Establish network for AMR surveillance in Asia Pacific region

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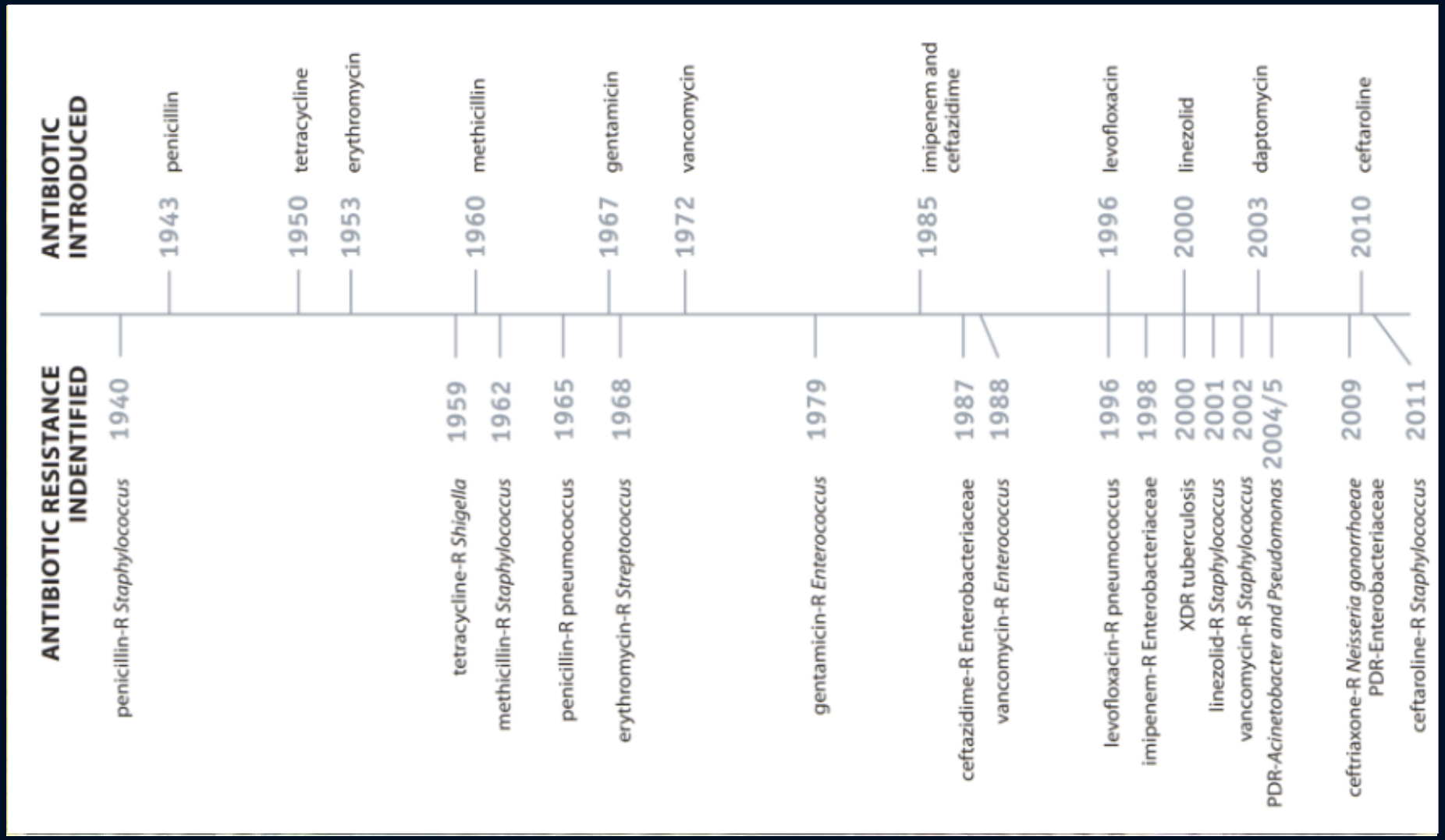
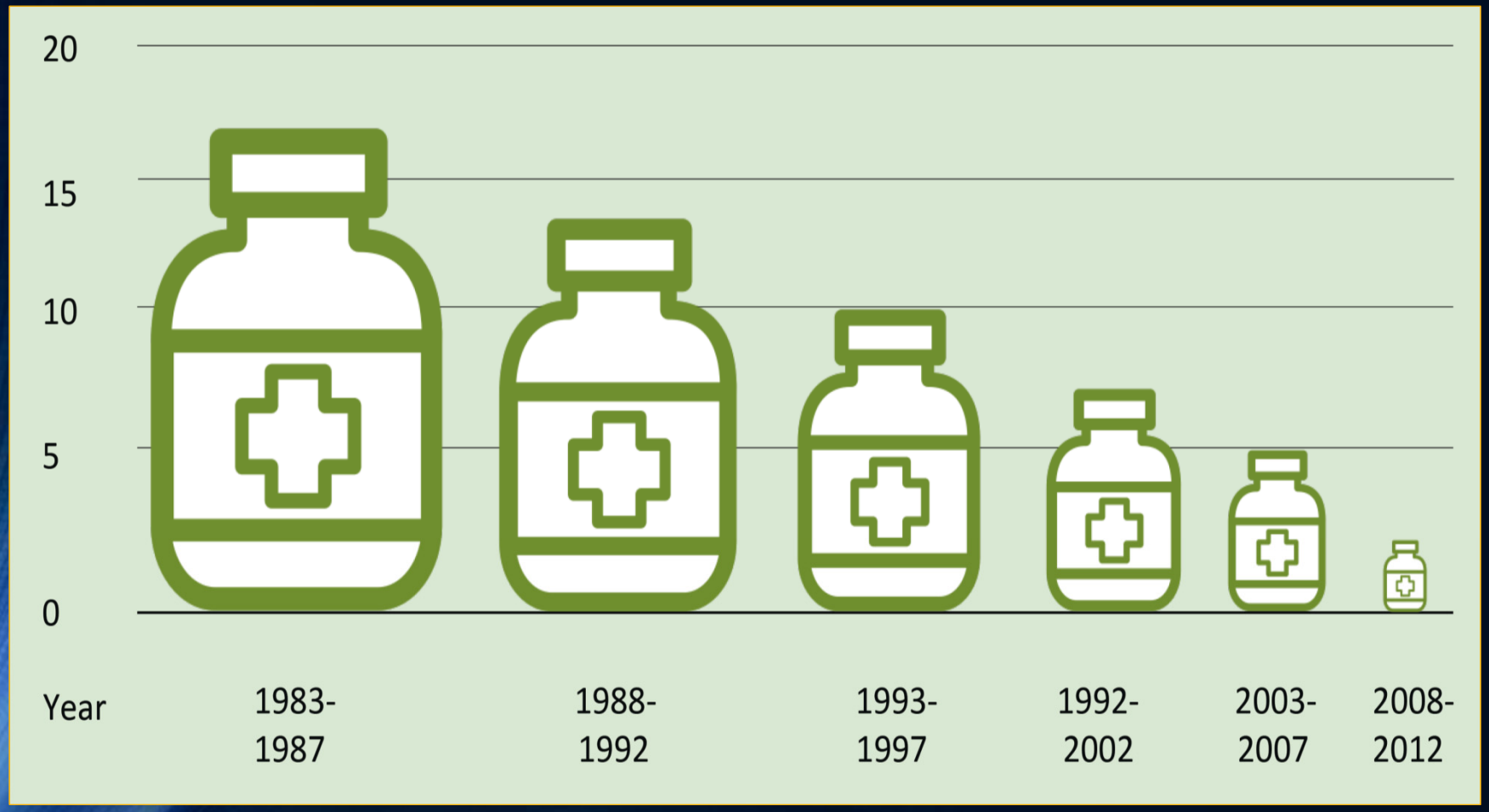
APAC REGIONAL MEDICAL THERAPEUTIC AREA LEAD, ANTI-INFECTIVES, *PFIZER INC.*

It would be an endless story ....



https://www.cdc.gov/drugresistance/about.html

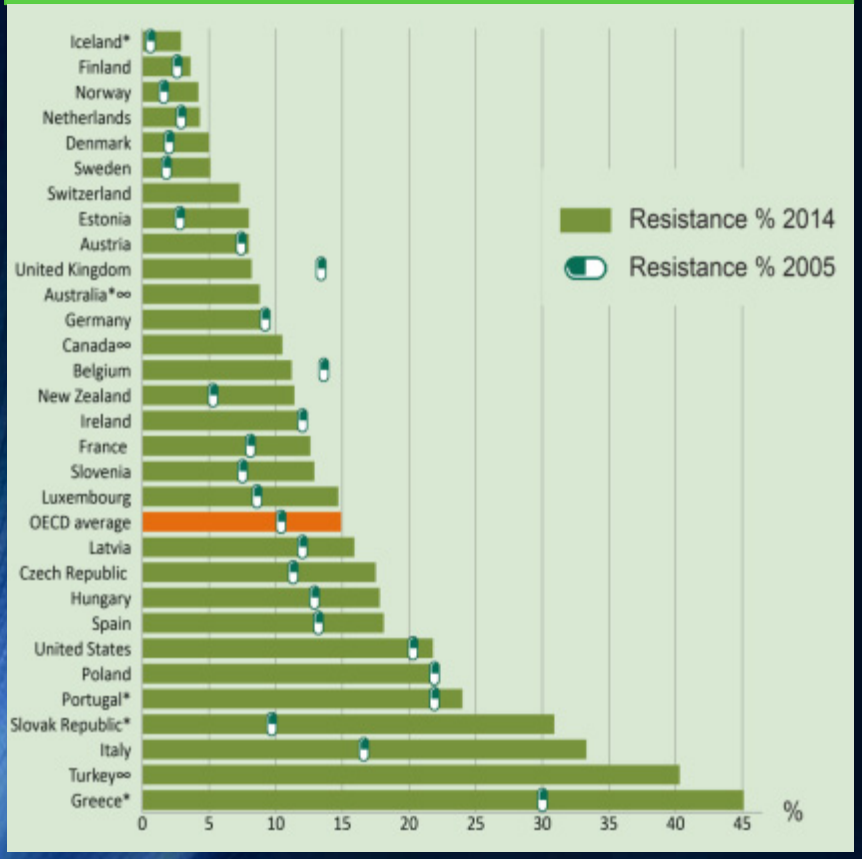
Number of new antimicrobials approved by the United States Food and Drug Administration since 1983



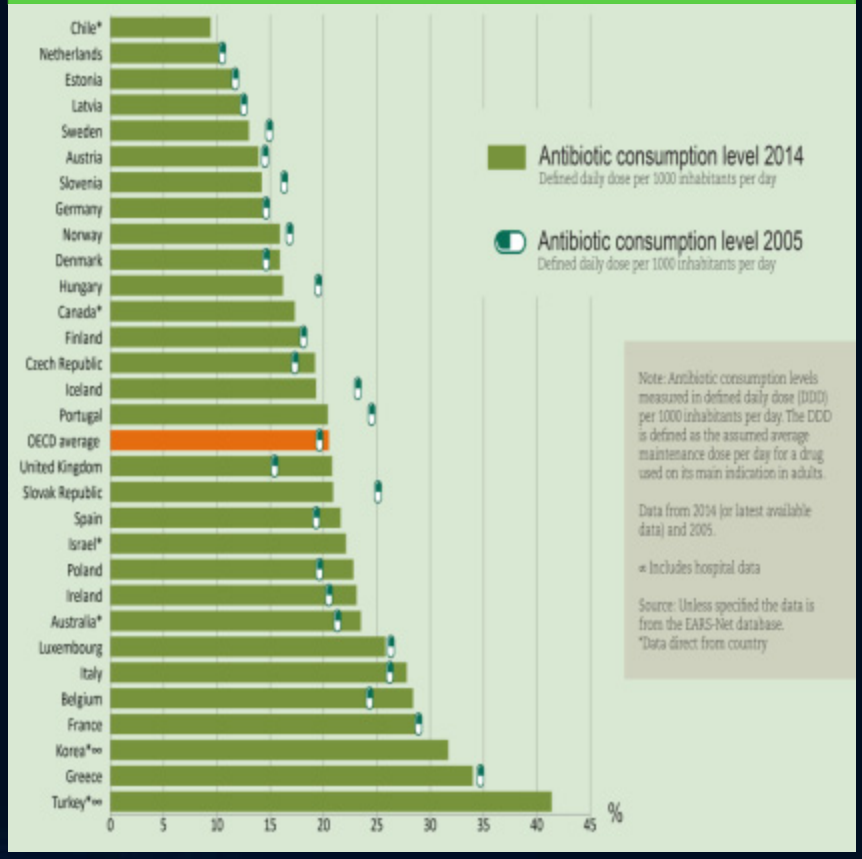
Source: OECD (2015). Antimicrobial resistance in G7 countries and beyond: economic issues, policies and options for action.

Antimicrobial resistance is a growing challenges across countries

TREND ACROSS OECD COUNTRIES ANTIBIOTICS RESISTANCE IS GROWING

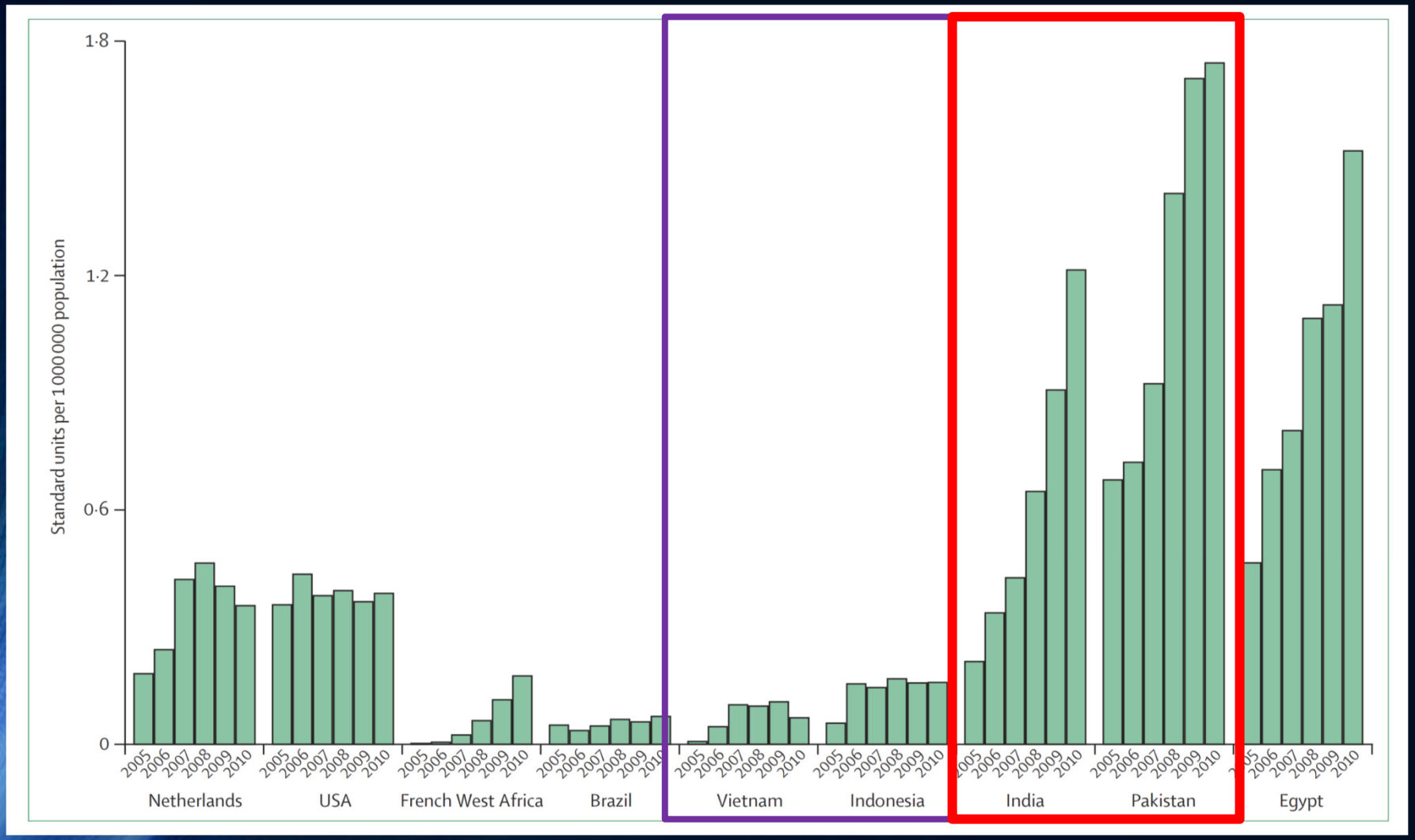


HUMAN CONSUMPTION OF ANTIBIOTICS REMAINED SUBSTANTIALLY STABLE BETWEEN 2005 AND 2014



www.oecd.org/health/antimicrobial-resistance.htm © OECD 2016

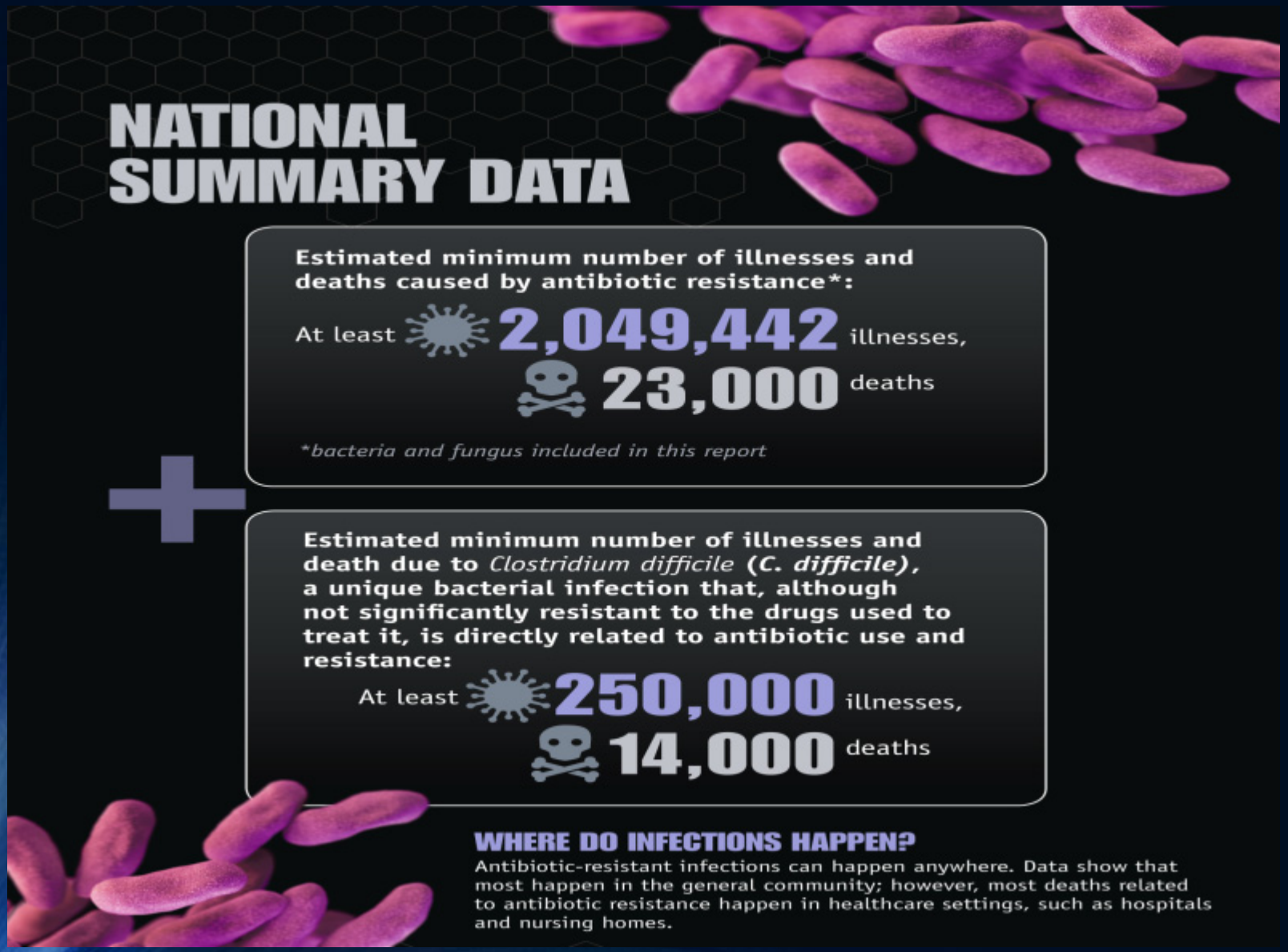
Trends in retail sales of carbapenem antibiotics for Gram-negative bacteria in different countries



Based on data obtained from IMS Health's MIDAS™ database.

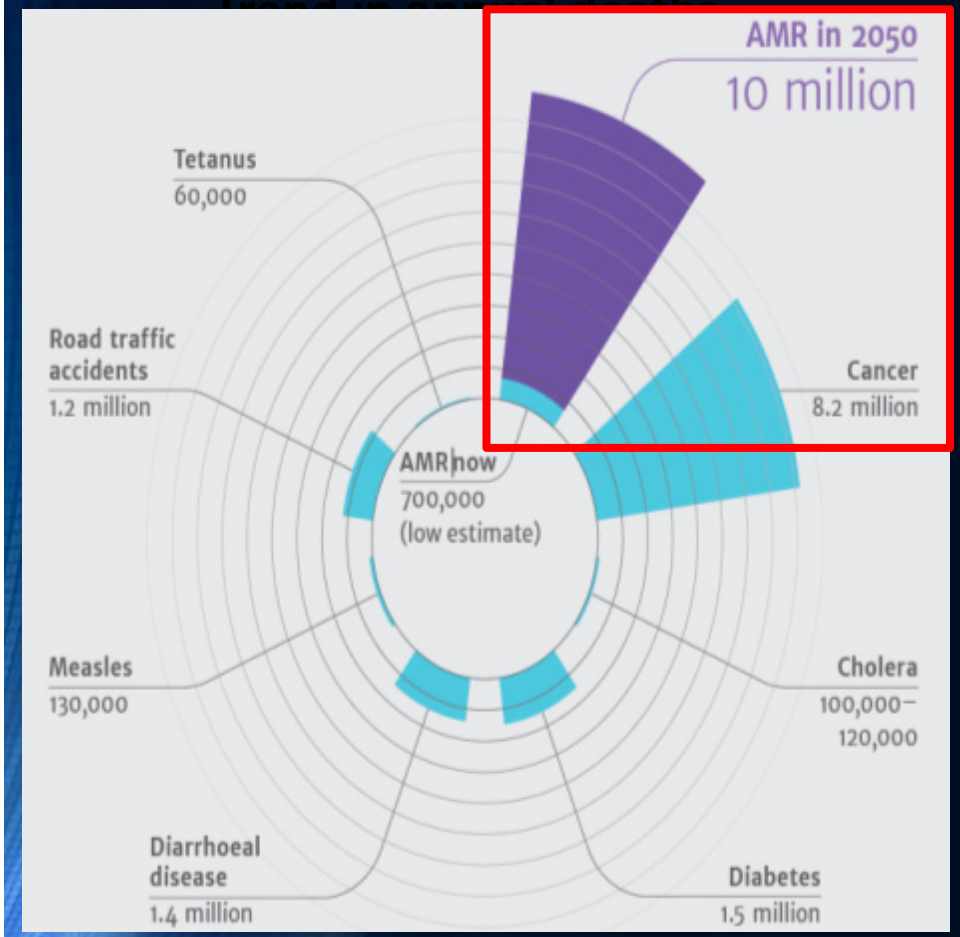
Ramanan Laxminarayan *et al Lancet Infect Dis* 2013 Nov. *at* http://dx.doi.org/10.1016/S1473-3099(13)70318-9

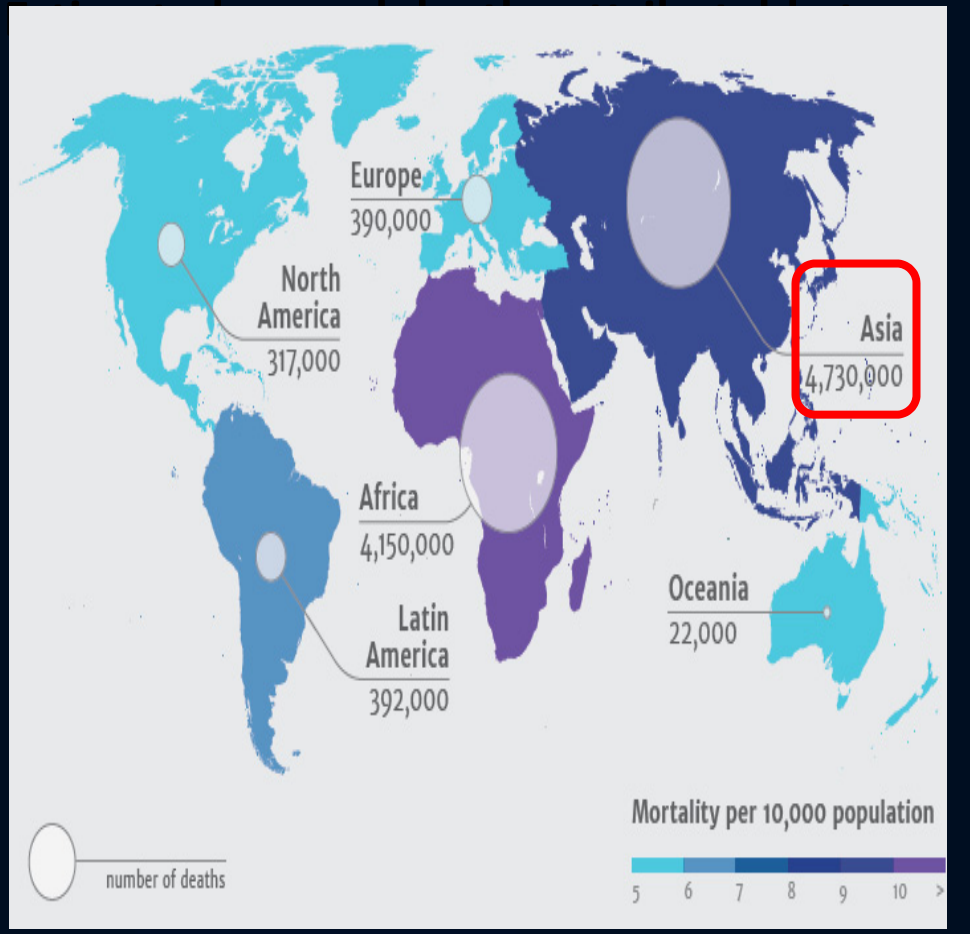
Impact of AMR to human community



https://www.cdc.gov/drugresistance/about.html

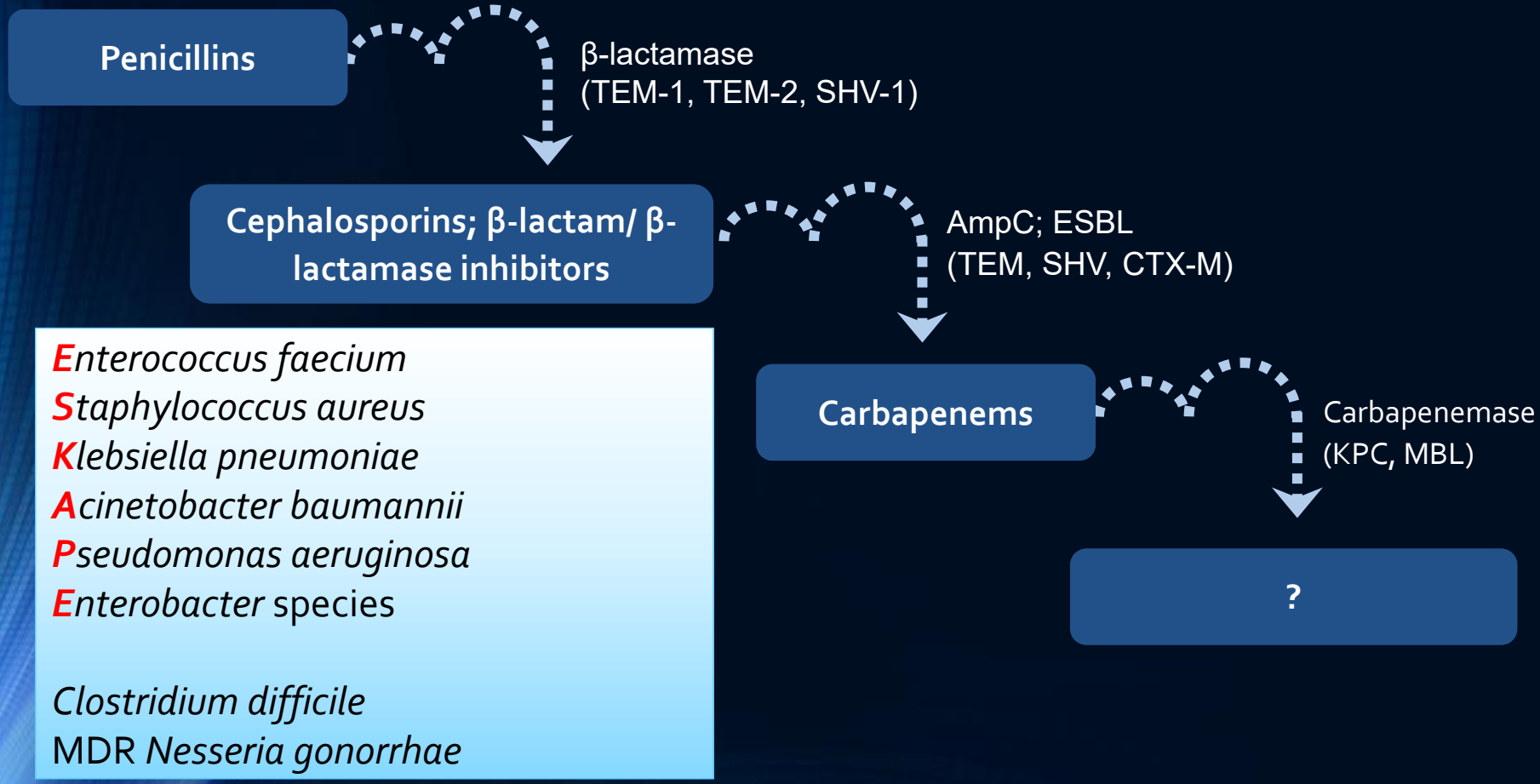
Increasing Antibiotic Resistance Has the Largest Impact in Emerging Markets





Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations. January 2016. Available at: http://amr-review.org/sites/default/files/Tackling%20drug-resistant%20infections%20-%20An%20overview%20of%20our%20work_LR_NOCROPS.pdf (accessed 18 Feb 2016)

Development of Antibiotics in Response to Resistance Due to β-Lactamases



MBL=metalllo-β-lactamase; TEM-1, TEM-2, SHV-1, TEM, SHV, CTX-M=types of β-lactamases.

Burgess DS, et al. *Am J Health-Syst Pharm*. 2008;65(suppl 2):S4-S15.

Mortality rate associated with resistant and MDR ESKAPE bacteria.

Authors	Hospital Wards	Bacteria	Mortality rate	P-value	References
Al Jarousha et al. (2009)	Neonatal ICU	MDR-*A. baumannii* (15/40)	37.5%	0.001	[54]
		Susceptible *A. baumannii* (12/100)	12%		
Anunnatsiri et al. (2011)	ICU	MDR-*A. baumannii* (22/24)	91.7%	0.001	[41]
		Susceptible *A. baumannii* (12/25)	48%		
Amer et al. (2015)	Emergency ICU /Pediatric ICU	CR-MBLP-*P. aeruginosa* (14/32)	43,8%	0.2	[64]
		CR-MBLN-*P. aeruginosa* (2/8)	25%		
Furtado et al. (2009)	ICU	Imipenem-resistant *P. aeruginosa* (31/63)	49%	0.02	[31]
		Imipenem-susceptible *P. aeruginosa* (61/182)	33%		
Marra et al. (2006)	ICU	ESBL-producing *K. pneumoniae* (18/56)	32.14%	0.042	[46]
		Non-ESBL *K. pneumoniae* (8/52)	15.38%		
Moreira et al. (2008)	ICU	ORSA (11/29)	37.9%	0.41	[47]
		OSSA (8/32)	25%		
Serefhanoglu et al. (2009)	ICU	MDR-ESBL-producing-*E. coli* and *K. pneumoniae* (7/30)	23.3%	0.606	[32]
		Non-MDR-ESBL-producing-*E. coli* and *K. pneumoniae* (12/64)	18.8%		
Tuon et al. (2012)	ICU	Carbapenem-resistant *P. aeruginosa* (13/29)	54.2%	0.043	[22]
		Carbapenem-susceptible *P. aeruginosa* (26/48)	44.8%		
Chen et al. (2012)	ICU	MRSA (25/75)	33%	0.01	[48]
		MSSA (8/43)	18.6%		
Fu et al. (2015)	ICU	XDR *A. baumannii* (31/39)	79.5%	0.1	[49]
		Non-XDR *A. baumannii* (38/86)	44.2%		
Jia et al. (2015)	ICU	Linezolid non-susceptible Enterococci (3/44)	6.8%	0.521	[50]
		Linezolid-susceptible Enterococci (2/44)	4.5%		
		Un-infected Control patients (3/176)	1.7%		
Yao et al. (2015)	ICU	MRSA (12/57)	21%	0.002	[35]
		MSSA (9/116)	8%		
Gomez Rueda et al. (2014)	ICU	Carbapenem resistant *K. pneumoniae* (31/61)	50.8%	0.042	[36]
		Carbapenem-susceptible *K. pneumoniae* (20/61)	32.7%		
		Un-infected control patients (25/122)	20.4%		
Kumar et al. (2014)	ICU	Carbapenem-resistant *A. baumannii* (9/33)	27.3%	0.074	[37]
		Carbapenem-susceptible *A. baumannii* (3/32)	9.4%		
Nazer et al. (2015)	ICU	MDR-*A. baumannii* (118/161)	73.3%	0.015	[53]
		Non-MDR-*A. baumannii* (142/232)	61.2%		
Deris et al. (2011)	ICU	Imipenem-resistant -*A. baumannii* (6/15)	42.9%	0.201	[39]
		Imipenem-susceptible *A. baumannii* (9/41)	24.3%		
Inchai et al. (2015)	ICU	MDR-*A. baumannii* (10/72)	13.9%	0.001	[44]
		XDR- *A. baumannii* (88/220)	40%		
		PDR-*A. baumannii* (7/12)	58.3%		
Jamulitrat et al. (2009)	ICU	Imipenem-resistant-*A. baumannii* (35/67)	52.2%	0.001	[59]
		Imipenem-susceptible *A. baumannii* (26/131)	19.9%%		
Thatrimontrichai et al. (2016)	ICU	Carbapenem-resistant *A. baumannii* (10/63)	15.9%	0.01	[19]
		Carbapenem-susceptible *A. baumannii* (1/13)	7.7%		
		Un-infected control patients (0/25)	0%		
Topeli et al. (2000)	ICU	MRSA (15/46)	32.6%	0.02	[21]
		MSSA (7/55)	12.7%		

RC Founou *et al* PLOS ONE https://doi.org/10.1371/journal.pone.0189621 December 21, 2017

Foster the development of new innovative antimicrobial agents

U.S. Department of Health & Human Services

FDA U.S. FOOD & DRUG ADMINISTRATION

GAIN Act and Qualified Infectious Disease Product Program (QIDP)

	Year initiated	Benefits	Data required	Antibacterial examples and approval year	Notes
Accelerated Approval Pathway	1992	• FDA approval based on surrogate end point, offering shorter development time • Clinical trials must be conducted post-approval to confirm clinical benefit	• Not specified, however must show advantage over existing therapies and effect on surrogate end point likely to predict clinical efficacy • Sponsor must discuss this pathway possibility with FDA during development	• Quinupristin/dalfopristin 1999 • Bedaquiline 2012	• Inception due to AIDS epidemic and need for zidovudine (AZT) on market • Majority of drugs approved by this pathway include oncological agents
Fast Track Designation	1997	• More frequent meetings with FDA • More frequent written communication from FDA • Rolling NDA review	• Preliminary nonclinical, mechanistic, or clinical data • Of note, typical Phase 3 data still required for FDA approval • Can be requested upon IND submission; FDA has 60 days to respond	• Ceftaroline 2010 • Fidaxomicin 2011 • Bedaquiline 2012 • Dalbavancin[a] 2014 • Oritavancin[a] 2014 • Tedizolid[a] 2014 • Ceftolozane/tazobactam[a] 2014 • Ceftazidime/avibactam[a] 2015	• Addresses broad range of diseases, including but not limited to HIV/AIDS, Alzheimer's, cancer, epilepsy, cardiovascular, endocrine • GAIN Act of 2012 enables QIDP designated drug candidates to receive Fast Track Designation
Priority Review	1992	• Shortens review of NDA from 10 months to 6 months	• Data contained in NDA submission • Must show significant improvement in safety or effectiveness of the treatment, prevention, or diagnosis of a serious condition	• Fidaxomicin 2011 • Bedaquiline 2012 • Dalbavancin[a] 2014 • Oritavancin[a] 2014 • Tedizolid[a] 2014 • Ceftolozane/tazobactam[a] 2014 • Ceftazidime/avibactam[a] 2015	• GAIN Act of 2012 enables QIDP designated drug candidates to have Priority Review
Breakthrough Therapy Designation	2012	• More frequent meetings with FDA • More frequent written communication from FDA • Rolling NDA review • Intensive guidance on efficient development program • Involvement of FDA to expedite development	• Preliminary clinical data • Must show substantial improvement on clinically significant end point(s) over available therapies	None	• Largely oncology and orphan diseases • Several new agents for Hepatitis C infection have received this designation • Microbiome therapeutic (SER-109) and microbiome restoration therapy (RBX2660) for recurrent *Clostridium difficile* infection and monoclonal antibody for *Staphylococcus aureus* infections have received status (pipeline agents)

EXPERT REVIEW OF ANTI-INFECTIVE THERAPY, 2017 VOL. 15, NO. 00, 425–433
http://dx.doi.org/10.1080/14787210.2017.1308251

Antibiotic Drug Details, Development Milestones, and ESKAPE Status: FDA-Approved Antibiotics, 2010-2015

Drug	IND Filed	NDA Filed	Approval Date	Current Manufacturer	Drug Class (Year of Discovery)	Method of Administration	Novel Mechanism of Action	Indications	In Vitro Activity Against ESKAPE Pathogens?
Ceftaroline	December 2004	December 2009	29 October 2010	Actavis	Cephalosporin (1928)	Intravenous	No	ABSSSI; CABP	Yes
Fidaxomicin	August 2003	November 2010	27 May 2011	Cubist Pharmaceuticals (subsidiary of Merck)	Macrolide (1948)	Oral	No	CDAD and prevention of recurrences	No*
Bedaquiline	November 2006	June 2012	28 December 2012	Janssen Research and Development (Johnson & Johnson)	Diarylquinoline (1997)	Oral	Yes	Pulmonary tuberculosis caused by multidrug-resistant tuberculosis	No†
Dalbavancin	July 2000	September 2013	23 May 2014	Actavis	Lipoglycopeptide (1953)	Intravenous	No	ABSSSI	No
Tedizolid	November 2007; August 2009	October 2013	20 June 2014	Cubist Pharmaceuticals (subsidiary of Merck)	Oxazolidinone (1955)	Oral; intravenous	No	ABSSSI	No
Oritavancin	August 1996	December 2013	6 August 2014	The Medicines Company	Glycopeptide (1953)	Intravenous	No	ABSSSI	No
Ceftolozane-tazobactam	July 2009	April 2014	19 December 2014	Cubist Pharmaceuticals (subsidiary of Merck)	Cephalosporin (1928) + β-lactamase inhibitor	Intravenous	No	CIAI; CUTI	Yes
Ceftazidime-avibactam	January 2008	June 2014	25 February 2015	AstraZeneca/ Actavis	Cephalosporin (1928) + β-lactamase inhibitor	Intravenous	No	CIAI; CUTI	Yes

ABSSSI = acute bacterial skin and skin-structure infection; CABP = community-acquired bacterial pneumonia; CDAD = *Clostridium difficile*-associated diarrhea; CIAI = complicated intra-abdominal infection; CUTI = complicated urinary tract infection; ESKAPE = *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumonia, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterobacter* species; IND = investigational new drug; NDA = new drug application.

* *Clostridium difficile* is a Centers for Disease Control and Prevention urgent-threat pathogen.

† Multidrug-resistant tuberculosis is a global health priority.

Ann Intern Med. 2016;165:363-372. doi:10.7326/M16-0291

Global action plan on antimicrobial resistance
from WHO

- Alert to this crisis, the May 2015 World Health Assembly adopted a global action plan on antimicrobial resistance, which outlines five objectives:
- to **improve awareness and understanding** of antimicrobial resistance through effective communication, education and training;
- to strengthen the knowledge and evidence base through **surveillance and research**;
- to reduce the incidence of infection through effective **sanitation, hygiene and infection prevention measures**;
- to **optimize the use of antimicrobial medicines** in human and animal health; and
- to develop the economic case for **sustainable investment** that takes account of the needs of all countries and to increase investment in **new medicines, diagnostic tools, vaccines and other interventions.**

http://www.who.int/antimicrobial-resistance/publications/global-action-plan/en/

Four Core Actions to Fight Resistance

US CDC

1 PREVENTING INFECTIONS, PREVENTING THE SPREAD OF RESISTANCE

Avoiding infections in the first place reduces the amount of antibiotics that have to be used and reduces the likelihood that resistance will develop during therapy. There are many ways that drug-resistant infections can be prevented: immunization, safe food preparation, handwashing, and using antibiotics as directed and only when necessary. In addition, preventing infections also prevents the spread of resistant bacteria.

2 TRACKING

CDC gathers data on antibiotic-resistant infections, causes of infections and whether there are particular reasons (risk factors) that caused some people to get a resistant infection. With that information, experts can develop specific strategies to prevent those infections and prevent the resistant bacteria from spreading.

3 IMPROVING ANTIBIOTIC PRESCRIBING/STEWARDSHIP

Perhaps the single most important action needed to greatly slow down the development and spread of antibiotic-resistant infections is to change the way antibiotics are used. Up to half of antibiotic use in humans and much of antibiotic use in animals is unnecessary and inappropriate and makes everyone less safe. Stopping even some of the inappropriate and unnecessary use of antibiotics in people and animals would help greatly in slowing down the spread of resistant bacteria. This commitment to always use antibiotics appropriately and safely—only when they are needed to treat disease, and to choose the right antibiotics and to administer them in the right way in every case—is known as antibiotic stewardship.

4 DEVELOPING NEW DRUGS AND DIAGNOSTIC TESTS

Because antibiotic resistance occurs as part of a natural process in which bacteria evolve, it can be slowed but not stopped. Therefore, we will always need new antibiotics to keep up with resistant bacteria as well as new diagnostic tests to track the development of resistance.

2 TRACKING

CDC gathers data on antibiotic-resistant infections, causes of infections and whether there are particular reasons (risk factors) that caused some people to get a resistant infection. With that information, experts can develop specific strategies to prevent those infections and prevent the resistant bacteria from spreading.

https://www.cdc.gov/drugresistance/about.html

The key objective of AMR surveillance system

- To providing early warning of emerging problems
  - monitoring changing patterns of resistance,
  - targeting and evaluating prevention and control measures
- Assisting researchers in developing new drugs
- Providing good patient care
  - Development of clinical guidance of empirical treatment of infectious diseases
- Improve understanding of the relationship between drug use and resistance, identify and anticipate gaps in availability of existing drugs, and help identify preventive interventions.

https://www.cdc.gov/drugresistance/actionplan/surveillance1.html

Lancet Infect Dis 2018: 18 e99-e106

The key directives of impact by well established surveillance system

- Therapy guidelines *
- Antibiotic formulary *
- Antibiotic stewardship programmes *
- Public health interventions
- Infection control policies
- Antimicrobial development.

***The elementary and starting goals of surveillance program**

Lancet Infect Dis 2018: 18:e99-106

The key merits of well functioned AMR surveillance system to address the objectives

- Accurate
- Reliable
- Flexible access
- Timely updated

Difference of various surveillance program

- **Isolate based**
  - Data on resistance patterns within the **bacterial population**
    - Percentage of resistance to a variety of antimicrobial agents
    - Clinical driven and impacted by clinical behavior
    - Potentially biased with under- or over -estimated of AMR challenges
- **Sample based***
  - Data of both basic insight into patterns and the extent of AMR in **the tested populations**
    - Incidence of stratified tested population
    - allows detecting the most frequent type of resistant infections within that population and it allows stratification to identify AMR patterns and strategic foci

2018 GLASS report
* Preferred program by GLASS

Difference of various surveillance program (cont'd)

Passive surveillance	Active surveillance	Sentinel surveillance*
data from **voluntary reporting** without stimulating report by reminder or controlled protocol.	Driven by **protocol** with active monitoring of reporters' performance and data quality (protoocl-driven)	data collection from **selected ,** either randomly or intentionally**, a small group** of health workers with protocol guidance
requested of each health worker is minimal	specific feedback to improve their performance	Sentinel reporters should be trained
few incentives for reporters	stimulus to reports in the form of individual feedback or other incentives	Incentives for reporters
data would be **incomplete**	**more complete** data collection	more detailed data on cases of illness
least costly	substantially more time and resources needed	requires more time and resources

* may be the best type of surveillance if more intensive investigation of individual case is needed

http://conflict.lshtm.ac.uk/page_02.htm

Snapshot of AMR surveillance system across APAC countries (I)

Country	Surveillance program	accessibility	Key natures
Japan	JANIS https://janis.mhlw.go.jp/english/about/index.html	Website access of the annual report (since 2013)	Passive surveillance 1000+ sites send the report to repository monthly
Korea	KONSAR since 1997	Publication of specific analysis report	Passive surveillance
Philippines	http://arsp.com.ph/ (25 years)	Annual report since 2014 to 2017	24 sentinel sites to send results to central lab with WHONET
Thailand	NARST since 1998 http://narst.dmsc.moph.go.th/	Website access of annual report and AMR data	Passive surveillance guided with well structured manual

Snapshot of AMR surveillance system across APAC countries (II)

Country	Surveillance program	Accessibility	Key natures
Hong Kong	CHP https://www.chp.gov.hk/en/statistics/data/10/641/697/3345.html	Website access of the annual report of antimicrobial susceptibility data of targeted pathogens (since 2014))	Passive surveillance
Australia	AURA https://www.safetyandquality.gov.au/antimicrobial-use-and-resistance-in-australia/about-aura/	Website access of the annual report of since 2011 (updated to 2017)	Passive surveillance

Snapshot of AMR surveillance system across APAC countries (III)

Country	Surveillance program	Accessibility	Key nature
Indonesia		Assessment Tool for Laboratory and Antimicrobial Resistance (ATLASS) kicked off in Oct. 2017	
Malaysia	NSAR since 2002 http://www.imr.gov.my/en/component/content/article/75-english-content/national-collabration/1469-nsar-main.html	Website access of the annual report of since 2002	Passive surveillance
Singapore*	Driven by NAT in 2011, NARCC in 2014, and National Strategic Action Plan on Antimicrobial Resistance in 2015	Publications	Passive surveillance among public hospitals

*NAT: the National Antimicrobial Taskforce ; NARCC: National Antimicrobial Resistance Control Committee . It is integrated surveillance for antimicrobial resistance and antimicrobial utilization across sectors for human, animals, food and environment.

Snapshot of AMR surveillance system across APAC countries (IV)

Country	Surveillance program	Accessibility	Key nature
Vietnam	National Action Plan to Combat Antimicrobial Resistance since 2017#	NA yet	sentinel surveillance system involving 16 laboratories and six model hospitals.
India	NCDC	Access report at website	10 Network laboratories to initiate antimicrobial resistance surveillance on four common bacterial pathogens*
	ICMR - ICMR's surveillance network at http://14.139.60.53/iamrsn/	Accessible report at website since 2014 and published articles	Isolates driven

US CDC collaborates with WHO-Vietnam, Oxford Clinical Research Unit, American Society for Microbiology, Association of Public Health Laboratories, and PATH to directly support implementation of Vietnam's National Action Plan to Combat Antimicrobial Resistance

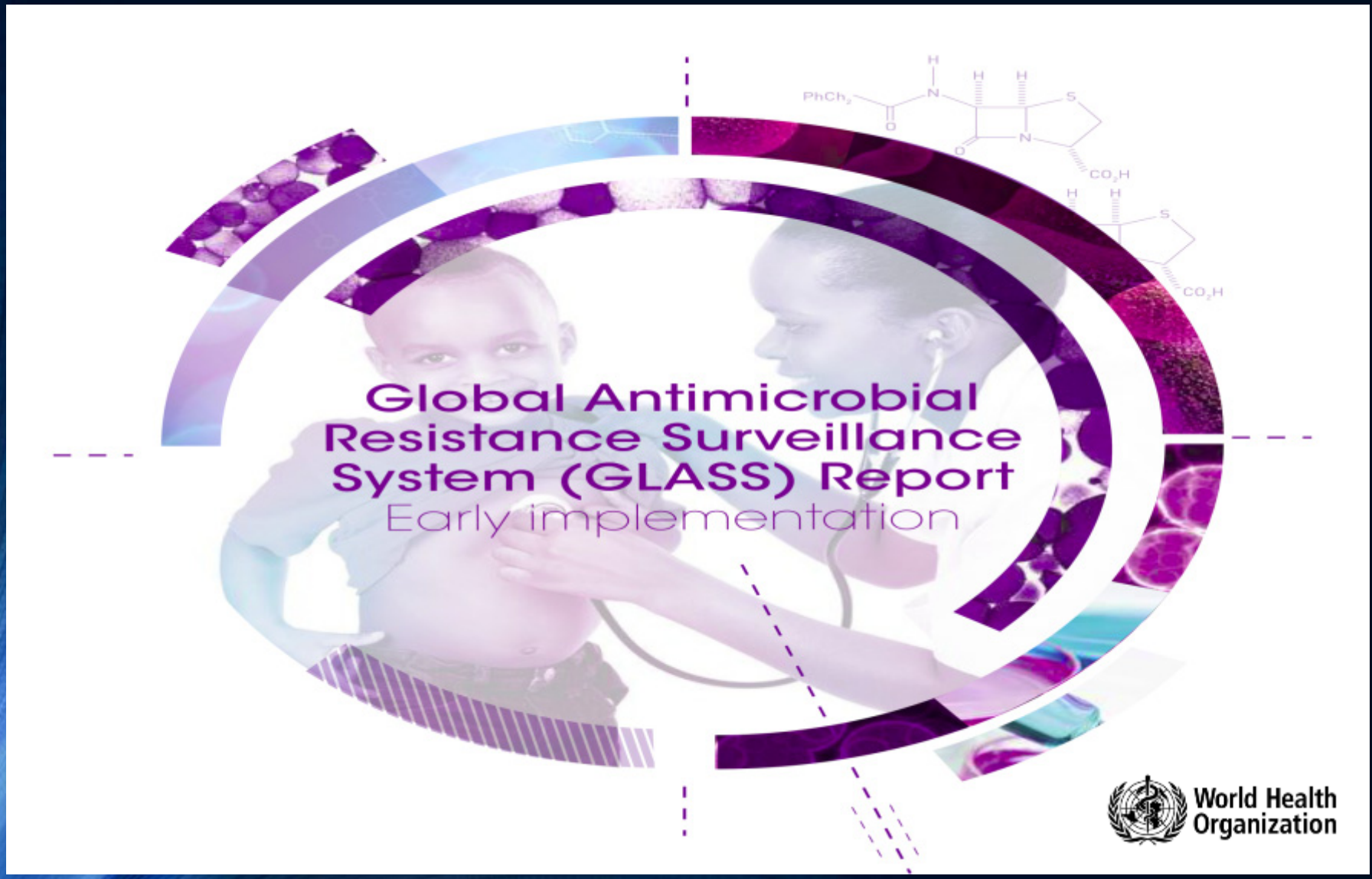
* *Klebsiella*, *Escherichia coli*, *Staphylococcus aureus*, *and Enterococcus* species

GLASS Report- Early implementation 2016-17

Great variation of the status of country implementation of surveillance system

- Bangladesh, Bhutan, India, Indonesia, Maldives, and Myanmar are at the early stage of surveillance set up, and surveillance guidelines have been developed but not fully implemented. AMR surveillance data exist but are not centralized, with limited analysis and representativeness.
- Three countries (Nepal, Sri Lanka, and Thailand) possess standardized national AMR surveillance data. However, surveillance development is at an early stage and the scope of antibiotics under surveillance is limited
- 11 countries, including Australia, Cambodia, China, Fiji, Japan, Malaysia, Mongolia, New Zealand, Philippines, Republic of Korea and Viet Nam have already developed their National Action Plans, with Viet Nam currently undertaking its first review of its plan

On 22 October 2015 WHO launched the Global Antimicrobial Resistance Surveillance System (GLASS)



The GLASS objectives

- Foster national surveillance systems and harmonise global standards;
- Estimate the extent of AMR globally by monitoring selected indicators;
- Collect surveillance data needed to inform and estimate AMR burden;
- Routinely analyse and report global data on AMR;
- Detect emerging resistance and its international spread;
- Assess the impact of interventions.

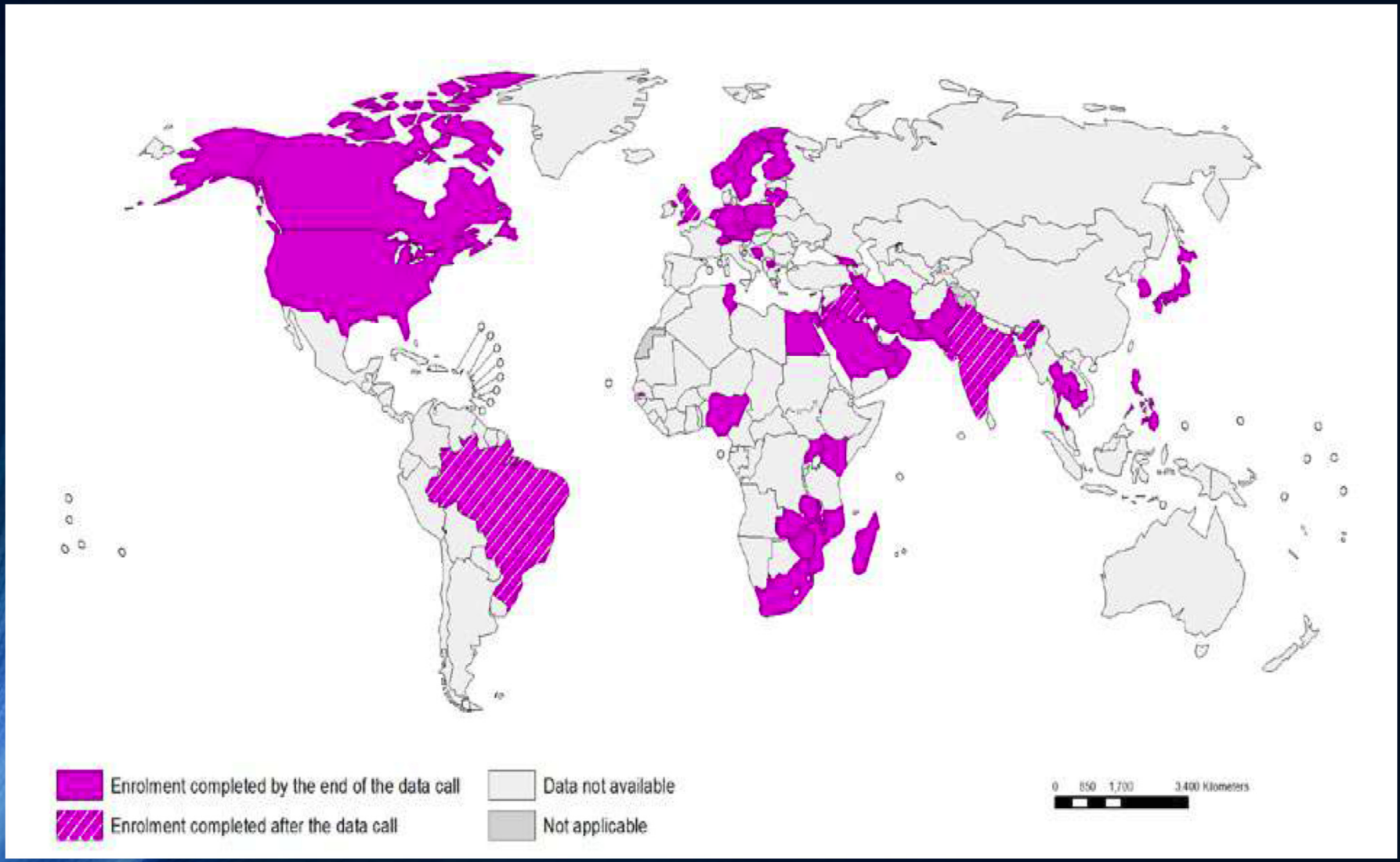
Global Antimicrobial Resistance Surveillance System (GLASS) Report- Early implementation 2016-17

GLASS

- GLASS is a system that enables standardised global reporting of official national AMR data. It collaborates with **existing regional and national AMR surveillance networks** to produce timely and comprehensive data.
- GLASS **relies upon countries to conduct their own national surveillance**. GLASS promotes the use of globally agreed and standardised methods for compiling data both locally and nationally, and the gathering of information on selected AMR indicators in a harmonised way across and within countries.

Global Antimicrobial Resistance Surveillance System (GLASS) Report- Early implementation 2016-17

GLASS Enrolment map in 2017



Global Antimicrobial Resistance Surveillance System (GLASS) Report- Early implementation 2016-17

Asian Network for Surveillance of Resistant Pathogens(ANSORP)

- ANSORP is the first and only international study group for the surveillance of AMR in the Asian region and over the past 18 years
- It is a very unique model worldwide, given that it was **voluntarily organised by physicians**, specifically focuses on AMR and infectious diseases
  - 14 hospitals from 11 Asian countries in 1996
  - 120 hospitals in 14 countries or areas in 2014
- **A series of international studies – 20 publications found at PubMed**
  - ***Streptococcus pneumoniae***
  - **MRSA**
  - **MDR GNB (metallo β lactamase producers)**
  - **VRE**

SENTRY Antimicrobial Surveillance Program

- Establishment by JMI Laboratory in 1997
- Monitors worldwide pathogens and the changes in resistance patterns over time through **centralized testing** and **utilizing reference susceptibility methods**
- Sites submitting organisms through a **prevalence based approach** across a number of different types of infections, including bloodstream, skin and soft tissue, respiratory, urinary tract, pathogens from patients hospitalized with pneumonia, intra-abdominal and invasive fungal infections.
- New compounds and other agents can easily be integrated into the SENTRY platform by establishing agreements at the beginning of the calendar year and transferring the client compound and request to be incorporated into the panel production process.
- There are over 200 sites worldwide that participate annually.
- 2019 publications, including 497 full articles searched at PubMed and other posters and abstracts

https://www.jmilabs.com/sentry-surveillance-program/
sentry-mvp.jmilabs.com

Study for Monitoring Antimicrobial Resistance Trends (SMART)

- SMART monitors the in vitro susceptibility of clinical bacterial isolates to antimicrobials in **intra-abdominal** and **urinary tract infections** worldwide since 2002 and 2009, respectively.
- The program is sponsored by Merck & Co., *Inc.*, Started in 2002 and 198 countries are involved
- **Isolates based surveillance**:
  - Each site need to collect up to 100 consecutive aerobic and facultative gram-negative bacilli from patients with intra-abdominal infections and Record the duration of hospitalization (<48 hours or ≥8 hours) at time of isolate recovery
- A total of 21,584 clinical bacterial isolates were collected in 2011.
  - 13,356 were intra-abdominal infection isolates
  - 7,989 were urinary tract infection isolates
- 39 published articles and 56 congress posters were developed up to 2012
- Data is accessible at website (http://www.globalsmartsite.com/smart/index.aspx) by registered visitors

http://partnerships.ifpma.org/partnership/study-for-monitoring-antimicrobial-resistance-trends-smart

Antimicrobial Testing Leadership and Surveillance (ATLAS)

- ATLAS includes a fully-searchable database initially built since 2004 with data from the TEST (Tigecycline Evaluation Surveillance Trial) surveillance program, but now also encompassing data from the AWARE (Assessing Worldwide Antimicrobial Resistance Evaluation) and INFORM (International Network for Optimal Resistance Monitoring) programs.
- **Isolates based surveillance**
  - Each site will collect, identify, store, and ship fresh clinical Gram-positive and -negative aerobic isolates from documented cIAI, cUTI, cSSSI, LRTI and blood sources with information of sources (ICU, wards, etc.). All isolates will be sent to International Health Management Associates, Inc. (IHMA's) central laboratory, in Schaumburg, Illinois where the isolates will be further evaluated (phenotyping and genotyping) and stored. Only isolates considered to be the potential causative agent of the patient's infection should be included in this study.
- The registered user is able to analyze the data from either or both programs, and produce reports in tabular and graphical formats by visiting the website at https://atlas-surveillance.com
- The ATLAS database will be regularly updated (every 6 to 8 months).

Antimicrobial Testing Leadership and Surveillance (ATLAS)

	TEST	INFORM/AWARE	Combined
Total Number of Isolates	415,388	218,432	631,680
Total Number of Countries Contributing Data	70	40	73*
Total Number of Sites Contributing Data	689	234	780*
Total Number of Pathogens	196	146	287
Total Number of Antimicrobials	21	40	44
Years Contributing Data	2004-2017	2012-2017	2004-2017

* There are duplicates of countries and sites between TEST and INFORM/AWARE

- 650 posters and 63 full articles were developed up to 2017

The differences among the international surveillance programs

	GLASS	ANSORP	SENTRY	SMART	ATLAS
Sponsor	WHO	Academia (APFID)	JMI Lab	Merck &Co. Inc.	Pfizer Inc.
Nature	Passive	Passive	Passive	Passive	Passive
Surveillance types	Variable	Isolates based	Protocol driven	Protocol driven	Protocol driven
Specific diseases focus	none	Project driven	Variable per client's needs	cIAI cUTI	cIAI , cUTI, cSSSI, LRTI, BSI
Accessibility	Annual report	publications	Publications	Website and publications	Website and publications
Validation process	absent	absent	Central laboratory validation	Central laboratory validation	Central laboratory validation
Timely update	Annual	variable	Annual report	Annual report	Every 6-8 months

cIAI: complicated intra-abdominal infections, cUTI: complicated urinary tract infection, cSSSI: complicated skin and skin structure infection, LRTI: lower respiratory tract infection, BSI: blood stream infection

Value of international surveillance programs

- Provide reliable global in vitro susceptibility data
- Identify changes in the resistance rates of global, regional and local pathogens
- Recognize the emergence of new resistance mechanisms
- Detect trends in multidrug resistance by analysing data longitudinally over time

Features of 42 European national and regional surveillance systems on antimicrobial resistance included in review

Despite the efforts of European Centre for Disease Control and Prevention (ECDC) and other organizations, wide heterogeneity in procedures and indicators still exists.

Characteristic	Variable	*n* (%)
Source of data	Laboratory only	33 (78.5)
	Laboratory and patients' charts	8 (19.0)
	Unknown/not reported	1 (2.3)
Duplicates policy	Duplicates excluded	25 (59.5)
Case definition	Isolates from clinical samples	22 (52.3)
	Infections	10 (23.8)
	Unknown/not reported	10 (23.8)
Indicators	Proportion of resistant isolates[a]	27 (64.2)
	Cumulative incidence[a]	11 (26.1)
	Incidence density[a]	12 (28.5)
	Unknown/not reported	8 (19.0)
Pathogens specified	*Streptococcus pneumoniae*	32 (76.1)
	Staphylococcus aureus	41 (97.6)
	Enterococcus spp.	31 (73.8)
	Escherichia coli	38 (90.4)
	Klebsiella pneumoniae	36 (85.7)
	Pseudomonas aeruginosa	34 (80.9)
	Acinetobacter baumannii	35 (83.3)
	Clostridium difficile	22 (52.3)

[a] Not mutually exclusive.

M. Núnez-Núnez *et al.* *Clinical Microbiology and Infection* 24 (2018) 105 - 109

Limitations of surveillance program

Lessons learned from EARS-Net (ECDC)

Structural Problems

- **Different objectives**
- **Insufficient coordination and sharing of information**
- **Inadequate standardization** of data collected and methods of microbiological testing (including susceptibility testing), and data sharing policies
- **Delay in publication** and insufficient publication for food surveillance data

Laboratory-based surveillance issues

- **Insufficient associated** and relevant epidemiological, clinical, and outcome data
- **Genetic typing** and characterization not routinely included
- **Biases** introduced by sample collection protocols

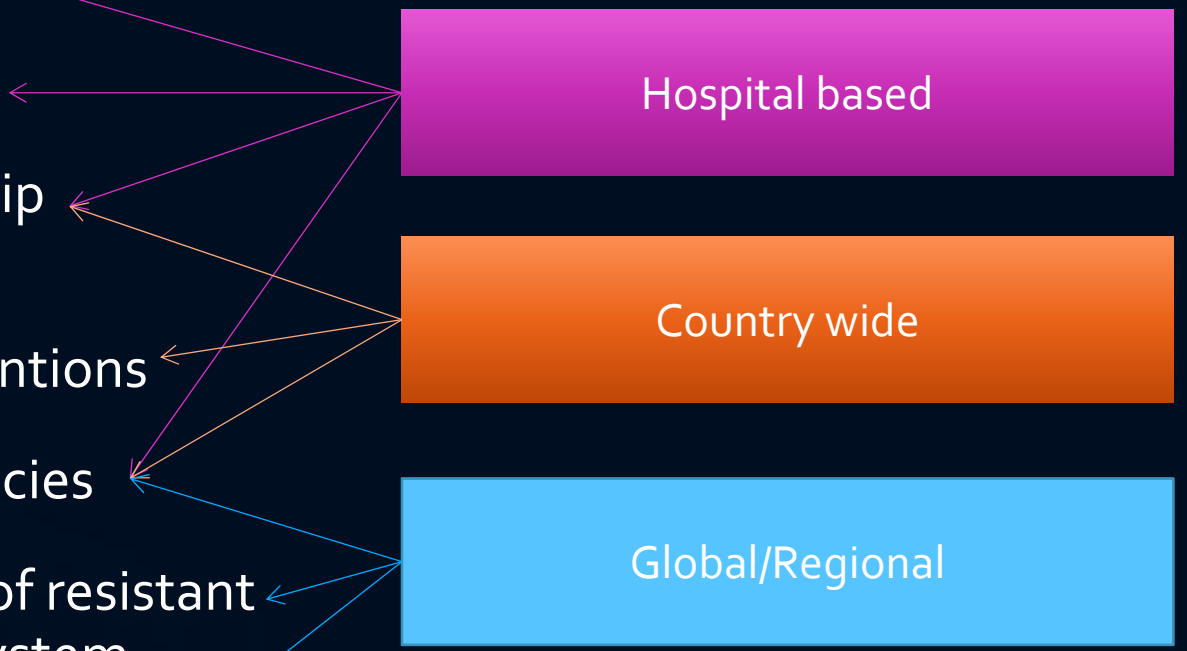
Insufficient coordination between human, animal, and food systems

- Data collection in animals directed at disease eradication and not detection of resistance to either animal or human drugs
- Coverage of only veterinary pathogens and antibiotics in animal and food surveillance systems

Lancet Infect Dis 2018: 18 e99-e106
http://dx.doi.org/10.1016/S1473-3099(17)30485-1

The key utility of different surveillance programs

- Therapy guidelines
- Antibiotic formulary
- Antibiotic stewardship programmes
- Public health interventions
- Infection control policies
- Identify emergence of resistant bugs with warning system
- Antimicrobial development.



Necessity of surveillance program across levels:
Hospital based, country wide, international (region or global)

The key elements of collaborative surveillance programs

- Standardized methodology of susceptibility tests
- Common objectives with key foci
- Unified protocol of isolates collections
- Timely updated data accessibility to guide the treatment and antimicrobial stewardship
- Generation of clinical impact
  - Enhancement the benefits and minimize for patients
  - Changes of clinicians' behavior
  - Impact on appropriate uses of antimicrobial agents in agricultures and veterinary industry

It is critical to have collaboration among all stakeholders

- Government
- Academia
- Clinical institutes
- Pharmaceuticals
- Industries