THE PEW CHARITABLE TRUSTS

Antibiotic stewardship in animal agriculture

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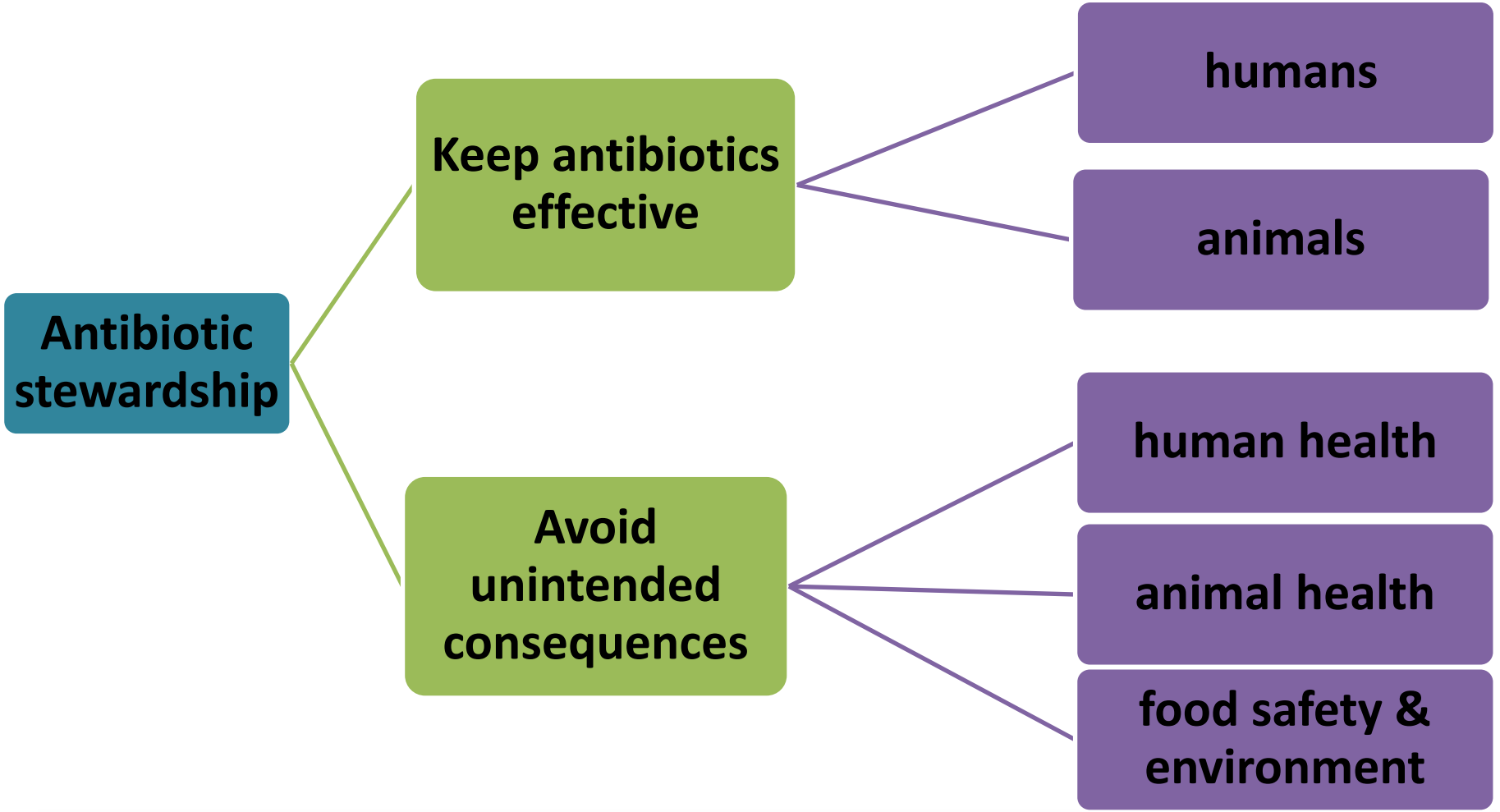
October 29, 2019

Overview: Topics of today's presentation

- What is antibiotic stewardship & why does it matter?
- The role of antibiotic alternatives in stewardship
- The role of behavior research in stewardship
- The way forward

Stewardship = careful & responsible management of resources



The need for antibiotic stewardship: Human health perspective

63% of infectious disease doctors have treated patients with infections that **did not respond to any antibiotics.**

2 million Americans

acquire **serious infections** caused by antibiotic-resistant bacteria each year. **23,000 people die** each year as a direct result of these infections.

Antibiotic use is associated with adverse patient outcomes, such as *Clostridium difficile* infections, which cause at least

14,000 deaths

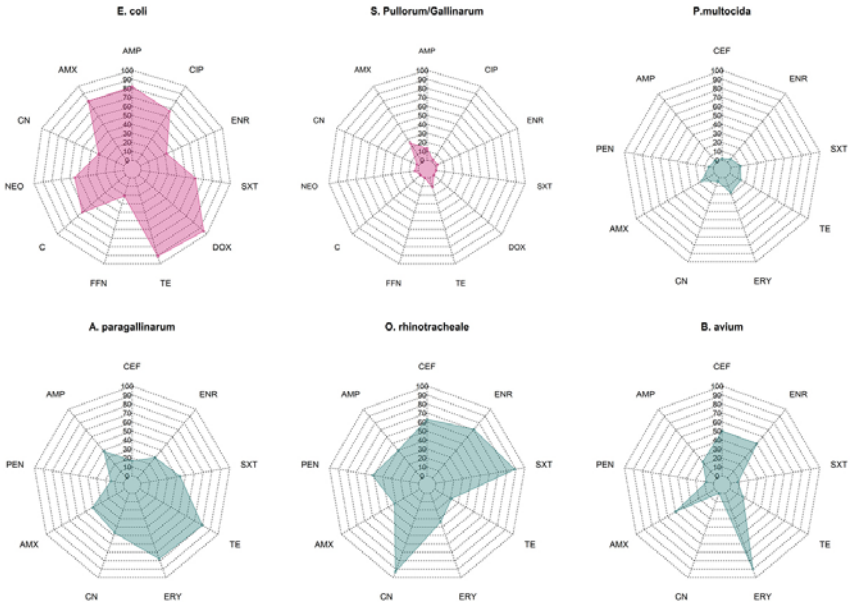
in the United States each year.

Source

http://www.pewtrusts.org/~/media/assets/2015/02/antibioticoveruseinfographic_artfinal_v5.pdf?la=en

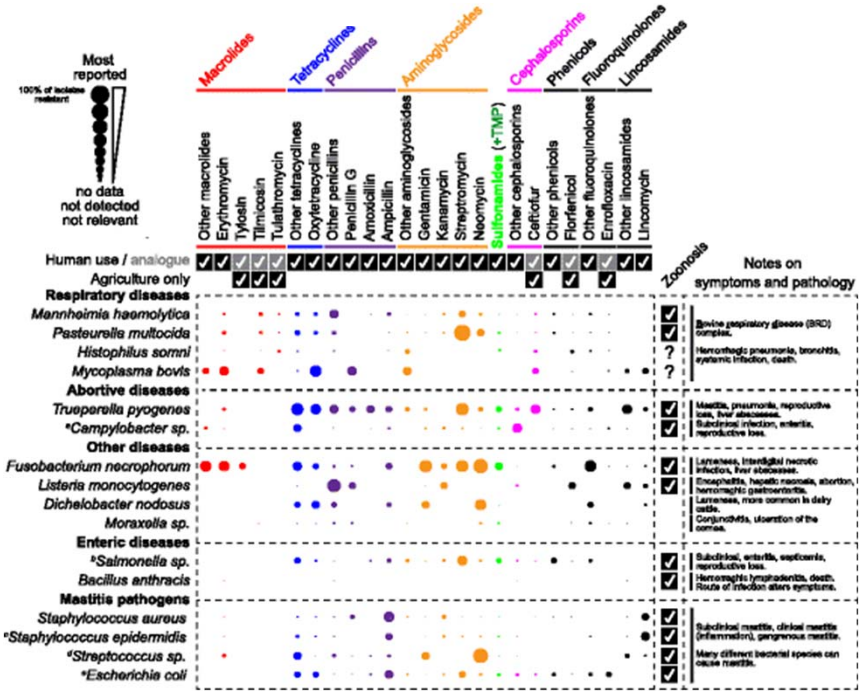
The need for antibiotic stewardship: Animal health perspectives

Antibiotic resistance in poultry disease pathogens



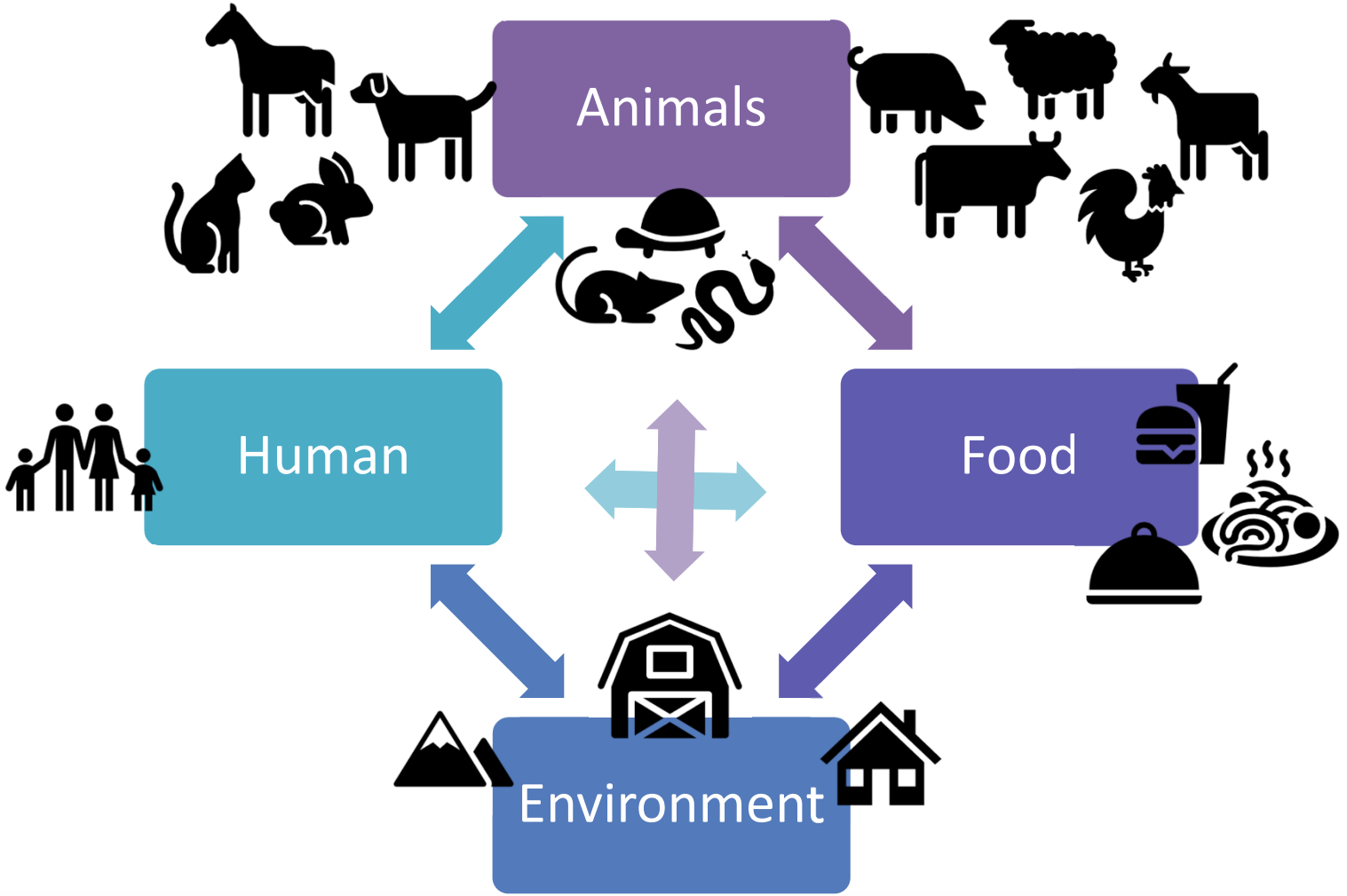
Source:
Thi Nhug, N., Chansiripornachi, N., Carrique-Mas, J.J., Front. Vet. Sci. 2017. Antimicrobial Resistance in Bacterial Poultry Pathogens: A review. Available at https://www.frontiersin.org/articles/10.3389/fvets.2017.00126/full

Antibiotic resistance in cattle disease pathogens



Source:
Cameron, A., McAllister, T.A., 2016. Antimicrobial usage and resistance in beef production. *Journal of Animal Science and Biotechnology* 7, 68.

The need for antibiotic stewardship: One health perspective



Private sector policy : Defining core components of stewardship

	Foundation	Implementation	Evaluation
	Know what to do, why, and communicate actions	***Implement foundation of knowledge***	***Continuous Assessment of stewardship practices***
1. Commitment and culture	Know about antibiotic stewardship and why it is needed	Caregivers understand and embrace their role in stewardship	Demonstrate commitment to stewardship
2. Veterinarian guidance and partnership	Understand VCPR and its importance	Have a valid VCPR and animal health plan in place	Demonstrate that veterinarian has an appropriate oversight role
3. Disease prevention strategies	Know spectrum of options to prevent diseases	Implement appropriate husbandry, biosecurity and other prevention practices	Demonstrate protocols and prevention practices
4. Optimal treatment approaches	Know how to recognize signs of disease and when and how to seek veterinary engagement	Have sound diagnostic treatment practices and protocols in place	Demonstrate that disease treatment outcomes are monitored
5. Record Keeping	Understand importance and value of accurate record keeping	Have appropriate record keeping systems in place	Demonstrate actionable record keeping

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The need for antibiotic alternatives is growing & not fully met

Alternatives for priority diseases of key importance

- Few diseases drive most antibiotic use
- Commercial vaccines available for many of the key priority diseases
- Many of the vaccines have several limitations
- Other promising alternatives exist but require further research

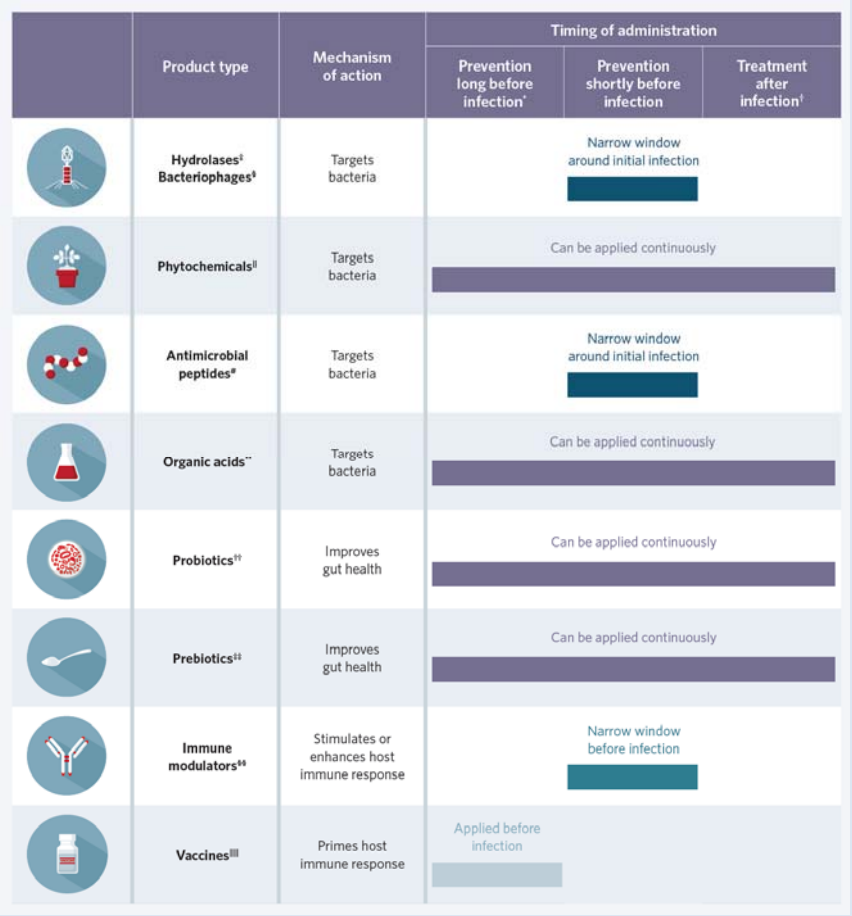
	Priority diseases for broiler chickens*			Disease-specific vaccines†			Other promising alternative approaches requiring more research‡
	Disease	Agent	Antibiotic use	Commercial availability	Major constraints	R&D priority	
Enteric diseases	Necrotic enteritis	Bacterial toxin	High	Yes	• Short-lasting and limited immunity • Application inconvenient, no mass application	High	• Phytochemicals • Prebiotics and probiotics • Immune modulators (e.g., egg yolk antibodies) • Antimicrobial peptides • Substances that bind the bacterial toxin (e.g., clays) • Bacteriophages
	Coccidiosis	Parasite, antibiotic use for secondary bacterial infection	High	Yes	• No cross-protection across strains • Current vaccines can cause disease	High	• Essential oils • Other phytochemicals (e.g., saponins)
	Infectious bronchitis	Virus, antibiotic use for secondary bacterial infection	Medium	Yes	• Protection across strains suboptimal • Virus mutates rapidly	Medium	
Generalized infection	*Escherichia coli*	Bacterium, infection possibly secondary to other diseases (e.g., yolk sac infection)	High	Yes	• Protection across strains suboptimal • No vaccine for some primary conditions that predispose for secondary *Escherichia coli*	High	

http://www.pewtrusts.org/~/media/assets/2017/07/alternatives_to_antibiotics_in_animal_agriculture.pdf

Developing antibiotic alternatives poses scientific challenges

Alternatives often more complex than antibiotics

- Heterogeneous group of products
- Include large molecules & complex mixtures of living organisms
- Mechanism of action varies & often poorly understood
- Use of multiple products together, with largely unknown & hard-to-predict results



	Product type	Mechanism of action	Timing of administration: Prevention long before infection*	Prevention shortly before infection	Treatment after infection†
	Hydrolases‡ Bacteriophages§	Targets bacteria		Narrow window around initial infection	
	Phytochemicals‖	Targets bacteria		Can be applied continuously	
	Antimicrobial peptides#	Targets bacteria		Narrow window around initial infection	
	Organic acids**	Targets bacteria		Can be applied continuously	
	Probiotics††	Improves gut health		Can be applied continuously	
	Prebiotics‡‡	Improves gut health		Can be applied continuously	
	Immune modulators§§	Stimulates or enhances host immune response		Narrow window before infection	
	Vaccines‖‖	Primes host immune response	Applied before infection		

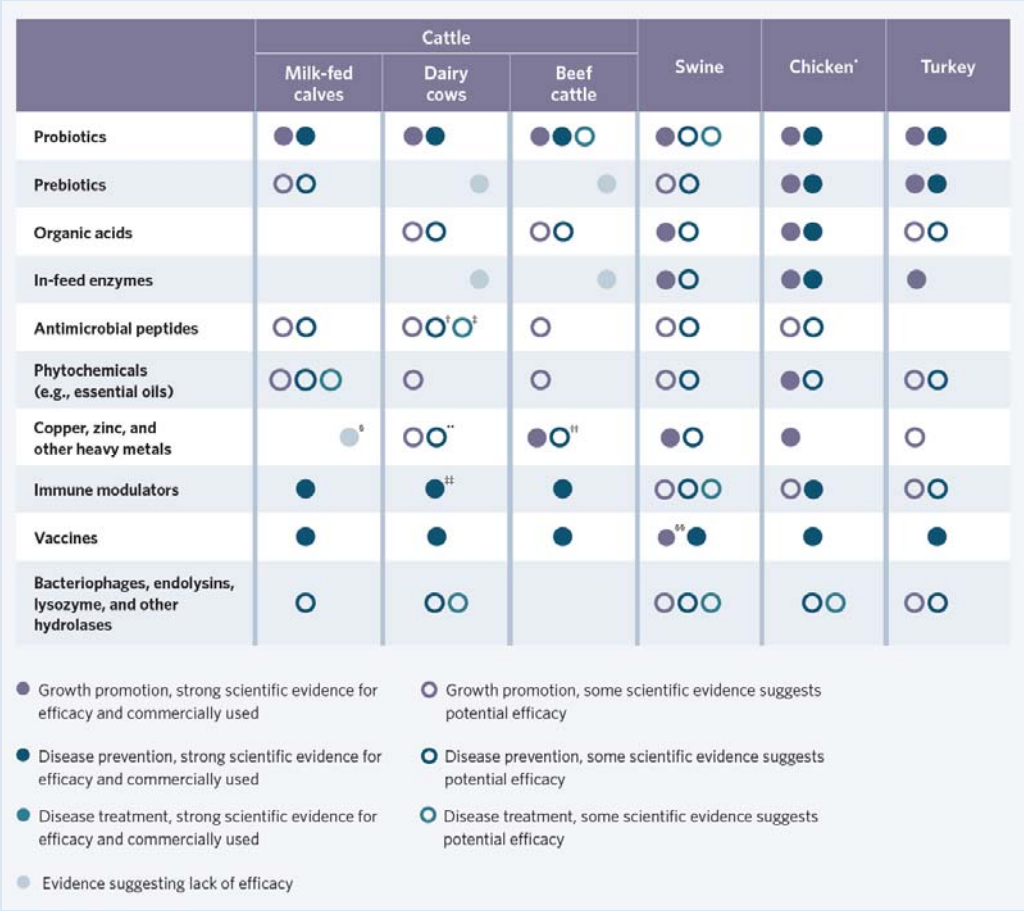
http://www.pewtrusts.org/~/media/assets/2017/07/alternatives_to_antibiotics_in_animal_agriculture.pdf

Several product types hold promise as antibiotic alternatives

Current options for growth promotion & prevention

- More products have shown efficacy for growth promotion & disease prevention than for treatment
- Currently more products exist with proven efficacy for chicken than for other species
- Alternatives often have a narrower spectrum of action & lower efficacy than traditional antibiotics
- Efficacy often varies across trials for largely unknown reasons

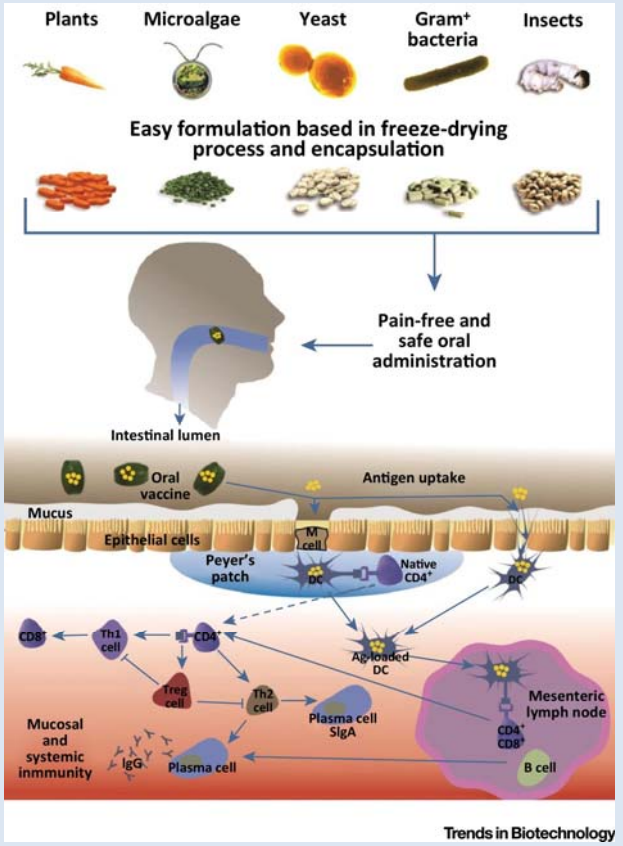
http://www.pewtrusts.org/~/media/assets/2017/07/alternatives_to_antibiotics_in_animal_agriculture.pdf



Veterinary vaccines can become effective antibiotic alternatives

Scientific progress in 4 key areas can make vaccines effective antibiotic alternatives

- **Safety improvements** (*e.g.*, vectored vaccines & new adjuvants) to minimize unintended consequences
- **Efficacy improvements** (*e.g.*, combination/ recombinant vaccines & protocol optimization) to generate robust & durable protection against broad range of pathogens (including in very young animals)
- **Easier administration** (*e.g.*, new oral vaccination strategies & increased stability) to permit easy mass vaccination
- **Cost reductions** to make use economically feasible and cost-effective



Source:
Hoelzer, K., Bielke, L., Blake, D.P., Cox, E., Cutting, S.M., et al. *Vet Res*. 2018: 49:64; **and** Hoelzer, K., Bielke, L., Blake, D.P., Cox, E., Cutting, S.M., et al. *Vet. Res*. 2018 49:70.

Source:
https://www.cell.com/trends/biotechnology/fulltext/S0167-7799(15)00247-4

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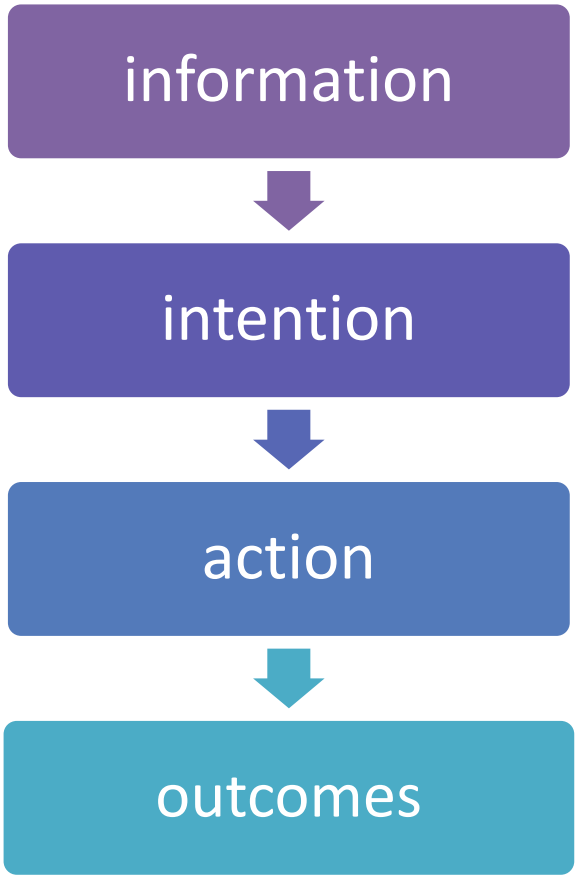
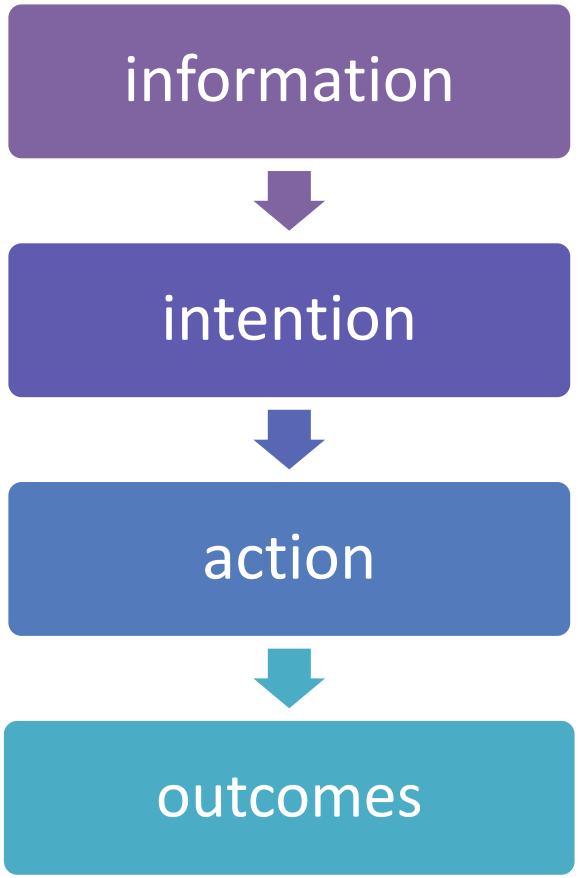
Implementing stewardship: 'traditional' behavior change model



Implementing stewardship: 'traditional' behavior change model

Human behavior is not that simple!

Human behavior is more complex than the 'traditional' model



Why behavior change may not work

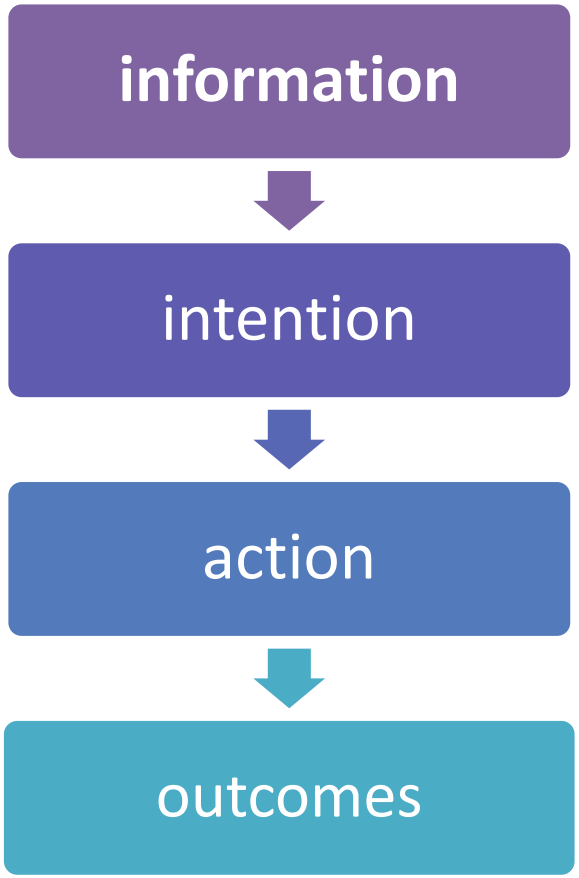
- Transmission of information
  - access to information
  - effective communication

- Competing interests

- Contextual influences
  - socio-economic, situational, choice set, etc.
- Heuristics & biases in decision-making
  - cognitive biases
  - behavioral biases
  - affect, emotion and attitude
  - risk aversion & uncertainty

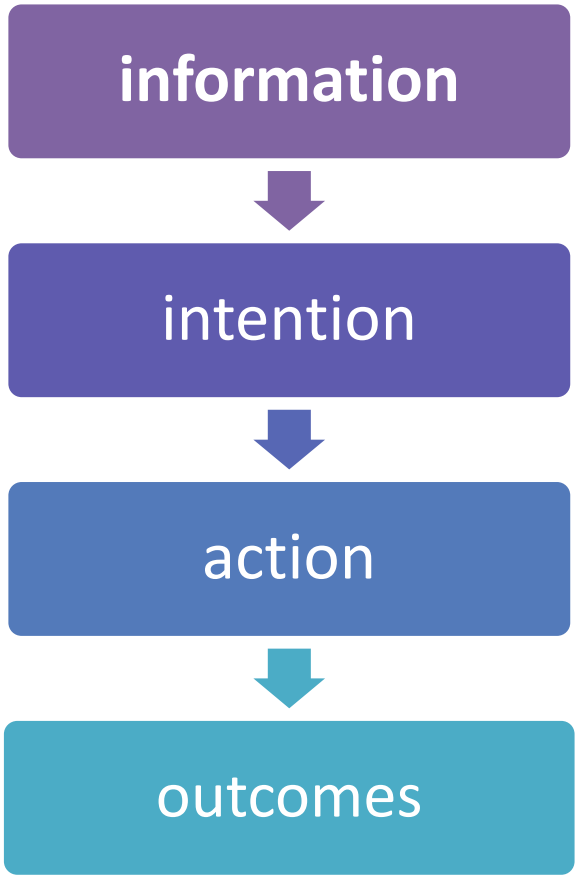
- Personality type and management style
- ……

What the literature tells us: how farmers access information



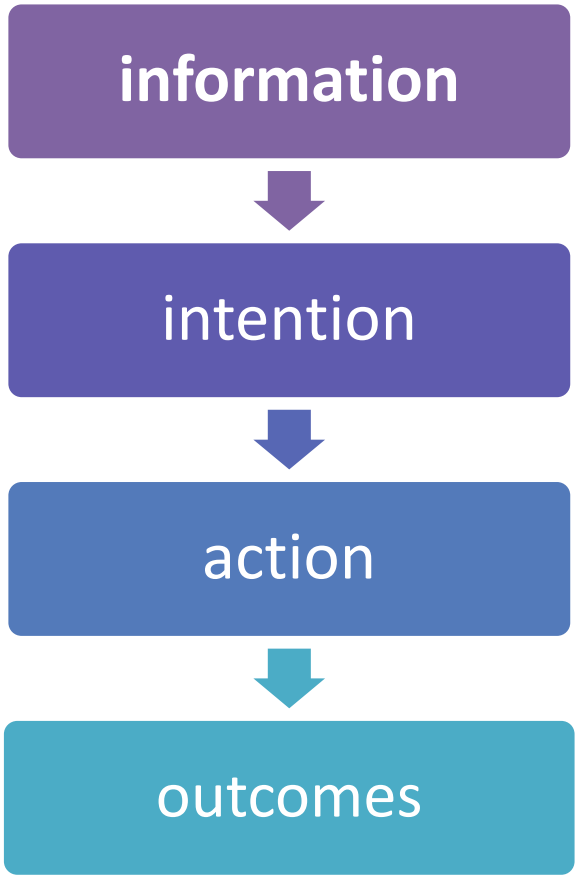
Key sources of information for farmers
• Veterinarians
• Peers & colleagues
• Other trusted farm advisors (e.g., nutritionists)
• Other authoritative sources, e.g.: - Universities - Animal Health Organizations - Government agencies
• Trade publications, other media
• Other sources

What the literature tells us: how well veterinarians communicate



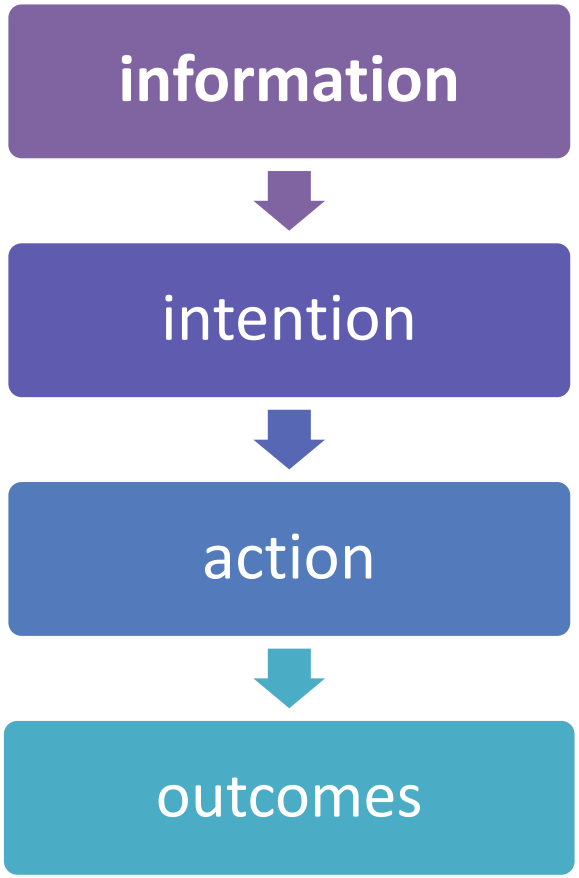
Limitations in veterinarians' ability to advise farmers
• Understanding of farm goals, challenges & priorities - *Real* or *perceived* lack of understanding
• Communication skills
• Motivation - *Farmers* may lack motivation to change - *Veterinarians* may lack motivation to effect change
• Lack of trust in veterinary advice - Incongruent with farmer's experience - Incongruent with other advisors
• Time, tools and resources
• Lack of follow-up and follow-through
• …….

What the literature tells us: factors that impact decision-making



'Competing interests' shown to impact decision-making
• *Perceived* or *real* demands & pressures - Risk of disappointing expectations - Risk of losing clients - Risk of blame if issues arise later on - Heightened pressure if initial treatment failed
• Ethics & values - Professional & personal values - Moral and ethical obligations to clients & animals
• Business operations - Economic & financial constraints - Logistic & time constraints
• *Perceived* or *real* social pressures
• ……

What the literature tells us: heuristics & biases in decision-making



Factors shown to influence decision-making process
• Age, years of experience & overall competency
• Overall level of confidence
• Educational background, gender, geographic region etc.
• Prior relevant experience with disease / condition
• Views of/recognition by peers & other key influencers
• Awareness of antibiotic resistance problem
• Feelings and emotions, in particular despair
• Risk perception and risk aversion
• Uncertainty (in particular about magnitude of loss)
• ……

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Take-home message: what we do and do not know

What we know

Why: stewardship is needed

Who: public & private partners are committed

What: implementation of core components

How: change behavior of farmers & veterinarians

What existing research tells us

Veterinarians and farmers are important partners in stewardship

Their **decision-making behavior** is not fully linear

Various conflicts, biases & emotions influence the decision-making process

What we don't know

How to **effectively change the behavior** of farmers and veterinarians

Very little **behavior change research** in animal agriculture so far

Contact me with questions & to learn more about our work

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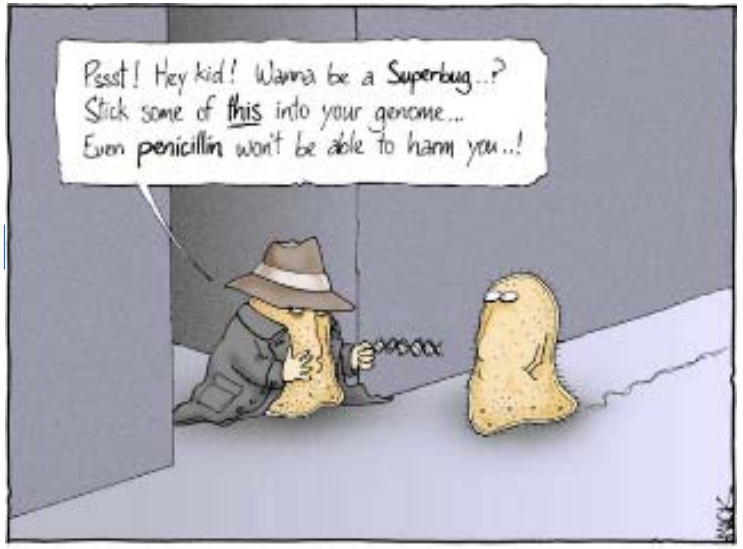

It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

Source: http://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.0050112