Antimicrobial Resistance

Structuring the problem and containing it

Online Media Workshop
Antimicrobial Resistance in Africa: A Growing Scourge
Aug 27-28, 2020

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What is Antimicrobial Resistance?

- **Antimicrobial resistance** happens when microorganisms (such as bacteria, fungi, viruses, and parasites) change when they are exposed to antimicrobial drugs (such as antibiotics, antifungals, antivirals, antimalarials, and anthelmintics) (WHO)

- **Antibiotic resistance** happens when germs like bacteria develop the ability to defeat the drugs designed to kill them. That means the germs are not killed and continue to grow. (CDC)

- How does AMR develop?
  - Occurs **naturally over time**; accelerates by misuse and overuse of antimicrobials
  - Antibiotic use exerts **greater selection pressure** on bacteria, causing resistant ones to survive
  - At a cellular level, resistance is acquired through **transfer of genetic material** from one bacteria to another

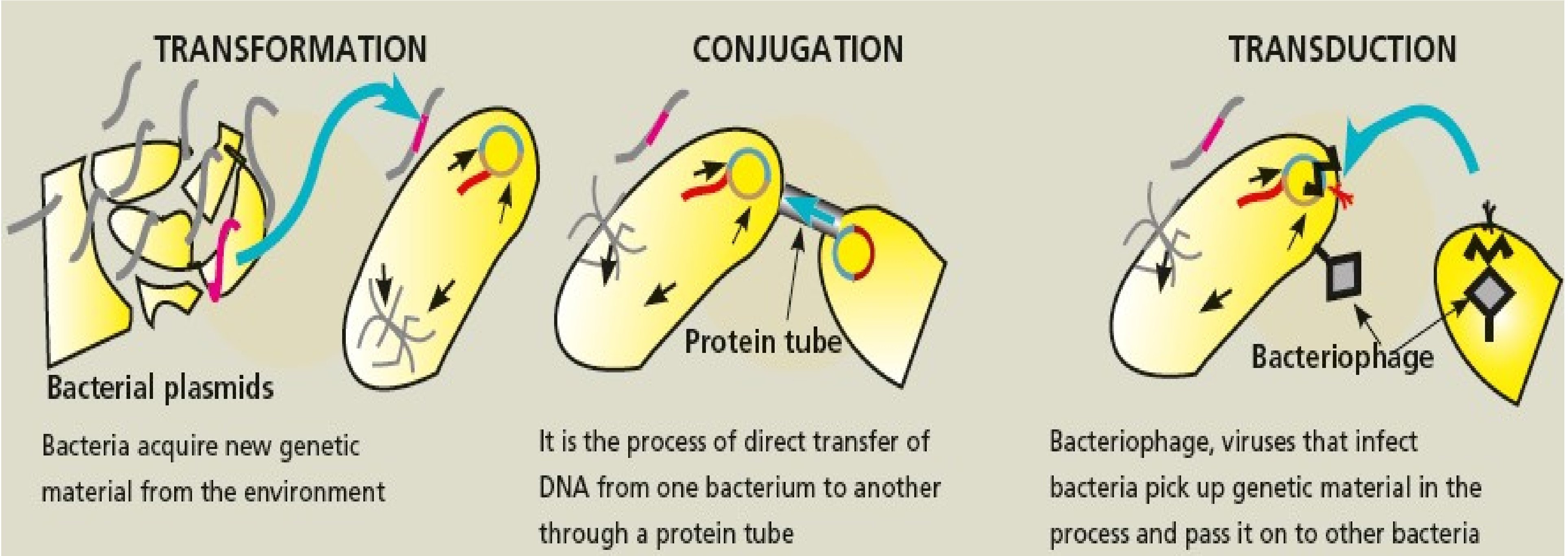


Figure source: Down to Earth

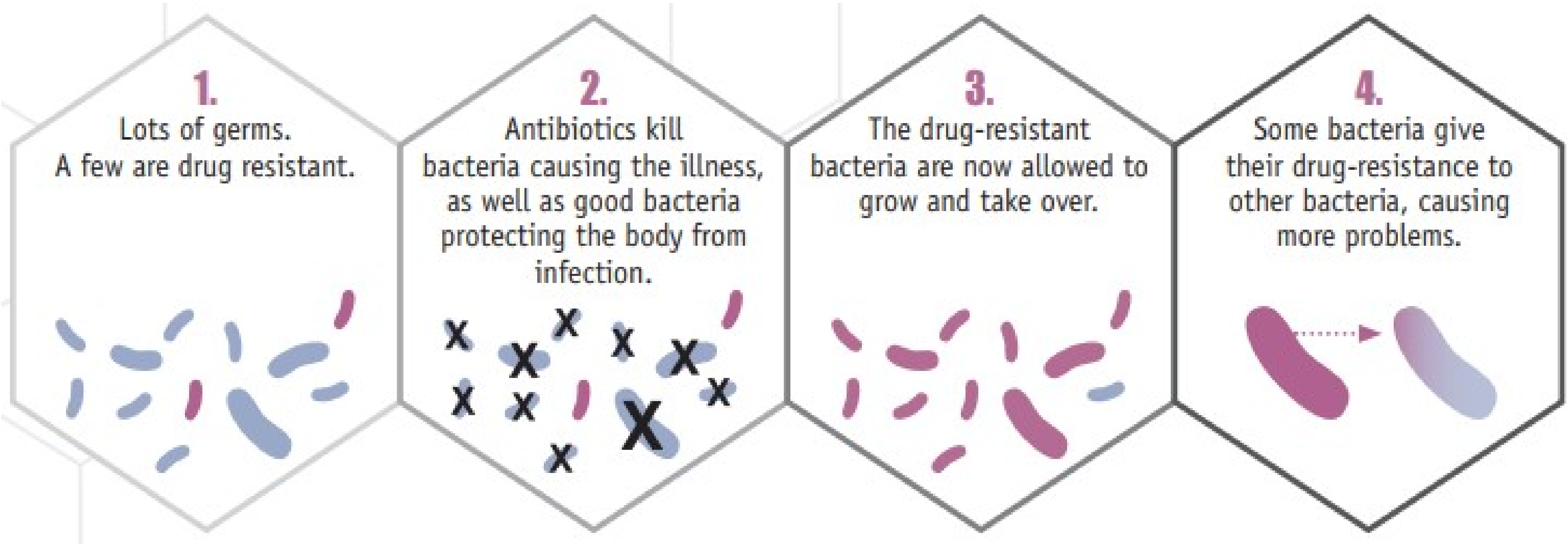


Figure source: CDC

Scale and impact of the AMR problem is huge

- **Multiple microorganisms** (bacteria, virus, fungi, parasite)
- **Different types of a bacteria** (e.g. Gram positive bacteria, Gram-negative bacteria)
- **Infections of multiple organ systems/body tissues** (gut, respiratory, urinary, blood etc.)
- **Different sources of infection** (community-acquired, hospital-acquired, food-borne)
- **Impacts outcome of infectious diseases**, **non-communicable diseases** (e.g. chemotherapy in cancer, diabetic foot), **post-surgical infections** (e.g. hip transplant, cardiac surgery)
- **Resistance against almost all antibiotics** (old antibiotics like tetracycline, penicillin; new antibiotics like 3rd, 4th, 5th generation cephalosporins; last resort like colistin)
- **Prevalent across globe, all age groups**

Antibiotics becoming ineffective leading to untreatable infections, longer hospital stays, expensive treatments, more morbidity and deaths; Economy, livelihood, food security and safety, attainment of several SDGs can be severely impacted

AMR is cross cutting; has strong multi-sectoral linkages w.r.t. both cause and effect

Animal health and production

- Poultry, fisheries, dairy, swine
- Intensive production systems
- Routine antibiotic use for growth promotion, disease prevention
- Use of critically important antibiotics (CIA) for humans

Human health

- Self medication
- Over prescription
- Over-the-counter sale
- Access vs excess issue

AMR

Waste and Environment

- Point and non-point sources
- Hotspots include waste from farms, factories, healthcare settings and sewage/water treatment plants
- Non-point sources include rivers etc.

Plants

- Routine use of antibiotics as fungicides in crops to prevent diseases;
- Use of streptomycin, a CIA used in certain Tuberculosis cases such as in India

High annual deaths due to AMR leading to huge cumulative damage vis-à-vis viral pandemics of the 21st century (which are acute crisis of a limited duration)

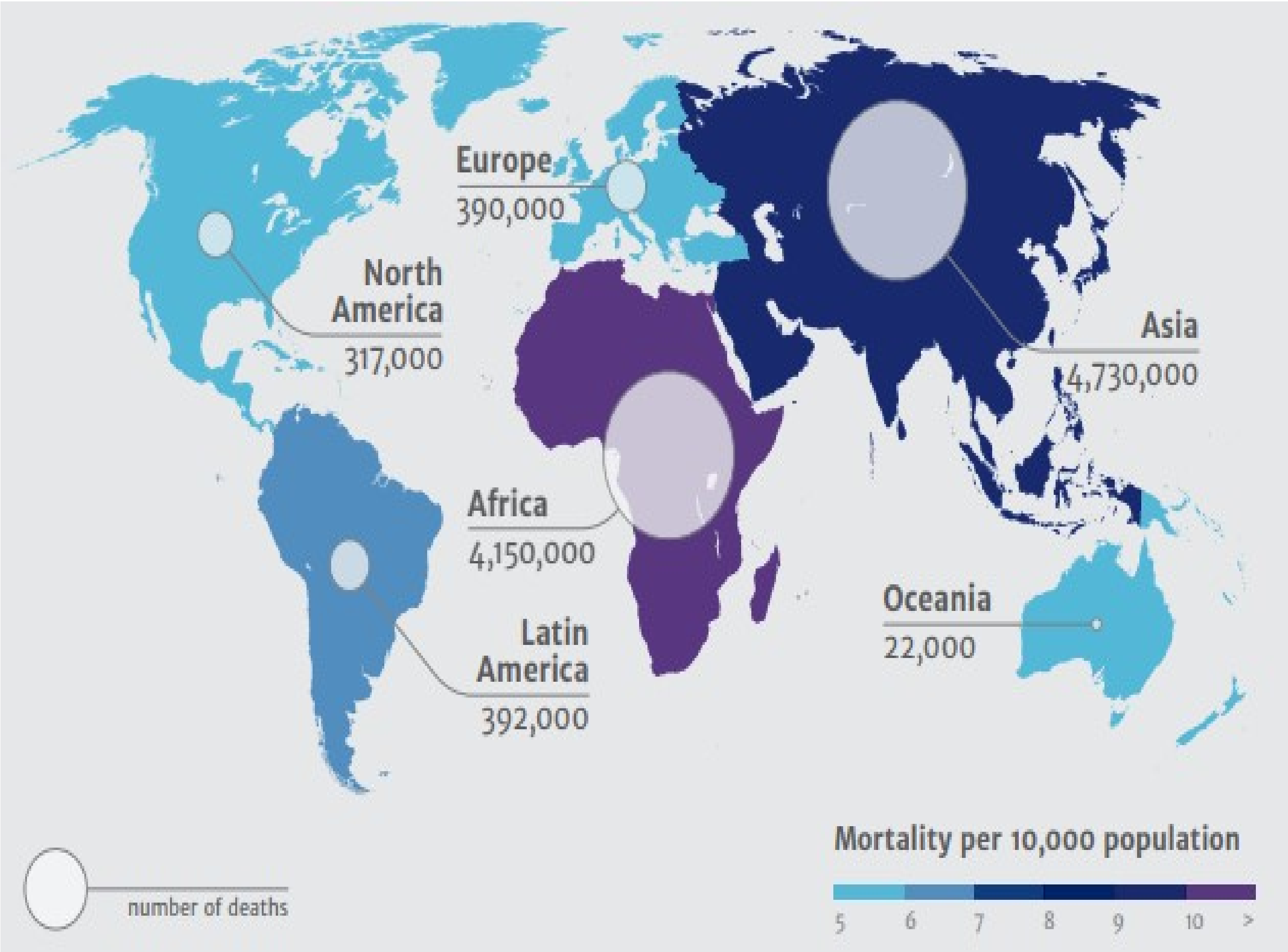
- **700,000** deaths globally every year estimated due to AMR (Review on AMR, 2016)
- **2,30,000** deaths globally in 2017 due to multidrug-resistant (MDR) or rifampicin-resistant TB (WHO, 2018)
- **45% of deaths** in both Africa and South-East Asia to MDR bacteria (WHO GLASS Report 2014)
- **USD 100 trillion** – cumulative cost to global economic output by 2050
- **3.8%** expected **loss in annual GDP** globally by 2050 in a high AMR-impact scenario (World Bank, 2017)

Pandemic	Causative organism	Worldwide deaths
Spanish Flu (1918-19)	Influenza A (H1N1) virus	20-50 million
Asian Flu (1957-58)	Influenza A (H2N2) virus	1.1 million
Hong Kong Flu (1968)	Influenza A (H3N2) virus	1 million
After 2000		
SARS (2003)	SARS CoV virus	916 (Nov 2002- Aug 2003)
Swine Flu (2009)	Influenza A (H1N1) virus	0.15-0.57 million (during first year)
MERS (2012)	MERS-CoV virus	858 (since Sept 2012)
Ebola (2014-16)	Ebola virus	11 310
Covid19 (2019-20 ongoing)	SARS-CoV2 virus	>0.8 million (as on August 27, 2020)

Source: WHO and CDC

AMR - a chronic pandemic of huge cumulative damage

10 million lives a year estimated to be at risk by 2050, if AMR not contained; About 90 per cent to be in Asia and Africa



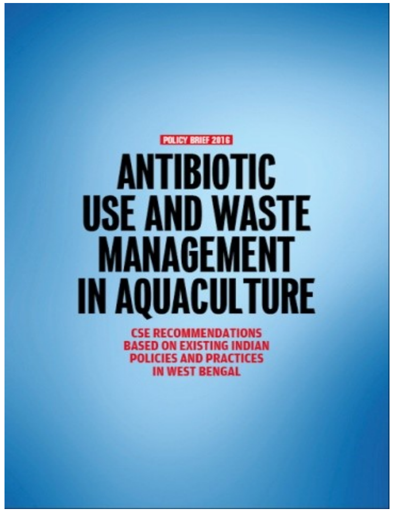
Deaths attributable to AMR every year by 2050

Source- AMR: Tackling a crisis for the health and wealth of nations

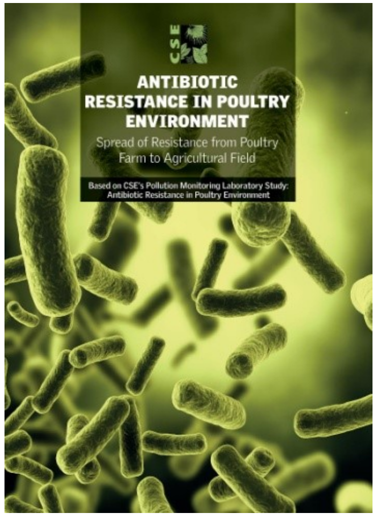
CSE's work to help contain AMR in animal and environmental sectors

2010 (Honey)

2014 (Poultry)



2016 (Fish)

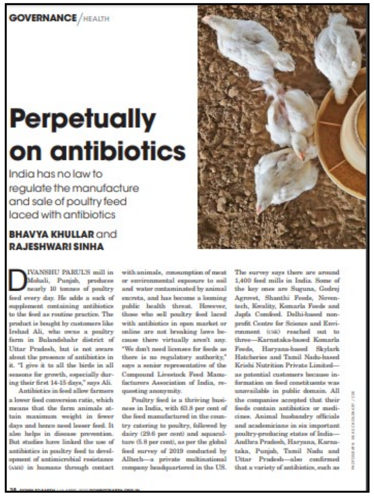


2017 (Poultry farms)

2017 (Fast food)

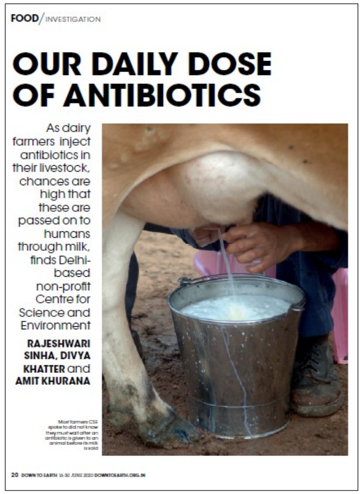
2019 (Crops)

2019 (Unused drug disposal)



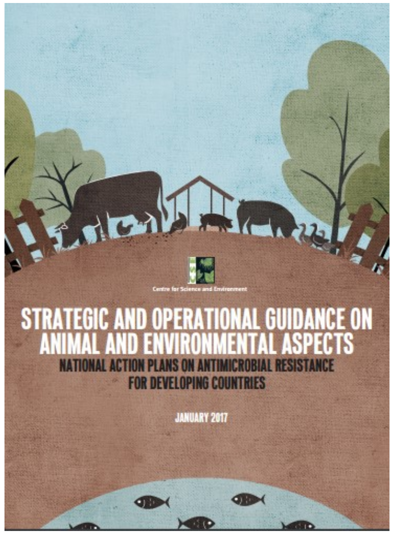
2020 (Feed)

2020 (Fast food)

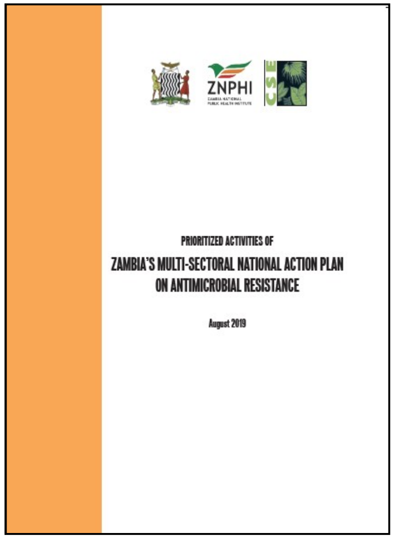


2020 (Dairy)

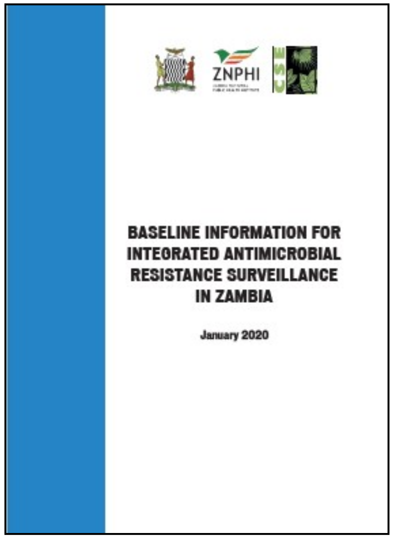
CSE's work to support NAP implementation in developing countries including African countries



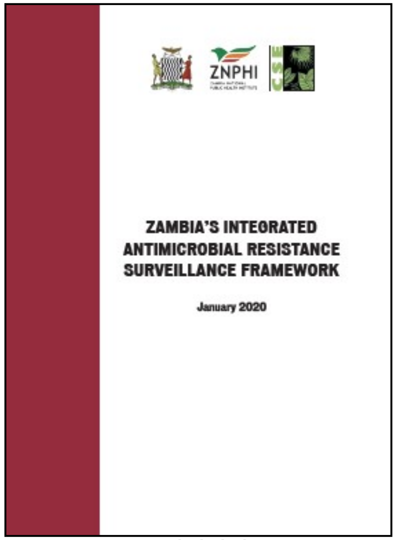
2016-17



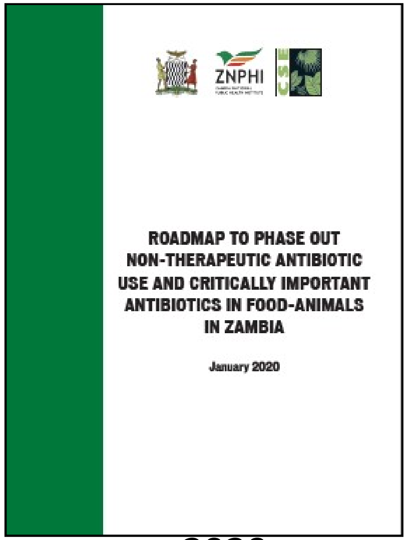
2019



2020



2020



2020

- Pan-Africa Workshops to help support implementation of National Action Plans (NAP) on AMR
- Collaboration with Zambia to help implementation of Multisectoral NAP-AMR
- Beginning collaborations in Zimbabwe to support implementation of One-Health AMR NAP

Antibiotic use in food systems

Intensive food-animal farming

More food is now grown in intensive settings; the very nature of such industrial production can create crisis

- In **high income countries**, most of food from animals is grown in intensive settings
- In **low and middle income countries** intensification is growing due **to animal protein demand**

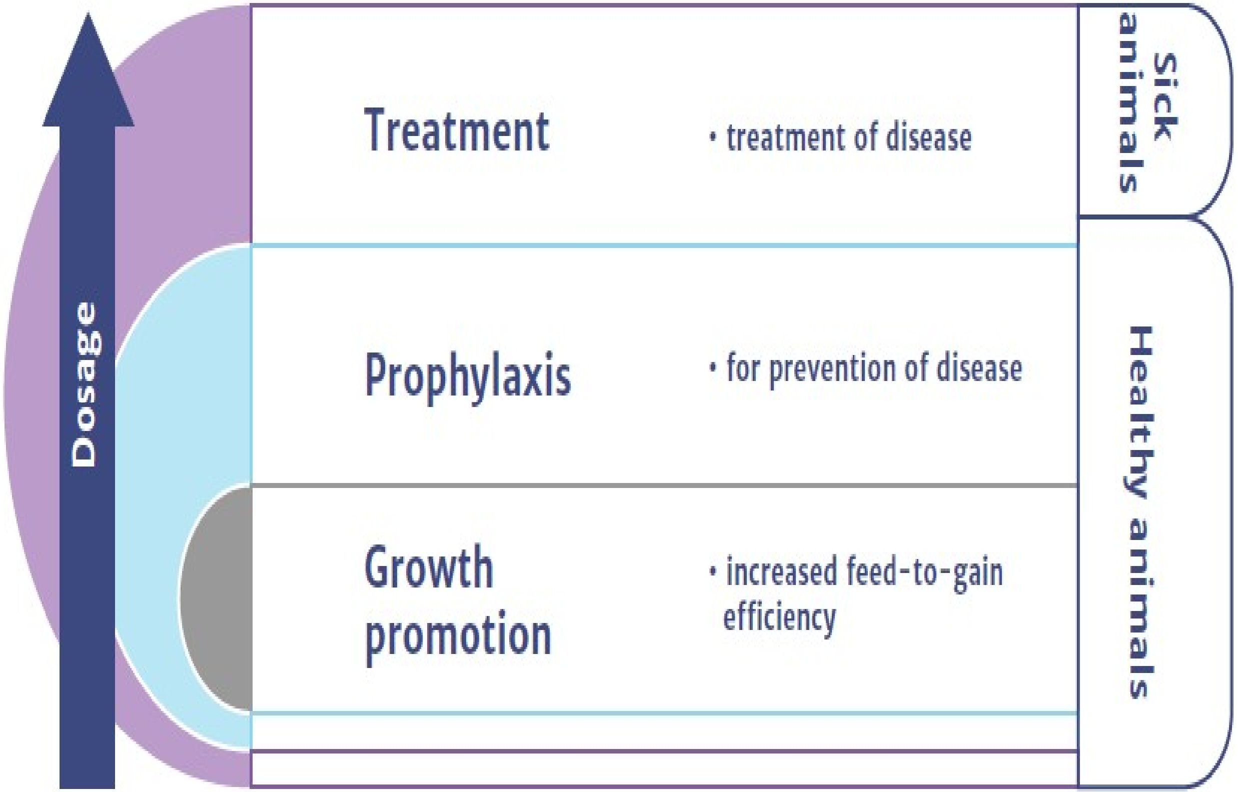
But the very nature of such production systems can create crisis

- **Large-scale units** with **high stocking density** of animals/birds/fish
- **Genetically selected breeds** for productivity (not disease resilience)
- Confined conditions; **limited focus on animal husbandry**
- Dependence on **commercial feed**, inputs (also known as animal feeding operations, factory farms)
- Often **geographically concentrated**; vertically integrated by large players; involves contract farming
- Industrial systems but considered agriculture; do not get required **regulatory attention**

High use of **chemicals and drugs** (easy/economical substitute)

Intensive food production is also linked to several pandemics

Antibiotic use in livestock

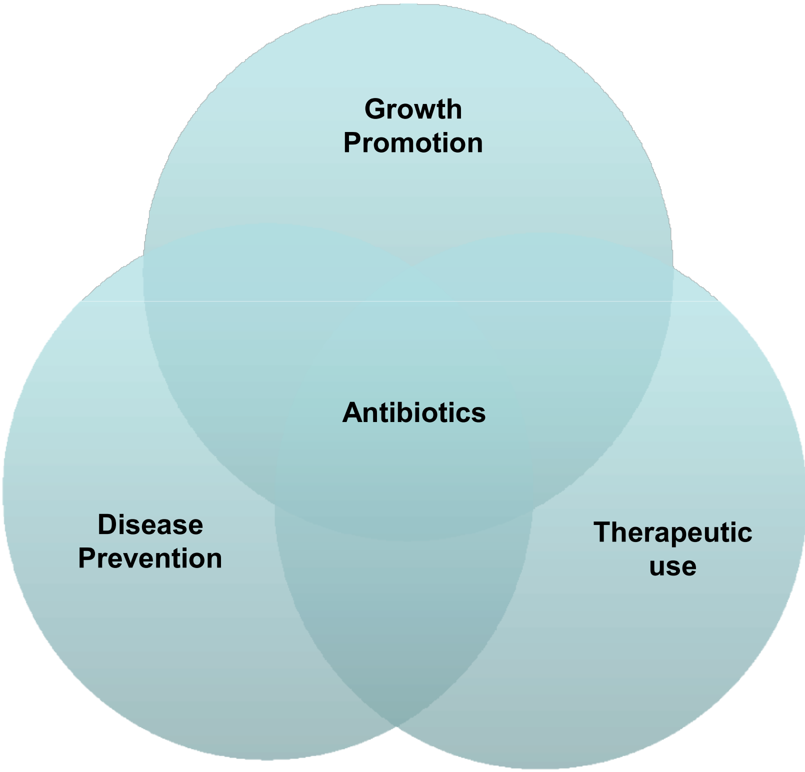


Non-therapeutic antibiotic use

- **Routine** antibiotic use to promote faster **growth** and **prevent diseases** despite no clinical sign
- Use of medically important antibiotics including **critically important** and last-resort

Source: Review on AMR-Antimicrobials in agriculture and the environment: reducing unnecessary use and waste

Only collective action on both growth promotion and disease prevention would solve the purpose



- **Antibiotic use in animals>> humans;** ~70% of medically important antibiotics for human health sold in the US and >50% percent in most countries are used in livestock
- **Non-therapeutic use** a big contributor
- Focus so far on **restricting growth promotion**
- **No fine line** – segregating where one role stops and other begins
- Need for **collective action**
  - EU banned all growth promoter use in food-animals in 2006, rise in antimicrobial use for disease prevention
  - Based on its learnings, EU will enforce ban on preventive mass medication in animals from 2022

*WHO Guidelines on Use of Medically Important Antimicrobials in Food-Producing Animals (2017); IACG Report "No Time to Wait" (2019)

Countries need to regulate the way food is grown; re-think the relationship – how it is produced and its overall impact

- Ban antibiotic use for **growth promotion**; regulate feed well – antibiotics not to be allowed
- Restrict **mass disease prevention** (i.e. group preventative use); regulate **over-the-counter sale** of antibiotics
- Limit use of **critically important antibiotics**; preserve those with **highest priority** for human use (quinolones, macrolides, 3^{rd},4^{th}, 5^{th} gen cephalosporins, polymyxins, glycopeptides)
- **Reduce need for chemicals** by focusing on animal husbandry, bio-security, alternatives, diagnostics, and veterinary extension systems
- **Reduce dependence** on intensive systems; grow more food in other settings

Necessary policies, surveillance, awareness, capacity building and budgets must go hand-in-hand with the above

Antibiotic use in food systems

Crops

- Antibiotic use in crops is a **common practice**
- In many geographies, antibiotics are registered as **fungicides** (e.g., India)
- Use for **treatment** and **prevention** of diseases such as blight, canker
- **Unapproved use** on other crops; use in **higher doses and frequency**
- **Streptomycin** is commonly used
- Antibiotic use is made in **combination with other fungicides**
- A recent analysis from 32 countries also indicated similar wider practices

WHAT'S THE NORM ANYWAY?

Streptocycline is used on a large number of crops despite Central insecticide board (CIBRC) allowing its use on eight

Recommended use on crops and for disease	Used but not recommended by CIBRC	Not recommended by CIBRC but by KVK*
Bean (halo blight), potato (blackleg and soft rot, bangle disease), tea (blister blight), tobacco (wildfire) and tomato (bacterial leaf spot)	Apple gourd, bottle gourd, brinjal, cabbage, carrot, cauliflower, chenopodium, chilli, coriander, cucumber, fenugreek, garlic, gram, lady finger, onion, radish and spinach	Betel vine, brinjal cabbage, cauliflower, onion and ginger
Apple (fire blight) and citrus (citrus canker)	Grape, mango and pomegranate	Banana, mango, pomegranate, and watermelon
Paddy (bacterial leaf blight)	Mustard	Gram and sesame

Source: Central Insecticide Board and Registration Committee; *Krishi Vigyan Kendra

Source: Too much too often (Down to Earth)

Antibiotic use in food systems

Crops

Areas for action

- **Regulate the misuse** of antibiotic use in crops
- **Re-categorize antibiotics** from fungicides to antibacterials/bactericides
- **Limit the use of CIAs** in crops
- **Monitor** the amounts of **antibiotics used** in crops
- **Surveillance of plant-derived food produce** for residual antibiotics

Structuring the environment sector w.r.t AMR

Point Sources

Farms

Waste from:

- Animal farms – poultry, dairy, pig, fish etc.
- Agriculture farms

Factories

Effluents from:

- Pharma manufacturing
- Feed mills
- Slaughter houses
- Processing units (meat, dairy)
- Effluent treatment plants

Households/ Community

- Effluents from Sewage treatment plants
- Disposal of unused, expired drugs

Healthcare Settings

- Hospital sewage
- Waste from veterinary care settings

Non-point Sources

Rivers, Reservoirs

Groundwater

Agricultural soil

Three AMR determinants that travel across the systems, sectors: Antibiotic resistant bacteria, Antibiotic resistance genes, Antibiotic residues

AMR in the environment is a cross cutting issue. Continuous and perhaps ever-lasting interplay among AMR determinants sets the ground for resistance growing like a chain reaction

AMR in environment has been a neglected agenda

- Focus has been on ‘what is going in’ and not on ‘**what is coming out**’. Missing the complete picture

- AMR containment in the waste and environment sector has largely been a neglected agenda
  - Global deliberations now include environment, but **no specific guidance** yet
  - Environment is not the key mandate of WHO-FAO-OIE tripartite; **UNEP only recently included**
  - Country level National Action Plans have outlined approaches to address the environmental AMR routes, but there is still **inadequate action on the ground**
  - **Limited awareness** and **buy-in** of policymakers and environmental regulators on the issue; **limited expertise on microbiology** related aspects
  - No **environmental standards** w.r.t. residual antibiotics or resistant bacteria

- Mixed scientific opinion due to complexity of the issue

It is time we re-think, re-prioritize and put the environment first; at par with human and animal sectors

Tackling AMR from the environment – policies to practice

A **comprehensive approach** is required to address this complex issue. A **precautionary principle** should be considered

- Antibiotics in the environment could be considered as a **hazardous chemical**; **AMR centric waste management approaches should be adopted**
- **Standards for residual antibiotics** in environment and **waste management guidelines** should be developed
- **Surveillance** of waste/effluents, litter, manure for AMR determinants, particularly from hotspots, should be carried out
- Policies that help keep a check on **land application of farm litter** should be developed
- Policies for **drug take-back** under **Extended producer Responsibility** for unused and expired medicines from human, animal sector should be developed and implemented
- **Guidelines** on siting, biosecurity, sanitation and hygiene for different point sources should be developed
- Ongoing research should **continue to inform** future policy and plans

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