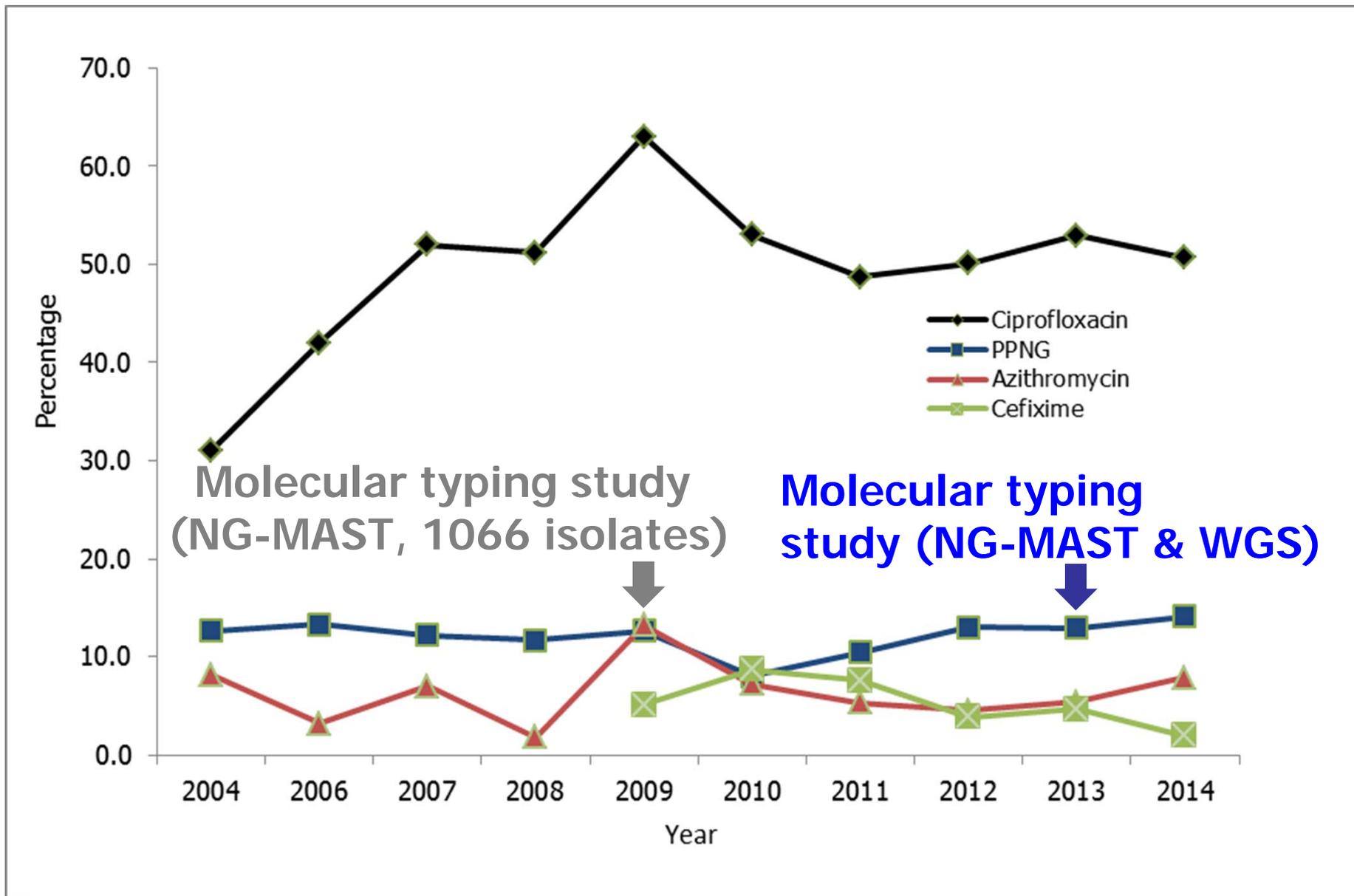
- Can develop high-level ceftriaxone resistance (F89 "superbug")

No

countries

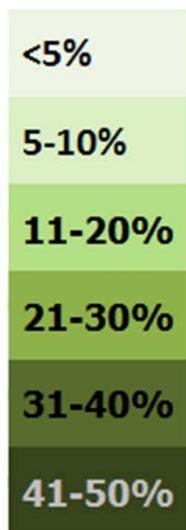


# Antimicrobial resistance in the EU/EEA, 2004-2014

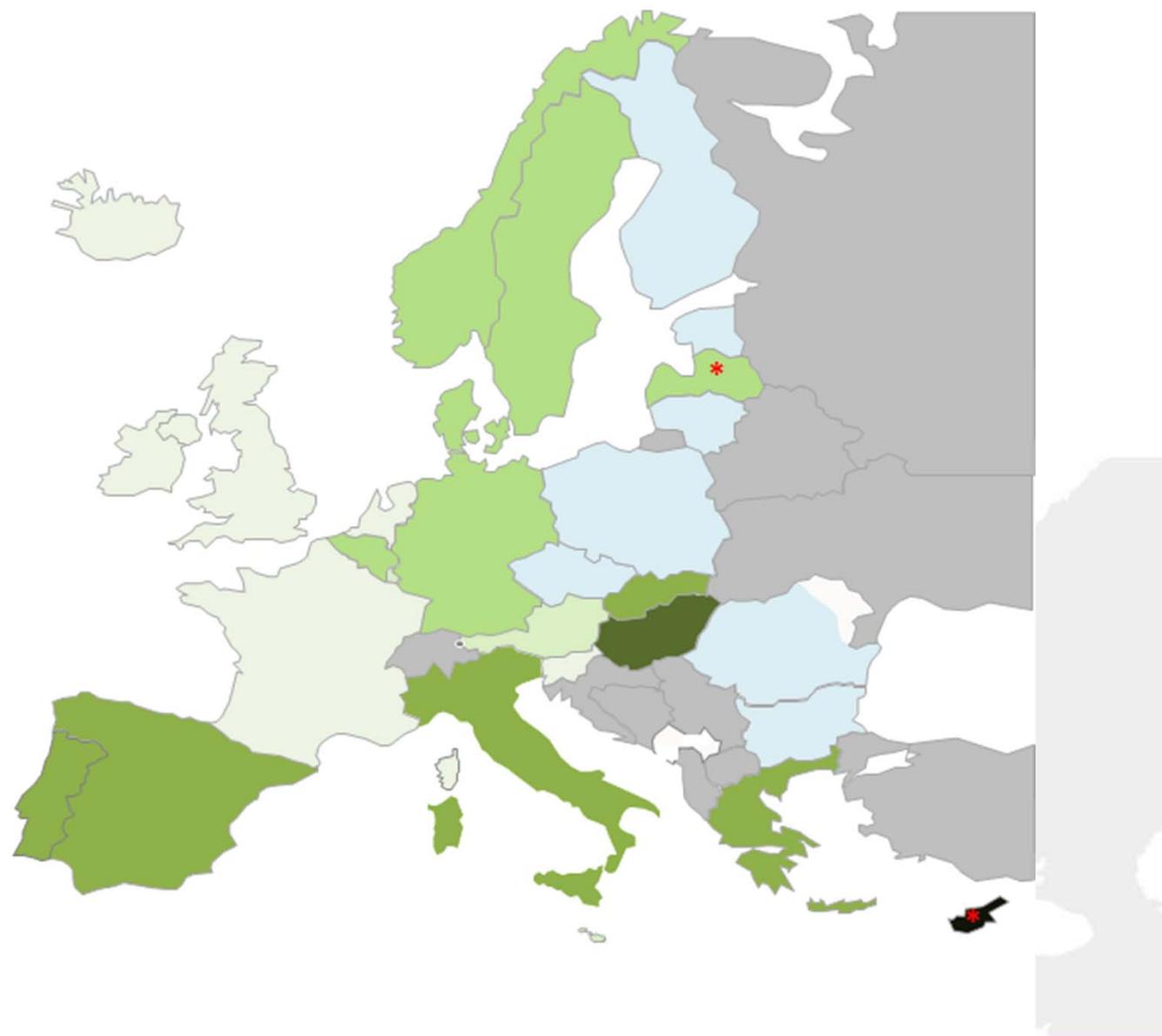


**Ceftriaxone resistance (1 isolate in 2015, 5 in 2014, and 7 in 2013)**

# NG-MAST G1407 in EU/EEA, 2013

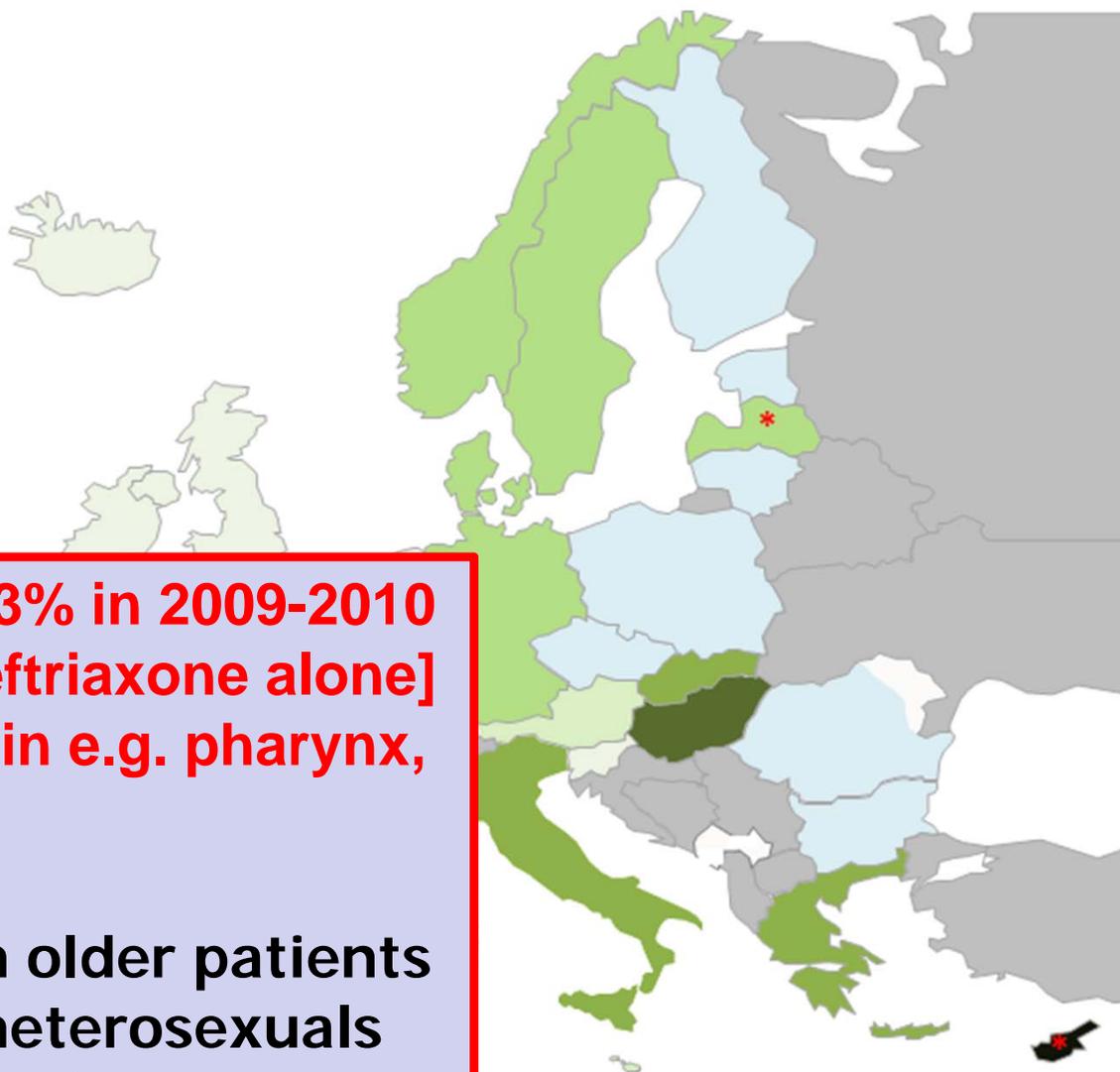
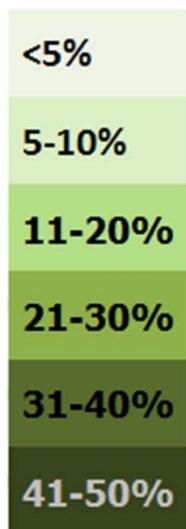


Non-participating countries



\* Low numbers of isolates tested

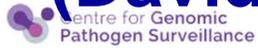
# NG-MAST G1407 in EU/EEA, 2013



- G1407: 15.4% versus 23.3% in 2009-2010 (effect of dual therapy [/ceftriaxone alone] targeting G1407 reservoir in e.g. pharynx, MSM?)

- G1407: associated with older patients (>45 years of age) and heterosexuals (more among MSM in 2010)

# User-friendly, open access NG WGS web tools at Sanger Institute (David Aanensen and Simon Harris)



## Whole Genome Sequence Analysis <http://www.wgsa.net/>

A web application for the processing, clustering and exploration of microbial genome assemblies.

Get started with *Staphylococcus aureus*



Upload genome assemblies and metadata, or view all publicly available genomes.



Generate results including MLST, AMR predictions, clustering of genomes, and interactive visualisation of metadata.

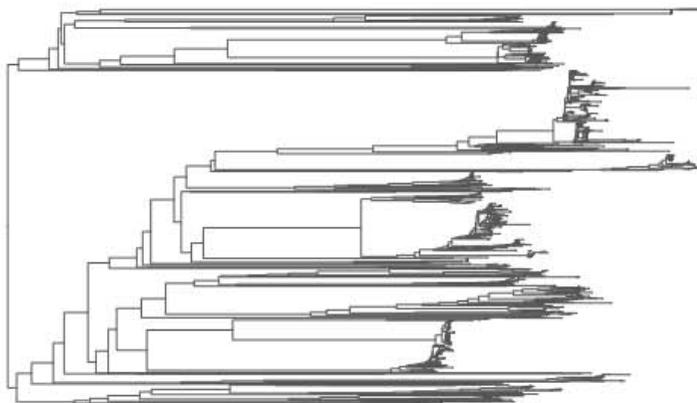


Compare results with publicly available genomes within a species reference tree.



# Links between the WGS and all metadata

Collection



HISTORY

346.27

Metadata Antibiotics SNPs Genes

	NAME	DATE	WGSA REFERENCE	ST	PROFILE	NG-MAST	POR	TBPB	CORE
	ECDC_CY13_005	28th June 2013	WHO_O_ST1902	6726	377_39_67_237_149_153_133	-	6332	189	1694
	ECDC_GE13_094	29th November 2013	WHO_O_ST1902	6726	377_39_67_237_149_153_133	11613	982	1992	1691
	ECDC_AT13_487	24th September 2013	WHO_O_ST1902	6726	377_39_67_237_149_153_133	11576	6783	189	1697
	ECDC_DK13_497	15th October 2013	WHO_O_ST1902	11177	109_39_764_237_148_153_65	1993	1257	6	1700

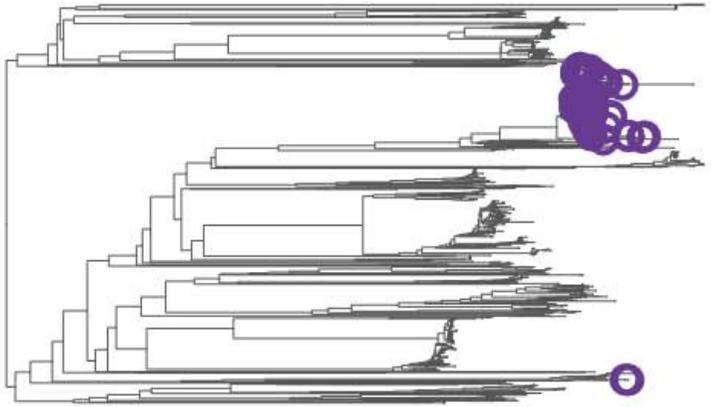
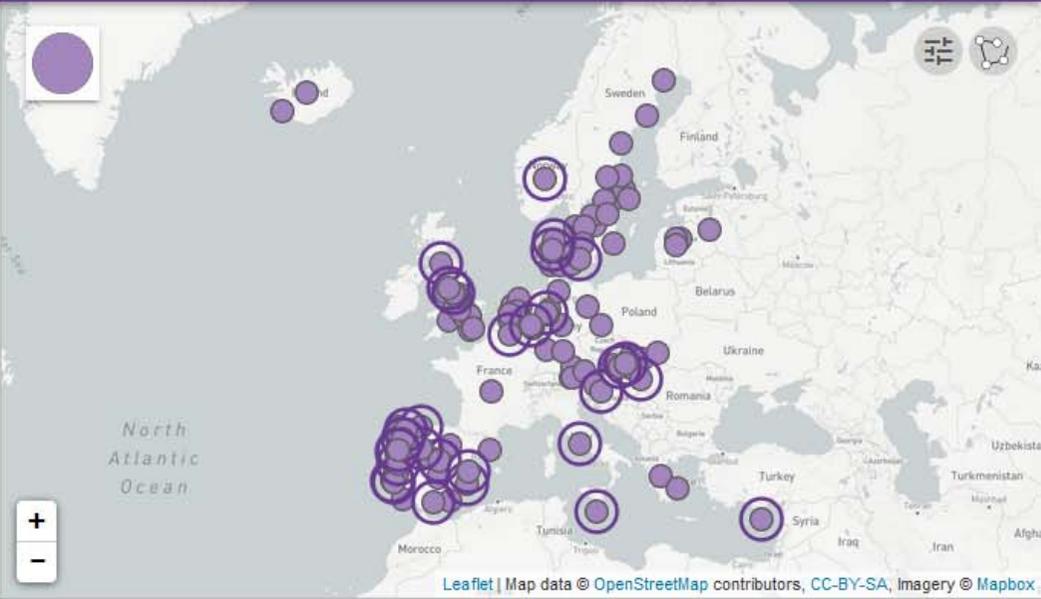


Leaflet | Map data © OpenStreetMap contributors, CC-BY-SA, Imagery © Mapbox

# NG-MAST STs and genogroups

WGSA 1407 78 of 1054 DOWNLOADS

Collection

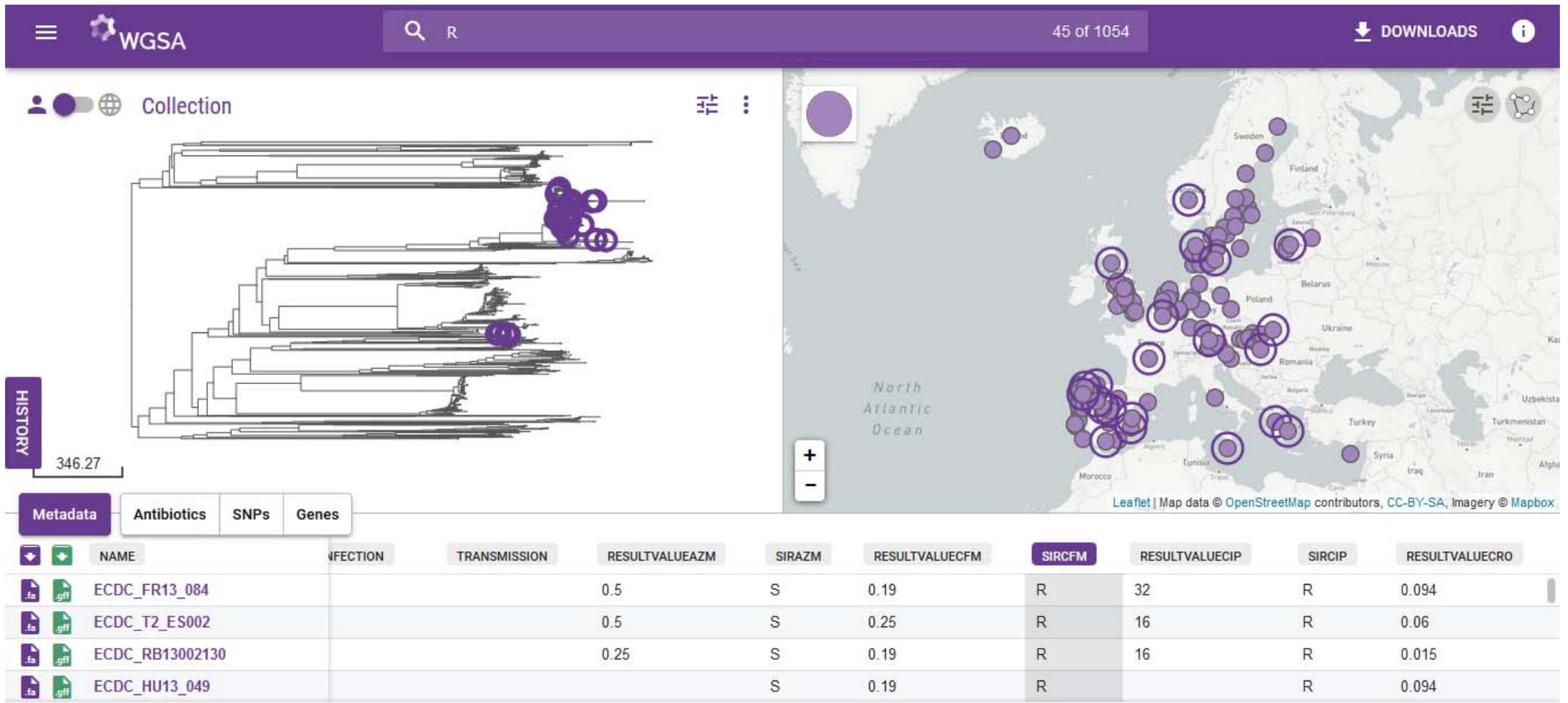
HISTORY 346.27

Metadata Antibiotics SNPs Genes

	NAME	DATE	WGSA REFERENCE	ST	PROFILE	NG-MAST	POR	TBPB	CORE MATCHES	% C
 	ECDC_DK13_482	15th October 2013	WHO_Y_ST1901	1901	109_39_170_111_148_153_65	1407	908	110	1705	99.6
 	ECDC_GC_062	18th September 2013	WHO_Y_ST1901	1901	109_39_170_111_148_153_65	1407	908	110	1705	99.6
 	ECDC_GC_063	18th September 2013	WHO_Y_ST1901	1901	109_39_170_111_148_153_65	1407	908	110	1705	99.6
 	ECDC_T2_ES002	4th April 2013	WHO_Y_ST1901	1901	109_39_170_111_148_153_65	1407	908	110	1705	99.6

Leaflet | Map data © OpenStreetMap contributors, CC-BY-SA, Imagery © Mapbox

# Cefixime resistance



# Antimicrobial resistance mutations

**Prediction of resistance/susceptibility** to sulphonamides, penicillin, tetracycline, spectinomycin, rifampicin, fluoroquinolones, azithromycin, and cephalosporins with relatively adequate sensitivity and specificity!

NAME	CIP					CRO				CFM					ponA1_				
	parC_	S88P	S87R	gyrA_	D95G	D95N	S91F	penA_	P551S	G545S	I312M	V316T	penA_	P551S	G545S	I312M	V316T	ponA1_	L421P
ECDC_FR13_084			●		●		●			●	●	●			●	●	●		●
ECDC_T2_ES002			●		●		●			●	●	●			●	●	●		●
ECDC_RB13002130			●		●		●			●	●	●			●	●	●		●
ECDC_HU13_049			●		●		●			●	●	●			●	●	●		●

## Main challenges with using WGS in Euro-GASP

- ~~Publically available, user-friendly web tool~~
- **Improve metadata reporting**, e.g. level, additionally city, previous and concurrent STI, sexual orientation..
- **Improve sampling** (no. and representativeness)
- WGS on **non-cultured specimens valuable!**
- **Quality assurance of WGS for future decentralised WGS** (2016 WHO reference strains)

# The novel 2016 WHO *Neisseria gonorrhoeae* reference strains for global quality assurance of laboratory investigations: phenotypic, genetic and reference genome characterization

Magnus Unemo<sup>1\*</sup>, Daniel Golparian<sup>1</sup>, Leonor Sánchez-Busó<sup>2</sup>, Yonatan Grad<sup>3,4</sup>, Susanne Jacobsson<sup>1</sup>, Makoto Ohnishi<sup>5</sup>,  
Monica M. Lahra<sup>6</sup>, Athena Limnios<sup>6</sup>, Aleksandra E. Sikora<sup>7</sup>, Teodora Wi<sup>8</sup> and Simon R. Harris<sup>2</sup>

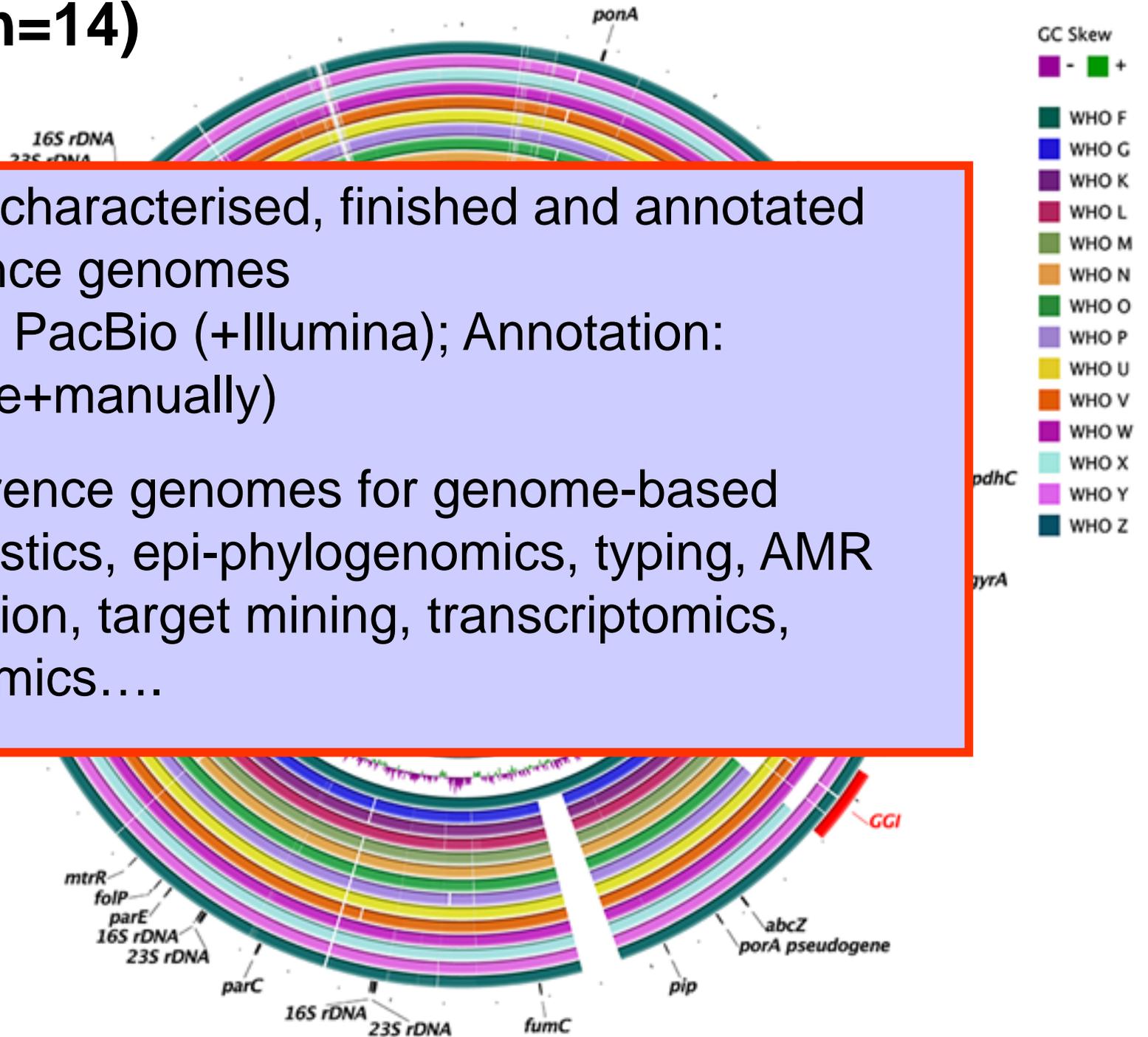
**J Antimicrob Chemother. 2016**

- Available AMR phenotypes for 20 antimicrobials (previous, current, and future treatment globally)
- All known genetic AMR determinants
- [Reference genomes](#)



# 2016 WHO NG reference strains – reference genomes (n=14)

- Fully characterised, finished and annotated reference genomes (WGS: PacBio (+Illumina); Annotation: pipeline+manually)
- Reference genomes for genome-based diagnostics, epi-phylogenomics, typing, AMR prediction, target mining, transcriptomics, proteomics....



**Performance of the MIC test strip (Liofilchem), M.I.C.Evaluators (Oxoid) and Ezy MIC strip (HiMedia) compared with the Etest for *N. gonorrhoeae***

**Jönsson A, Jacobsson S, Unemo M**

**In manuscript**

- **102 temporally, geographically and genetically diverse isolates**
- **All described AMR patterns and determinants**
- **Ceftriaxone, cefixime, azithromycin, spectinomycin, ciprofloxacin, penicillin G, tetracycline and gentamicin**

# Number of minor/major/very major errors (CLSI) in SIR category – HiMedia most errors and also several quality issues

<i>Antimicrobial</i>	<i>Liofilchem</i>	<i>Oxoid</i>	<i>HiMedia</i>
<i>Ceftriaxone<sup>±</sup></i>			
<i>Cefixime<sup>±</sup></i>			
<i>Azithromycin</i>			
<i>Spectinomycin</i>			
<i>Ciprofloxacin</i>			
<i>Penicillin G</i>			
<i>Tetracycline</i>			
<i>Gentamicin</i>			
<i>Total SIR categorical agreement %</i>			


**True MIC: <0.016 mg/L**

# Future treatment of gonorrhoea?

## ~~1. Increased doses of ceftriaxone~~

~~Limited time period (based on the MICs of *N. gonorrhoeae*  
Superbugs, pharmacodynamics and resistance emergence)!~~

## 2. Dual antimicrobial therapy

### **Already introduced first-line (when susceptibility unknown)**

- i) Ceftriaxone 250 mg + Azithromycin 1 g (USA<sup>1</sup> +Canada)
- ii) Ceftriaxone 500 mg + Azithromycin 1 g (UK<sup>2</sup> +Australia)
- iii) Ceftriaxone 500 mg + Azithromycin 2 g (Europe)<sup>3</sup>  
(Ceftriaxone 500 mg + Azithromycin 1.5 g [e.g. Germany])

**- Empirical treatment eradicating also Chlamydia, and many *M. genitalium* infections (useful in syndromic management)**

<sup>1</sup>CDC. MMWR. 2010, 2012 and 2014

<sup>2</sup>Bignell & Fitzgerald. Int J STD AIDS. 2011

<sup>3</sup>Bignell & Unemo. Int J STD AIDS. 2013

# Future treatment of gonorrhoea?

~~1. Increased doses of ceftriaxone~~

~~Limited time period (based on the MICs of *N. gonorrhoeae*~~

~~Superbugs, pharmacodynamics and resistance emergence)!~~

## 2. Dual antimicrobial therapy

### Effective, but for how long?

1. Already resistance to both antimicrobials

2. Too expensive (and inconvenient) for wide use in less-resourced settings

**3. First global treatment failure recently verified!**

many *M. genitalium* infections (useful in syndromic management)

<sup>1</sup>CDC. MMWR. 2010, 2012 and 2014

<sup>2</sup>Bignell & Fitzgerald. Int J STD AIDS. 2011

<sup>3</sup>Bignell & Unemo. Int J STD AIDS. 2013

# FIRST GLOBAL FAILURE OF DUAL ANTIMICROBIAL THERAPY IN TREATMENT OF GONORRHEA

**Fifer H, Golparian D, Natarajan U, Alexander S, Hughes G, Jones L, and Unemo M**

**New Engl J Med. 2016**

- **Ceftriaxone 500 mg×1 plus azithromycin 1 g×1**
- **Heterosexual male with pharyngeal gonorrhoea in United Kingdom, but infected in Japan**
- **XDR strain: Resistant to ceftriaxone, cefixime, azithromycin, penicillins, tetracyclines, and fluoroquinolones, but susceptible to spectinomycin**

## New treatment – use or repurpose old antimicrobials

- **Spectinomycin** – Valuable to have widely available again!
  - **Gentamicin** (Brown, et al. *STD*. 2010; Chisholm, et al. *JAC*. 2011; Dowell & Kirkcaldy. *PMJ*. 2013) – Rare bacterial resistance, but not 95% cure rate?
  - **Ertapenem** (Unemo, et al. *AAC*. 2012)? - Only *in vitro* data, affected by ESC resistance mechanisms, less promising?
  - **Fosfomycin** (Barbee et al. *JAC*. 2014; Hauser et al. *AAC*. 2015; Tesh et al. *IJAA*. 2015)? - Only recent *in vitro* data, rapid resistance selection, not 95% cure?
- More data crucial (clinical, extragenital site, PK/PD, selection of resistance, relationship genetics-MIC-treatment outcome, SIR breakpoints)  
⇒ none ideal, only considered for dual therapy?

# Recent or ongoing randomized clinical trials (uncomplicated gonorrhoea; Phase 2-3)

---

- **Gentamicin IM** (Ongoing; Phase 3 [Aim: 718 participants])

Gentamicin 240 mg versus ceftriaxone 500 mg

(azithromycin 1 g added to both arms)

- **Solithromycin oral** (Ongoing; Phase 3 [Aim: 300 participants])

Open-label, randomized, multi-center (Culture/NAATs: 7/21 days)

Solithromycin 1 g versus ceftriaxone 500 mg + azithromycin 1 g

- **AZD0914 oral** (Completed; Phase 2 [Aim: 180 participants])

Open-label, randomized, multi-center (Culture: 6 days)

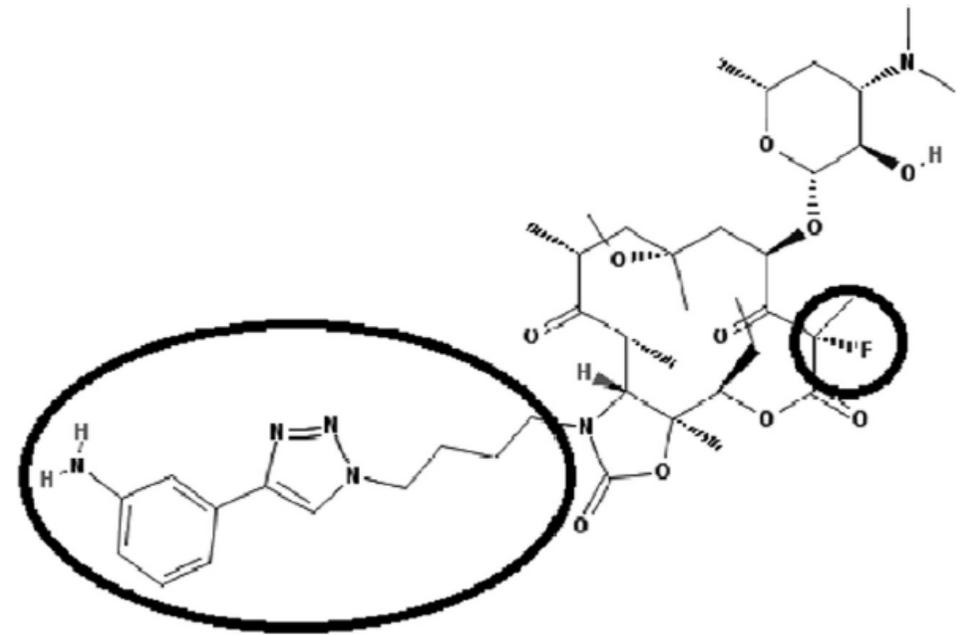
AZD0914 2 g (n=70) and AZD0914 3 g (n=70) versus

ceftriaxone 500 mg (n=40) – Results presented in Sept., 2016

- **Gepotidacin oral** (Ongoing; Phase 2 [Aim: 60 participants])

Open-label, randomized, multi-center, dose-ranging (Culture: 4-8 days)

Gepotidacin 1.5 g and gepotidacin 3 g



## Solithromycin (CEM-101)

- First fluoroketolide (class: macrolides)
- 3 ribosomal (23S rRNA) targets ( $\uparrow$  activity +  $\downarrow$  resistance)
- **AZM MIC > 256 mg/L (23S rRNA A2059G)  $\Rightarrow$  SOLI MIC = 4-32 mg/L (resistance!) ( $\uparrow$  MtrCDE and NorM  $\Rightarrow$  increased MIC)**  
(Golparian et al. AAC. 2012)
- Oral, single dose (well absorbed, high tissue distribution, and safe; Still et al. AAC. 2011)
- Effective *in vitro* against *C. trachomatis* and *M. genitalium*  
(Roblin et al. AAC. 2010; Jensen et al. AAC. 2014)

# A Phase 2 Trial of Oral Solithromycin 1200 mg or 1000 mg as Single-Dose Oral Therapy for Uncomplicated Gonorrhea

Edward W. Hook III,<sup>1</sup> Matthew Golden,<sup>2</sup> Brian D. Jamieson,<sup>3</sup> Paula B. Dixon,<sup>1</sup> Hanne S. Harbison,<sup>1</sup> Sylvan Lowens,<sup>2</sup> and Prabhavathi Fernandes<sup>3</sup>

**Clin Infect Dis. 2015**

Men and women (n=59) with uncomplicated urogenital infection

**Table 2. Microbiologic Outcomes Following Solithromycin Therapy for Uncomplicated Gonorrhea<sup>a</sup>**

**100% eradication of NG in culture**

Organism and Site	Solithromycin 1200 mg (n = 24)		Solithromycin 1000 mg (n = 22)	
	Culture	NAAT	Culture	NAAT
<i>Neisseria gonorrhoeae</i>				
Urogenital	22/0	23/2	20/0	20/4
Rectal	2/0	9/0	2/0	11/0
Throat	5/0	9/3	3/0	7/1
<b>Total</b>	<b>29/0</b>	<b>41/5</b>	<b>25/0</b>	<b>37/5</b>
<i>Chlamydia trachomatis</i>				
Urogenital	NA	8/1	NA	2/1
Rectal	NA	1/0	NA	1/0

Outcomes are shown as positive at enrollment/positive at follow-up. **7(-10) days**

**Mycoplasma genitalium: 10/3**

**Table 4. Adverse Events and Laboratory Abnormalities Among Participants Receiving Oral Solithromycin 1200 mg or 1000 mg**

Adverse Event	Solithromycin 1200 mg (n = 28), No. (%)	Solithromycin 1000 mg (n = 31), No. (%)
<b>Gastrointestinal</b>		
Diarrhea	17 (61)	13 (42)
Nausea	9 (32)	8 (26)
Vomiting	4 (14)	1 (3)
Abdominal pain	3 (11)	2 (7)
<b>Neurologic</b>		
Dysgeusia	2 (7)	2 (7)
Somnolence	0	1 (3)
<b>General</b>		
Fatigue/asthenia	0	3 (10)
<b>Dermatologic</b>		
Cutaneous papules	1 (4)	0
Pruritus	0	1 (3)

- Dose-related events  $\Rightarrow$  1 g in Phase 3 trial!

# Recent or ongoing randomized clinical trials (uncomplicated gonorrhoea; Phase 2-3)

## - **Solithromycin oral** (Ongoing; Phase 3 [Aim: 300 participants])

- Open-label, randomized, multi-centre (Culture/NAATs: 7/21 days)

- **Solithromycin 1 g** versus ceftriaxone 500 mg + azithromycin 1 g

**A) Initial patient cohort (262 patients): failure to demonstrate non-inferiority to dual therapy (91.3% cure rate compared to 100%) – no bacterial resistance (↑ dose [adverse effects], formula?)?**

**B) Hepatotoxicity? Synergistic toxicity in dual therapy?**

(<http://investor.cempra.com/releasedetail.cfm?ReleaseID=1014807>)

## - **Zoliflodacin oral** (Completed; Phase 2 [Aim: 180 participants])

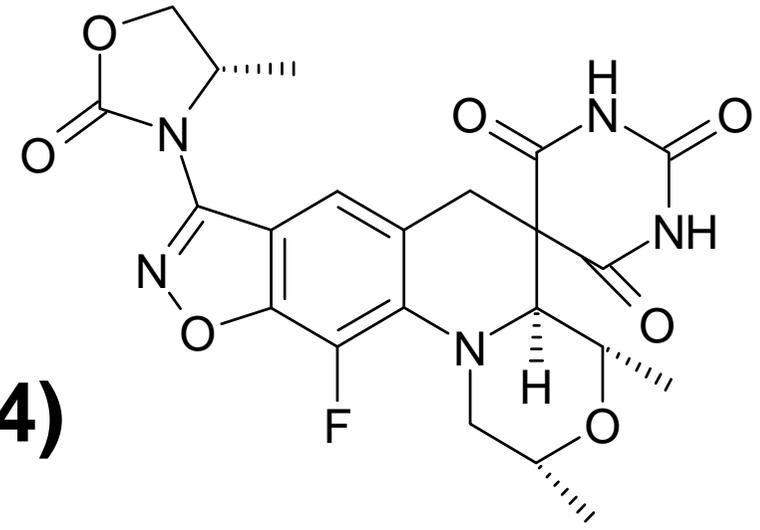
- Open-label, randomized, multi-centre (Culture: 6 days)

- **Zoliflodacin 2 g** (n=70) and **zoliflodacin 3 g** (n=70) versus ceftriaxone 500 mg (n=40) - **Promising (100% cure rate with 3 g and 98% with 2 g), despite not final formulation of zoliflodacin!**

## - **Gepotidacin oral** (Completed; Phase 2 [Aim: 60 participants])

Open-label, randomized, multi-centre, dose-ranging (Culture: 4-8 days)

**Gepotidacin 1.5 g and gepotidacin 3 g – Results not publically available!**



## Zoliflodacin (AZD0914, ETX0914)

- Spiropyrimidinetrione
- Dual DNA topoisomerase II inhibitor (target(s): GyrB!+ParE?)? - no resistance or resistance mutations in clinical isolates (Jacobsson et al. AAC. 2014; Unemo et al. AAC. 2015; Papp et al. IJAA. 2016)
- Oral, single dose
- Good tissue penetrance and bioavailability, and sufficiently high safety and tolerability, i.e. 200 mg to 4 g well tolerated (Lawrence et al. ICAAC. 2014)
- Effective *in vitro* against *C. trachomatis* and *M. genitalium*?

# A phase II trial of single-dose oral ETX0914 (AZD0914) for treatment of uncomplicated urogenital gonorrhea

Taylor SN, Marrazzo J, Batteiger BE, Hook EW, Seña AC, Wierzbicki MR, Kwak H, Johnson SM, Lawrence K, Mueller J. **CDC STD Prevention meeting. Sept. 2016**

---

## **Microbiological cure:**

- 48/49 (**98%**) with **zolidodacin 2 g**
- 47/47 (**100%**) with **zolidodacin 3 g**
- 21/21 (100%) with ceftriaxone 500 mg

## **Zolidodacin well tolerated:**

21/179 (12%) reporting 20 mild and 1 moderate adverse events (mostly gastrointestinal)

- **More pharyngeal infections required!**

# Ongoing or very recent randomized clinical trials (uncomplicated gonorrhoea; Phase 2-3)

- **Solithromycin oral** (Ongoing; Phase 3 [Aim: 300 participants])
  - Open-label, randomized, multi-centre (Culture/NAATs: 7/21 days)
  - Solithromycin 1 g versus ceftriaxone 500 mg + azithromycin 1 g
  - A) Evaluating initial patient cohort (262 patients): failure to demonstrate non-inferiority to dual therapy (91.3% cure rate for microbiologically evaluable compared to 100%) – no bacterial resistance but duration of solithromycin exposure at infection site suboptimal (↑ dose?)?
  - B) Hepatotoxicity with single dose? Synergistic toxicity in dual therapy?  
(<http://investor.cempra.com/releasedetail.cfm?ReleaseID=1014807>; 28 Feb)
- **Zoliflodacin oral** (Completed; Phase 2 [Aim: 180 participants])
  - Open-label, randomized, multi-centre (Culture: 6 days)
  - **Zoliflodacin 2 g** (n=70) and **zoliflodacin 3 g** (n=70) versus ceftriaxone 500 mg (n=40) - **Promising (100% cure rate with 3 g and 98% with 2 g), despite not final formulation of zoliflodacin ⇒ Phase 3 planned with 3 g, optimized formulation, and also pharyngeal and rectal infections**
- **Gepotidacin oral** (Completed; Phase 2 [Aim: 60 participants])
  - Open-label, randomized, multi-centre, dose-ranging (Culture: 4-8 days)

# Analysis of agar dilution MIC testing methods and variables and *in vitro* activity of Gepotidacin (GSK2140944) against *Neisseria gonorrhoeae*

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- Novel triazaacenaphthylene antimicrobial (DNA topoisomerase II inhibitor (Target(s): GyrA!, ParC?))
- MIC<sub>50</sub> and MIC<sub>90</sub> in 145 *N. gonorrhoeae* isolates: 0.25 mg/L and 0.5 mg/L, respectively
- 108 CIP-S MIC<sub>90</sub> of 0.25 mg/L vs. 37 CIP-NS MIC<sub>90</sub> of 1 mg/L (highest MIC recorded) – Cross-resistance?

**Scangarella-Oman et al. ASM Microbe. 2016. Abstract**

**Large *in vitro* evaluation addressing MDR and cross-resistance just finished (Unemo et al)!**

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  - Gepotidacin 1.5 g** and **gepotidacin 3 g** – **Results cannot be shared yet!**

# Conclusions

- AMR in *N. gonorrhoeae* widespread globally, azithromycin resistance increases rapidly but ESC resistance has decreased in many countries (effect of dual therapy (/ceftriaxone) targeting NG-MAST G1407?)
- Increased quality assured AMR surveillance crucial in many settings
- WGS, including AMR prediction, linked to AMR and metadata significantly strengthen the AMR surveillance in *N. gonorrhoeae*, nationally and internationally
- New antimicrobials essential, and solithromycin, gepotidacin and particularly zoliflodacin promising (in dual therapy!)
- The fight not lost but a vaccine only sustainable solution?

Women's Soccer World Cup 2015: Official Swedish slogan

#KLAPPAFÖRSVERIGE  
#CLAPFORSWEDEN



"The clap" = nickname of gonorrhoea since the 16th century