Antimicrobial Resistance & Consumption in Human Health

Intersectoral AMR Committee Meeting
13/04/16

Dr Karen Burns
Consultant Clinical Microbiologist
HSE-Health Protection Surveillance Centre (HPSC)

Presentation Overview

- Why should we be worried about AMR?
- What data do we currently have?
- What data would we like to have?
- What is required to achieve our objective?

COUNCIL OF THE EUROPEAN UNION **Brussels, 29 May 2012**

10. **STRESSES** that AMR is a growing European and global health problem in both humans and animals, leading to limited or poor options for treatment whilst diminishing the quality of life and to important economic consequences in terms of augmenting healthcare costs and productivity losses.

11. **RECOGNISES** that the development of AMR is accelerated by excessive and inappropriate use of antimicrobial agents which, together with poor hygiene or poor infection control practices, creates favourable conditions for the development, spread and persistence of resistant microorganisms in both humans and animals.

13. **UNDERLINES** the need for an active holistic risk based approach based on a "One Health" perspective with the purpose of reducing the use of antimicrobials as much as possible and to maximise coordinated efforts between the human health sector and the veterinary sector in the fight against AMR.

Annual Report of the Chief Medical Officer

Volume Two, 2011
Infections and the rise of antimicrobial resistance

UK Five Year Antimicrobial Resistance Strategy 2013 to 2018

Challenges and opportunities

- Antimicrobial resistance is increasing worldwide, the government needs to:
  - put antimicrobial resistance on the national risk register (specifically, the 'National security Risk Assessment')
  - implement effectively the UK 2013-2018 cross government antimicrobial resistance strategy
  - improve global leadership and action, particularly around the development of new antibiotics and preserving the effectiveness of existing antibiotics (antibiotic stewardship)

DATA ON ANTIBIOTIC USE IN HUMAN HEALTHCARE AND IN AGRICULTURE ARE NOT SYSTEMATICALLY COLLECTED

An Roinn Sláinte
DEPARTMENT OF HEALTH

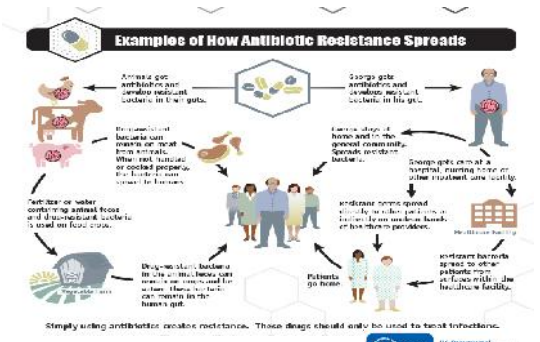
Department of Health / Department of Agriculture

Interdepartmental Discussion Paper:

An Intersectoral Response to the Spread of Antimicrobial Resistance (AMR) in the Human and Animal Health Sectors

2014

AMR: A Global Public Health Threat



AMR: Here and now…

- 2016: Irish pensioner presents to local ED – Influenza-like illness
- ICU admission for respiratory failure, refractory, despite ventilation x 1 week, acute kidney injury – Confirmed influenza pneumonia, suspected secondary bacterial pneumonia – multiple antimicrobials
- Transferred to tertiary critical care for haemodialysis
- Isolated on transfer, as known influenza infection
- Routine ICU admission rectal swabs CRE, VRE & MRSA swabs of nose, groin

Rectal swab: *Klebsiella pneumoniae*

AGENT	RESULT
Amoxicillin	RESISTANT
Co-amoxiclav	RESISTANT
Cefuroxime	RESISTANT
Cefotaxime	RESISTANT
Ceftazidime	RESISTANT
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Multi-drug resistant *K. pneumoniae* (MDR-KP) ESBL & carbapenemase producing OXA-48 CRE confirmed by reference lab in Galway

AMR: Here and now…

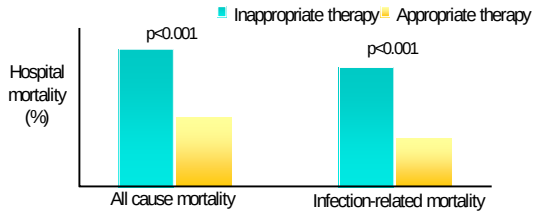
- Day 8 tertiary ICU (day 15 hospitalisation)
- Temperature, unstable, evolving sepsis
- Commenced colistin & amikacin in view of known CRE colonisation
- Blood cultures grew *Klebsiella pneumoniae* – CRE
- Infection source was central vascular catheter
- Improved with appropriate antimicrobial therapy & removal of catheter

AMR: Here and now…

- Require 10 days combination nephrotoxic treatment, monitoring antimicrobial levels, in context of recovering kidney function
- Strict isolation precautions maintained – gloves, long-sleeved gowns, isolation
- Transferred back to isolation in referral hospital

Picking the right antimicrobial for infection saves lives

- Inappropriate initial therapy is associated with increased mortality*
  - Relative risk mortality 2.37 (95CI 1.83-3.08)



 *Kollef et al. Chest 1999;115:462–474

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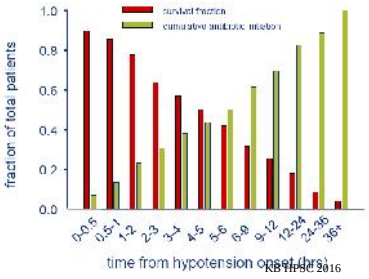
Giving antimicrobials quickly in severe infections saves lives



Mortality in septic shock related to duration of hypotension prior to initiation of antibiotic therapy*

*Kumar et al, *Crit Care Med* 2006

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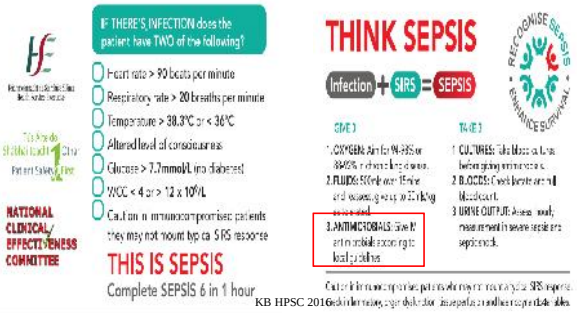
HSE sepsis guide



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AMR: Here and now…

- Fortunately, it was already known this patient was colonised with CRE – appropriate early treatment of sepsis was possible
- Review of Irish bloodstream infection data (2008 – 2013) reported attributable mortality of *K. pneumoniae* bloodstream infection = 15% (non-CRE) – Source: HPSC
- Reported attributable mortality of CRE bloodstream infections is >50%, based on many international studies

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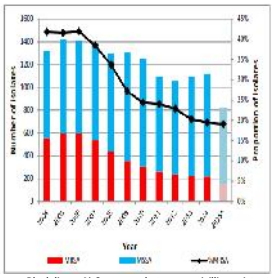
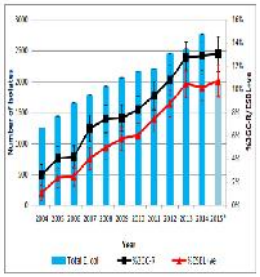
Annual *S. aureus* BSI Ireland 2004-2015 (Q3)



Black line = % *S. aureus* that are meticillin resistant i.e. MRSA

Annual *E. coli* BSI Ireland 2004-2015 (Q3)



Black line = % *E. coli* resistant to multiple antimicrobials

Source: HPSC

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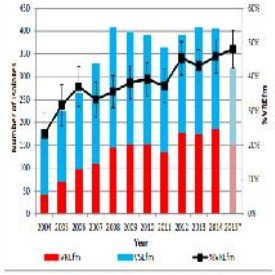
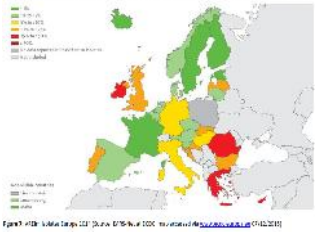
Annual *E. faecium* BSI Ireland 2004-2015 (Q3)



Black line = % *E. faecium* resistant to vancomycin (VRE)



Review of Irish bloodstream infection data (2008 – 2013) reported attributable mortality of bloodstream infection = 19%

Source: HPSC

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Multi-drug resistant *K. pneumoniae* (MDRKP)

- Notifiable to HPSC since Jan 2014. To end 2015:
- Widely-disseminated throughout the Irish healthcare system, with 915 cases reported by 50 hospitals:
  - **67% hospital** – Of those, 40% required treatment for infection & just 55% were placed in isolation within 24 hours of result
  - **13% long-term care facility**
  - **20% primary care**
- 84% from clinical samples: urine > swab > sterile site
- 16% picked up on rectal screening swabs
- **12% are also CRE**

Source: HPSC

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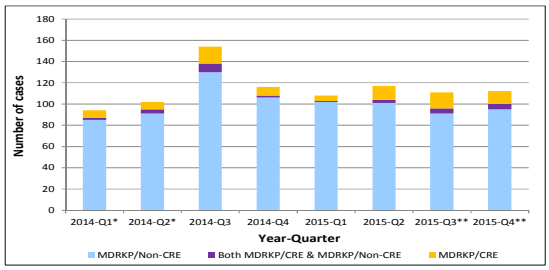

Prospective MDRKP (CRE and Non-CRE) reporting: distribution of all cases by quarter (data for Q1 2014-Q4 2015)
*No data from one tertiary hospital for Q1-2 2014; ** no data from one general hospital for Q3-4 2015

Source: HPSC

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Rapid communications

FIRST IDENTIFICATION OF CLASS A CARBAPENEMASE-PRODUCING KLEBSIELLA PNEUMONIAE IN THE REPUBLIC OF IRELAND

EUROSURVEILLANCE Vol. 14 - Issue 13 - 2 April 2009

LETTERS

First identified case of VIM-producing carbapenem-resistant Klebsiella pneumoniae in the Republic of Ireland associated with fatal outcome

Eurosurv Dec 2010

RAPID COMMUNICATIONS

First isolation and outbreak of OXA-48-producing *Klebsiella pneumoniae* in an Irish hospital, March to June 2011

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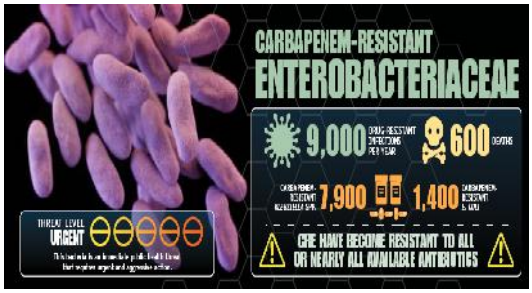

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CRE outbreak: Media 2011

Home News

Limerick hospital 'superbug' outbreak

Mid-Western patients hit by multi-drug resistant bug

Bug 'deadlier than MRSA'

Strain that can't be killed by most drugs is found in our hospitals for the first time

'It chops up antibiotics'

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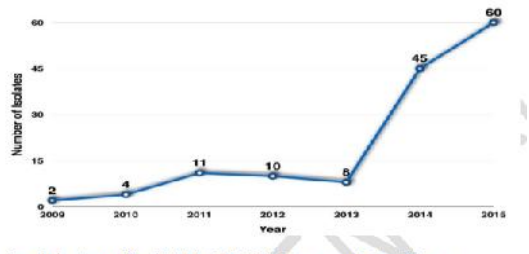
CRE in midwest of Ireland



Annual laboratory-confirmed CPE UHL 2009 – 2015: Data courtesy Dr Clara O'Connor

CRE was made notifiable in Ireland in 2011 and enhanced surveillance of CRE is conducted by HPSC

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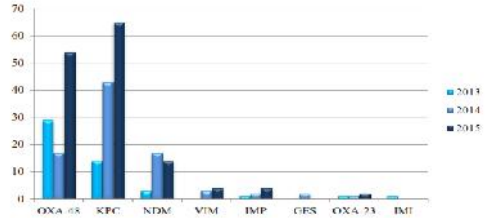
CRE national data

Figure 1: Carbapenemases detected in Ireland 2013 - 2015



81 confirmed CRE cases nationally in 2014 -> 140 in 2015 -> 23 Jan & Feb 2016
Data courtesy: Prof Martin Cormican, CPEARLS

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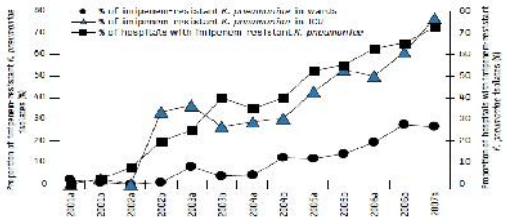
Carbapenem resistant *Klebsiella* (CRE) in Greece

Trends in proportion of imipenem-resistant *Klebsiella pneumoniae* isolates in hospitals in Greece, 2000-2006



Vatopoulos *et al – Eurosurveillance 2008*

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Carbapenem-resistant *Klebsiella* (CRE) in Italy

The first reported cases of KPC-Kp (ST258)

ST258, ST512 (CC258)

ST512
ST258
ST101
ST15
ST147-like

Data source: GM Rossolini, ARHAI Network Meeting, Berlin, Dec 2012

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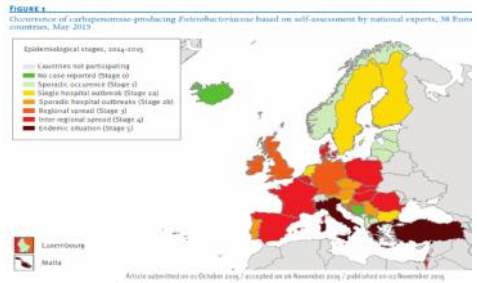
CRE in Europe



Albiger B *et al.* EUSCAPE working group: Eurosurveillance 2015

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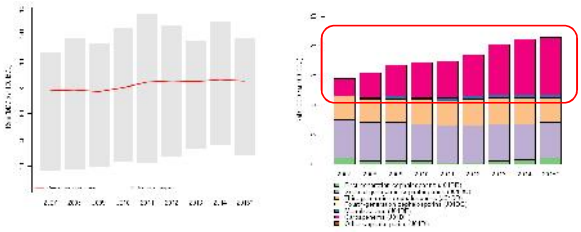
Concerns about AMR influence our empiric prescribing
Antimicrobial use drives AMR



Source: HPSC Source: HPSC

Significant increase in carbapenem (e.g., meropenem) use in Ireland
Emergence of carbapenem resistant *Enterobacteriaceae* (CRE) since 2009

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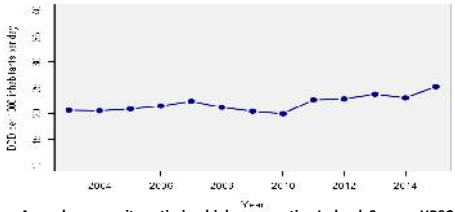

Annual community antimicrobial consumption Ireland. Source: HPSC

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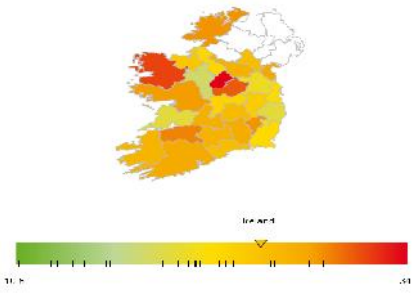

Regional variation in community antimicrobial consumption Ireland. Source: HPSC

Colistin resistance

RAPID COMMUNICATIONS

Colistin resistance superimposed to endemic carbapenem-resistant *Klebsiella pneumoniae*: a rapidly evolving problem in Italy, November 2013 to April 2014

M. Monaco[1,2], T. Giani[1,2], M. Raffone[1,2], F. Arena[1], A. García-Fernández[3], S. Pollini[1], Network EuSCAPE-Italy[4], H. Grundmann[5], A. Pantosti (annalisa.pantosti@iss.it)[1], G.M. Rossolini[1,2,6]

Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study

Yi-Yun Liu[1], Yang Wang[2], Timothy R Walsh, Ling-Xian Yi, Rong Zhang, James Spencer, Yohei Doi, Guobao Tian, Baolei Dong, Xianhui Huang, Lin-Feng Yu, Donata Gu, Hongwei Ren, Xiaojie Chen, Luchao Lv, Dandan He, Hongwei Zhou, Zisen Liang, Jian-Hua Liu, Jianzhang Shen

Summary
Background Until now, polymyxin resistance has involved chromosomal mutations but has never been reported via

Rectal swab: *Klebsiella pneumoniae*

AGENT	RESULT
Amoxicillin	RESISTANT
Co-amoxiclav	RESISTANT
Cefuroxime	RESISTANT
Cefotaxime	RESISTANT
Ceftazidime	RESISTANT
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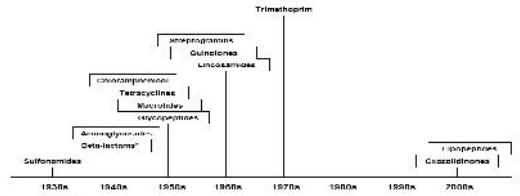
Last resort antimicrobials widely-used
No new agents in the pipeline

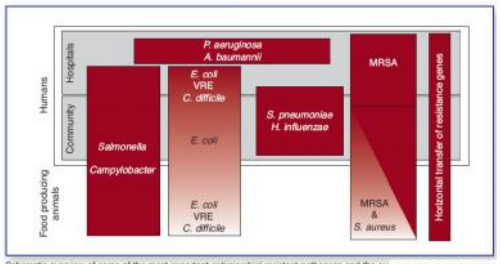
Figure 1. Discovery of new classes of antibiotics.



Source: (4, p 10)

© European Centre for Disease Prevention and Control, 2008. Reproduction is authorised, provided the source is acknowledged

Figure 4.2 Reservoirs of AMR bacteria causing human infections



Schematic overview of some of the most important antimicrobial resistant pathogens and the ov... © World Health Organization 2012
reservoirs. As indicated some pathogens are strictly confined within the human reservoir, whereas others have a mainly or partly animal reservoir.
Source: Reproduced from[8] with permission

Other AMR threats

- **Zoonotic bacteria:**
  - Campylobacter
  - Salmonella
- **Sexually-transmitted bacteria:**
  - *Neisseria gonorrhoea*
    - *1304 cases reported in Ireland in 2014*
    - *101 isolates available for testing*
    - *37% ciprofloxacin resistant, 34% azithomycin resistant*

http://amr-review.org/publications

Review on Antimicrobial Resistance

SCIENTIFIC REPORT

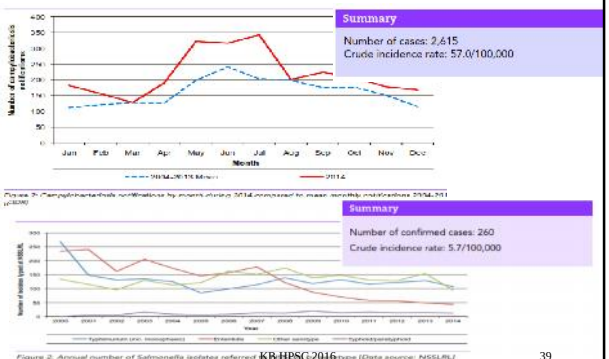
ecdc EFSA Journal

ADOPTED: 8 February 2016 PUBLISHED: 11 February 2016
doi:10.2903/j.efsa.2016.4380

The European Union Summary Report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2014

European Food Safety Authority
European Centre for Disease Prevention and Control

Human Salmonella isolates (2014) – 26% multi-drug resistant & colistin resistance also detected
Human campylobacter isolates (2014) – Ciprofloxacin resistance widely reported



http://www.hpsc.ie/AboutHPSC/AnnualReports/

Other AMR threats

- **Fungi:** Triazole resistant *Aspergillus fumigatus: Cyp51A* gene mutation
  - **Prior azole exposure**
  - **Azole fungicides for crop protection**
- Invasive aspergillosis associated with high mortality – azoles are cornerstone of treatment
- Difficult to diagnose and overseas referral of isolates for antifungal susceptibility testing required
- Affects patients with serious immunocompromise: leukaemia, transplant, chemotherapy, critically ill

ecdc

Thirty-First Meeting
26 September 2012
Upplands Väsby, Sweden

Risk assessment on the impact of the environmental usage of triazoles on the development and spread of resistance to medical triazoles in *Aspergillus* spp.

In order to understand the epidemiology and origin of azole-resistant *A. fumigatus* in Europe and to encounter and battle this very significant problem, it is essential to:

1. To obtain good and reliable data from the EU concerning *A. fumigatus* resistance in the patient population and the environment,
2. To further identify the cause or the sources of the resistant development in both the clinical setting and the environment.

Clinical Infectious Diseases

INVITED ARTICLE

IDSA hivma

HEALTHCARE EPIDEMIOLOGY: Robert A. Weinstein, Section Editor

Azole Resistance in *Aspergillus fumigatus*: Can We Retain the Clinical Use of Mold-Active Antifungal Azoles?

Paul E. Verweij,[1] Anuradha Chowdhary,[2] Willem J. G. Melchers,[1] and Jacques F. Meis[1,3]
[1]Department of Medical Microbiology, Radboud University Medical Centre, Nijmegen, The Netherlands; [2]Department of Medical Mycology, Vallabhbhai Patel Chest Institute, University of Delhi, India; and [3]Department of Medical Microbiology and Infectious Diseases, Canisius Wilhelmina Hospital, Nijmegen, The Netherlands

Surveillance = Information for Action

9.0 Healthcare-Associated Infections, Antimicrobial Consumption and Resistance
9.1 C. difficile infection
9.2 Alcohol Hand Rub Surveillance
9.3 Hand Hygiene Compliance
9.4 Antimicrobial Consumption
9.5 Antimicrobial Resistance
Enhanced surveillance of Carbapenem Resistant Enterobacteriaceae (CRE)

http://www.hpsc.ie/AboutHPSC/AnnualReports/

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Surveillance = Information for Action

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DANMAP Annual Report 2014

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WE CAN'T MANAGE IT IF WE'RE NOT MEASURING IT

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Suggested actions to tackle AMR

- National intersectoral & interdepartmental SMART AMR strategy
  - Five-year plan
  - Governance and leadership clearly-defined
  - Specific objectives, measurable, attainable, timelines and outputs clearly-defined
- Adopted as government policy
- Ring-fenced funding
- Designated expertise to critically evaluate data, ask research questions, support collaboration
- Invitation for an external review of strategy by ECDC recommended

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Actions to tackle human AMR in hospitals, long-term care facilities and community

- **General:**
  - Healthcare infrastructure: single rooms, *en suite* toilets, critical care, oncology, haematology, transplant
  - Healthcare occupancy & ED occupancy
  - Healthcare staffing:
    - General patient care, reflecting case mix and dependency
    - Specialist infection prevention and control
    - Specialist antimicrobial stewardship
  - IT infrastructure that support IPC and antimicrobial stewardship activities

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Actions to tackle human AMR in hospitals, long-term care facilities and community

- **Specific:**
  - Integrated surveillance systems at national, regional, hospital group, community care area, hospital and long-term care facility
  - Timely analysis and feedback of surveillance data
  - Timely analysis and feedback of prescriber level data
  - Implementation of national guidelines, MDRO & MRSA guideline recommendations
  - Active screening for MDRO in accordance with guidelines

Actions to tackle human AMR in hospitals, long-term care facilities and community

- **Specific:**
  - Strengthen microbiology reference laboratory surveillance capacity:
    - Expanded resistance surveillance in *Enterobacteriaceae*
    - Enterococci
    - Aspergillus
    - *Clostridium difficile*
  - Collaborative working with veterinary and food safety
  - Strengthen public health functions, epidemiological support for surveillance and outbreaks
  - Epidemiological carriage studies in high risk acute hospital populations (ICU, chemotherapy, transplant) and in long-term care facilities

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Thank you for your attention