# BAD BUGS, NO DRUGS

WHY IPC IS AT THE FOREFRONT

**OF AMR ACTIONS** 

### Martin Kiernan

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### ALEXANDER FLEMING (1881-1955)

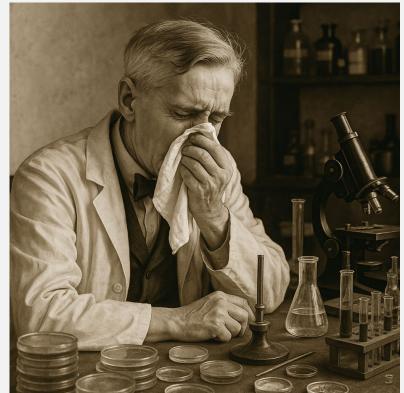
- Following experiences in WWI, became interested in natural antibacterial action – antiseptics did more harm than good
- Antiseptics worked well on the surface, but deep wounds tended to shelter anaerobic bacteria
  - antiseptics seemed to remove beneficial agents produced that protected patients in these cases at least as well as they removed bacteria
    - Fleming, A., The Physiological and Antiseptic Action of Flavine (with Some Observations on the Testing of Antiseptics). The Lancet, 1917. 190(4905): p. 341-345.

THE PHYSIOLOGICAL AND ANTISEPTIC ACTION OF FLAVINE (with some observations on the testing of ANTISEPTICS).

BY ALEXANDER FLEMING, F.R.C.S. ENG., TEMPORARY LIEUTENANT, R.A.M.C. (From a Research Laboratory of a Base Hospital in France.)

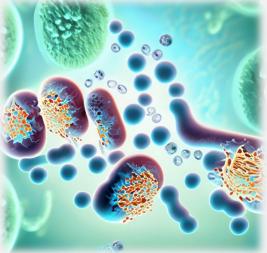
### ALEXANDER FLEMING AND THE RUNNY NOSE (1921)

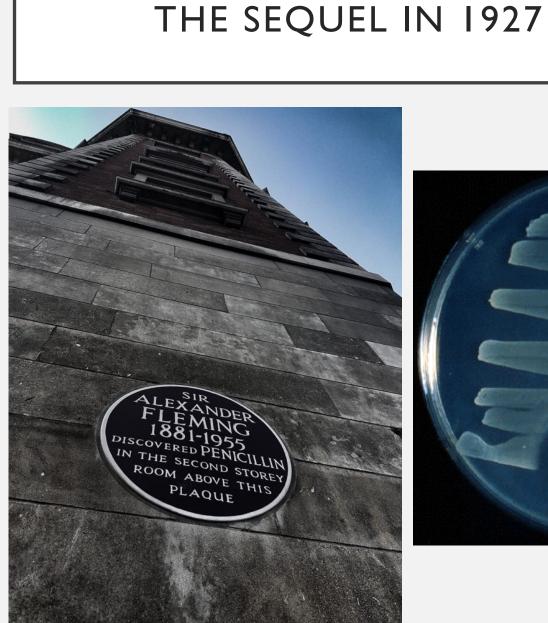
- In the midst of a cold he 'put' some mucus from his nose on an agar plate and added it to the clutter on his workbench
  - Along with the usual mixture of organisms he noted that some bacteria were dissolving
- He extended his tests using tears contributed by co-workers
  - "The demand by us for tears was so great, that laboratory attendants were pressed into service, receiving threepence for each contribution."



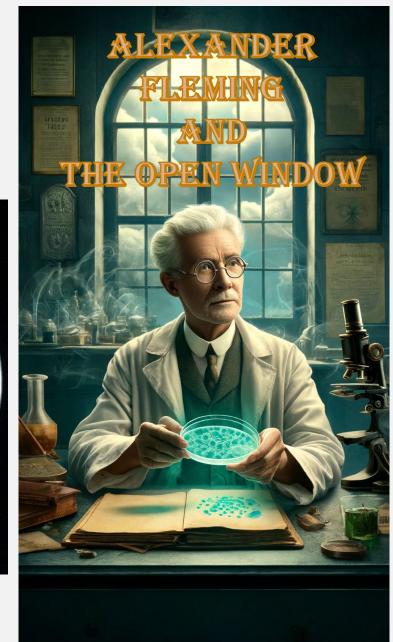
### HE HAD DISCOVERED LYSOZYME

- Lysozyme: a combination word derived from lysis (the ability to dissolve something else), and enzyme
  - found in the milk of lactating women, he concluding that this might have something to do with protecting the body from airborne bacteria because it showed up in most of the main entrances to the body
  - Never isolated the active agent, effective only against non-pathogens
  - 4 papers published, lectures given, and all ignored however the processes turned out to be useful (titration methods and blood assays)



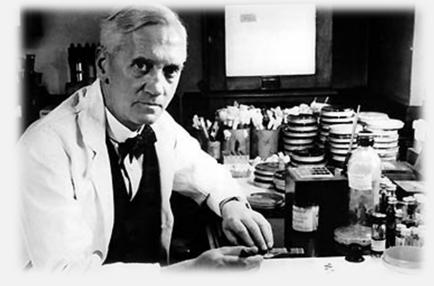






### A SEQUENCE OF FORTUNATE EVENTS

- A stray mould spore
- An unincubated plate of bacteria
- A drop in temperature at precisely the right time to inhibit bacterial growth
- Fleming's return from vacation in Suffolk in time to see the mould's effectiveness before it overran the plate



 Pure luck in re-examining a petri dish he had put on the stack of dishes to be cleaned in the tub of disinfectant

### PENICILLIN

- Fleming was not able to produce penicillin in a usable form and there was a distinct lack of interest from the medical profession
  - Although discovered in 1927, it was 1940 before the structure was described by Florey and Chain, leading to the possibility of manufacture
- Fleming predicted the future
  - "the microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out ... In such cases the thoughtless person playing with penicillin is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted."

### PC ALBERT ALEXANDER

- Injured during a bombing raid in Oxford (1941)
  - became infected by Streptococci and Staphylococci, spread to eyes and scalp, given a sulfa drug that did nothing to alleviate infection but did give him a rash
  - abscesses drained, but could not save his eye
  - Given 200 mg of penicillin, followed by three doses of 100 mg every three hours. Within 24 hours there was "dramatic improvement"
  - Penicillin extracted from urine and re-administered all looked well
  - 10 days later, infection returned however all available drug had been used up and he did not survive



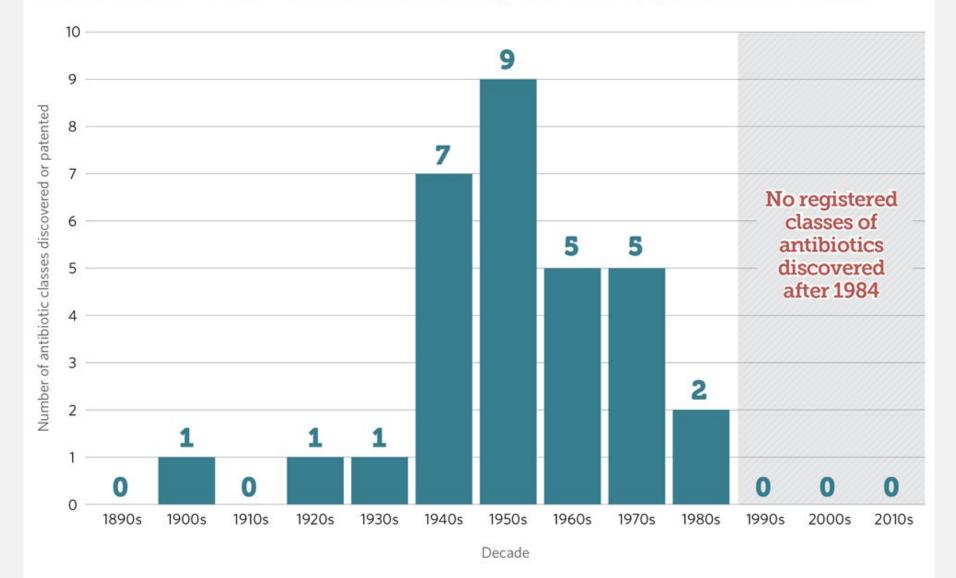




### DISCOVERY VS RESISTANCE

| Antibiotic Class                                  | First Human Use | Origin                                  | Resistance Seen |
|---|-----------------|---|-----------------|
| Penicillin  | 1941            | Penicillium notatum                     | 1947            |
| Aminoglycosides<br>(Streptomycin)<br>(Gentamicin) | 944<br> 963     | Streptomyces griseus                    | 946<br> 967     |
| Methicillin                                       | 1959            | Semi-synthetic penicillin<br>derivative | 1960            |
| Quinolones  | 1967            | From chloroquine                        | 1970s           |
| Glycopeptides                                     | 1958            | Streptomyces orientalis                 | l 980s          |
| Carbapenems<br>(Imipenem)                         | 1985            | Streptomyces cattleya                   | 1996            |
| Cephalosporins                                    | 1964            | Acremonium spp. (fungus)                | l 980s          |
| Polymyxins (Colistin)                             | 1959            | Bacillus polymyxa                       | 2015            |

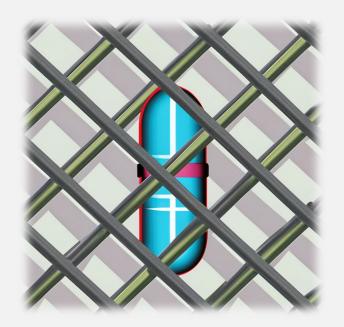
#### More than 30-Year Void in Discovery of New Types of Antibiotics



Source: Adapted from Lynn L. Silver, "Challenges of Antibacterial Discovery," Clinical Microbiology Review (2011)

### GREAT! A NEW ANTIBIOTIC IS DISCOVERED

- Antibiotics were <5% of all drug discovery funding 2003-2013
- A course is 5 days not long term
  - Not commercially viable
- It will be restricted as a treatment of last resort
  - Fear of resistance occurring
  - So not many will get it
- Economics of antibiotic R&D is a major disincentive to investment
- Will take global action by governments

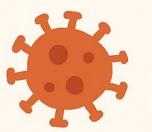


### WILL VACCINES FOR BACTERIAL INFECTIONS SAVE US?

| Organism                 | Phase I | Phase 2 | Phase 3                           | In use |
|--------------------------|---------|---------|-----------------------------------|--------|
| Neisseria gonorrhoeae    | I       | Х       | Х                                 | X      |
| Clostridioides difficile | Х       | Х       | l but<br>reduced<br>severity only | X      |
| E. Coli                  | Х       | Х       | l – failed                        | Х      |
| Klebsiella pneumoniae    | I       | Х       | Х                                 | X      |

### **Scope of the Problem**

### Antimicrobial Resistance



## **1.27 MILLION** DEATHS ANNUALLY

More deaths per year than HIV/AIDS or malaria

### **Asia-Pacific Focus**



## 700,000 AMR-RELATED DEATHS IN 2019

This region's large population and antibiotic use burden make it a major hotspot

ANNUAL AMR DEATHS WORLDWIDE COULD CLIMB TO **10 MILLION BY 2050** 

### AMR IN ASIA AND AUSTRALASIA

#### • High Resistance Rates

- Many Asian countries report very high resistance in common pathogens: e.g. over 30% resistance to first-line antibiotics for hospital infections
- In Pakistan, 81% of Klebsiella pneumoniae from burn infections are resistant to colistin
  - Mathu R, et al. Antibiotic resistance in the Middle East and Southern Asia: a systematic review and meta-analysis. JAC Antimicrob Resist 2025;7(1): https://doi.org/10.1093/jacamr/dlaf010

#### Comparative Perspective

- Australasia currently has comparatively lower rates of some resistant infections, but rising trends are noted
  - Australian Commission on Safety and Quality in Health Care. AURA 2023: fifth Australian report on antimicrobial use and resistance in human health. Sydney: CSQHC; 2023.

### PREVALENCE OF COLISTIN RESISTANCE IN FRESH VEGETABLES

- 3.6% overall; highest in carrot (14.3%), pakchoi (13.3%) and green pepper (7.7%)
  - Sequenced plasmids similar to clinical isolates and animals in various countries
    - Liu BT, et al . Colistin-Resistant mcr-Positive Enterobacteriaceae in Fresh Vegetables, an Increasing Infectious Threat in China. Int J Antimicrob Agents 2019;54(1):89-94.
  - Also in fruit
    - Yang, F., et al (2019). <u>Infect Drug Resist</u> 12: 385-389.





### Call for concern over the use of the new agricultural fungicide, ipflufenoquin, in Australia.

#### 3 JUNE, 2024

The Australia and New Zealand Mycoses Interest Group (ANZMIG), of the Australasian Society for Health approach to address significant concerns regarding the use of the new agricultural fungicia

To this end, it seeks dialogue with the Australian Pesticides and Veterinary Medicines Authority (A

#### 1. Use of ipflufenoquin in Australia

• ANZMIG notes the APVMA's approval and recent, restricted, registration of the fungicide, ipflufe diseases.

van Rhijn N, et al Aspergillus fumigatus strains that evolve resistance to the agrochemical fungicide ipflufenoquin in vitro are also resistant to olorofim. Nat Microbiol 2024;9(1):29-34

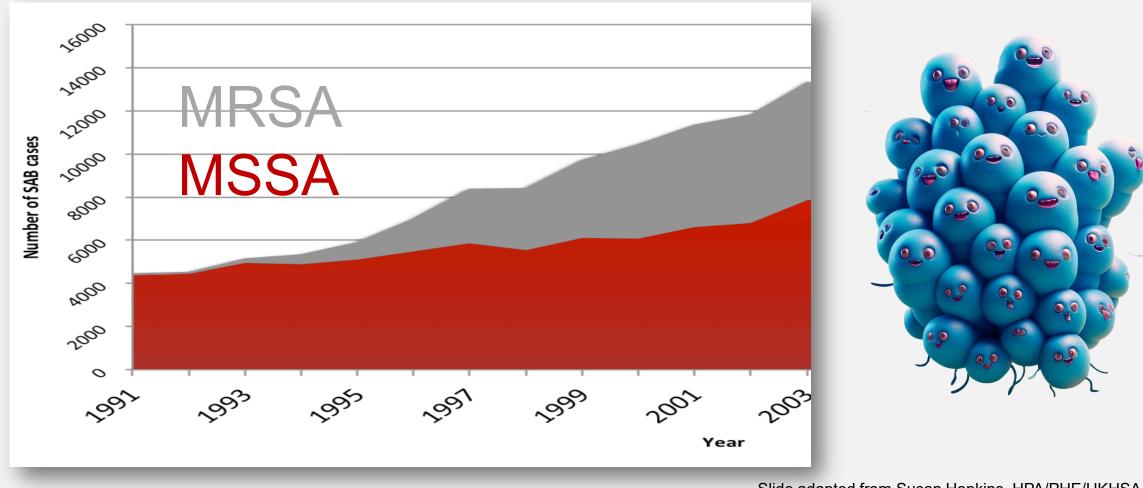


| Antibiotic Class  | Use in Animals                                       | Rationale in Veterinary Use   | Potential Human Impact  |
|---|--|---|---|
| Tetracyclines   | Widely used in poultry, swine, cattle                | countries), treatment of respiratory,   | Development of resistant E. coli, Salmonella, and<br>Campylobacter; cross-resistance affects human<br>therapy     |
| Macrolides  | Poultry, swine, cattle                               | I Ireatment of respiratory intections   | Selection of resistant Campylobacter and<br>Streptococcus; concern over erythromycin and<br>azithromycin efficacy |
| Fluoroquinolones  | Poultry and cattle                                   |   | Fluoroquinolone-resistant Campylobacter and Salmonella transmitted via food chain                                 |
| Aminoglycosides   | Swine, poultry, cattle                               | ILISED TOP SEDSIS ENTERITS  | Resistance genes plasmid-borne and transferable to human pathogens  |
| Beta-lactams (incl.<br>penicillins and<br>cephalosporins) | Used in most food-producing species                  |   | Resistant E. coli, Klebsiella from animals can<br>transfer to humans via direct contact or food                   |
| Polymyxins (e.g., colistin)                               | Common in pigs and poultry in some countries         | Last-resort treatment for enteric infections; growth promotion (historically) | Emergence of <b>mcr-1</b> gene (plasmid-mediated colistin resistance); global AMR concern                         |
| Sulfonamides  | Widely used in livestock                             | Treatment of respiratory and gastrointestinal infections                      | Resistance widespread in zoonotic pathogens; co-<br>resistance with other drug classes common                     |
| Glycopeptides (e.g.,<br>avoparcin)                        | Formerly used in growth promotion (now banned in EU) | Growth promoter (not for treatment)   | Use of avoparcin linked to emergence of<br><b>vancomycin-resistant enterococci (VRE)</b> in<br>humans             |

### THE COMPLACENCY ISSUE

- Antibiotics are a squandered resource no-one thought about sustainability and antibiotics were heavily marketed, so overused
  - "it's probably a virus, but here are some antibiotics anyway"
- No infection control in hospitals
  - "we can treat them anyway"
  - First Infection Control Nurse in the world was in Torbay (1959) because of the number of Staphylococcal infections (but not in patients)

### RISE OF S. AUREUS BLOODSTREAM INFECTIONS ENGLAND 1991-2003



Slide adapted from Susan Hopkins, HPA/PHE/UKHSA

### **MRSA\_THE** FORGOTTEN MASSACRE THE PLAGUE 2004 Filthy NHS wards kill 5,000 a year

### **OUR SQUALID HOSPITALS**

### The deadly superbug that puts Britain's hospitals to shame

# Daily Record

News

### KILLER RAPIST HAS MRSA IN PERVS' JAIL

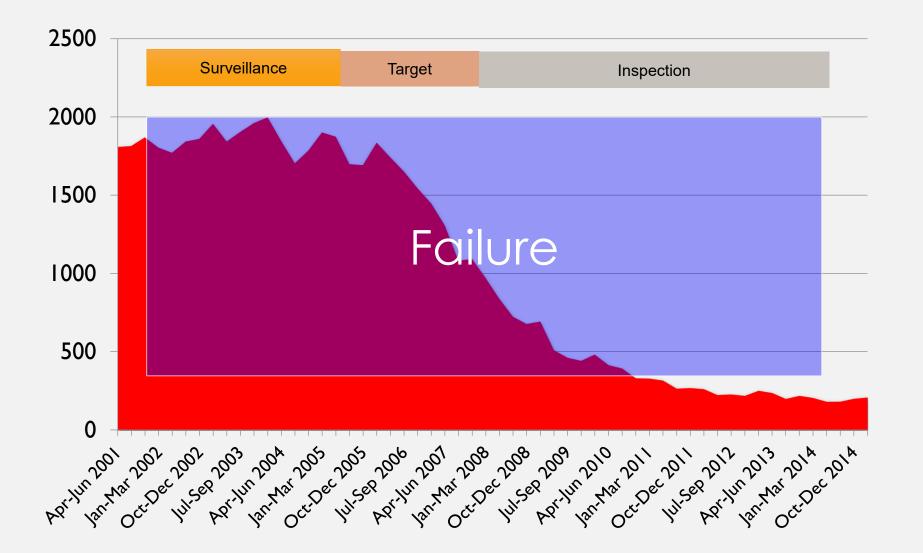
Oct 16 2004 **Superbug scare** By Amy Devine

A NOTORIOUS murderer and serial rapist is carrying the deadly superbug MRSA in jail.

Thomas Young has been moved to the hospital wing at Peterhead prison where bosses have reminded cons to wash their hands and have placed extra soap and paper towels in its halls.

But a source at the jail, where some of Scotland's worst sex offenders are held, said: 'Inmates and staff are scared to go near the health centre in case they catch this horrible bug.

### Quarterly MRSA Bloodstream Infections England: 2001-15



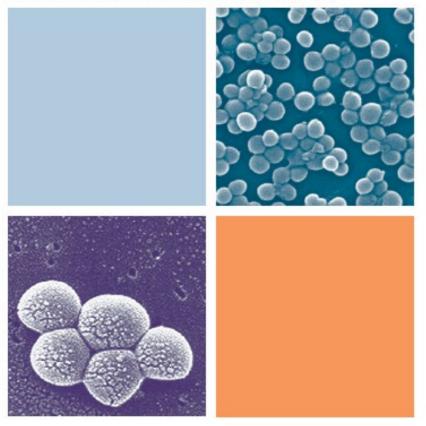
### WHY DID IT COME DOWN?

- Government action and policies
  - Nothing to do with the organism itself, new antibiotics etc
- It was all about stopping an organism from doing damage when it gets to where it should not
  - Screening, so that skin suppression could take place
  - The bloodstream via medical devices
- MRSA was the low-hanging fruit





National Confidential Study of Deaths Following Meticillin-Resistant Staphylococcus aureus (MRSA) Infection



'After 8 days the PVC inserted on admission showed signs of infection with a purulent discharge.' Case study 4

'Six days post-operatively the patient was noted to have pus coming from a cannula site.' Case study 6

'For almost half of the cases reviewed, The source of the MRSA infection was an invasive device, particularly PVC and CVC.'

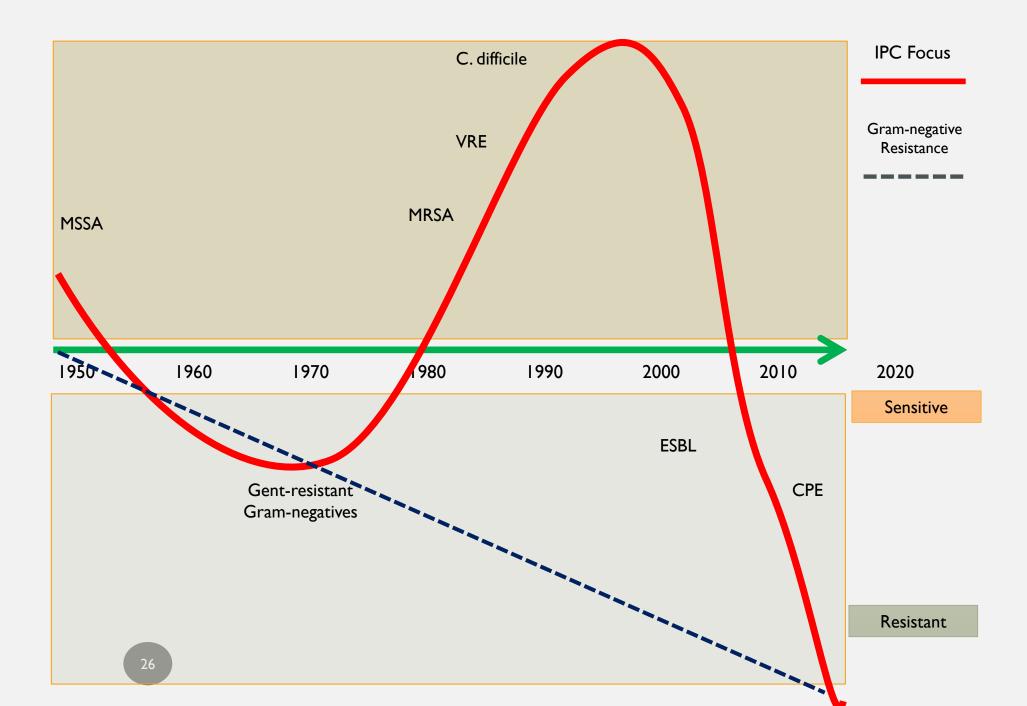
### SURGE PATHOGENS

### • Gram-Negatives on the Rise

- Hospital-acquired Gram-negative bacteria (like CRE carbapenem-resistant Enterobacteriales, Acinetobacter baumannii, Pseudomonas) are increasing. Globally, deaths associated with carbapenem-resistant infections jumped to over 1 million by 2021, outpacing most other resistance trends
  - In parts of Asia, endemic CRE outbreaks are routine in ICU settings

### • Emerging Fungal Threats

 Drug-resistant fungi have also appeared. Candidozyma auris, for instance, has simultaneously emerged in over 40 countries across multiple continents and caused difficult-to-control hospital outbreaks



#### **JULY 2004 : MEDIA DISCOVERS ESBL**

#### **Scientists fear 28 people** killed by new superbug

#### **James Meikle** Health correspondent

Scientists are urgently assessing the threat from new superbugs that are wrecking antibiotic treatments for hundreds in the year to March.

nary tract infections such as hospital treatment. cvstitis and cases of blood poisoning caused by strains of the scientists is that there is no E coli bug resistant to most antibiotics.

increasingly dreaded acronym not developed resistance is 28 had died. available in tablet form.

months the Health Protection

than 400 samples from 60 labs across Britain. The agency is assessing these results and will report next month.

It may prove difficult to be two classes of antibiotics, penispecific on how many people of patients and may have have died as a result of the killed 28 people in Shropshire bug, or where it was a contrib-

utory factor. Patients may have Laboratories have reported had underlying medical cona surge in the number of uri- ditions or been receiving other this county is that every ESBL-

> mandatory reporting system. unlike for MRSA. Yesterday

The bugs, represented by an Michael Gwynne, coroner for Telford and the Wrekin in ESBL, are not only striking in Shropshire, said there had hospitals, but also turning up in been 200 clinical infections in GP surgeries, and only one class the county over 12 months, of antibiotic to which they have and among the first 105 cases,

The outbreak started in patients did not respond to They are still not as preva- March 2003, but coroners conventional antibiotic treatlent as the notorious MRSA found out only when Shrewsfamily but over the last 12 bury and Telford Hospital NHS Trust sought advice on refer-

Agency has been sent more ring deaths of patients who had died from extended spectrum beta lactamases (ESBLs). These are enzymes produced by E coli bacteria which are resistant to

> cillins and cephalosporins. Mr Gwynne said: "I think it is alarming to say the least. The steps I have taken and agreed with other coroners for related death must be referred

One of the problems for the to the coroner and we can decide individually if we wish to have an inquest."

He is planning to reopen the inquest on a local woman because he has been told her death was attributable to ESBL. Pat Troop, chief executive of the Health Protection Agency, said GPs had been alerted to send samples to laboratories if

ments and the agency was also consulting specialists around the world to assess the threat.

Coroner fears new superbug outbreak

, 2004 THE DAILY TELEGRAPH

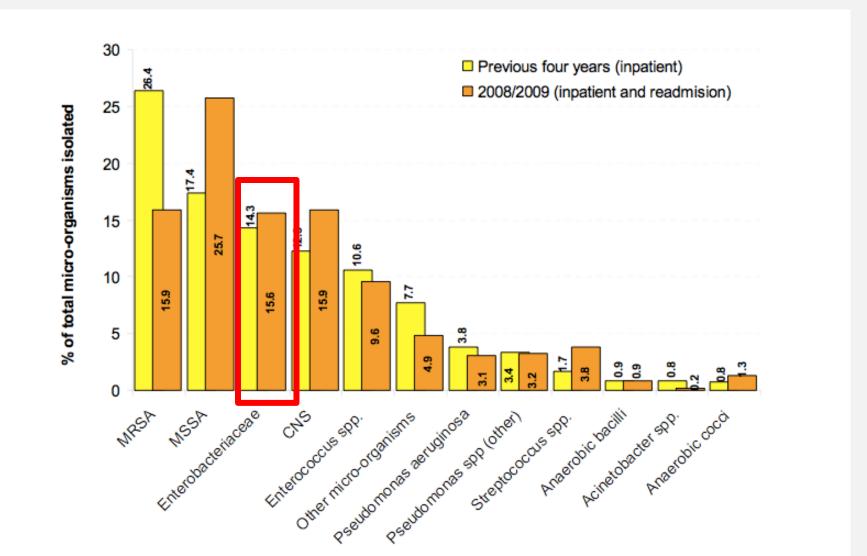
By Roger Highfield SCIENCE EDITOR

A CORONER called vesterday for greater efforts to deal with antibiotic-eating bacteria, a different kind of superbug to MRSA, which had been linked to 28 deaths in the past year in his area.

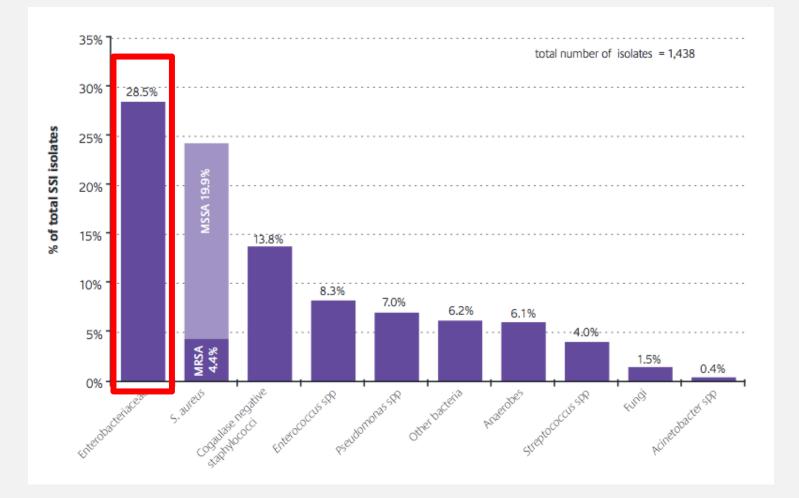
Prompted by his concerns, the Health Protection Agency admitted there had been an increase in urinary tract infections and blood poisoning caused by antibioticdigesting strains of the gut bacterium E coli.

# **EVIL SUPER BUG LEAGUE** ESB

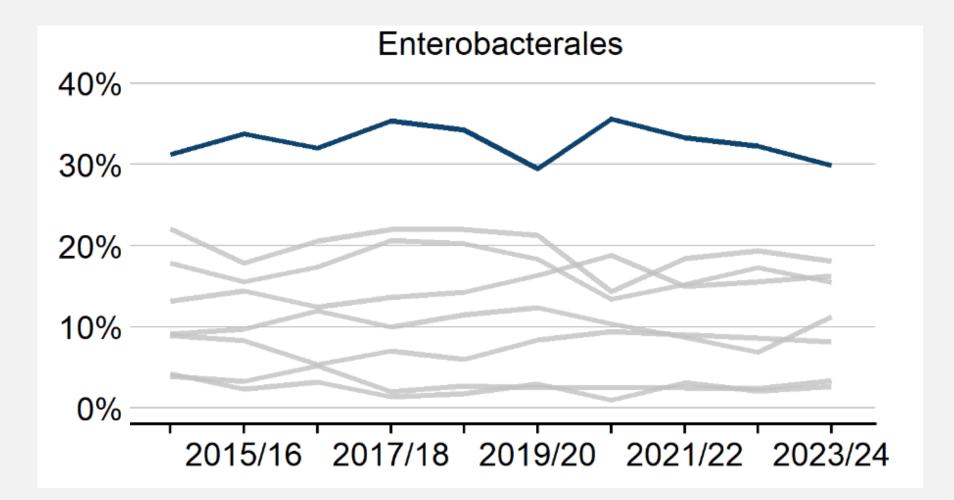
#### ORGANISMS CAUSING SURGICAL WOUND INFECTIONS ENGLAND 2004-9



### ORGANISMS CAUSING SURGICAL WOUND INFECTIONS ENGLAND 2012



### SURGICAL WOUND INFECTIONS ENGLAND 2012-2024



### SSI IN CABG IN VICTORIA 2010-23

- Predominant pathogens
  - Staphylococcus aureus, Serratia marcescens, Staphylococcus epidermidis, and Klebsiella pneumoniae
  - proportion of sternal and donor site SSIs involving Gram-negative pathogens increased from 38% to 59%
    - Tanamas SK, Lim LL, Bull AL, Malloy MJ, Brett J, Dickson Z, et al. Surgical Site Infections Complicating Coronary Artery Bypass Graft Surgery in Australia: time trends in infection rates, surgical antimicrobial prophylaxis and pathogens using a comprehensive surveillance network, 2010-2023. J Hosp Infect 2025. https://doi.org/10.1016/j.jhin.2025.04.027.

| ses  | Results M    | icro Devices (0)        | Conditions I          | nfections | Notes | Locations           | Isolation Ta       | igs (1) | Tasks (1/2) Ol | bs Alerts    |                         |   |
|--|--------------|-------------------------|-----------------------|-----------|-------|---------------------|--------------------|---------|----------------|--------------|-------------------------|---|
| Showing : Active results  - Add specimen Add selected organisms to infection |              |                         |                       |           |       |                     |                    |         |                |              |                         |   |
| Spe  | cimens       |                         |                       |           |       |                     |                    |         |                |              |                         |   |
|  | Specimen No. | Specimen Date           | Specimen Type         | Hosp      | ital  | ward                | Orga               | nisms   | Result Statu   | s Superseded | Import Date             |   |
|  |              |                         |                       |           | _     |                     |                    |         |                | All 👻        |                         |   |
| +  | 14M8444222   | 31-Jul-2014<br>00:00:00 | Urine (mid<br>stream) | Sefton PC |       | Roe Lane<br>Surgery | Coliform s         | p Case  | e Final        | No           | 02-Aug-2014<br>09:35:07 | 6 |
| +  | 14M8440100   | 02-Jul-2014<br>00:00:00 | Urine (mid<br>stream) | Sefton PC |       | Roe Lane<br>Surgery | Coliform s         | p Case  | e Final        | No           | 04-Jul-2014<br>11:45:17 | • |
| +  | 14M8435920   | 02-Jun-2014<br>00:00:00 | Urine (mid<br>stream) | Sefton PC |       | Roe Lane<br>Surgery | Coliform s         | p Case  | e Final        | No           | 04-Jun-2014<br>10:12:02 | • |
| +  | 14M8391196   | 08-Apr-2014<br>15:00:00 | Urine (mid<br>stream) | Sefton PC |       | Roe Lane<br>Surgery | Coliform s         | p Case  | e Final        | No           | 11-Apr-2014<br>12:23:21 | • |
| +  | 14M8386916   | 25-Feb-2014<br>00:00:00 | Urine (mid<br>stream) | Sefton PC |       | Roe Lane<br>Surgery | Escherichi<br>Case | a coli  | Final          | No           | 03-Mar-2014<br>09:27:40 | • |
| +  | 14M8365826   | 10-Feb-2014<br>00:00:00 | Urine (mid<br>stream) | Sefton PC |       | Roe Lane<br>Surgery | Coliform s         | p Case  | e Final        | No           | 12-Feb-2014<br>09:40:18 | 6 |
| +  | 13M8358997   | 23-Dec-2013<br>10:00:00 | Urine (mid<br>stream) | Sefton PC |       | Roe Lane<br>Surgery | Coliform s         | p Case  | e Final        | No           | 24-Dec-2013<br>10:40:04 | 6 |
| +  | 13M8307073   | 19-Nov-2013<br>09:00:00 | Urine (mid<br>stream) | Sefton P  |       | Roe Lane<br>Surgery | Coliform s         | p Case  | e Final        | No           | 21-Nov-2013<br>11:35:25 | 6 |
| +  | 13M8304288   | 30-Oct-2013<br>00:00:00 | Urine                 | Sefton PC |       | Roe Lane<br>Surgery | Coliform s         | p Case  | e Final        | No           | 01-Nov-2013<br>12:40:09 | • |
| +  | 13M8302090   | 15-Oct-2013<br>09:00:00 | Urine (mid<br>stream) | Sefton PC |       | Roe Lane<br>Surgery | Coliform s         | p Case  | e Final        | No           | 17-Oct-2013<br>10:55:17 | • |
| +  | 13M8297213   | 09-Sep-2013<br>10:00:00 | Urine (mid<br>stream) | Sefton PO |       | Roe Lane<br>Surgery | Coliform s         | p Case  | e Final        | No           | 11-Sep-2013<br>09:25:09 | • |
| +  | 13M8252595   | 27-Jun-2013<br>00:00:00 | Urine (mid<br>stream) | Sefton PC |       | Roe Lane<br>Surgery | Coliform s         | p Case  | e Final        | No           | 29-Jun-2013<br>09:55:05 | • |

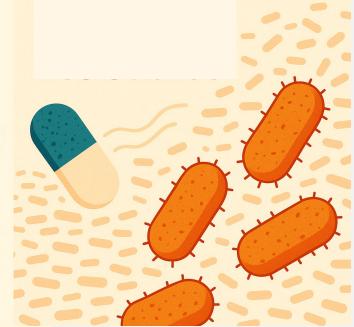
### IMMUNE SYSTEM – OVER TO YOU..

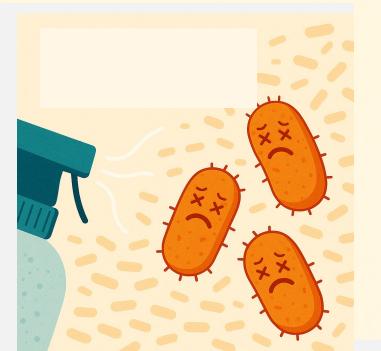
| 30 Jun 2014 00:00 | BC - Blood culture            | AICU - AICU | CNS - Coagulase Negative<br>Staphylococcus<br>GPC - Unidentified Gram posit<br>SE - Staphylococcus epiderm  |   |
|-------------------|-------------------------------|-------------|---|---|
| 30 Jun 2014 00:00 | ASC - Ascitic fluid           | AICU - AICU | KP - Klebsiella pneumoniae  | ۲ |
|                   | Organism<br>KP - Klebsiella p | pneumoniae  | AK - AmikacinRAMP - AmpicillinRAUG - AugmentinRCAZ - CeftazidimeRCOL - ColistinRCP - CiprofloxacinRCPD - CefpodoximeRCXM - CefuroximeRERT - ErtapenemRGEN - GentamicinRMER - MeropenemRTAZ - Pip/TazobactamRTRI - TrimethoprimR |   |

|             | Antibiotic   | Disinfectant  |
|-------------|--|---|
| Specificity | <ul> <li>Highly specific, targets single protein or metabolic pathway</li> <li>Bacteria only</li> <li>Susceptibility varies between genus/strain and isolate</li> </ul>                            | <ul> <li>Non-specific, targets global cellular structures<br/>and classes of biomolecules</li> <li>Not limited to bacteria</li> <li>Disinfectants claimed 'bactericidal' are<br/>normally effective against most bacteria,<br/>regardless of genus or family</li> </ul>         |
| Dose        | <ul> <li>Based on MIC</li> <li>Sufficiently high to be effective, as<br/>low as possible to not harm the<br/>patient</li> <li>Strong dilution after<br/>administration, variable during</li> </ul> | <ul> <li>High concentrations - 100 - 1000 x MIC; As highly concentrated as necessary; Uses defined log<sub>10</sub> reductions</li> <li>No/little dilution during application, constantly high during use, assuming correct application and no dilution at interface</li> </ul> |
| Exposure    | <ul> <li>Hours/days/weeks (even low doses<br/>over a long time)</li> </ul>   | <ul> <li>High dosage over short exposure time</li> </ul>  |
| Formulation | <ul> <li>Generally one active agent</li> </ul>   | <ul> <li>Complex formulation; often mixtures of<br/>different active substances</li> </ul>  |

### **Antibiotic resistance**

- Ability of bacteria to survive and proliferate despite the presence of an antibiotic that would normally inhibit or kill them
- Often acquired genetically through plasmids or mutations





### **Disinfectant tolerance**

- Reduced susceptibility of microorganisms to disinfectants although in-use concentrations are normally adequate
- May be intrinsic or selection-based Most often single Quaternary Ammonium Compounds, dependent on formulation

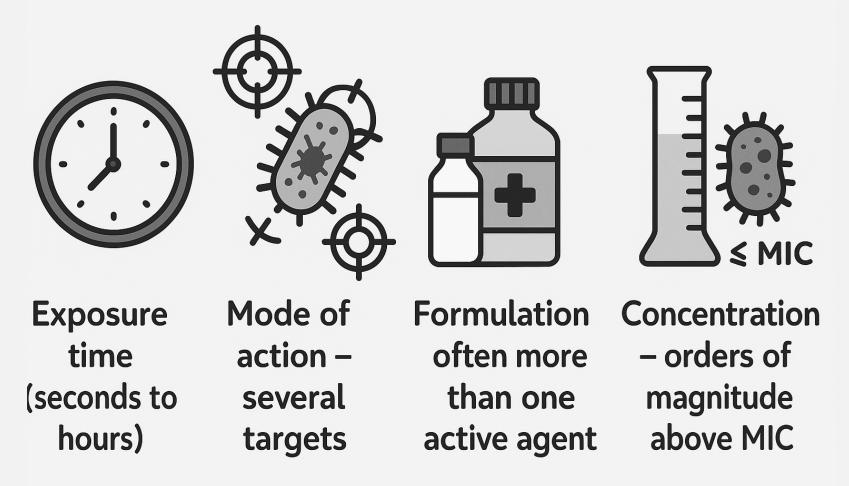
### DISINFECTANT TOLERANCE

| Disinfectant                               | First Use    | Tolerance      | Resistance          |
|--|--------------|----------------|---------------------|
| Ethanol                                    | 19th century | 2000s          | No                  |
| Sodium hypochlorite (Bleach)               | 1785         | 2000s          | No                  |
| Chlorine dioxide                           | 1814         | 2010s          | No                  |
| Hydrogen Peroxide                          | 1818         | 2010s          | No                  |
| Isopropanol                                | 1920         | 2000s          | No                  |
| Benzalkonium chloride                      | 1935         | <b>1980</b> s  | No                  |
| Glutaraldehyde                             | 1960         | <b>1980</b> s  | Yes - Mycobacterium |
| Didecyldimethylammonium chloride<br>(DDAC) | 1962         | 1990s          | No                  |
| Peracetic Acid (PAA)                       | 1985         | Not documented | No                  |

#### RESISTANCE

- Antibiotics
  - Average time to resistance 2-10 years; some within a year
- Disinfectants
  - Average time to resistance decades (if at all)
  - Mean tolerance 40-70 years
  - clinical impact of disinfectant tolerance is less clear and generally less significant due to high in-use concentrations and multi-target action

#### WHY IS DISINFECTANT RESISTANCE RARE?



Krewing M, et al . Resistance or tolerance? Highlighting the need for precise terminology in the field of disinfection. J Hosp Infect 2024;150:51-60

# DISINFECTANT TOLERANCE

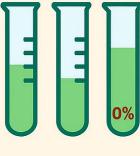
- Disinfectants are usually used at concentrations much higher than laboratory studies that show increased MICs (minimum inhibitory concentration) and MBCs (minimum bactericidal concentration) but problems arise when:
  - Surfaces are not cleaned properly first, reducing effectiveness
  - Contact time is too short
  - Disinfectants are diluted too much (either intentionally or by error)
    - Boyce JM. Quaternary ammonium disinfectants and antiseptics: tolerance, resistance and potential impact on antibiotic resistance. Antimicrob Resist Infect Control 2023;12(1):32 https://doi.org/10.1186/s13756-023-01241-z.

### DILUTION AT LOCAL LEVEL

- Automated dispensers that dilute concentrated Quaternary ammonium compounds with water are commonly used in healthcare in the USA
  - Cadnum JL et al. Dilution dysfunction: evaluation of automated disinfectant dispenser systems in 10 hospitals demonstrates a need for improved monitoring to ensure that correct disinfectant concentrations are delivered. Infect Control Hosp Epidemiol 2024;45(11):1362-5. https://doi.org/10.1017/ice.2024.148.



9 of 10 hospitals using dilutable disinfectants had 1 or more malfunctioning dispensers



Twenty-nine of 107 systems dispensed product with lowerthan-expected concentrations, including 15 with no detectable disinfectant

#### IS TOLERANCE A CLINICAL ISSUE?

- While studies highlight the risk and mechanisms of disinfectant tolerance and a potential to increase infection rates, direct clinical studies documenting a rise in infections due to disinfectant-resistant organisms are rare
  - Most evidence is indirect, and systematic reviews show that improved disinfection reduces MDRO infections, implying that MDROs cause more infections when not effectively eliminated
    - Peters A, et al. Impact of environmental hygiene interventions on healthcareassociated infections and patient colonization: a systematic review. Antimicrob Resist Infect Control 2022;11(1):38. https://doi.org/10.1186/s13756-022-01075-1.

### MITIGATION

- If you have an antibiotic-resistant organism, IPC procedures must be 100% as there are no alternative treatments
- If you have a disinfectant-tolerant organism, consider switch to alternative/higher-level agent
- No tolerance/resistance issues reported in:
  - Ethanol, Propanol, Peracetic acid, Povidone iodine, Hydrogen peroxide
- Is it time to consider rotation of agents?
  - Caution with surface compatibility; staff unfamiliarity etc

# AMR – TURNING THE TIDE I

- Antimicrobial Stewardship
  - Programs for appropriate prescribing, avoidance of antibiotics for viral or self-limiting conditions
- Diagnostic Stewardship
  - Appropriate testing
    - Lim LL, et al. Implementation of an intervention to reduce urine dipstick testing in aged care homes: a qualitative study of enablers and barriers, and strategies to enhance delivery. BMJ Open 2024;14(3):e081980. https://doi.org/10.1136/bmjopen-2023-081980.
  - Use of rapid diagnostics and point-of-care tests to distinguish between bacterial and viral infections, enhanced laboratory capacity for culture and sensitivity testing to guide targeted therapy and use of biomarkers (e.g., procalcitonin)
- Public and professional education
  - Combat misinformation and expectation

# AMR – TURNING THE TIDE 2

#### Immunisation Programs

- Increase uptake of vaccines (e.g., influenza, pneumococcal, Haemophilus influenzae type b) to prevent infections that often result in antibiotic use and promote animal vaccination to reduce the need for antibiotics in livestock
- Regulatory and Policy Interventions
  - Enforce prescription-only antibiotic access—ban over-the-counter antibiotic sales
- Agriculture and Veterinary Use
  - Reduce non-therapeutic use of antibiotics in animals (e.g., growth promotion, routine prophylaxis)
  - Promote One Health surveillance and action plans across human-animalenvironment interfaces

# AMR – TURNING THE TIDE 3

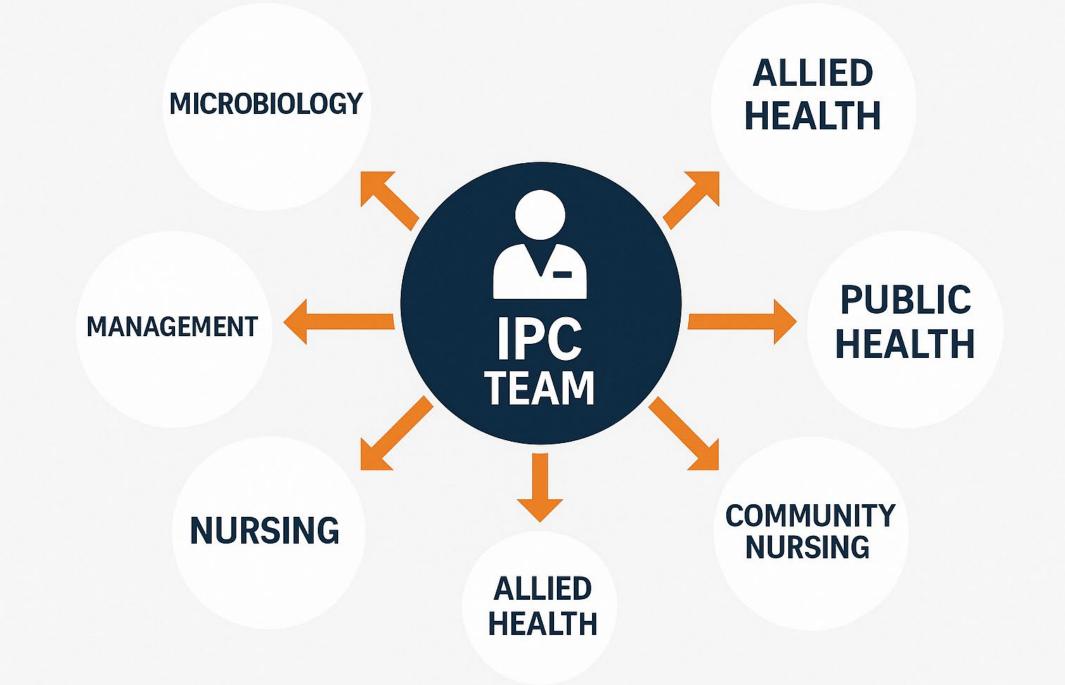
- Surveillance and Monitoring
  - Implement and strengthen systems for monitoring antibiotic use and resistance patterns in humans and animals
  - Use data to inform stewardship programs, policy decisions, and public reporting
- Research and Innovation
  - Invest in alternatives to antibiotics, such as bacteriophages, immunotherapies, and probiotics
    - Hu P, et al. Isolation and identification of Klebsiella pneumoniae phage PhiK2046: optimizing its antibacterial potential in combination with chlorhexidine. Antimicrob Resist Infect Control 2025;14(1):42.
  - Promote behavioural research into prescribing practices and compliance

#### IPC CAN CUT THE BURDEN AND THE COST

- Hand and environmental hygiene are the most cost-saving IPC measures, cutting AMR-related mortality by over 50% and reducing long-term complications by at least 40%.
  - Global report on infection prevention and control. Geneva: World Health Organization; 2022
- Implementing IPC measures like hand hygiene, antibiotic stewardship, and environmental cleaning can cut AMR burden by 85% and yield a seven-fold return on investment (OECD)
  - Slawomirski L, Klazinga N. Economics of patient safety: from analysis to action. Paris: Organisation for Economic Cooperation and Development; 2020

### AMR – TURNING THE TIDE

- Preventing infections = reducing resistance
  - WHO emphasises that improved infection prevention and control in healthcare is the single most important action to curb AMR
    - World Health Organization. Antimicrobial resistance: accelerating national and global responses: WHO strategic and operational priorities to address drug-resistant bacterial infections in the human health sector, 2025–2035. Geneva: WHO; 2023
- Prevent infections that would require the use of antibiotics
  - Strengthen IPC practices in healthcare to reduce HAIs, reducing the need for antibiotics
  - Promote hand hygiene, vaccination, aseptic technique, and environmental hygiene
  - Invest in WASH (water, sanitation, and hygiene) infrastructure, especially in lowresource settings



#### THE IPC WORLD ACCORDING TO WHO

# 33%-45%

of countries had no national IPC programme or an inactive one (surveys conducted in the last two years)

# 15.2%

of facilities met all IPC minimum requirements

92.9% met at least half of the requirements

# 3.8%

of countries had all IPC minimum requirements in place (WHO study)

77.4% met half of the requirements

FACILITY IPC PROGRAMMES CLASSIFIED IN 2019

INADEQUATE BASIC INTERMEDIATE average "basic" level in LICs

#### CONCLUDING

- Prevention is better than cure, especially when there isn't one..
- IPC Teams often operate behind the scenes and are often underappreciated or under-resourced
  - Successes (infections that **didn't** happen) are invisible
  - The better you do your job, the more invisible you become
- But you are frontline workers who are in a prime position to intercept unnecessary antibiotic usage and it is time that you were recognised as such