

Title: Drug Resistant Organisms
Antibiotics resistance : opportunities & challenges

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- Common targeted Antimicrobial Resistance organisms
- Developing resistance vs One Health approach
 - Global strategy Antimicrobial resistance
- ESKAPE Members
- Definitions of MDR, XDR, PDR – Standard definition ??
- Current Antibiotic Resistance Threats, by Microorganism (CDC)
- Challenging –
 - WHAT CAN WE DO ? -ASWP
 - Preauthorization
 - Prospective audit
- To Differentiate - Significant Infection or Colonization:



Introduction -Resistant Bacteria

- Antibiotic resistance is a **major challenge in the healthcare sector.**
- **Global threat.**
- Its emergence rests on
 - antimicrobial **overuse** in humans
 - food-producing **animals**;
 - **globalization**
 - **suboptimal infection control**
- Difficult decisions for **clinicians selecting optimal treatment.**
- **Challenging** : Antimicrobial stewardship programs (ASWPs)- **WHAT CAN WE DO?**
 - Significant Infection vs Colonization (**clinical & microbiological** significance):
 - **Preauthorization**
 - **Prospective audit**
 - **Training /Education**

Essential - Audit to Optimize Treatment (*ref : CDC 2017*)





Targeted common multi-drug resistant bacteria

GPB

- *Vancomycin-resistant enterococci (VRE)*
- Methicillin-resistant *Staphylococcus aureus* (MRSA)

GNB

- Extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae*
(examples of common *Enterobacteriaceae* are *Klebsiella pneumoniae* and *Escherichia coli*)
- **Carbapenemase-producing *Enterobacteriaceae***
(e.g. *Klebsiella pneumoniae*)
- **Multidrug-resistant *Acinetobacter* / *Pseudomonas aeruginosa***
- MDR *Enterobacter* species



How Antibiotic Resistance Happens

1. Lots of germs. A few are drug resistant.



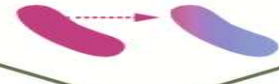
2. Antibiotics kill bacteria causing the illness, as well as good bacteria protecting the body from infection.



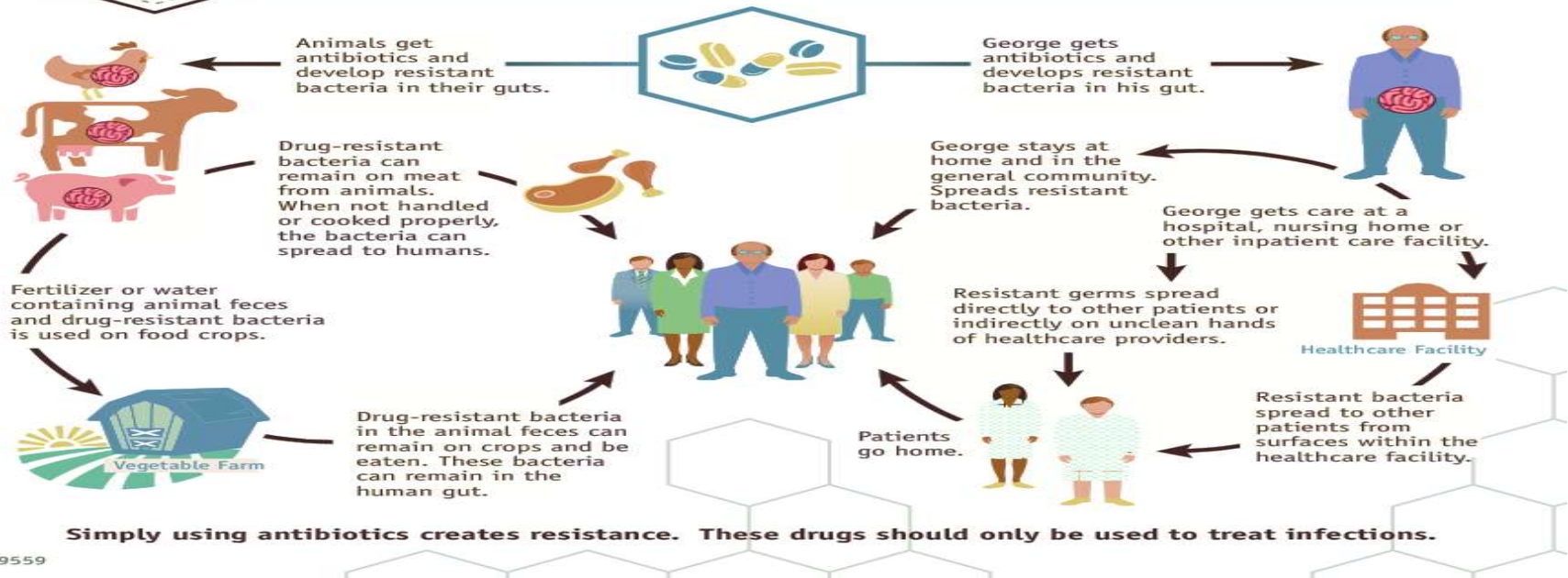
3. The drug-resistant bacteria are now allowed to grow and take over.



4. Some bacteria give their drug-resistance to other bacteria, causing more problems.



Examples of How Antibiotic Resistance Spreads



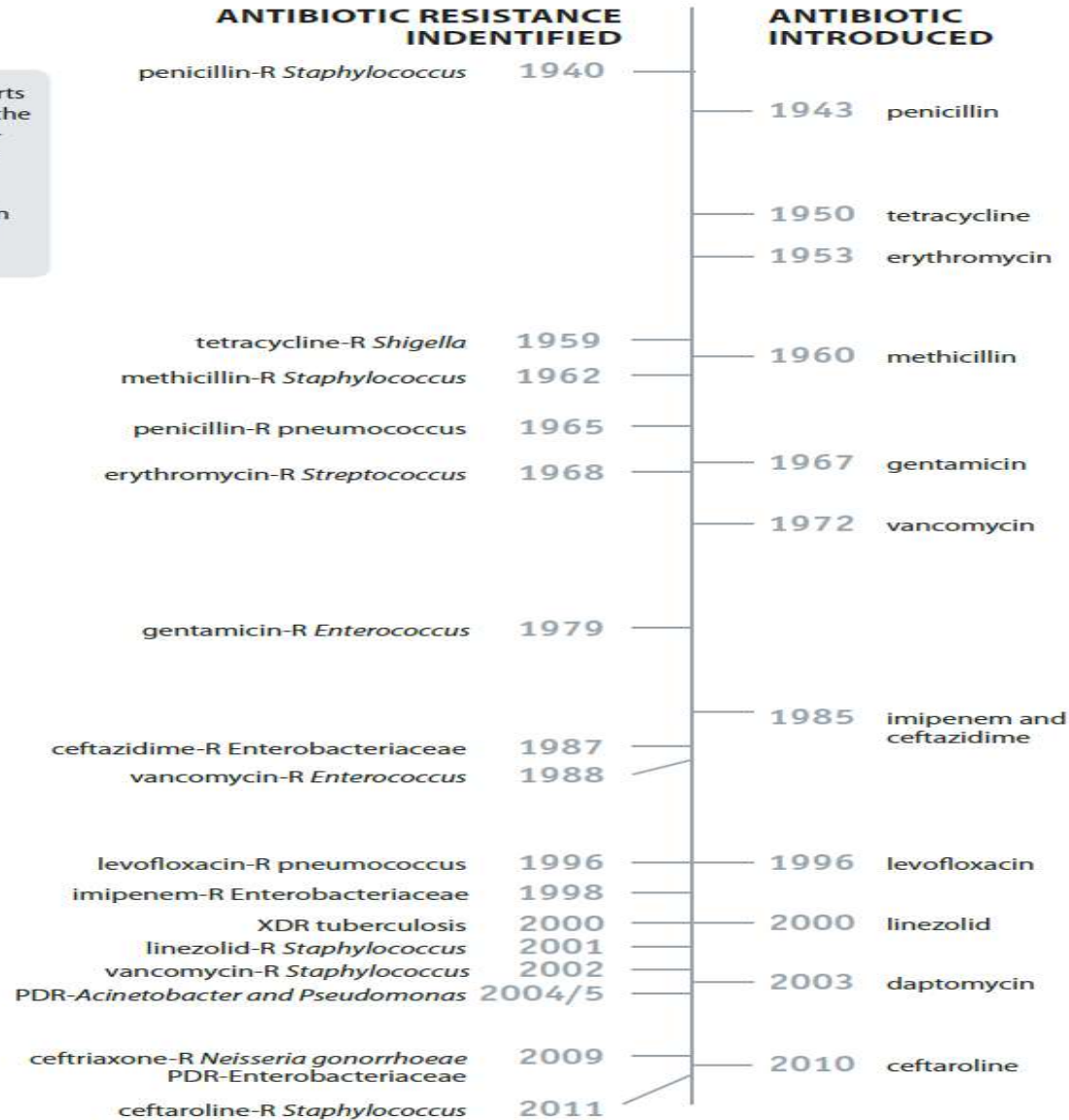
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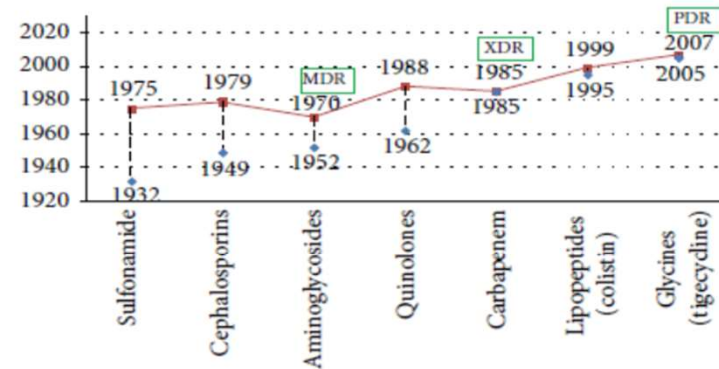
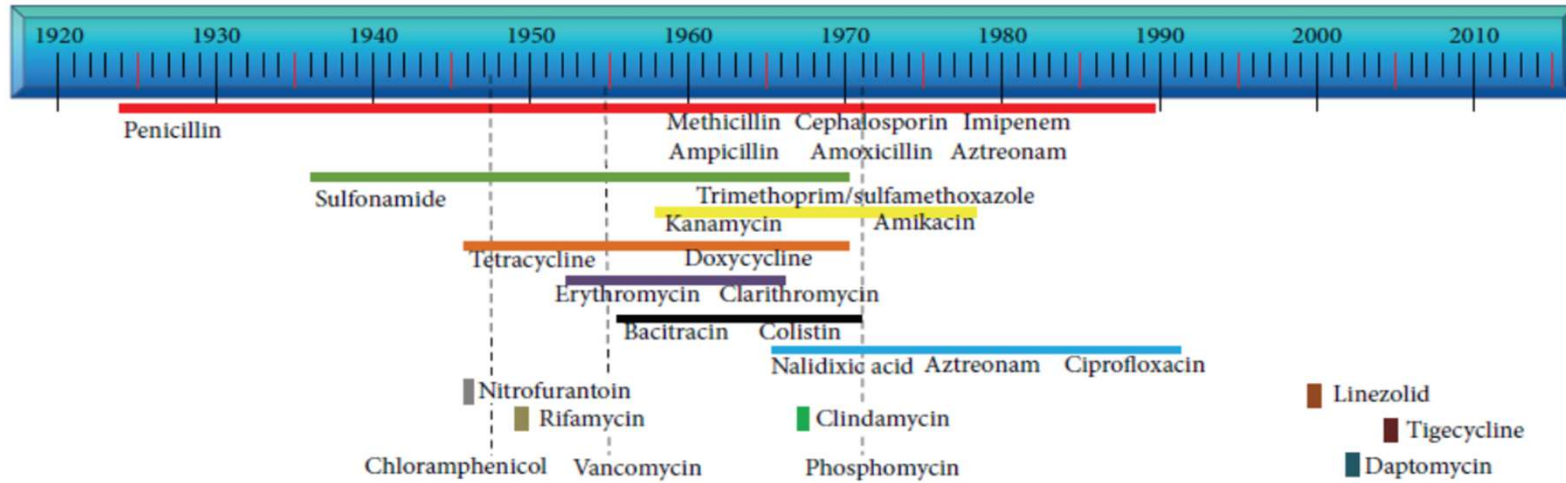
ANTIBIOTIC RESISTANCE THREATS in the United States, 2013

Developing Resistance

Timeline of Key Antibiotic Resistance Events

Dates are based upon early reports of resistance in the literature. In the case of pan drug-resistant (PDR)-*Acinetobacter* and *Pseudomonas*, the date is based upon reports of healthcare transmission or outbreaks. Note: penicillin was in limited use prior to widespread population usage in 1943.





Antibiotic color key:

- β-lactamics
- Sulfonamide
- Aminoglycosides
- Tetracycline
- Macrolides
- Polypeptide
- Quinolones
- Glycylcycline
- Nitrofurans
- Lincosamides
- Oxazolidinones
- Ansamycins
- Lipopeptides

- ◆ Date of introduction of antimicrobials
- *A. baumannii*

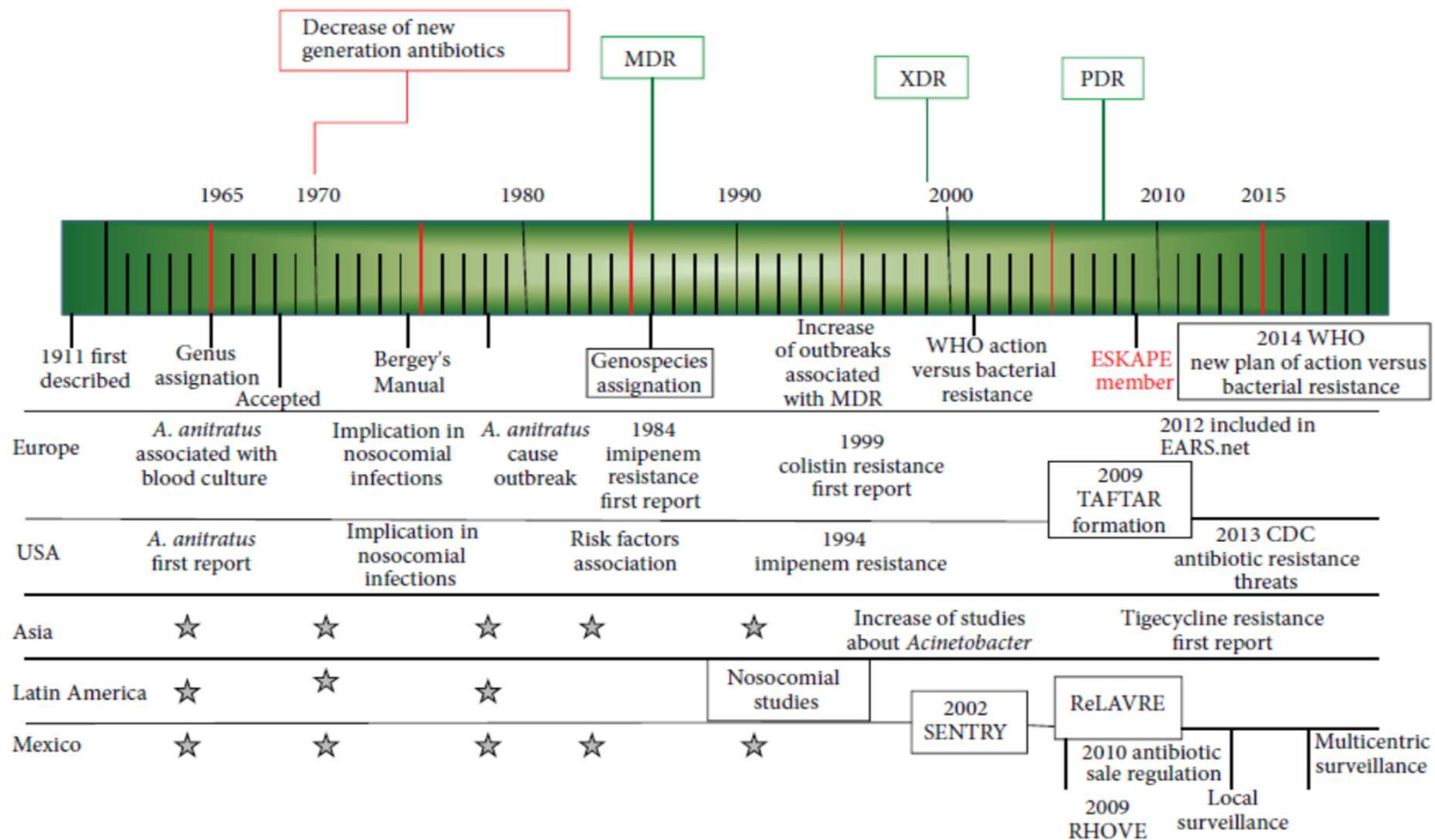


FIGURE 2: Brief history of the incorporation of *Acinetobacter baumannii* as one of the successful multidrug-resistant nosocomial pathogens. This has led to the strategic alliance of different countries and continents in monitoring resistant bacteria, and it has resulted in the formulation of a new action plan against bacterial resistance in 2015.

Ref: AnaMaria Gonzalez-Villoria¹ and Veronica Valverde-Garduno, Review Article
 Volume 2016, Article ID 7318075,
<http://dx.doi.org/10.1155/2016/7318075>



Definitions

ESKAPE

- *Enterococcus* , *Staph aureus*, *K.pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacter* species. –

PLUS??

- *How about -E.coli ?? (ESBL positive and Cip resistance)*

Antimicrobial Resistance Gram negative bacteria (GNB)

- **MDR**, consisted of those isolates that non-susceptible to at least 1 agent in 3 or more different classes (**MDR**).
- **XDR-**, consisted of those isolates that were resistant to all groups/classes of antimicrobials except one defined as extended resistant isolates (**XDR**). **Non-susceptible to at least 1 agent in ALL but 2 different classes.**
- **PDR-** consisted of those isolates that non-susceptible to all agents. (**PDR**)

Ref: Magiorakos AP, Srinivasan A, et al..*Clin Microbiol Infect* 2012; 18: 268–281

Ref: SASCM -Updated proposal for national standardization of definitions 2018



Current Antibiotic Resistance Threats, by Microorganism

Urgent Threats

- *Clostridioides difficile*
- **Carbapenem-resistant Enterobacteriaceae (CRE)**
- Drug-resistant *Neisseria gonorrhoeae*

Concerning Threats

- Vancomycin-resistant *Staphylococcus aureus* (VRSA)
- Erythromycin-Resistant Group A *Streptococcus*
- Clindamycin-resistant Group B *Streptococcus*

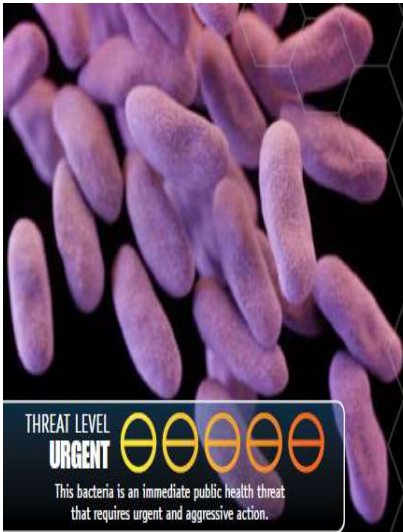
Serious Threats

- **Multidrug-resistant *Acinetobacter***
- Drug-resistant *Campylobacter*
- Fluconazole-resistant *Candida*
- Extended-spectrum Beta-lactamase producing *Enterobacteriaceae*
- Vancomycin-resistant *Enterococcus* (VRE)
- Multidrug-resistant *Pseudomonas aeruginosa*
- Drug-resistant non-typhoidal *Salmonella*
- Drug-resistant *Salmonella* Serotype Typhi
- Drug-resistant *Shigella*
- **Methicillin-resistant *Staphylococcus aureus* (MRSA)**
- Drug-resistant *Streptococcus pneumoniae*
- Drug-resistant Tuberculosis

Ref: CDC 2013



Threat level Example of MDR Bacteria



CARBAPENEM-RESISTANT ENTEROBACTERIACEAE

9,000 DRUG-RESISTANT INFECTIONS PER YEAR **600** DEATHS

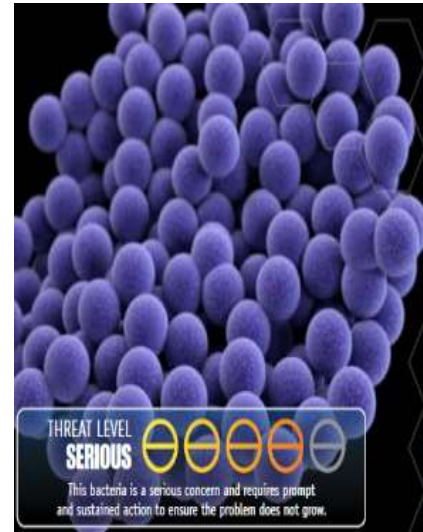
CARBAPENEM-RESISTANT **7,900** CARBAPENEM-RESISTANT **1,400**

KLEBSIELLA SPP. E. COLI

THREAT LEVEL URGENT ○○○○○○

This bacteria is an immediate public health threat that requires urgent and aggressive action.

CRE HAVE BECOME RESISTANT TO ALL OR NEARLY ALL AVAILABLE ANTIBIOTICS




METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA)

80,461 SEVERE MRSA INFECTIONS PER YEAR **11,285** DEATHS FROM MRSA PER YEAR

THREAT LEVEL SERIOUS ○○○○○○

This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.

STAPH BACTERIA ARE A LEADING CAUSE OF HEALTHCARE-ASSOCIATED INFECTIONS



MULTIDRUG-RESISTANT ACINETOBACTER

7,300 MULTIDRUG-RESISTANT ACINETOBACTER INFECTIONS **500** DEATHS FROM MULTIDRUG-RESISTANT INFECTIONS

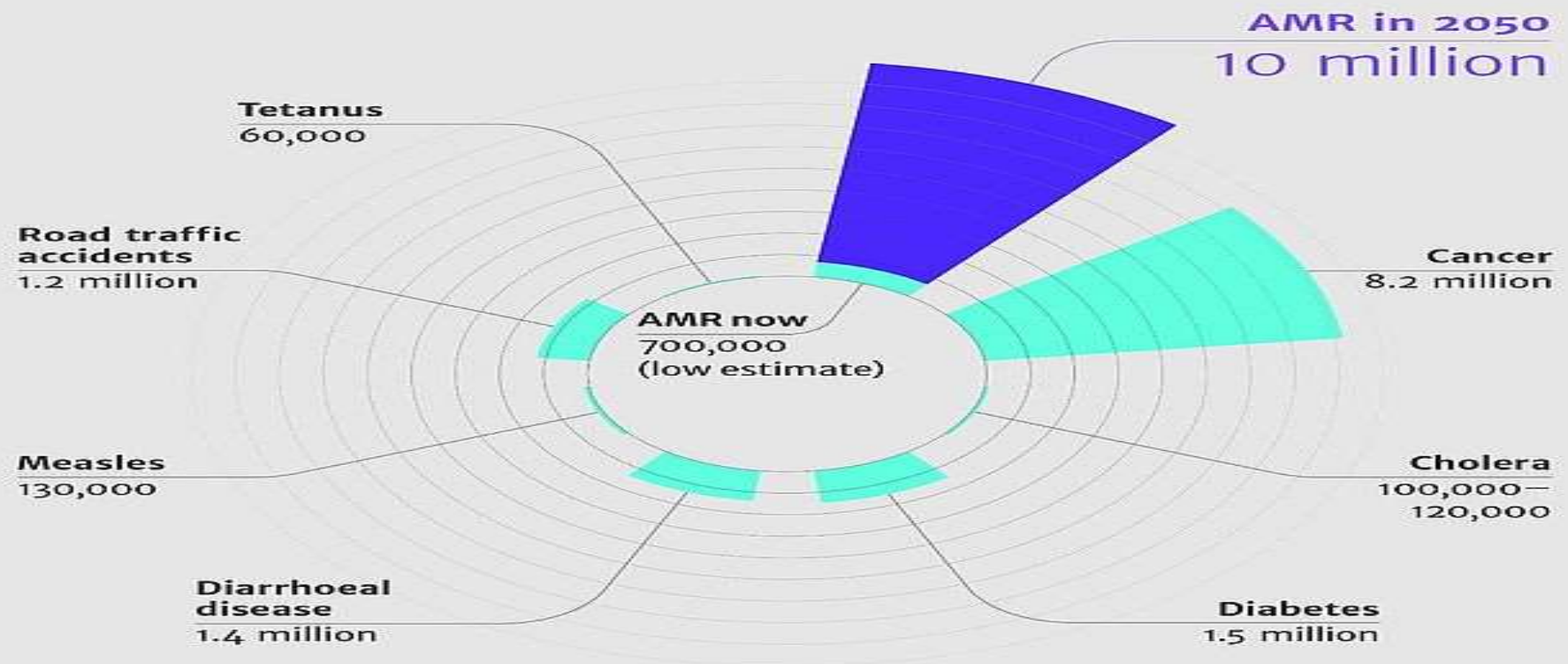
12,000 ACINETOBACTER INFECTIONS PER YEAR

THREAT LEVEL SERIOUS ○○○○○○

This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.

AT LEAST THREE DIFFERENT CLASSES OF ANTIBIOTICS NO LONGER CURE RESISTANT ACINETOBACTER INFECTIONS

Deaths attributable to AMR every year compared to other major causes of death



Sources

Diabetes
Cancer
Cholera
Diarrhoeal disease

www.who.int/mediacentre/factsheets/fs312/en/
www.who.int/mediacentre/factsheets/fs292/en/
www.who.int/mediacentre/factsheets/fs107/en/
www.sciencedirect.com/science/article/pii/S0140673612617280

Measles
Road traffic accidents
Tetanus

www.sciencedirect.com/science/article/pii/S0140673612617280
www.who.int/mediacentre/factsheets/fs338/en/
www.sciencedirect.com/science/article/pii/S0140673612617280



To achieve this overall goal, five strategic objectives have been identified.

Objective 1: Improve awareness and understanding of antimicrobial resistance through effective communication, education and training

Objective 2: Strengthen the knowledge and evidence base through surveillance and research

Objective 3: Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures

Objective 4: Optimize the use of antimicrobial medicines in human and animal health

Objective 5: Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions



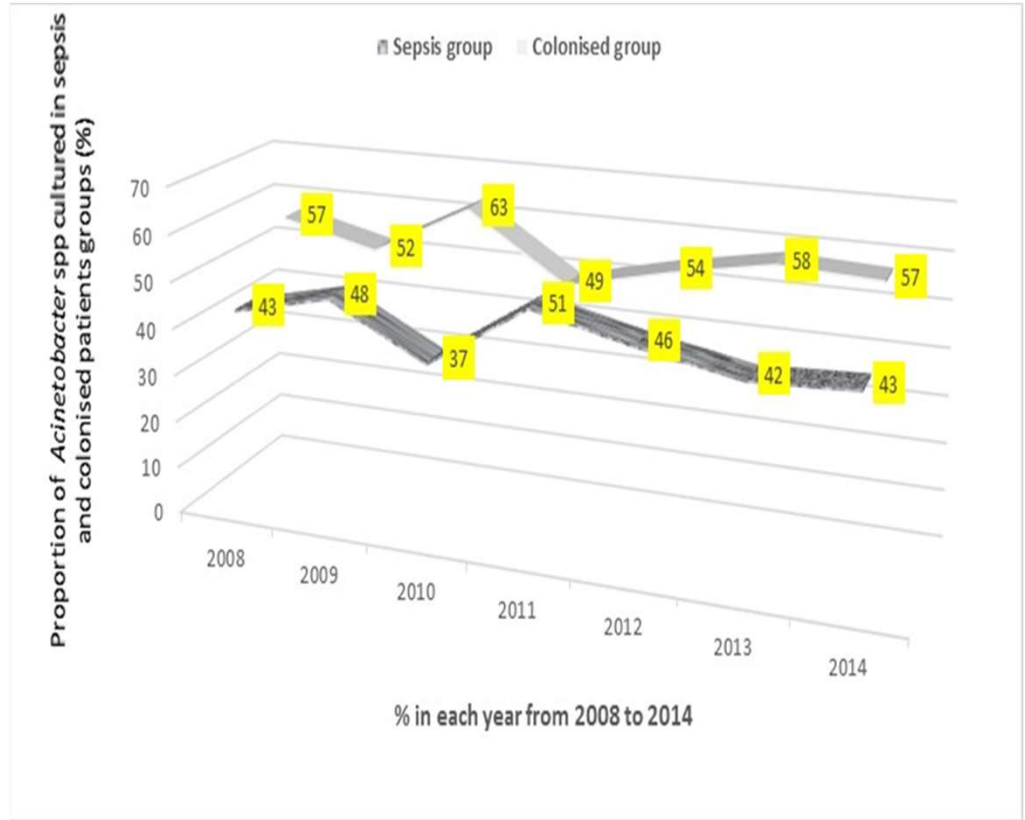
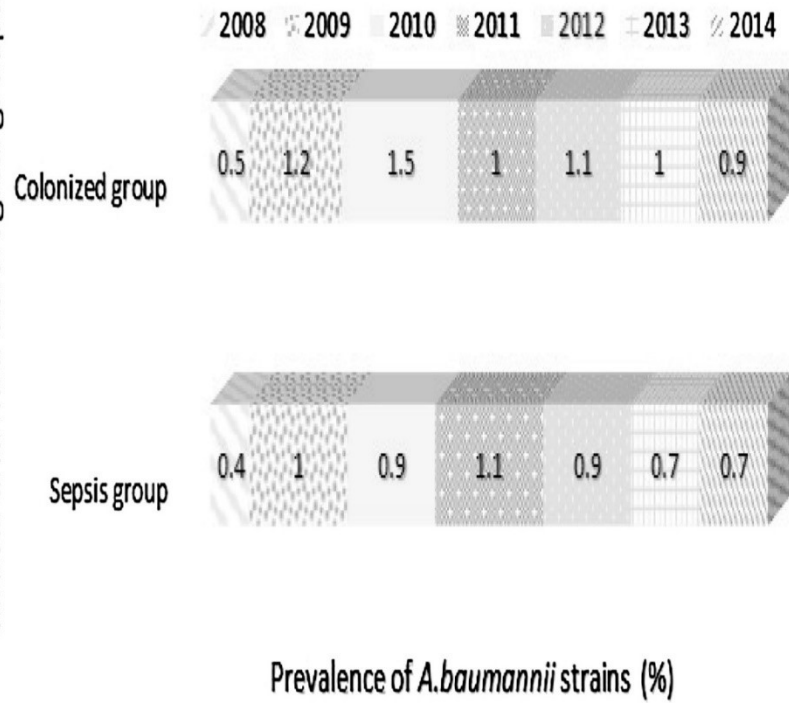
Local Surveillance study

Introduction:

- Antibiotic resistance organism (example- *Acinetobacter baumannii*)
 - serious problem in clinical settings worldwide, including South Africa.
- It significantly affects the optimal use of antibiotics/ ASWP.
 - Preauthorization ?? [Ref: IDSA 2016]
 - **Preauthorization** means that providers need approval to use antibiotics before they are prescribed.
 - **Prospective audit** allows antibiotic stewards to engage the prescribing clinician after the antibiotic has been used in order to optimize treatment.
 - The strategies may be used alone or in combination to reduce antibiotic misuse and decrease the development of resistance.
 - Hospitals should use one or both of these methods based on their local resources and expertise



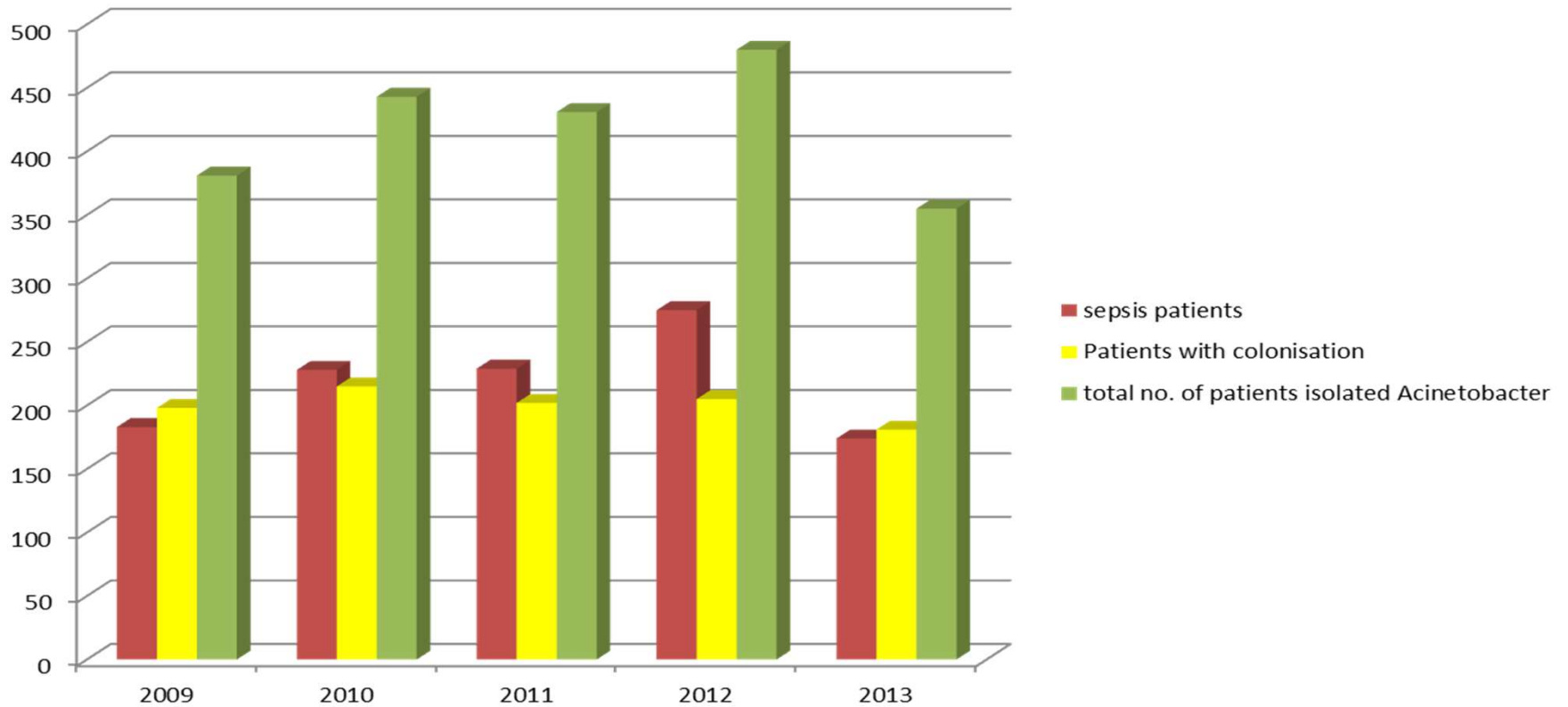
clinical and microbiological groups



Swe Swe-Han K *et al* 2017, Journal of Infection and Public Health DOI: <http://dx.doi.org/10.1016/j.jiph.2017.01.014>

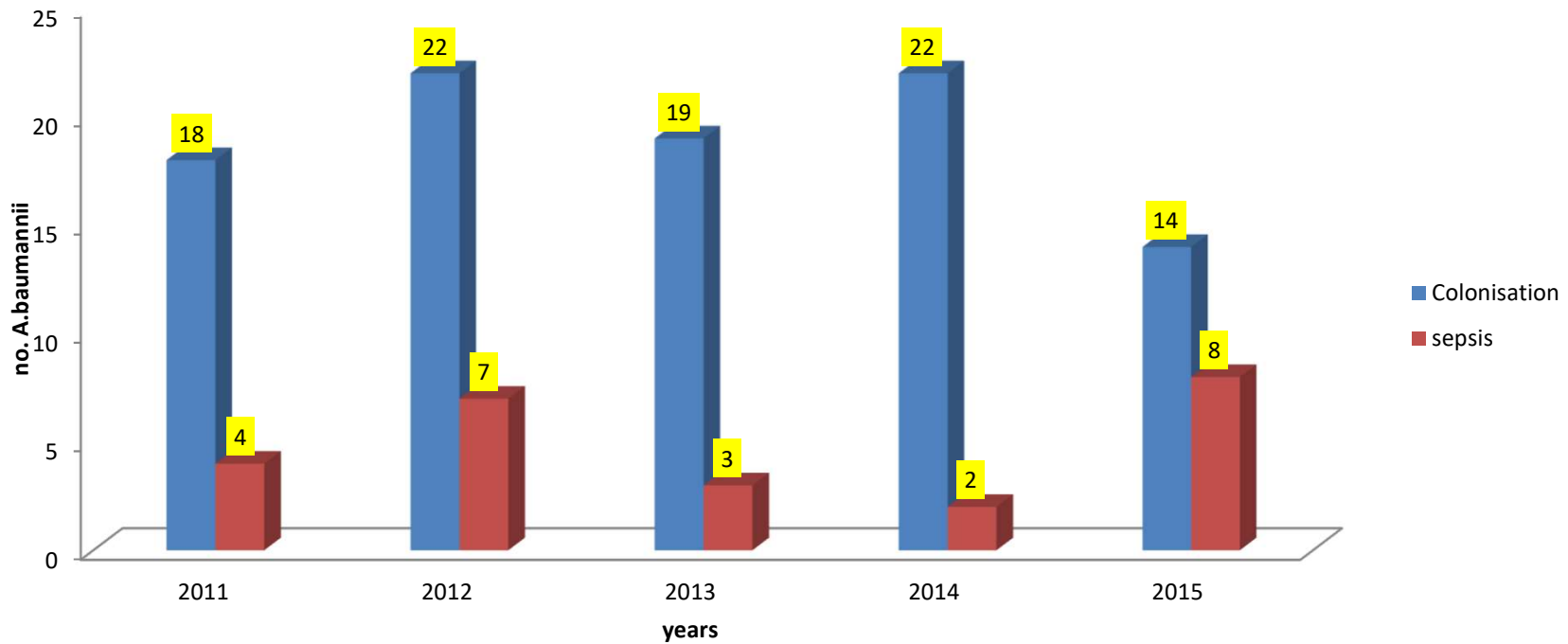


No. of Patients with Acinetobacter isolated (2009-2013) Central Referable Hospital ,Durban , South Africa





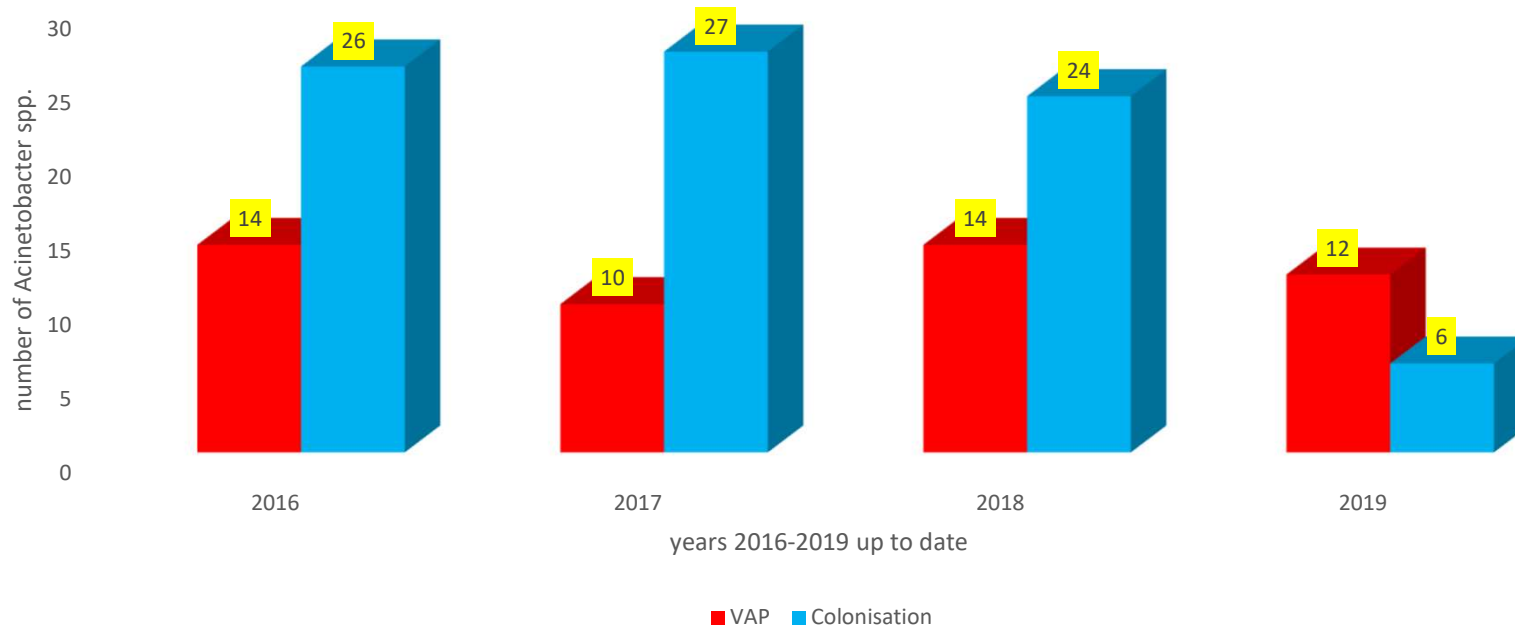
No. of patients Colonization vs significance- LRTI (2011-2015)- ICU

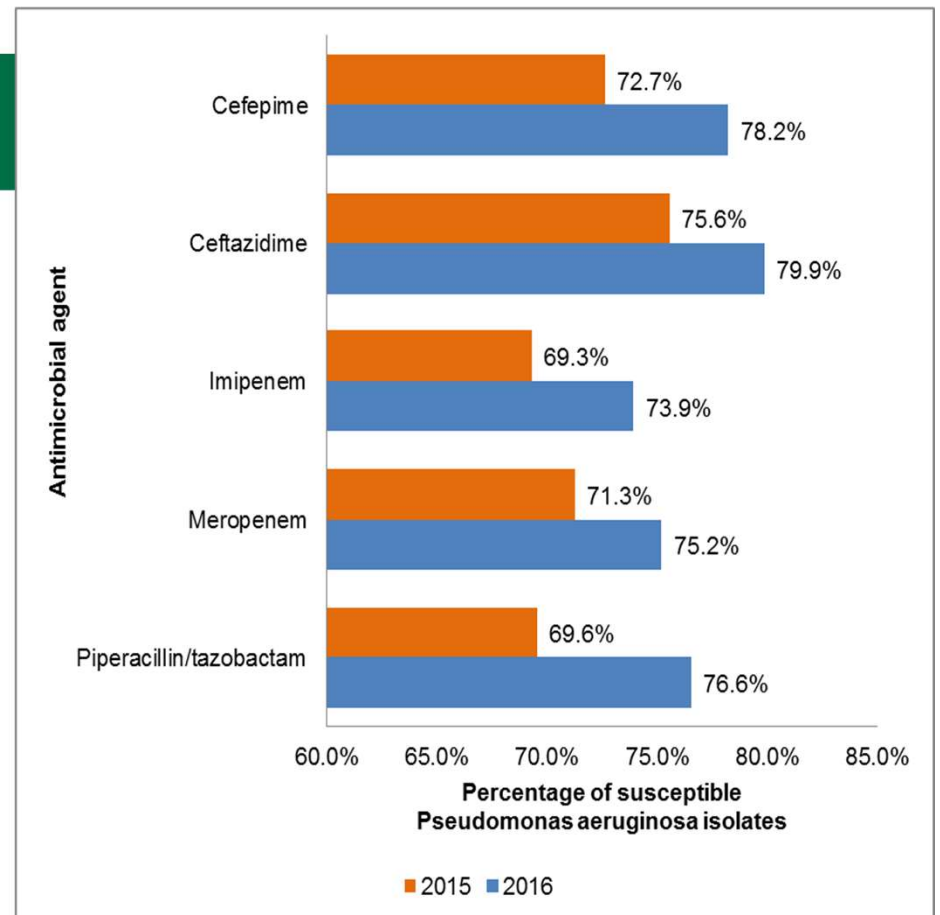
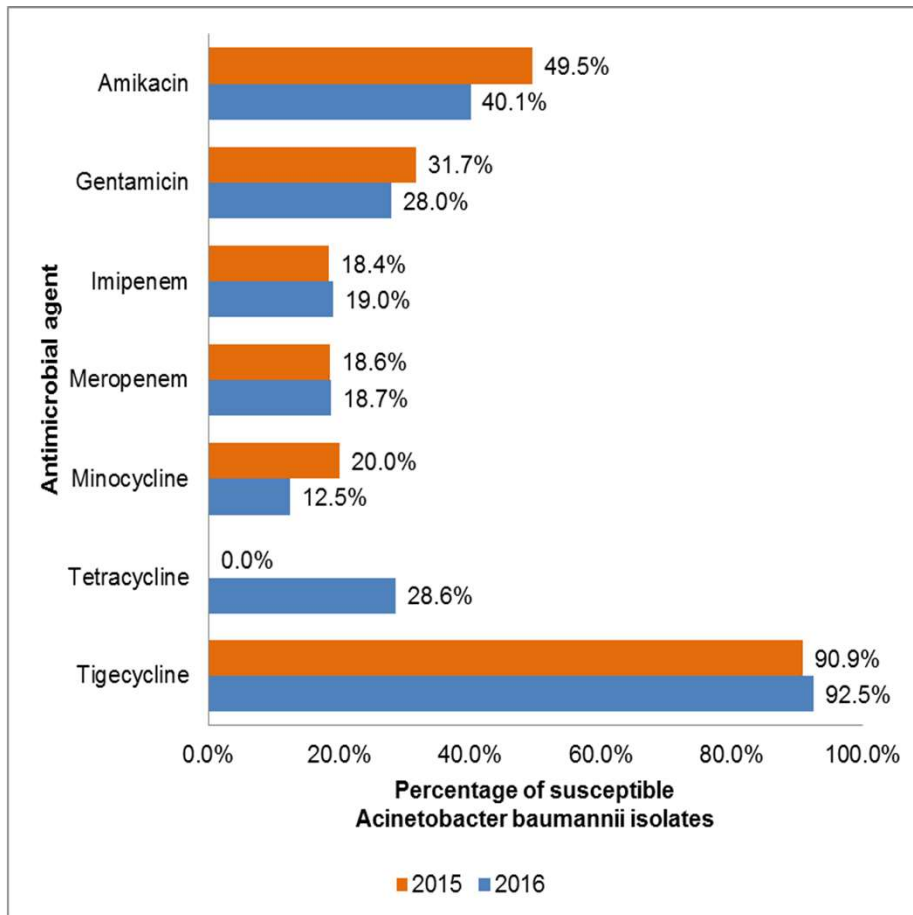




No. of patients Colonization vs Significance- LRTI (2016-2019 up to date)

No. of patients significant Pneumonia vs Colonization





Percentage of susceptible *Acinetobacter baumannii* and *Pseudomonas aeruginosa* isolates, 2015 to 2016.

Ref Olga et al; Antimicrobial Resistance Surveillance in the South African Public Sector Report | 2016



Challenging ?

- Differentiating colonisation from infection/sepsis
- indiscriminate unnecessary treatment

Example – colistin

- vancomycin
- limited selecting optimal treatment



Continue- Definition

Significant infection

Clinical significance:

Any GNB. GPB (Common example; *A.baumannii*) cultured from specimens from a clinically relevant site.

Colonisation

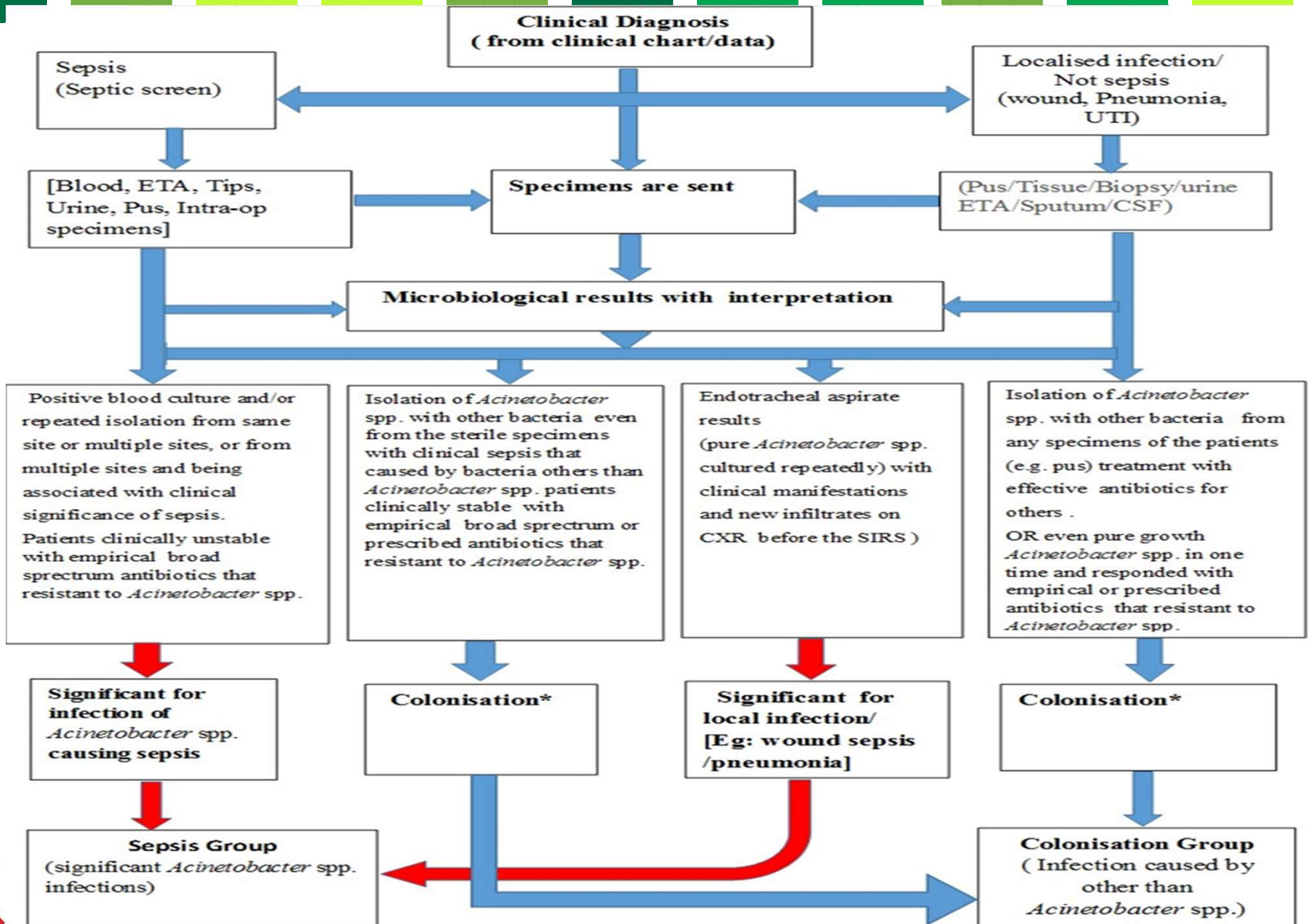
The following criteria were included in colonized group: The isolation of any bacteria (example: *A.baumannii* mixed with other bacteria) from non-sterile specimens of a patient who is clinically stable; or

The isolation of any bacteria (example- *A.baumannii*) from sterile specimens with clinically stable patients

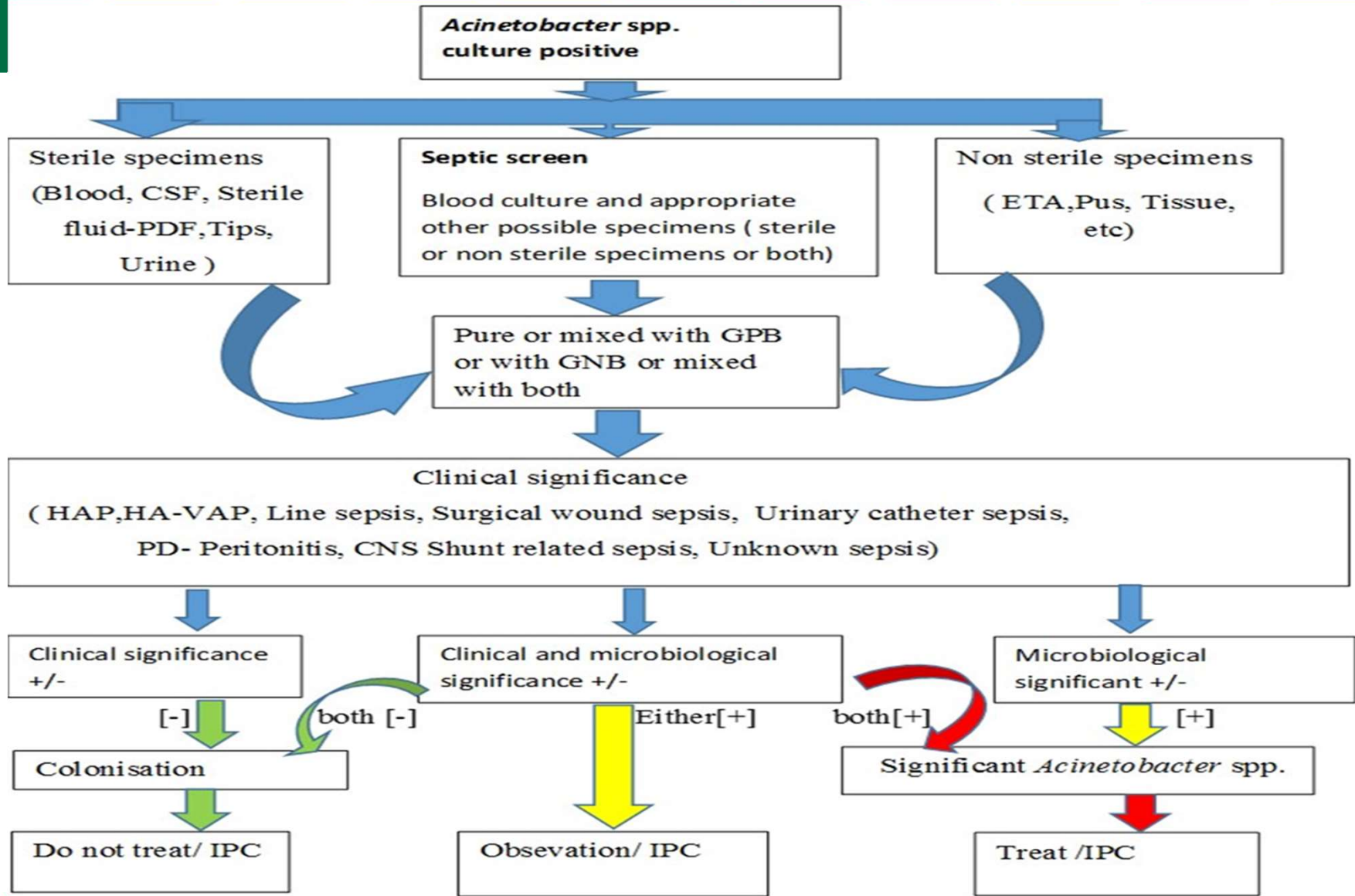
Ref: K Swe Swe- Han, K. Mlisana , M. Pillay (submitted –local study – manuscript)

Figure 1. Flow chart of clinical and microbiological criteria of sepsis and

colonisation



Preauthorisation decision assist the ASWP





Antibiogram – Local vs unit vs individual approach

- **Individual specific antibiogram approach**
(Drug resistant organisms)
- Continue **collaboration between clinicians and clinical microbiologists** in order to achieve the effective antibiotic stewardship programs in the hospital setting.
 - **Preauthorization- Crucial part –challenging (collaboration with Clinicians & Med Microbiologists)**
 - **Prospective audit – accurate tools ??**
- **Training /Education**



What Can We Do?

INDIVIDUALS

- Personal hygiene
- Educate others about the problem

HOSPITALS

- Improve hospital infection control
- Enforce regulations by patient safety oversight committees

DOCTORS

- Judicious use of drugs
- Educate patients about the proper use of antibiotics
- Collect more data on the extent of resistance

GOVERNMENTS

- Increase worldwide access to the appropriate drugs
- Revive R&D on antibiotic innovation
- Revive innovation of rapid diagnostic technologies
- Revive R&D for vaccines that target AMR organisms

Adapted from WHO, Alliance for Patient Safety, departmental report, 2007



Conclusion

Bacteria will inevitably find ways of resisting the antibiotics we develop, which is why aggressive action is needed now to keep new resistance from developing and to prevent the resistance that already exists from spreading.

There are **four core actions** that will help fight these deadly infections:

- preventing infections and preventing the spread of resistance (**IPC**)
- tracking resistant bacteria (**Surveillance**)
- improving the use of today's antibiotics (**Preauthorisation & Prospective audit**)
- promoting the development of new antibiotics and developing new diagnostic tests for resistant bacteria (**Research –innovative focus- Pharmacy & lab dx**)

NB- TRAINING AND EDUCATION

We are facing a bacterial Armageddon



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Acknowledgement:

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THANKS YOU !

28^h May 2019