

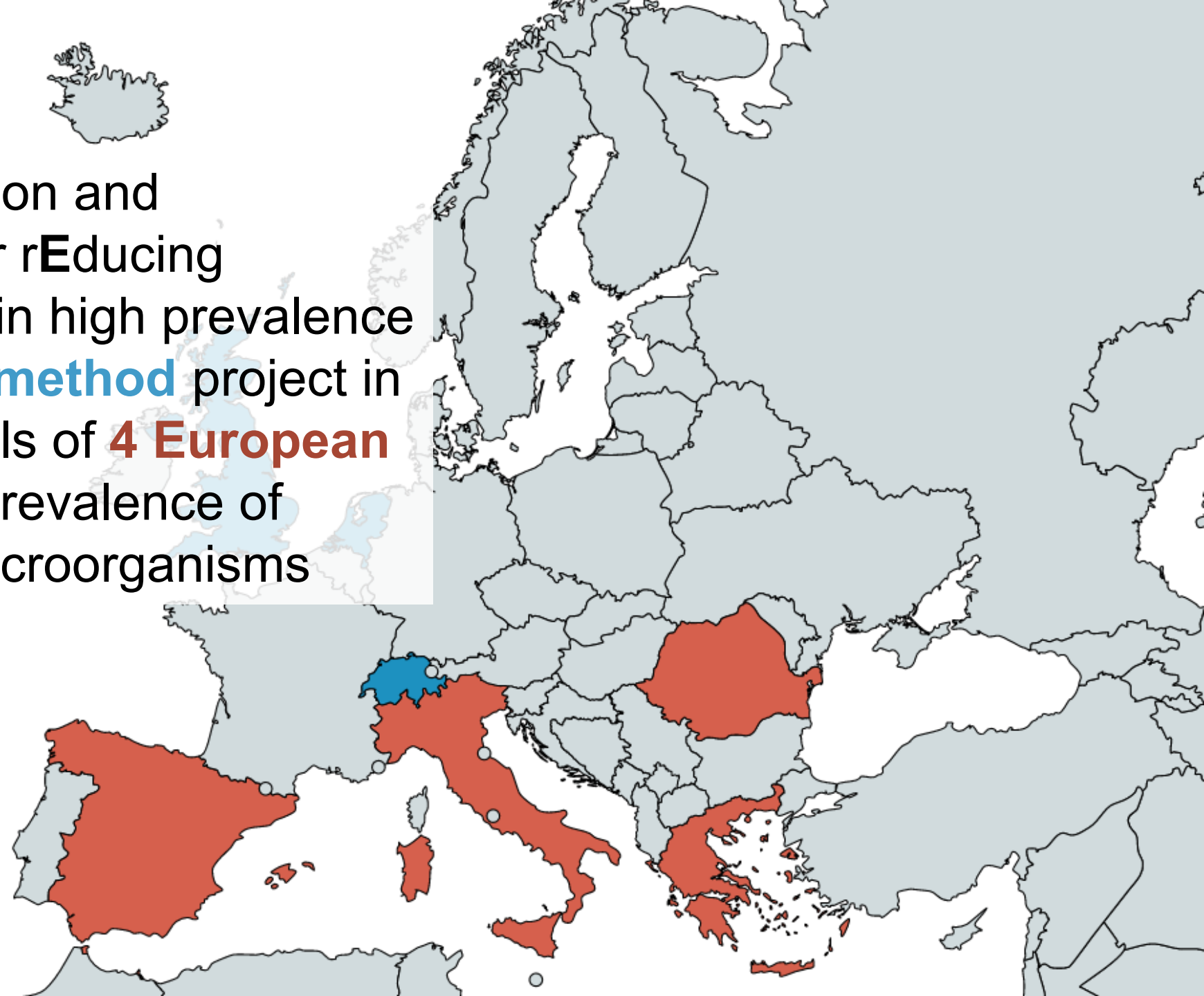
REVERSE Kick-Off Meeting, 17 September, Geneva, Switzerland

“REVERSE” antimicrobial resistance

(pREvention and management tools for rEducing antibiotic Resistance in high prevalence SEttings)

Walter Zingg, PD MD

REVERSE (pREVEntion and management tools for rEDucing antibiotic REsistance in high prevalence SETtings) is a **mixed-method** project in **24** acute care hospitals of **4 European countries** with high prevalence of multidrug-resistant microorganisms



Background

3.8 million (95%CI: 3.1–4.5 million) patients acquired a healthcare-associated infection each year in European acute care hospitals

Antimicrobial resistance to selected resistance markers was 31.6% in 2016/2017

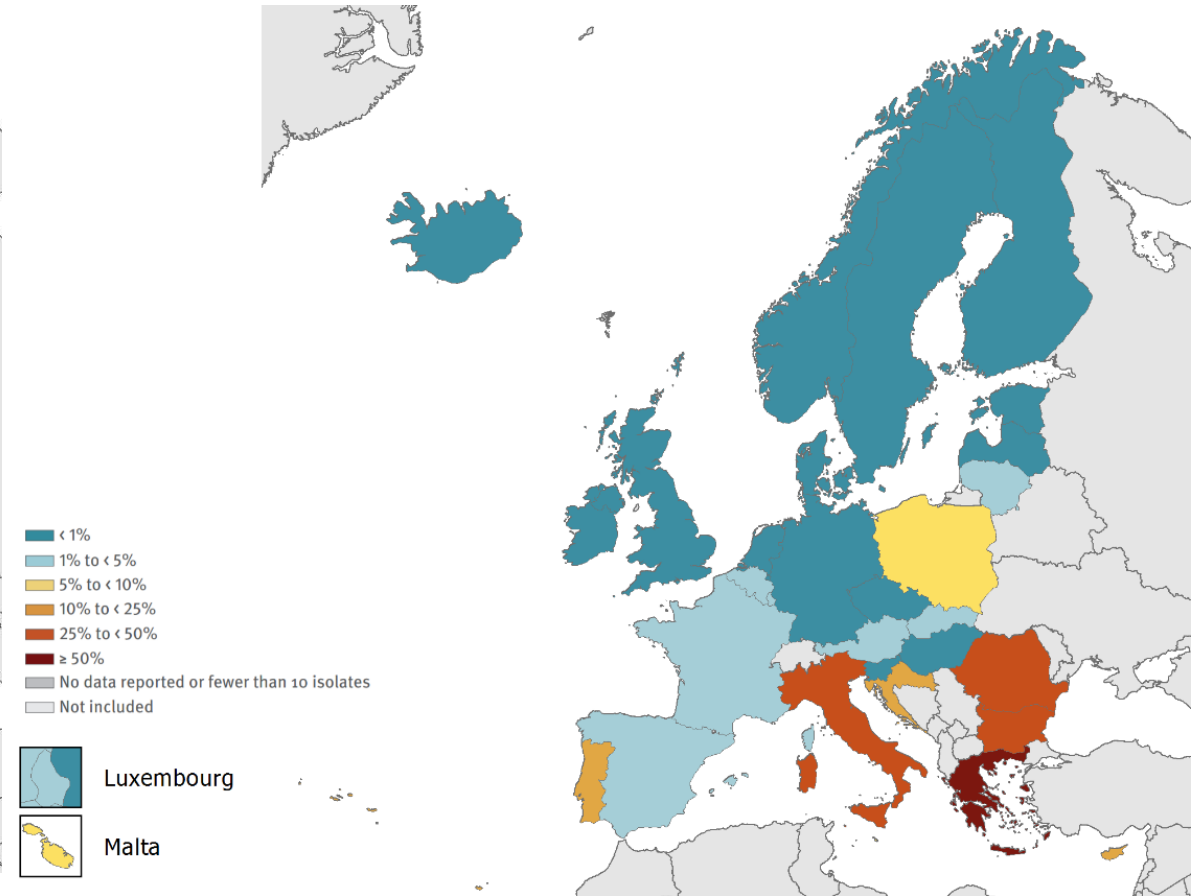
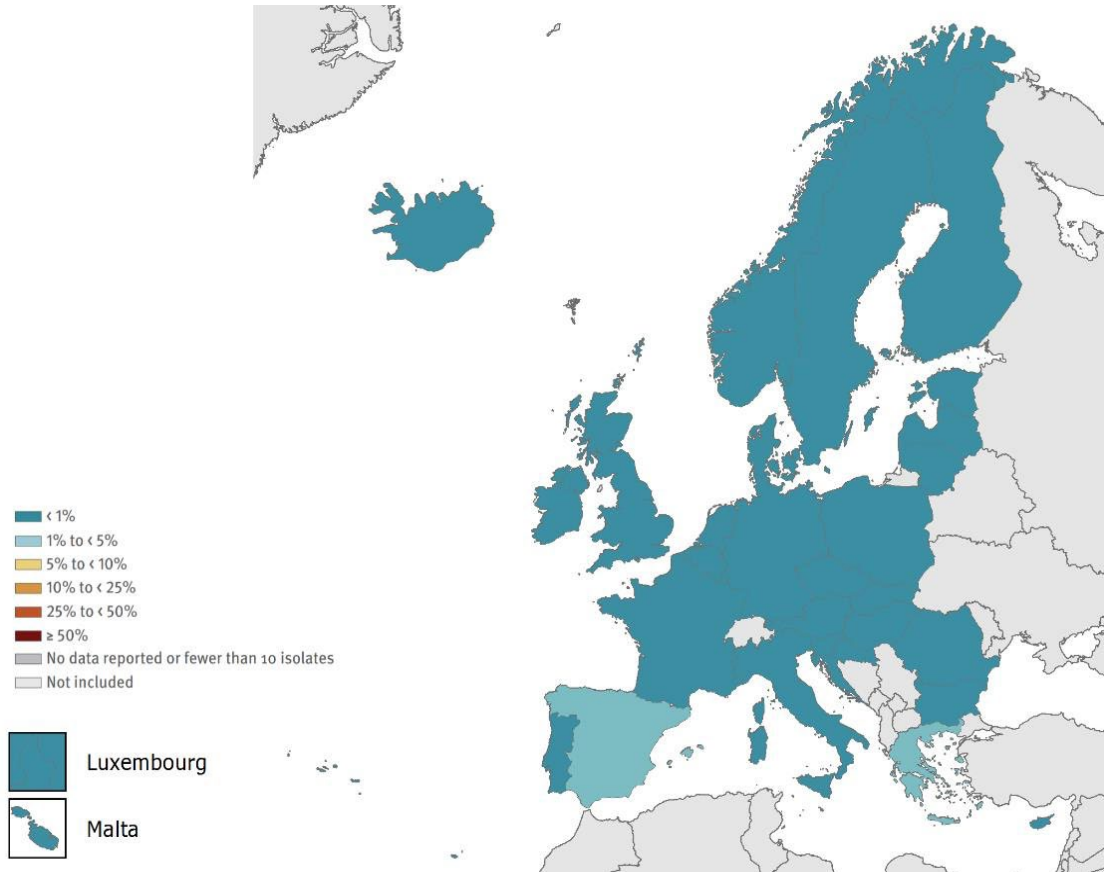
Prevalence, incidence, yearly cases

Switzerland – REVERSE countries

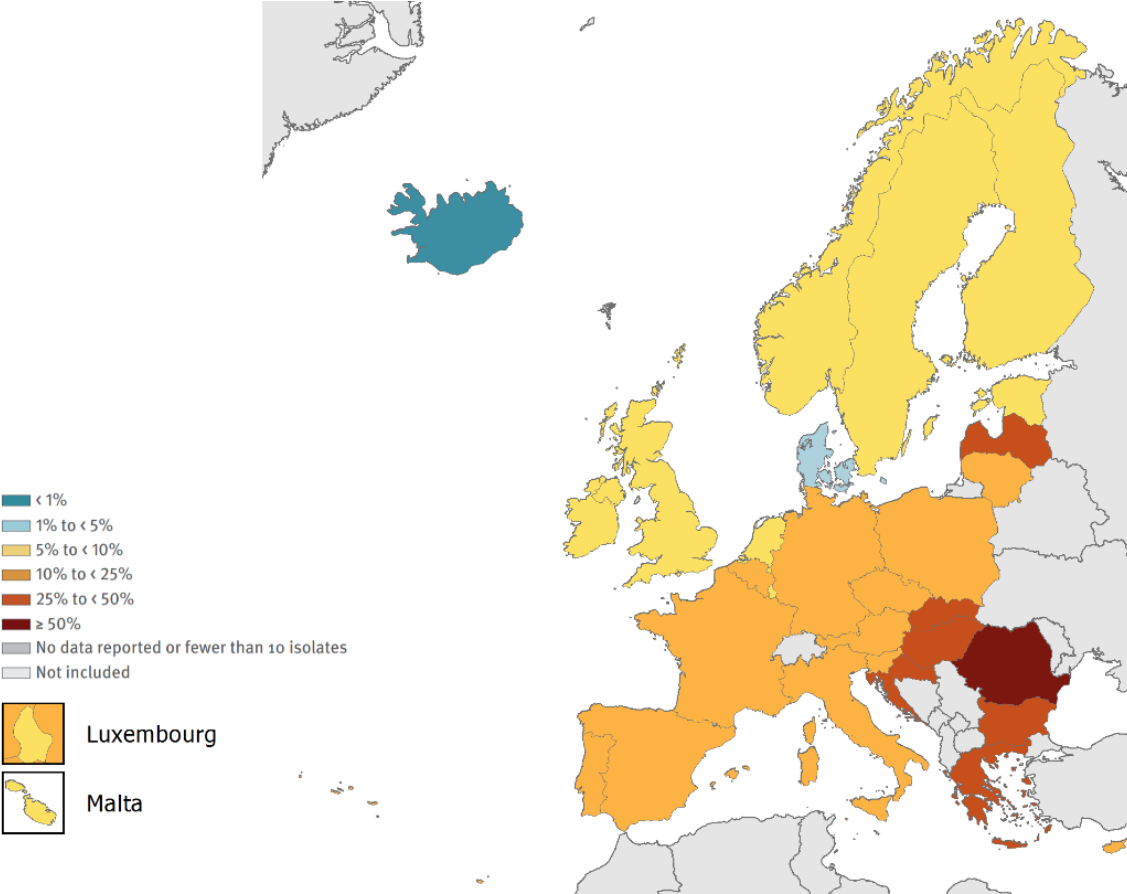
Country	Prevalence % (CI95%)	Incidence % (CI95%)	Cases N (CI95%)
Switzerland	5.9 (5.5–6.3)	4.5 (3.7–5.2)	59'100 (49'338–68'862)
Greece	10.0 (8.5–11.6)	4.3 (3.1–5.7)	66,487 (48,386–89,068)
Italy	8.0 (6.8–9.59)	6.0 (4.2–8.3)	534'709 (373'705–740'544)
Romania	3.6 (2.8–4.7)	2.6 (1.7–4.0)	97,257 (62,340–146,893)
Spain	7.8 (7.1–8.5)	4.9 (3.6–6.4)	255,169 (186,398–335,644)

Carbapenem-resistant *E. coli*

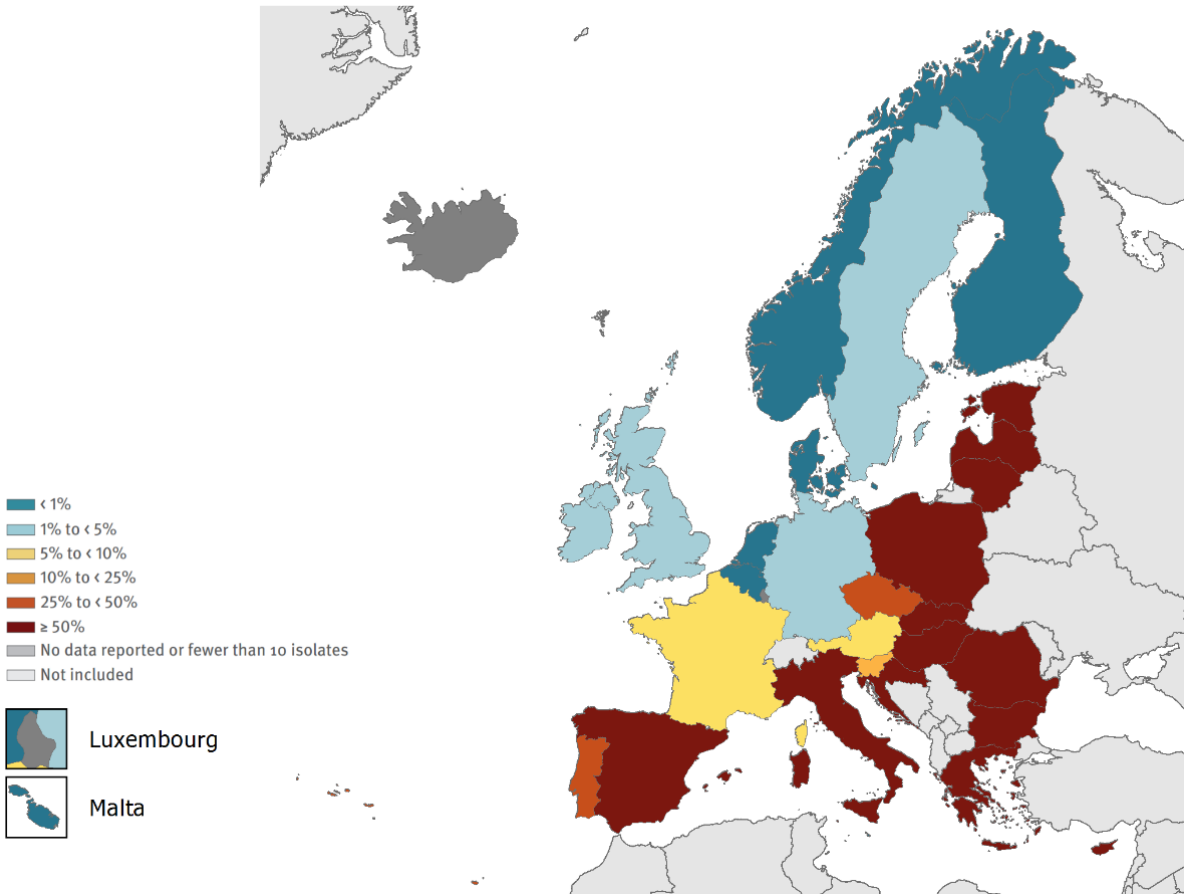
Carbapenem-resistant *K. pneumoniae*



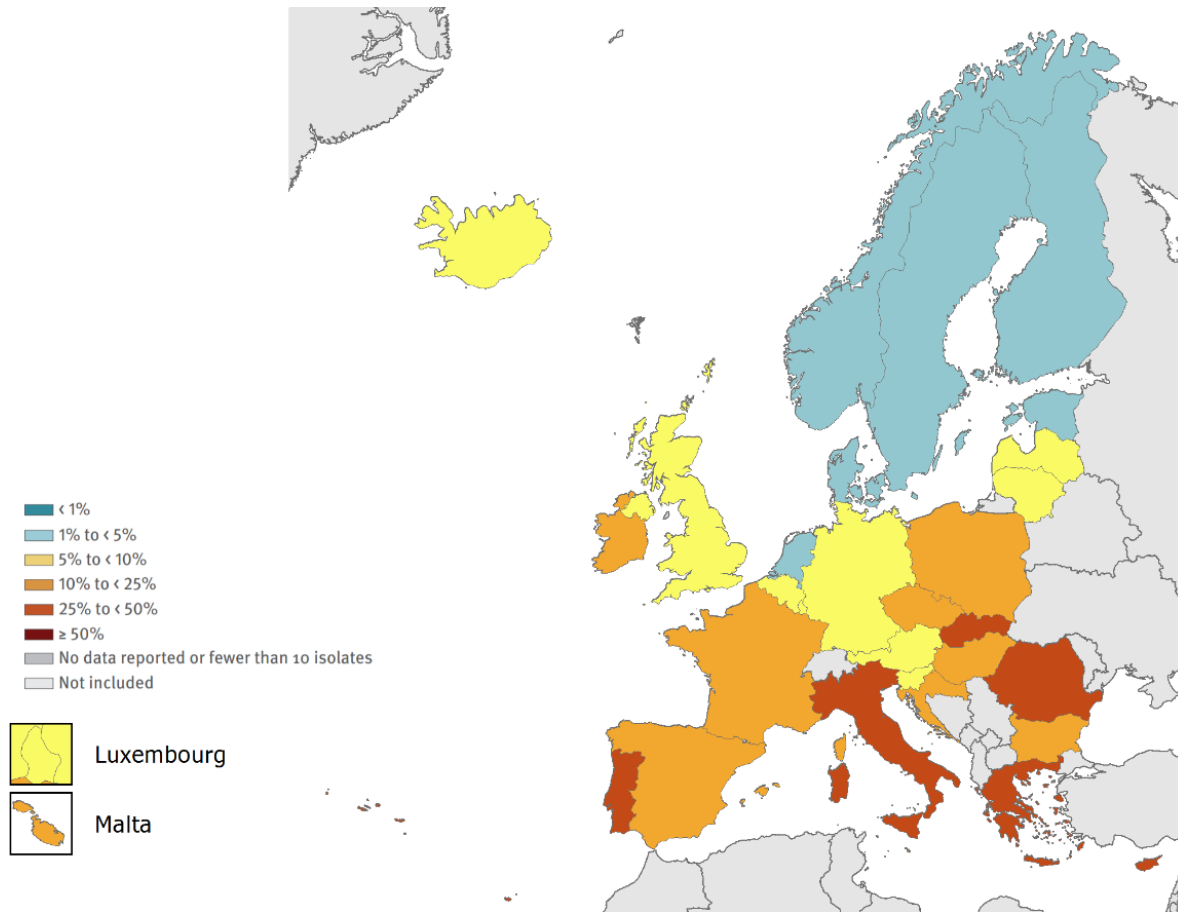
Carbapenem-resistant *P. aeruginosa*



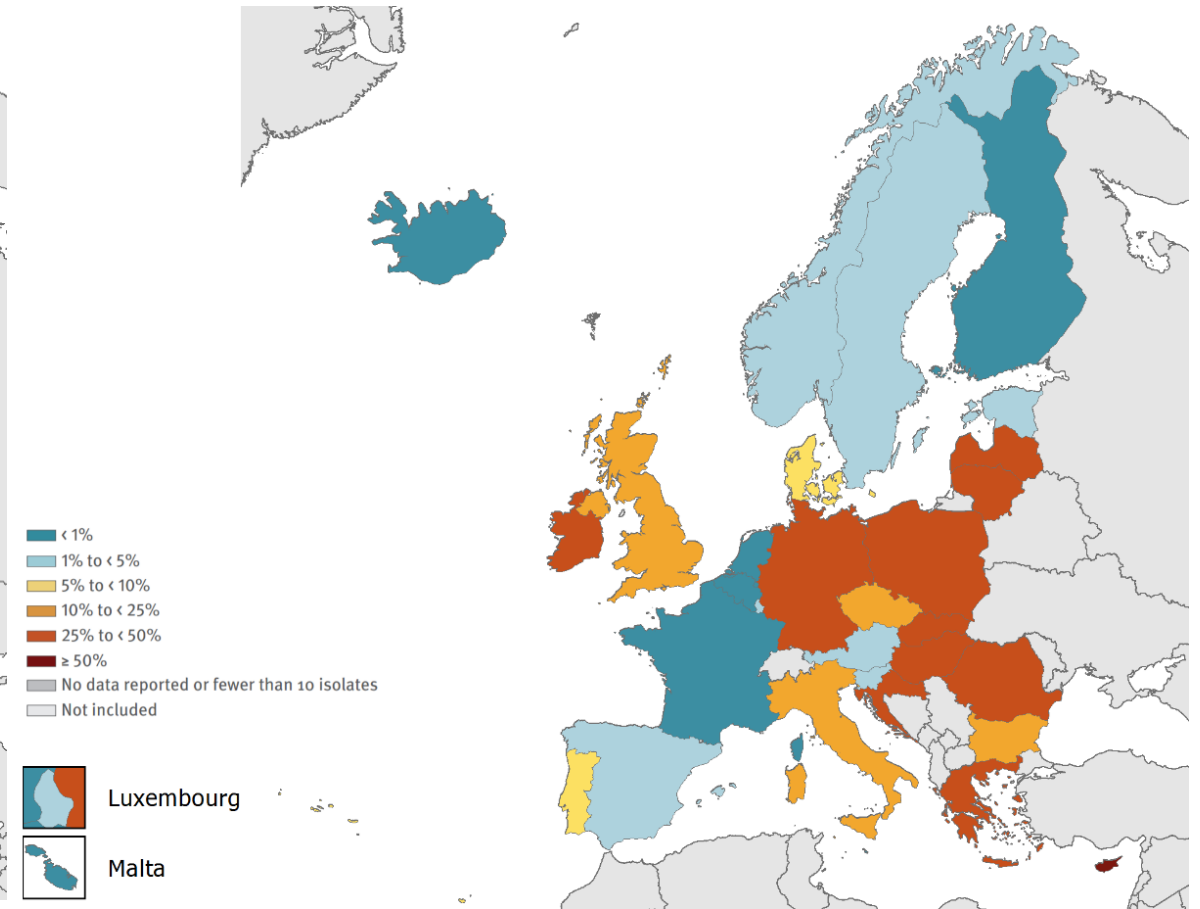
Carbapenem-resistant *A. baumannii*



Methicillin-resistant *S. aureus*



Vancomycin-resistant *E. faecium*



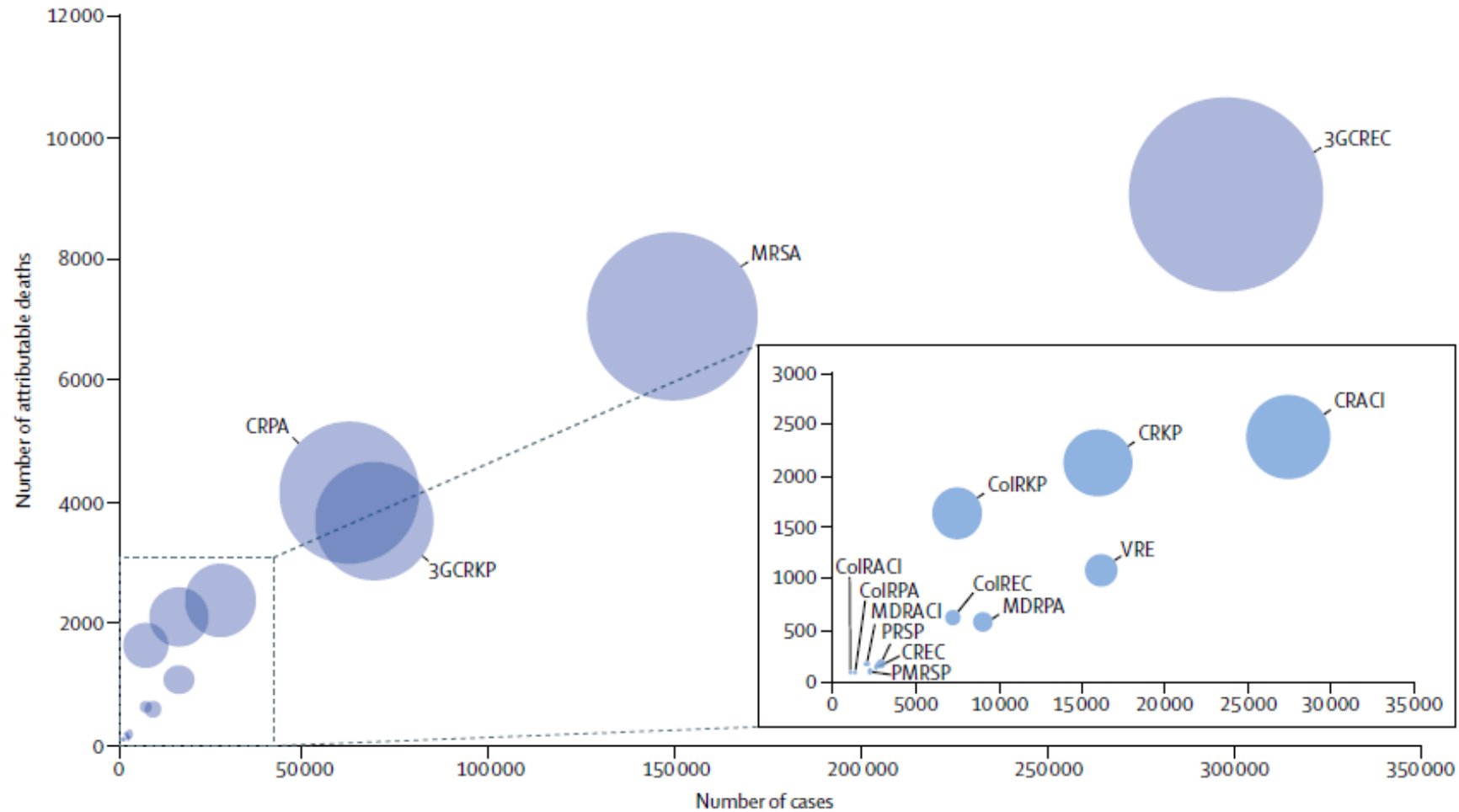
Composite index* of antimicrobial resistance in healthcare-associated infections

Switzerland – REVERSE countries, 2016/2017

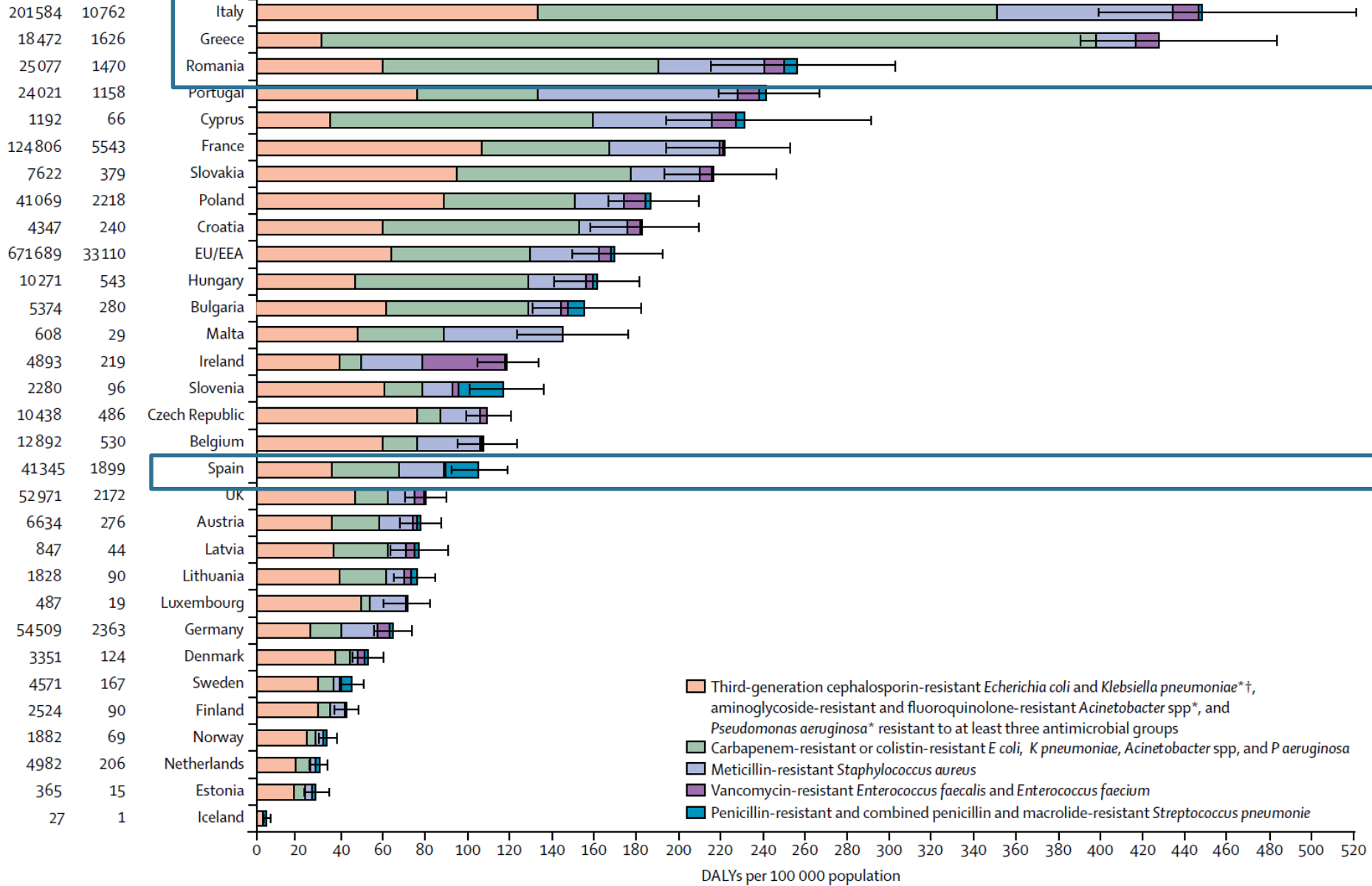
Country	Tested cases N	Composite index % (CI95%)
Switzerland	494	15.6% (12.4–18.8)
Greece	456	61.2%
Italy	555	42.3%
Romania	164	68.9%
Spain	926	26.6%

*MRSA, VRE, Enterobacteriaceae resistant to 3rd generation cephalosporins, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* resistant to carbapenems

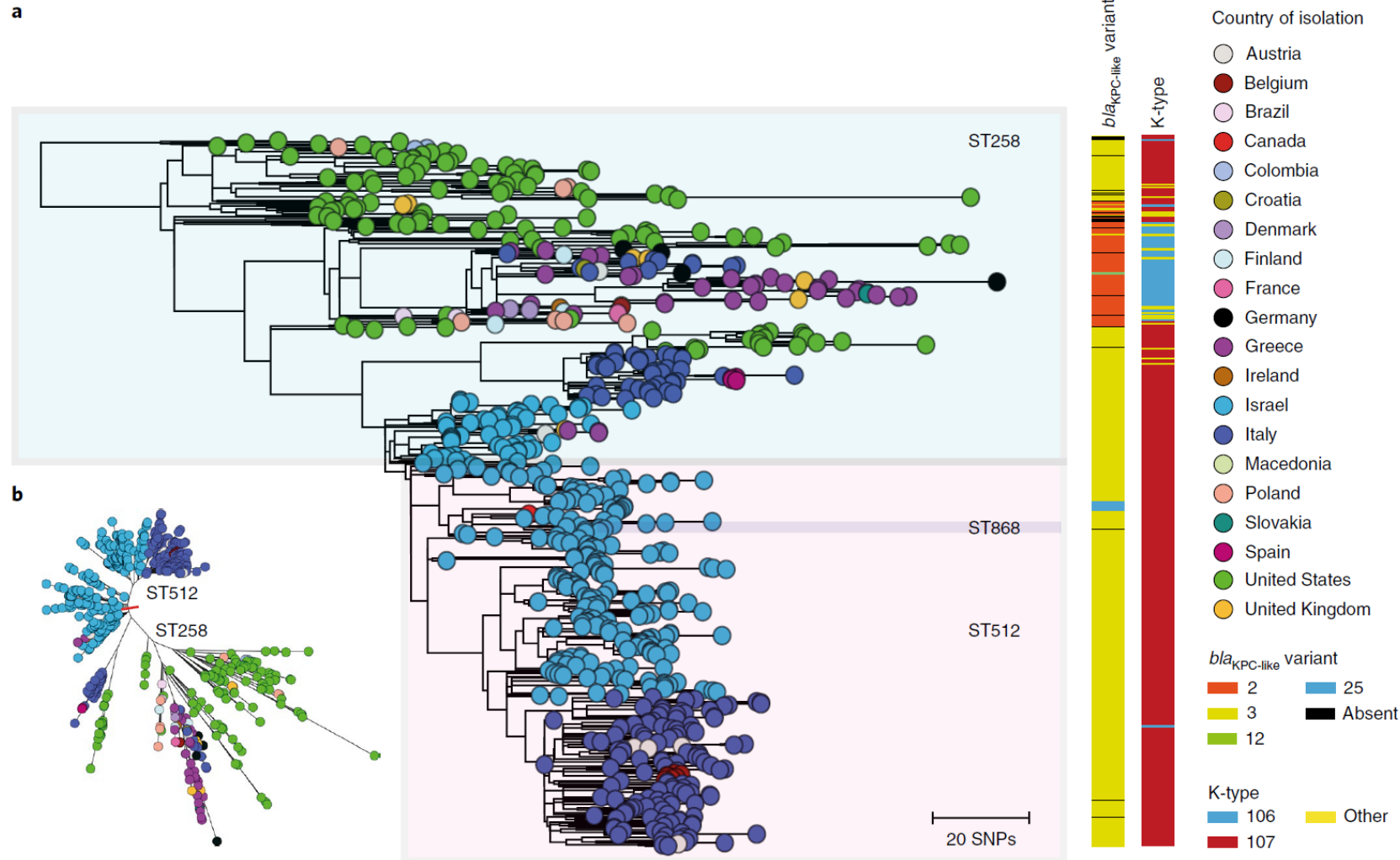
Burden healthcare-associated infections due to antibiotic-resistant microorganisms



Cases (median) Deaths (median)

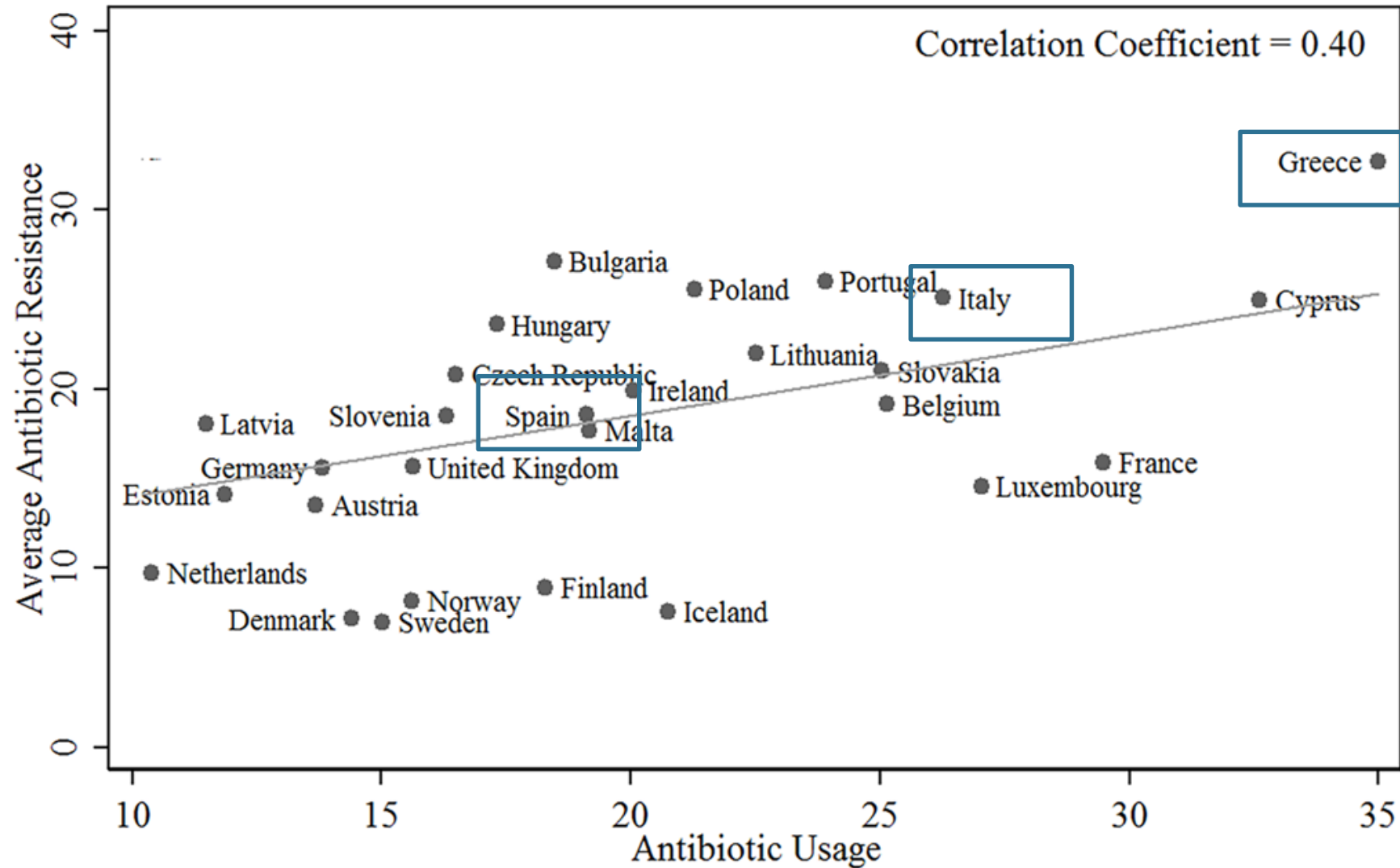


Hospital transmission is a driver for emerging resistance...

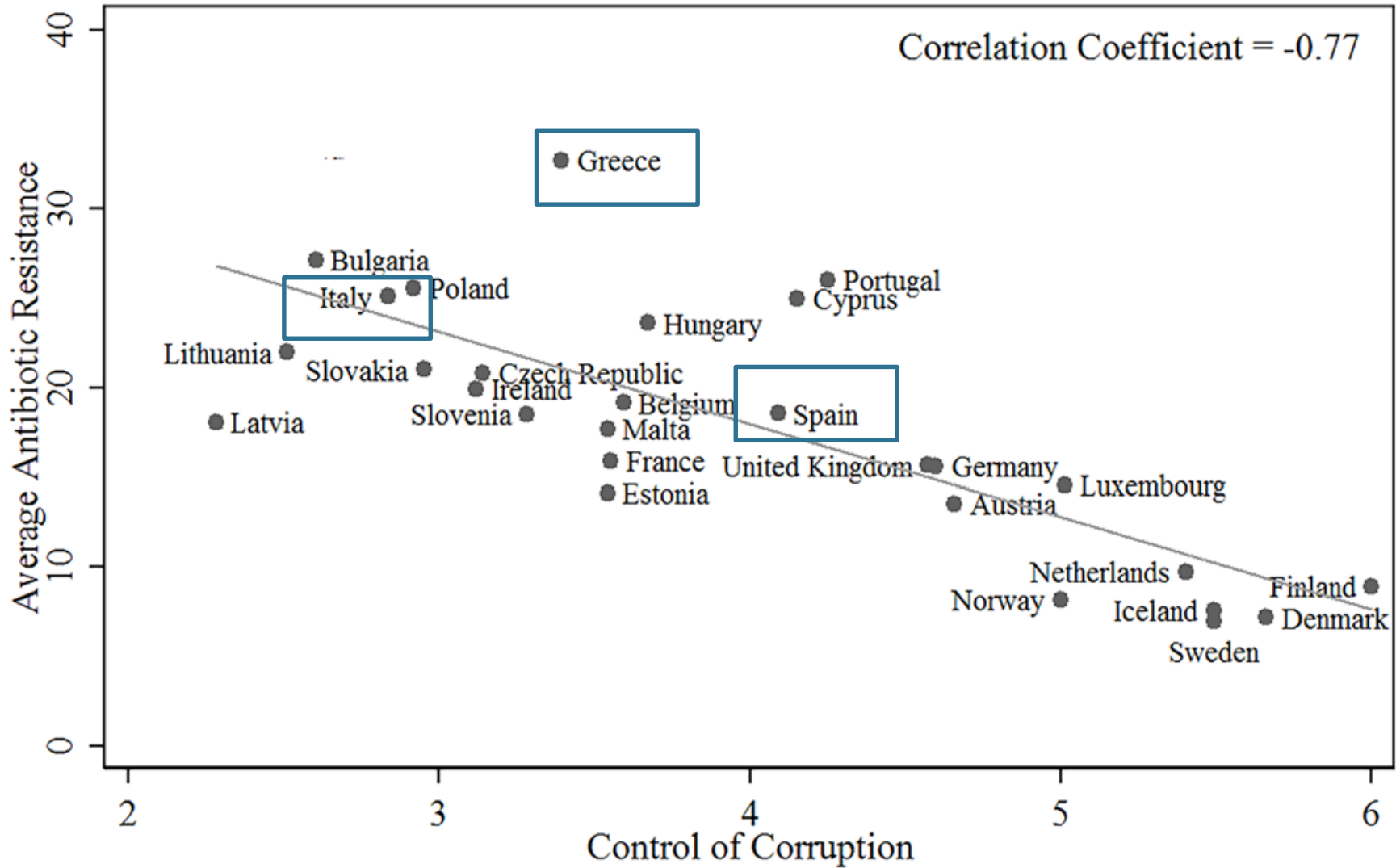


Over half of the hospitals that contributed carbapenemase-positive isolates to the study experienced hospital transmission, and interhospital spread was far more frequent within, rather than between, countries

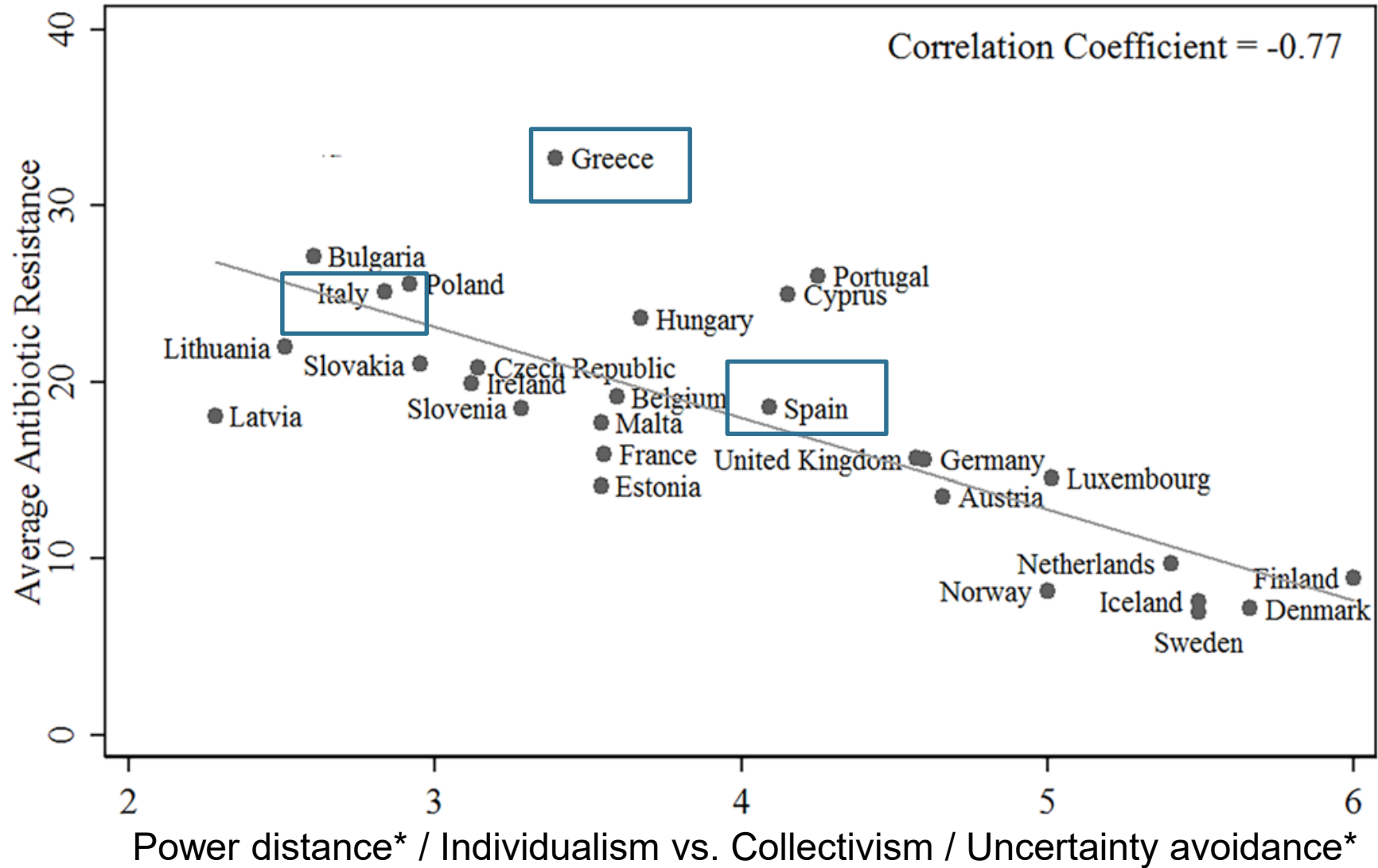
...as is antimicrobial consumption...



Explains **33%** of the total variation in antibiotic resistance



Explains 63% of the total variation in antibiotic resistance
 (in addition to antimicrobial use)



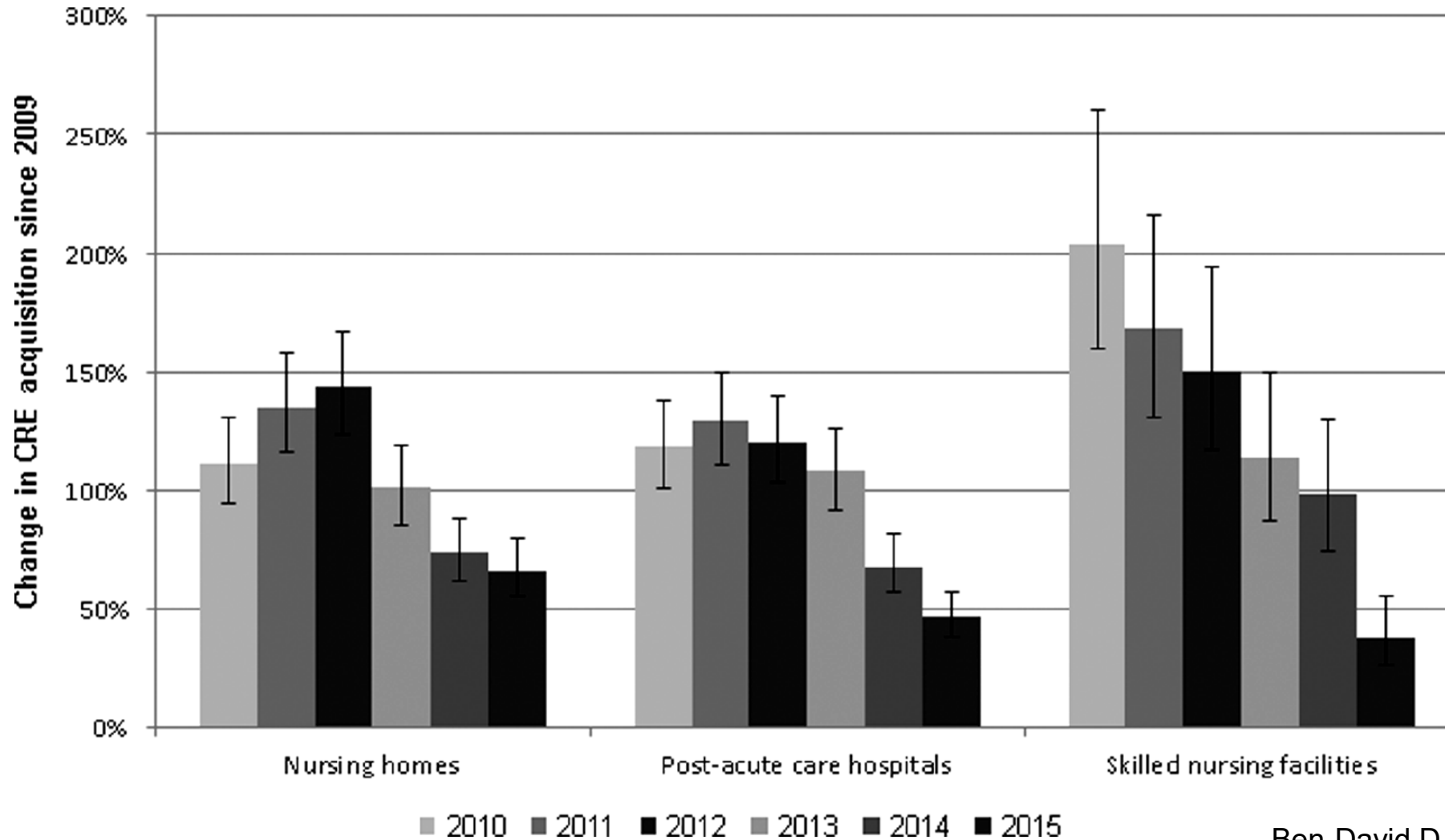
*positive correlation with ESAC data

*Deschepper R *BMC Health Services Research* 2008;8:123

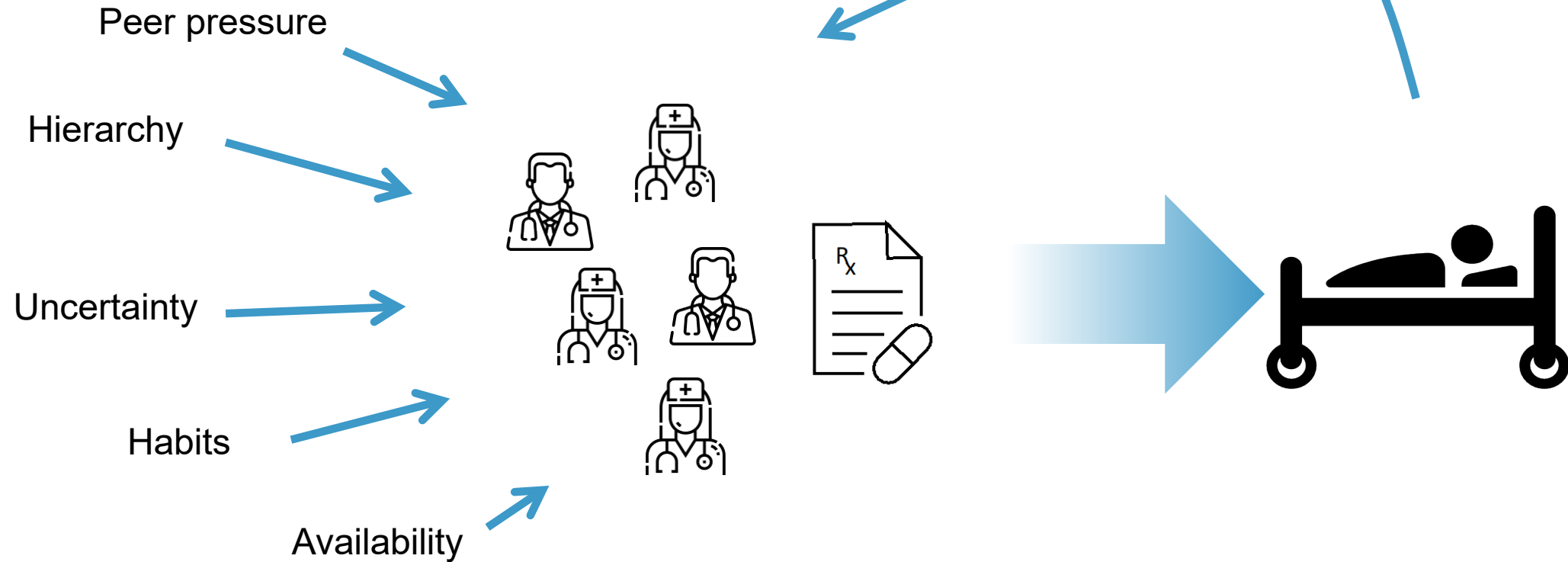
Infection prevention and control measures?

Variable	Post-Acute-Care Hospitals		
	Acute-Care Hospitals	Skilled Nursing/Chronic Ventilated/ Subacute Wards	Rehabilitation Wards
Room assignment	Private or cohorting with other CRE carriers	Private or cohorting with other CRE carriers	No regulation regarding room assignment
Dedicated nursing staff for CRE carriers	Required	Not required	Not required
Use of gloves and gowns in care of CRE carriers	Mandatory on room entrance	Mandatory on room entrance	According to standard precautions
Admission CRE screening of high-risk groups ^b	Required	Required	Not required, except in outbreak setting
CRE screening of patient contacts	Required	Required	Required
Participation in group activities	Prohibited	Allowed	Allowed
Standard protocol for discontinuation of contact isolation	Yes	Yes	Yes
Regular mandatory census reporting to NCIC	Yes	Yes	Yes

Infection prevention and control measures?



Antimicrobial stewardship?



Divergent goals of treating a present patient but preserving the efficacy of antibiotics for a future need make adherence to AMS difficult

In summary...

Antimicrobial resistance (AMR) is an endemic “under the radar“ problem

AMR is not the result of a single error in the “production line” of treating patients

AMR is driven by transmission and selection of resistant microorganisms and resistance genes due to breaches in infection prevention and control practices, limited diagnostic capacity, and prescription behaviour

There is evidence on specific infection prevention and control as well as antibiotic stewardship interventions working on isolated AMR challenges

Interventions on AMR must address “Behaviour” in hospitals that are complex, heterogenous organisations where problems rarely manifest in isolation

REVERSE

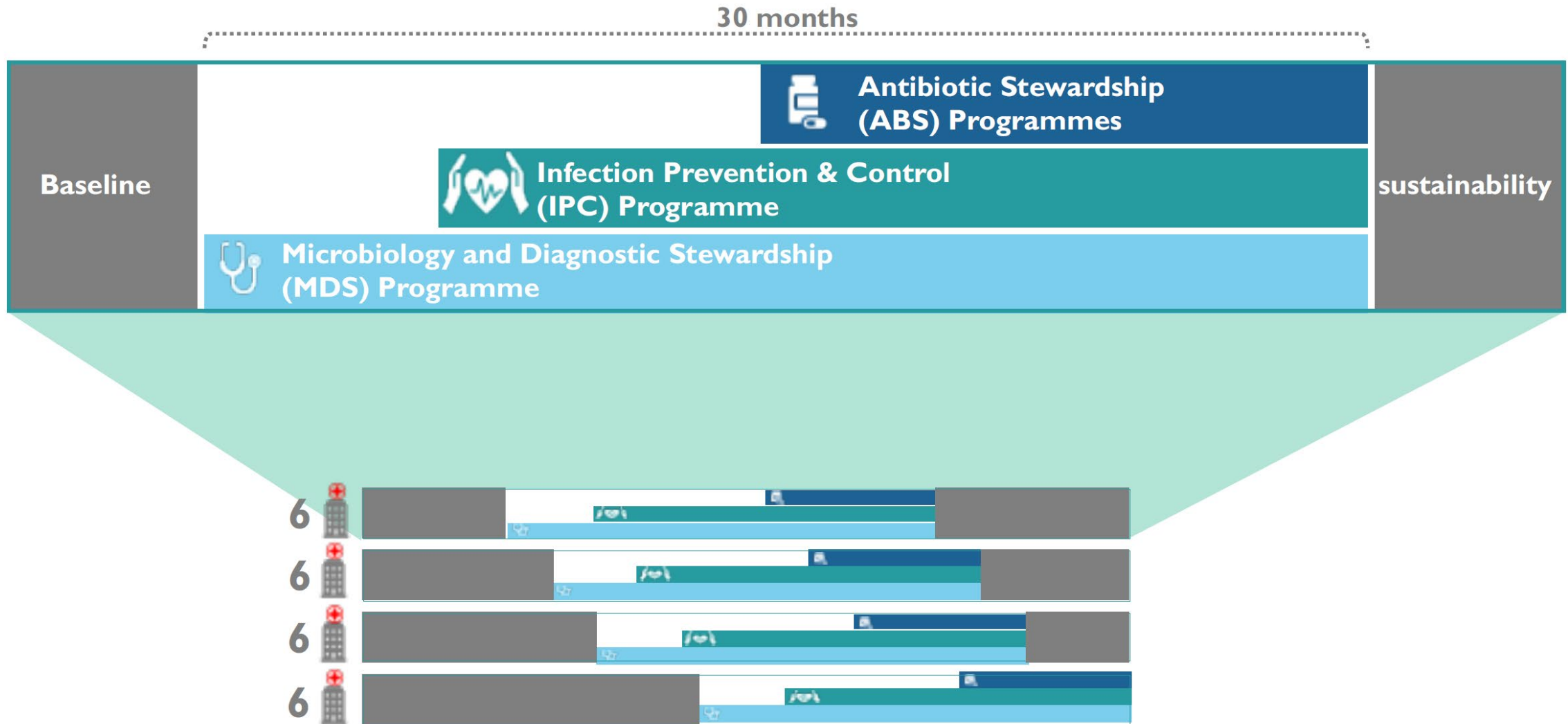
It is the concept of REVERSE that reducing antimicrobial resistance in acute care hospitals can only be achieved in a **collaborative approach** where various activities interact together in a large clinical trial that is sufficiently powered to provide actionable outcomes

Aims

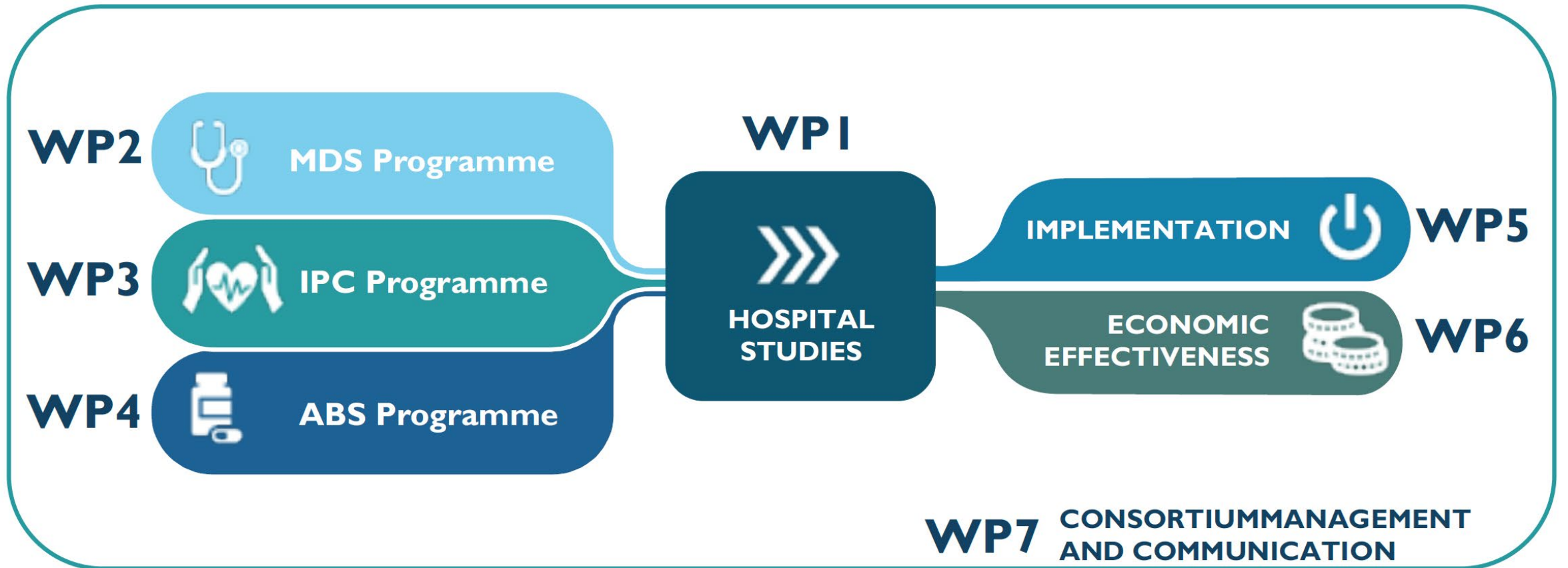
1. To design and evaluate an **integrated, modular strategy of evidence based intervention programmes** that can be implemented in the clinical management of hospitalized patients in high AMR prevalence settings;
2. To design and evaluate a **tailored enhanced implementation strategy versus a standard basic implementation strategy** to introduce evidence-based interventions in high AMR prevalence settings;
3. To estimate the **cost-effectiveness of the intervention programmes** for the prevention and clinical management of infections and colonization due to AMR pathogens;
4. To **develop recommendations and implementation strategies** on AMR prevention and clinical management strategies in high AMR prevalence settings in Europe, and to explore **transferability** of the proposed intervention programmes **to low-and-middle-income countries**;
5. To obtain a **change of the local organisational way of working** in the participating hospitals and to engage them as national and European **reference hospitals** for sustainability and further dissemination.

Study design

Cluster-randomized stepped-wedge design



Work packages



Interventions

Diagnostic stewardship

- Audits to assess microbiological capacity and stewardship in REVERSE hospitals
- Support establishing microbiological assays to reliably identify CRE, CRPA and CRAB in clinical samples where necessary
- Internal REVERSE quality control programme on correctly identifying CRE, CRPA and CRAB
- Increase the rate of blood culture sampling (positivity rates below 25/1000 patient-days)
- Four point prevalence surveys on CRE colonisation in inpatients with clonal relatedness analysis and identification of resistance genes

Interventions

Infection prevention and control

- Enhanced standard precautions
- Hand hygiene, with special emphasis on the use of alcohol-based hand rub
- Basic environmental hygiene
- Regular point prevalence surveys to detect previously unknown MDRO carriers
- Targeted MDRO screening in high-risk populations
- Audits and feedback on the basic IPC components in regular time intervals

- Universal MDRO screening at admission in high risk units
- Reinforced contact precautions for identified MDRO carriers
- Enhanced cleaning in high risk settings with point prevalence sampling surveys
- Improved information transfer within the hospital and along the referral pathways
- Root-cause analysis of newly detected cases

- Decolonization or decontamination of colonized patients or patients in high risk units using
- Molecular analysis and sequencing of isolates for outbreak investigation

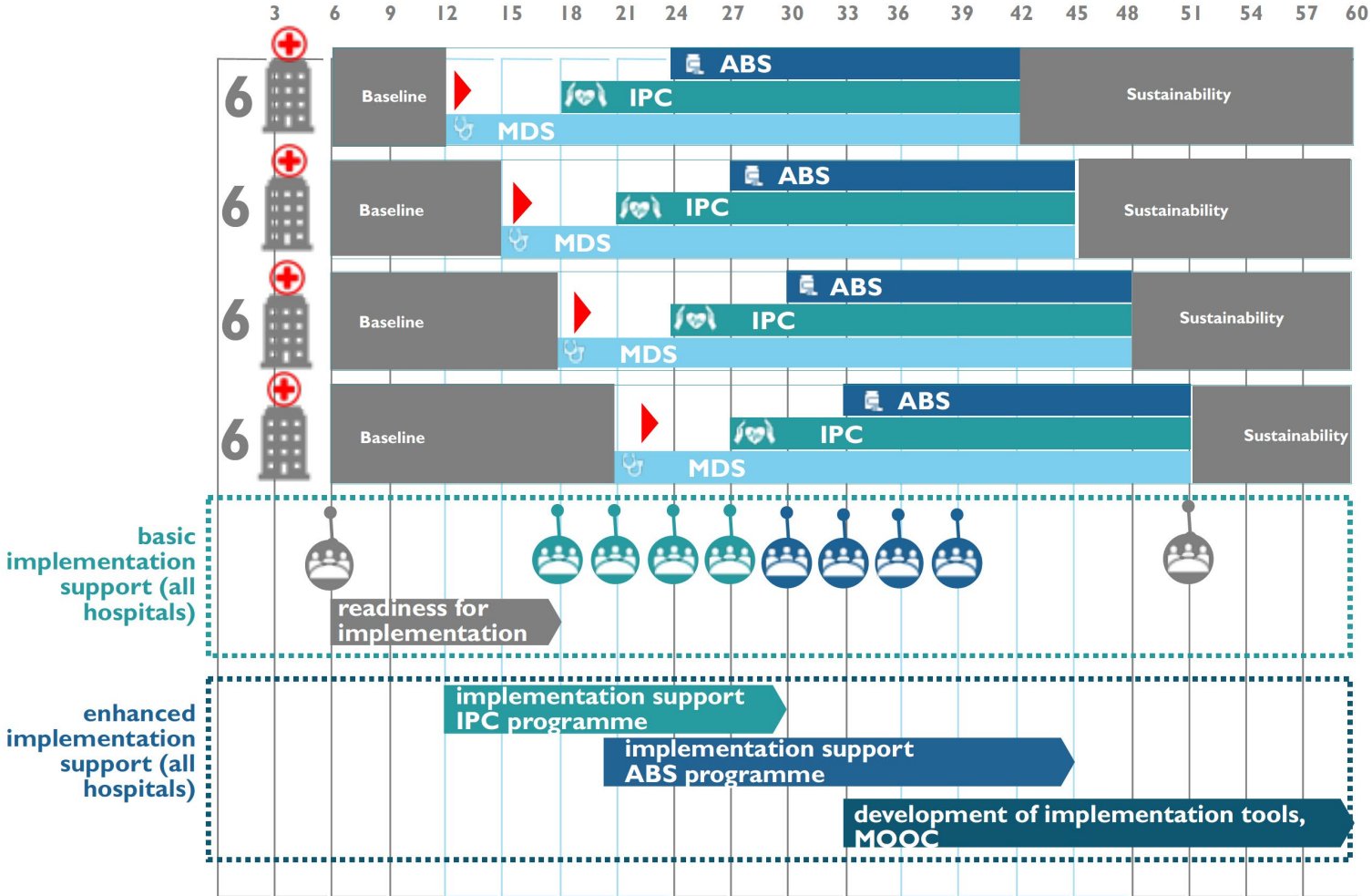
Interventions

Antimicrobial stewardship

- Best practice programme focusing on organisation, structure and available microbiology:
 - Adherence to national ABS plans
 - Multidisciplinary stewardship committees
 - Guidance documents on syndrome-specific treatment pathways
 - Dedicated recommendations for new drugs
 - Local ABS stewardship teams with ABS rounds
 - Surveillance of antibiotic consumption
 - Correct dosing (EUCAST)
- Technical interventions
 - Molecular characterization of resistance genes
 - Screening of patients in high-risk areas
 - Personalised surgical prophylaxis
 - Rapid molecular testing

Further analysis (intervention)

Implementation – Type 2 hybrid effectiveness-implementation trial



Further analysis

Cost-effectiveness analysis

- Systematic reviews on cost-effectiveness of ABS, IPC and MDS programmes
- Micro-costing of interventions and implementation
- Quality of life estimation
- Cost-effectiveness analysis from hospital perspective
- Cost-effectiveness analysis from a societal perspective
- Extrapolation to low-and-middle-income countries

The REVERSE consortium



University of Zurich
UZH



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ISGlobal
Barcelona Institute for Global Health



UNIVERSITY OF OXFORD



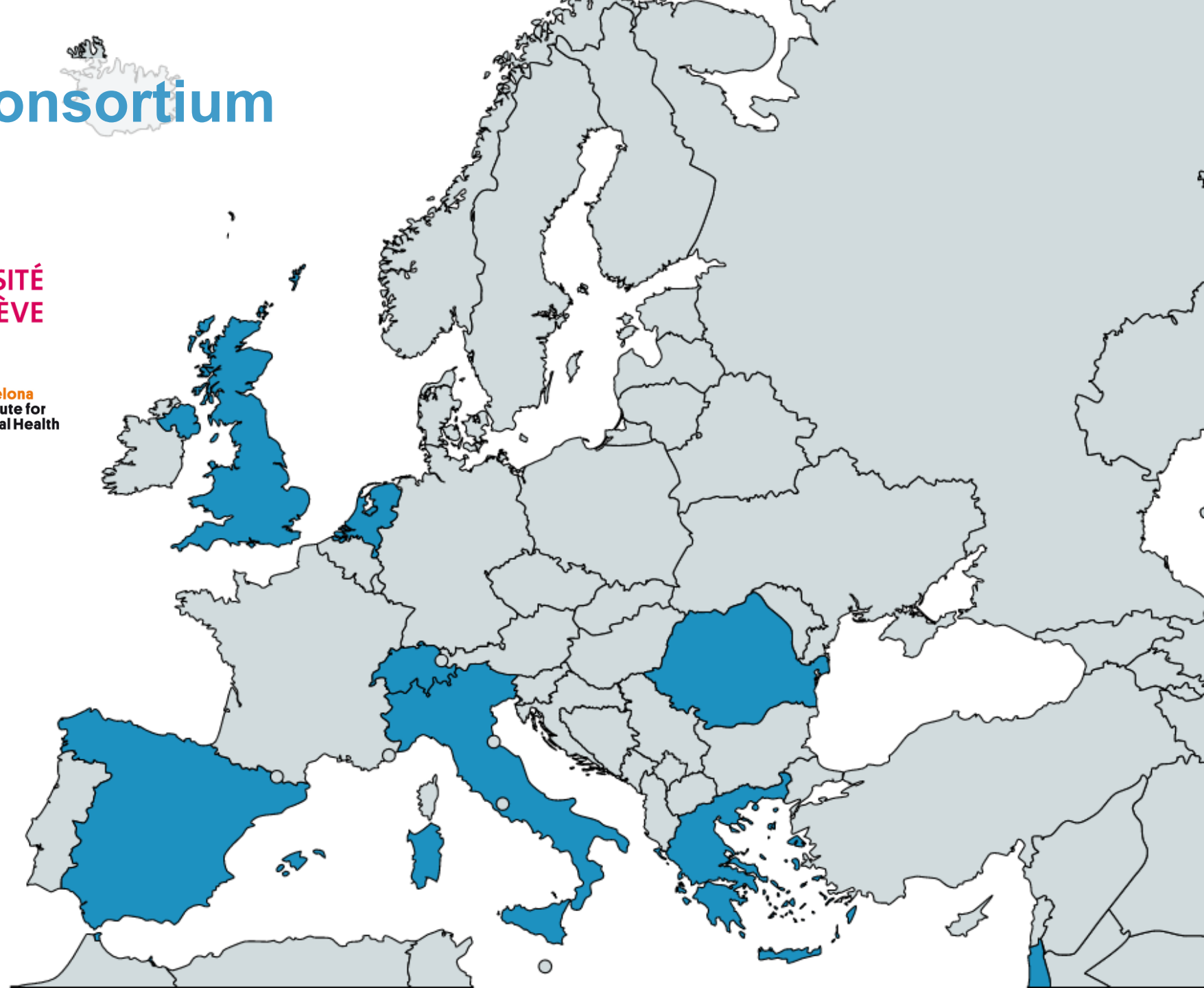
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REVERSE will be one of the independent partner projects of ECRAID

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explore
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Thank you for your attention

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