

# Antibiotic Use in Food Animals – A Dialogue for a Common Purpose

**H. Scott Hurd DVM, PhD**

Department of Production Animal Medicine

Director of World Health Organization Collaborating Center for Risk Analysis  
and Hazard Surveillance and Intervention in Food Animals

Former Deputy Undersecretary for Food Safety, USDA

Ames IA 50011, 515-231-3720

[shurd@iastate.edu](mailto:shurd@iastate.edu)

National Institute for Animal Agriculture, Chicago IL, October 26, 2011



# Objectives of this Meeting

- Dialogue
  - Where is consensus?
  - Where is science-based (dis)agreement?
  - Where is value-based (dis)agreement?
- Actions
  - Establish working committee
  - Identify and fill information and research (science) gaps
  - Establish criterion for decision making

# When science **CANNOT** help us make a decision

- When values play a large role in the possible choice
- When there only a limited number of choices
- When there is little uncertainty re: probability of some outcomes
- *Honest Broker, R.A Pielke, Cambridge Press*

# Possible Value Based Questions

- Is modern farming acceptable?
- Who should benefit and how much?
- How much suffering to animals should be permitted?
- How much vet oversight is “enough”?
- What is “over” or “unacceptable” use?
- What is acceptable risk?

# My Points

- 1. Concern (hazard) about antimicrobial resistant bacteria is not equivalent to risk.
- 2. Risk requires a connect causal pathway with case-by-case analysis
- 3. Alternative risk of sub-optimal animal health may be higher than the risk of on-farm antibiotic use.

# Antimicrobial resistant bacteria are a potential Hazard

- AMR found many places:
  - Farms – conventional and organic
  - Ground water, deep ocean trenches
  - Artic and sub-artic seals
  - Wild boars, Baboons
  - 30,000 year old permafrost
  - “..places which are relatively untouched by human civilization .... (Roberts, March.2011)

# Hazard Does Not Mean Risk

Hazard × **Dose (Exposure)** = Risk



Hazard

×



**Dose**

= Drowning

# Hazard Does Not Mean Risk

Hazard × **Dose (Exposure)** = Risk



Hazard

×



= Corrosive  
injury




# Example Hazardous Material

- Human Health Effects
  - cramps
  - nausea
  - dizziness
  - respiratory difficulties
  - convulsions capable of leading to death



# Example Hazardous Material = Oxygen

- Human Health Effects
  - cramps
  - nausea
  - dizziness
  - respiratory difficulties
  - convulsions capable of leading to death



**iSOC® Technology**

**Material Safety Data Sheet: Oxygen**

<b>Product Name:</b> Oxygen	<b>CAS:</b> 7782-44-7
Oxygen; Oxygen, compressed (D.O.T.)	<b>DOT I.D No.:</b> UN 1072
<b>Chemical Name and Synonyms:</b> Oxygen	<b>DOT Hazard Class:</b> Division 2.2
<b>Formula:</b> O <sub>2</sub>	<b>Chemical Family:</b> Oxidizer

**HEALTH HAZARD DATA**

**Time Weighted Average Exposure Limit:**  
None established (ACGIH 1994-1995). Oxygen is the "vital element" in the atmosphere in which we live and breathe.

**Symptoms of Exposure:**  
Breathing high concentrations (greater than 75 molar percent) causes symptoms of hyperoxia which includes cramps, nausea, dizziness, hypothermia, amblyopia, respiratory difficulties, bradycardia, fainting spells, and convulsions capable of leading to death. For additional information on hyperoxia, see Compressed Gas Association's Pamphlet P-14.

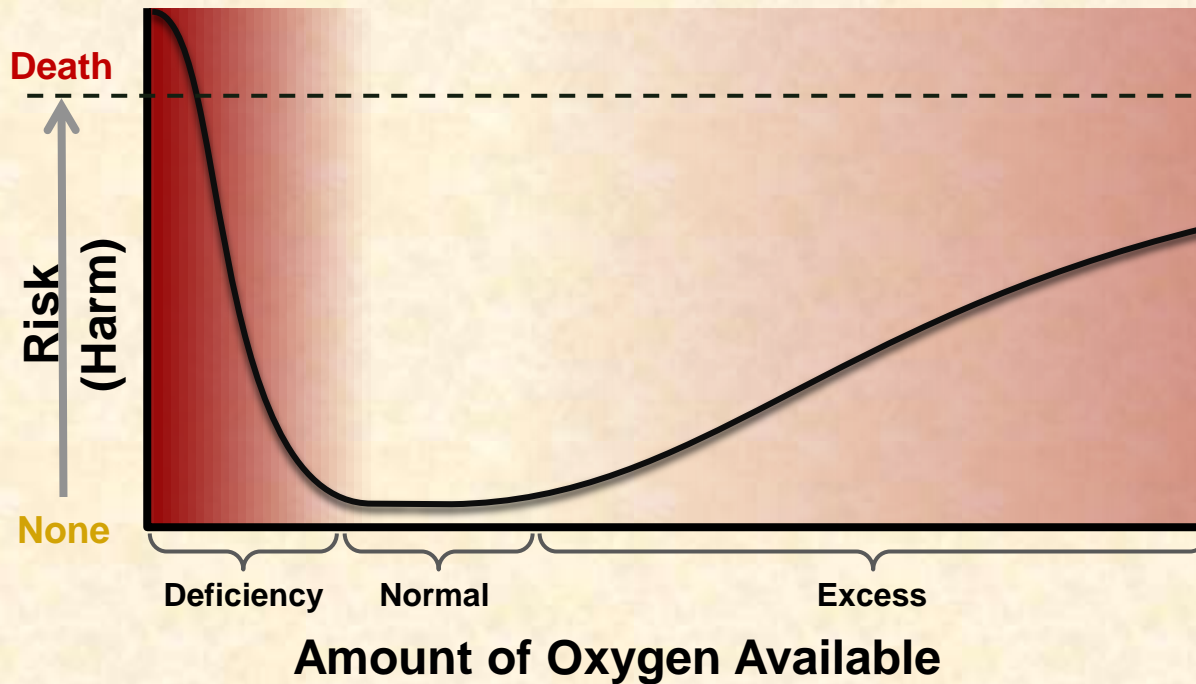
**Toxicological Properties:**

- The property is that hyperoxia which leads to pneumonia. Concentrations between 25 and 75 molar percent present a risk of inflammation of organic matter in the body.
- Oxygen is not listed in the LARC, NTP or by OSHA as a carcinogen or potential carcinogen.
- Persons in ill health where such illness would be aggravated by exposure to oxygen should not be allowed to work with or handle this product.

**Recommended First Aid Treatment:**  
Prompt medical attention is mandatory in all cases of overexposure to oxygen. Rescue personnel should be cognizant of extreme fire hazard associated with oxygen-rich atmosphere.

# Hazardous Material: Oxygen

## The Poison is in the Dose



# Concern to Infectious Disease Society

- **Staphylococcus infections (MRSA)** –mainly hospital nosocomial infections, occasionally associated with schools and athletic facilities. CDC said “not a foodborne infection and cannot be acquired by eating meat. “
- **Acinetobacter baumannii** is an opportunistic pathogen associated with a high rate of infections in soldiers wounded in Iraq.
- **Vancomycin Resistant Enterococcus (VRE)** hospital nosocomial infection due to extensive use of vancomycin in U.S. hospitals. Vancomycin or drugs in its class have never been approved for or used in food producing animals.
- **Pseudomonas aeruginosa** is another opportunistic pathogen found in intensive care units, occurs rarely in dairy mastitis
- **Streptococcus pneumoniae** is strictly a human pathogen that causes respiratory infections. no known connection to food producing or companion animals.
- **Neisseria gonorrhoea** strictly a human pathogen that causes venereal infections transmitted through human sexual contact.
- **Drug resistant tuberculosis and Klebsiella species** are other bacteria ..no known connection between these pathogens and food producing animals.
- <http://www.idsociety.org/Content.aspx?id=5650>. :

**HAZARD creates CONCERN**

**CONCERN  $\neq$  RISK**

“Probabilistic risk assessment should be used to reduce unnecessary conservatism associated with current regulatory requirements ...” (NRC, 1995)

Antibiotic resistant bacteria = Potential HAZARD

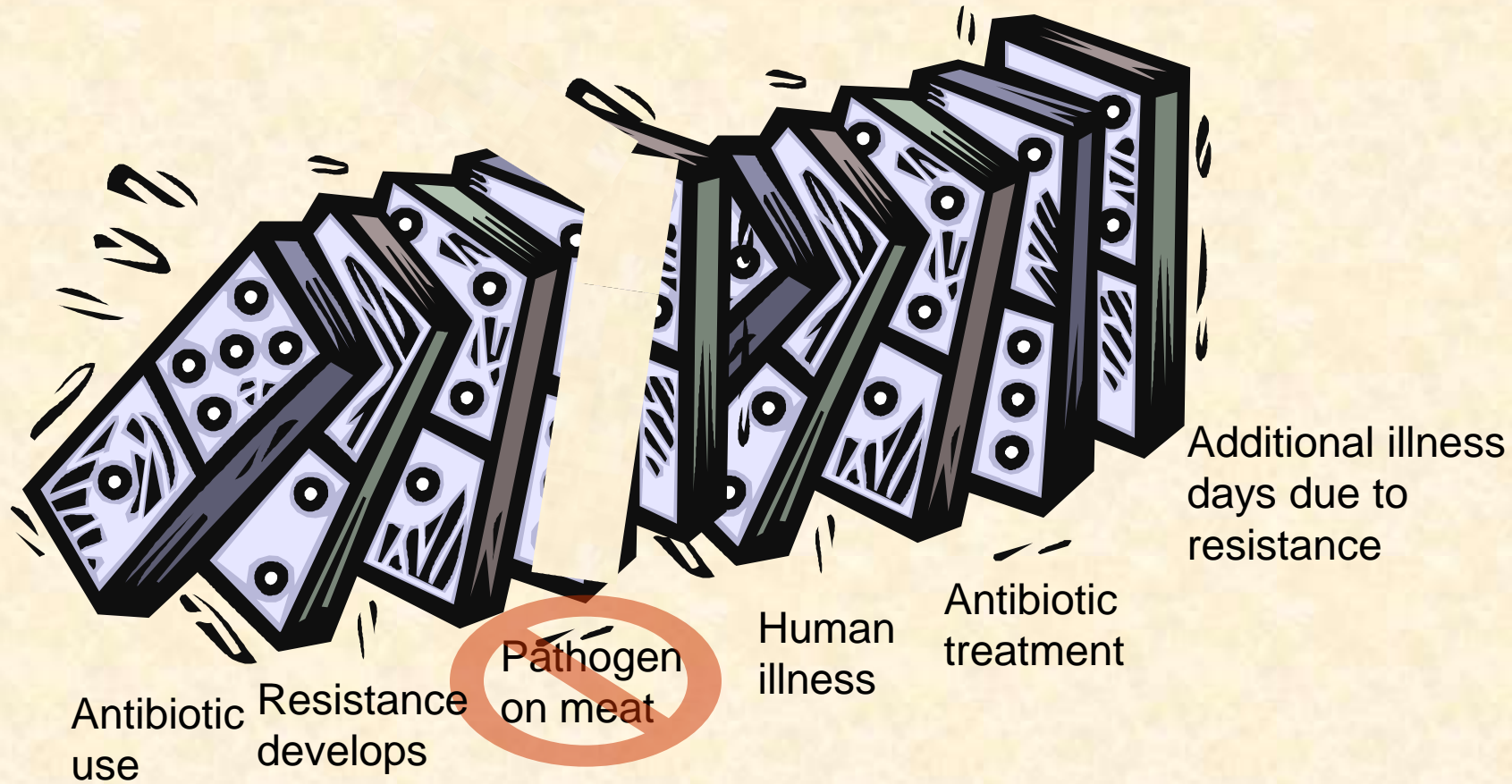
Risk assessment is needed to see if the causal pathway required does pose a RISK.

# Risk assessment estimates

## “Probability that:..

- 1) resistant bacteria are present in the target animal as a result of drug use
- **AND**
  - 2) humans to ingest bacteria in question from the relevant food commodity
- **AND**
  - 3) human exposure to resistant bacteria results in an adverse health consequence” (FDA Guidance 152).

# Without a causal pathway, you have NO risk

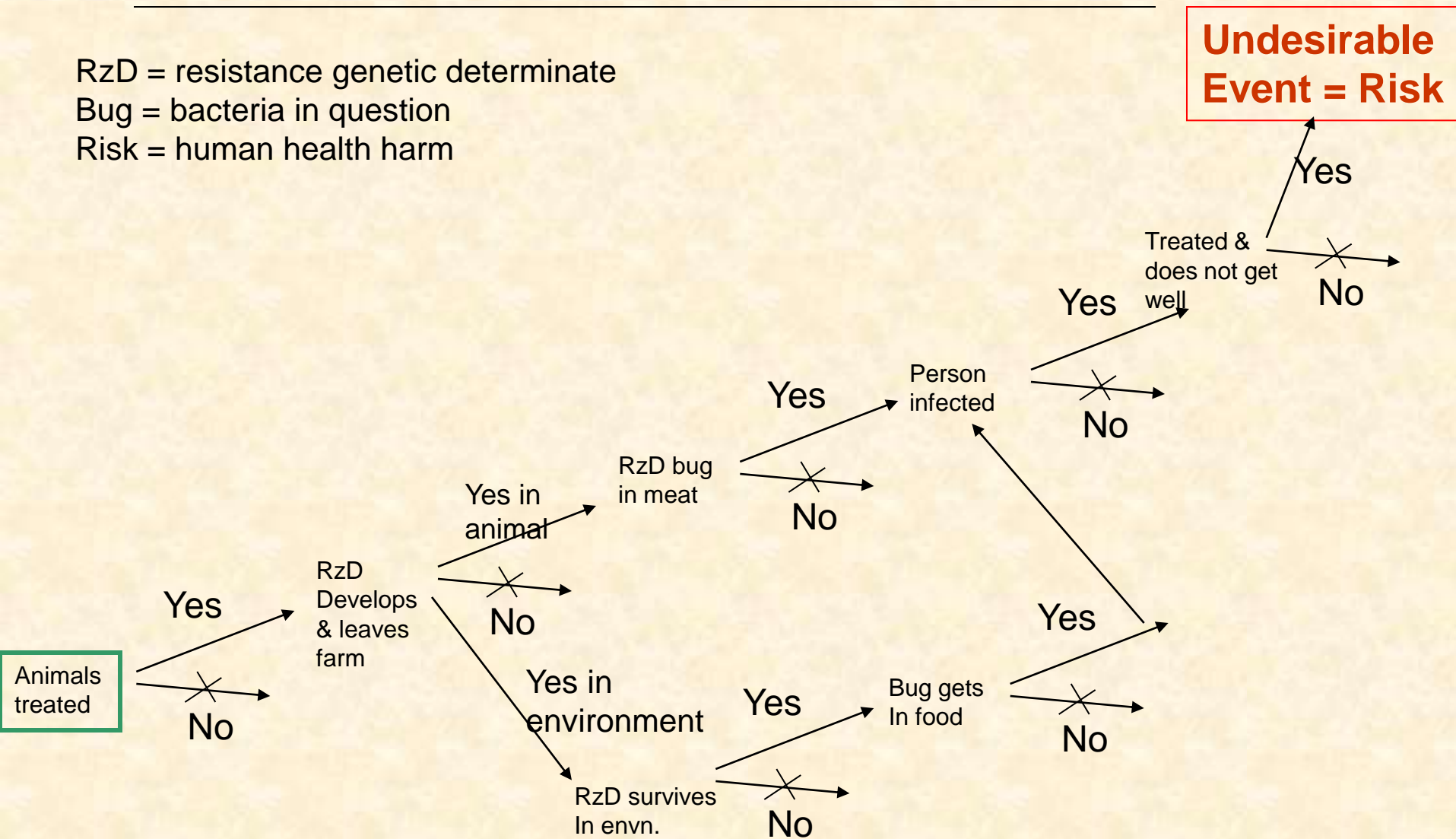


# Risk assessment must be implemented on case (bug) by case (drug) basis

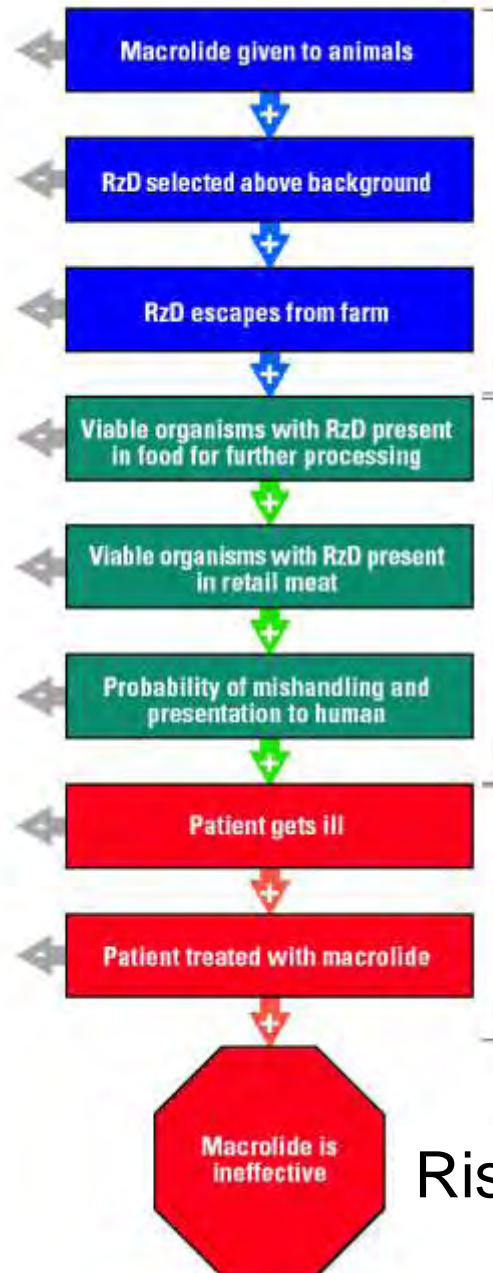
- *Campylobacter* & macrolides
- *Campylobacter* & fluoroquinolone
- *Salmonella* & macrolides
- Animal *Enterococci* do not colonize humans

## 2. Low risk of antibiotic use in livestock

RzD = resistance genetic determinate  
Bug = bacteria in question  
Risk = human health harm



# Pathway of Events Leading to the Risk



## FDA 152 methods

**Release Assessment:** Describes the probability that factors related to the antimicrobial use in animals will result in the emergence of resistant bacteria or resistance determinates (RzD).

**Exposure Assessment:** Describes the likelihood of human exposure to the RzD through particular exposure pathways.

**Consequence Assessment:** Describes the relationship between specified exposures to the RzD (the hazardous agent) and the consequences of those exposures (CVM-defined hazard)

Risk = 1 in 10 million per year

## 2. Risk Assessments have shown

Antimicrobial evaluated (target bacteria) on-farm use	Quantitative Risk	Comments, (Reference)
Enrofloxacin ( <i>Campylobacter</i> ) use in poultry to treat disease	1 in 30,000 of compromised treatment	Risk was termed as “low” by FDA. Methods overestimated attributable fraction and resulting risk (FDA 2001)
Enrofloxacin and macrolide ( <i>Campylobacter</i> ) use in poultry to treat disease	Removal is more hazardous to health than continued use	(Cox and Popken 2006)
All macrolide ( <i>Campylobacter</i> ) uses for production purposes, prevention, and treatment in cattle, swine, poultry	1 in 10 million of compromised treatment	(Hurd <i>et al.</i> 2004)
All macrolide ( <i>Campylobacter</i> ) uses for production purposes, prevention, and treatment in cattle, swine, poultry in Denmark	7 cases of resistant campylobacteriosis in Denmark per year	Most risk would come from imported product (Alban <i>et al.</i> 2008)
Macrolide ( <i>Campylobacter coli</i> ) use in swine	1 in 82 million	Stochastic model shows impact of uncertainty and variability in data (Hurd and Malladi 2008)
Streptogramin/Virginiamycin ( <i>Enterococcus faecium</i> )	~ 100 in 100 million of impaired treatment	Still a draft (FDA 2004)
Virginiamycin (Vancomycin resistant <i>Enterococcus faecium</i> )	Remove 1.8 treatment failures over 5 year period if banned	(Cox and Popken 2004)
Penicillin growth promoter ( <i>Enterococcus faecium</i> )	~4 in billion excess mortality	(Cox, Popken, and Mathers 2009)

Why take additional risk??



**3. Alternative risks maybe higher?**

# Example from poultry



ELSEVIER

Available online at [www.sciencedirect.com](http://www.sciencedirect.com)



ScienceDirect

Preventive Veterinary Medicine 79 (2007) 186–203

[www.elsevier.com/locate/prevetmed](http://www.elsevier.com/locate/prevetmed)

---

---

**PREVENTIVE  
VETERINARY  
MEDICINE**

---

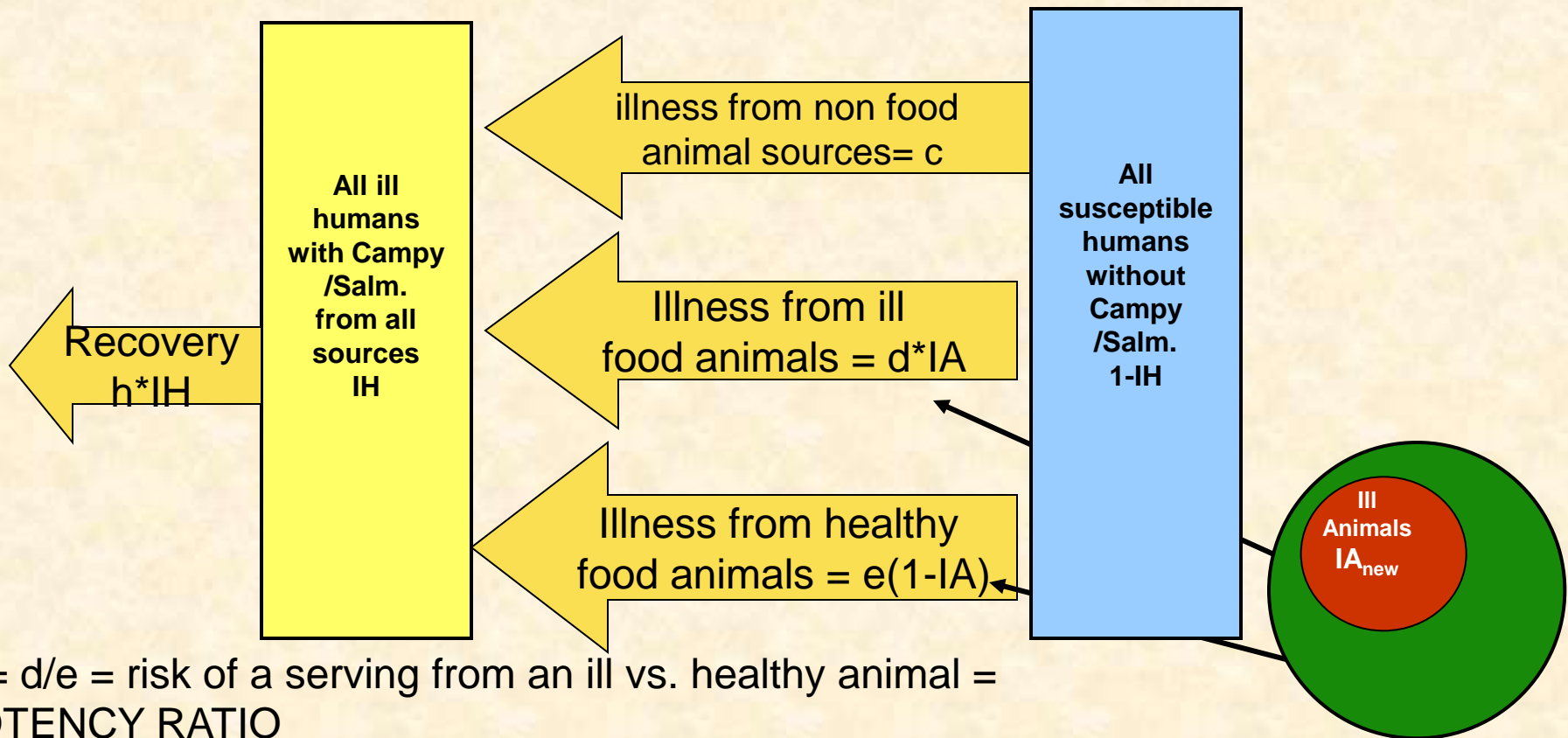
---

## Modeling the relationship between food animal health and human foodborne illness

Randall S. Singer<sup>a,b,\*</sup>, Louis A. Cox Jr.<sup>c</sup>, James S. Dickson<sup>d</sup>,  
H. Scott Hurd<sup>e</sup>, Ian Phillips<sup>f</sup>, Gay Y. Miller<sup>g</sup>

# Ordinary differential equation for ill (Campy/Salm) humans from all sources and responsive to proportion of ill animals consumed

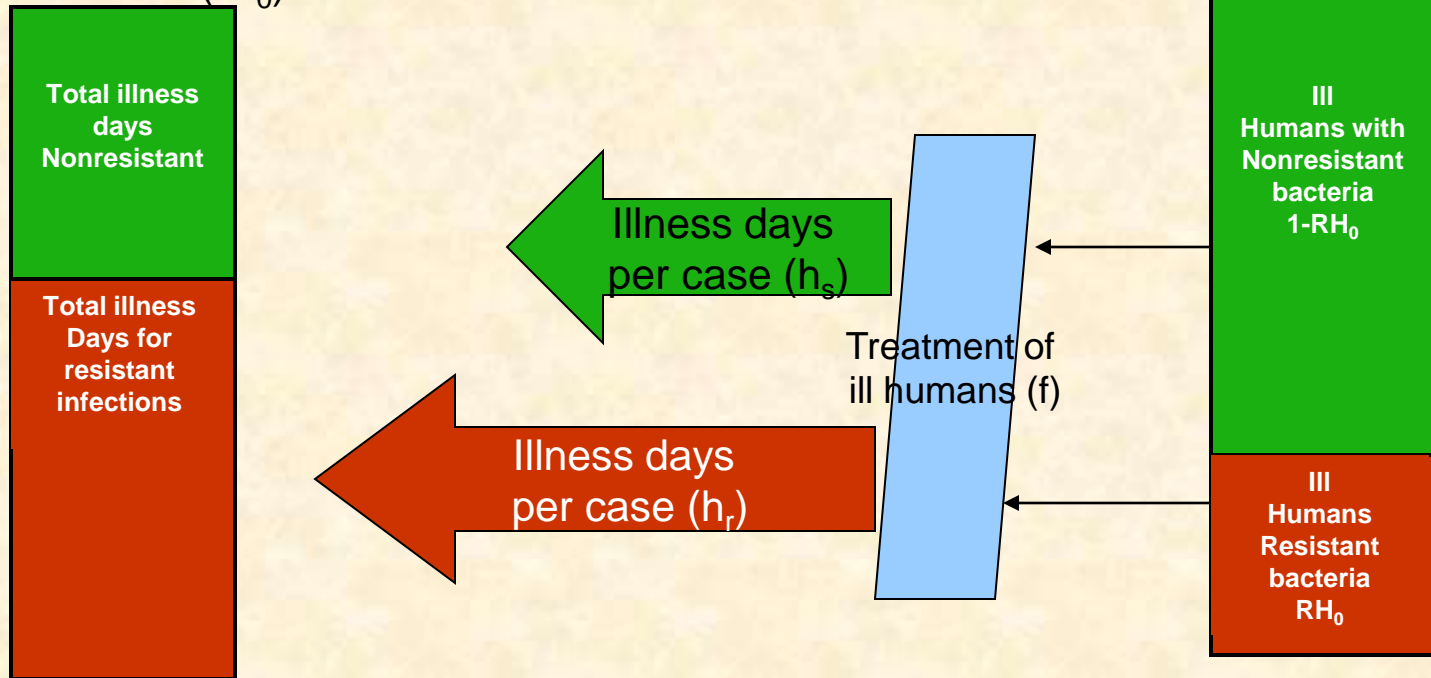
$$dIH / dt = [c + d * IA + e(1 - IA)] * (1 - IH) - h * IH$$



$D = d/e =$  risk of a serving from an ill vs. healthy animal = POTENCY RATIO

# Assume: Illness duration = 2 days longer if resistant infection

Total illness days at baseline ( $ID_0$ )



$$ID_0 = RH_0 * f * h_r + (1 - (RH_0 * f)) * h_s,$$

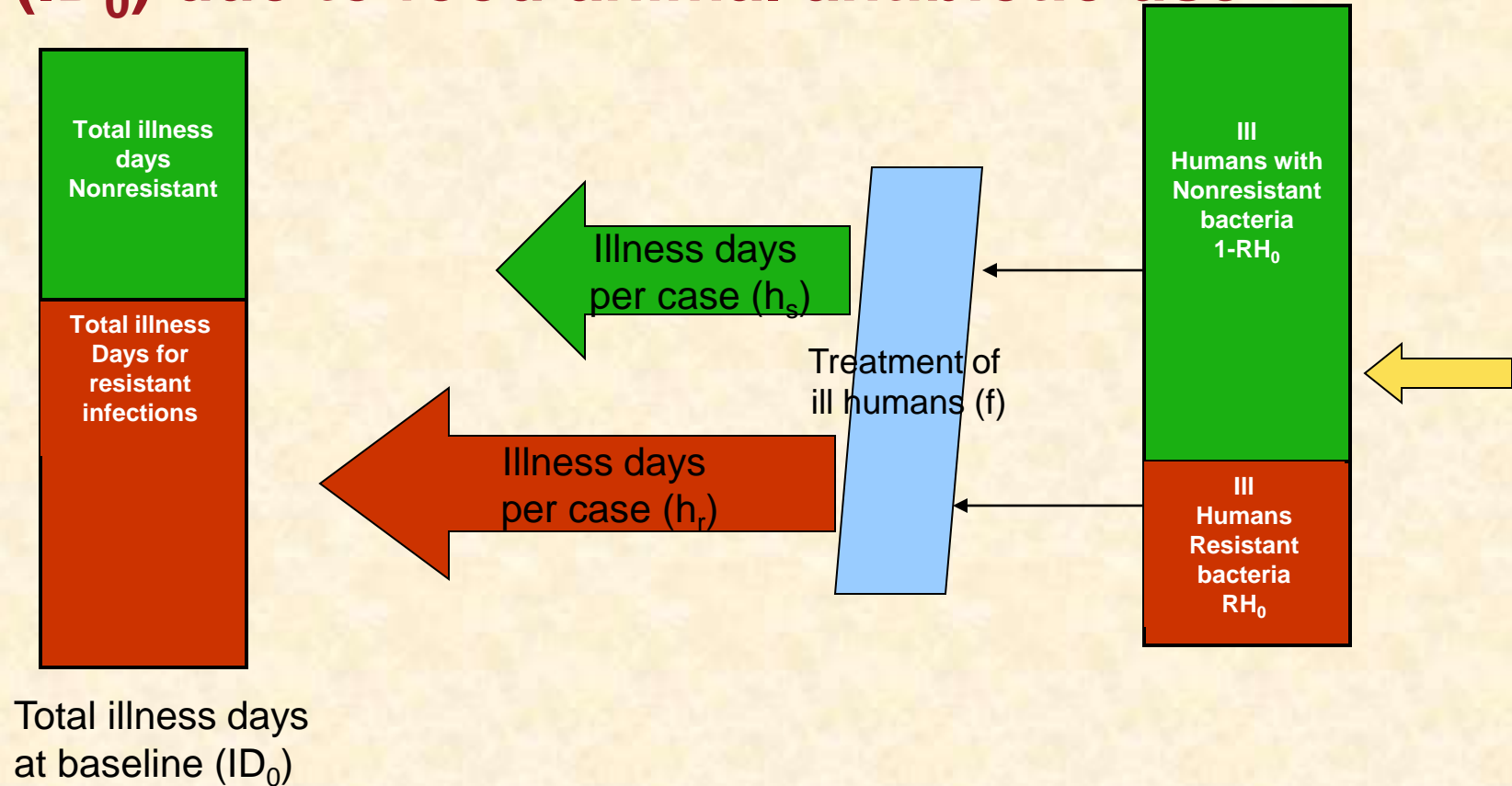
$RH_0$  is the fraction of human *Campylobacter* isolates that are resistant

$f$  is the fraction of patients receiving similar antibiotic treatment

$h_r$  and  $h_s$  are the durations of illness for resistant and susceptible

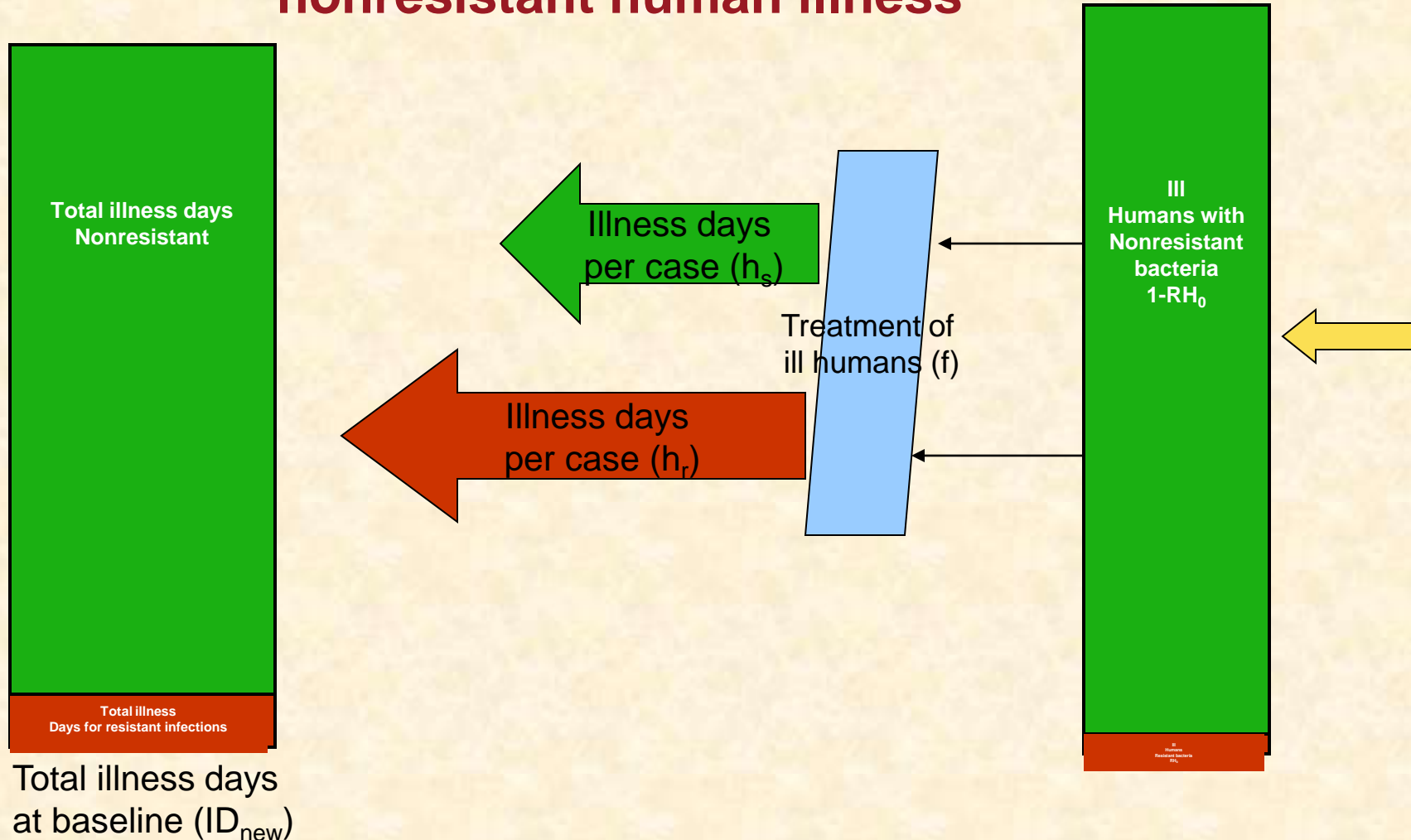
# BASELINE SCENARIO

Ratio of resistant to nonresistant human infections and impact on total illness days ( $ID_0$ ) due to food animal antibiotic use



# New SCENARIO

Increased total illness days ( $ID_{new}$ ) withOUT food animal antibiotic use → more “sick” birds more nonresistant human illness



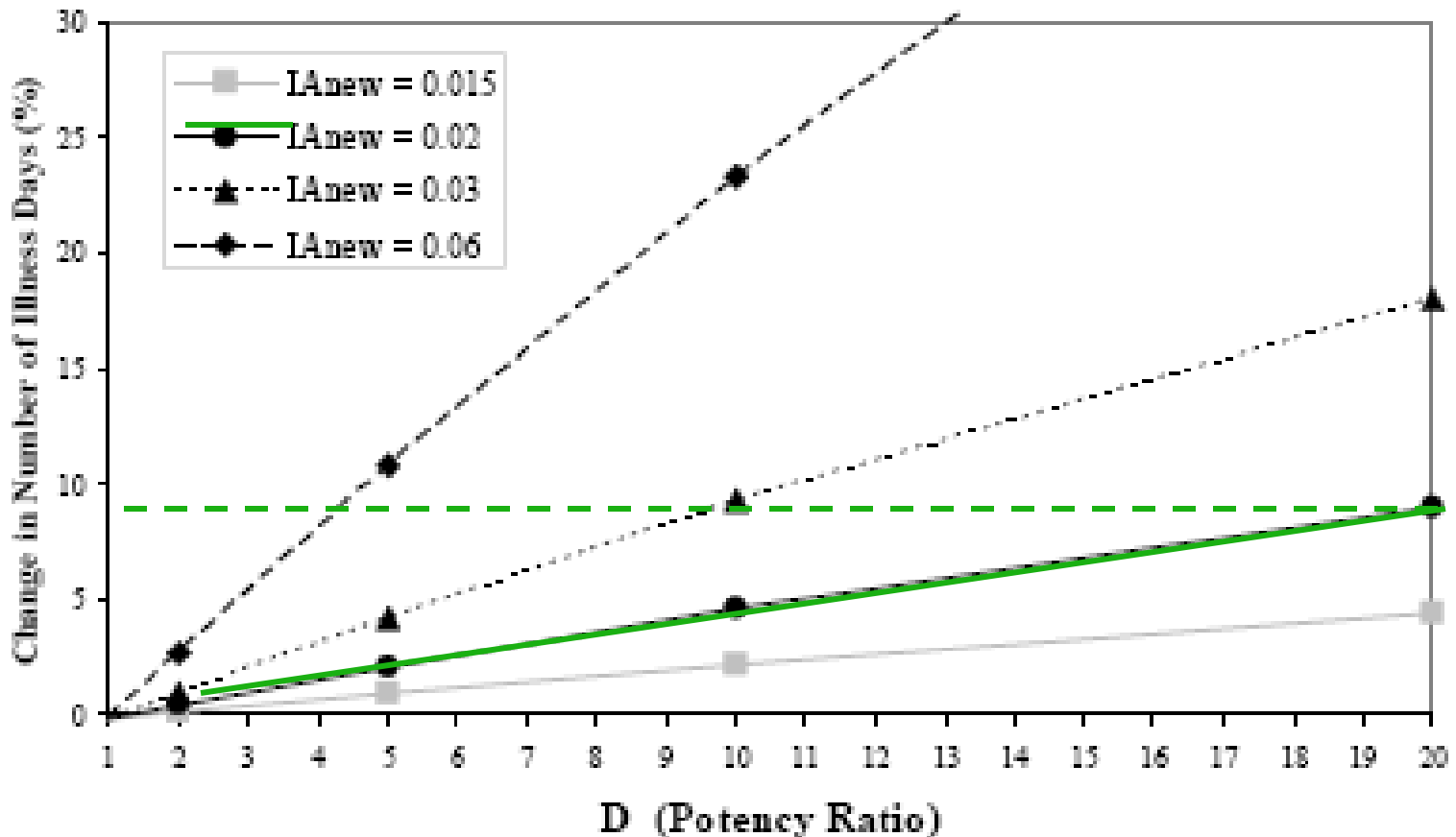
# Outcome measures of interest

- Percentage change in human illness days
  - $(\text{New Illness days} - \text{Old}) / \text{Old illness days}$
- Risk:benefit ratio:
  - Illness days caused per one illness day prevented
  - $\text{Excess days} / [(\text{ID}_0 - \text{ID}_{\text{new}}) * (\text{Old illness days} / \text{ID}_0)]$
  - ID = illness duration
- Parameters used for chicken, Campylobacter and tylosin (antibiotic)

# RESULTS

- As potency ratio (D) increases so does human illness, D is very uncertain
- Small increases in ill animals → large increases in human illness days
- e.g. If  $IA_0 = 0.01 \rightarrow IA_{\text{new}} = 0.02$  then human illness days increased 0.56% to 9.1% as D went from 2 to 20

**Percentage change in human illness days  
for prevalence of animal illness ( $IA_{new}$ ),  
relative to original prevalence ( $IA_0=0.01$ )  
over a range of potency ratios (D)**



# Results: increase in human campylobacteriosis

- e.g. 1% increase in the incidence of animal illness following the removal of tylosin from chickens is predicted to cause an additional 2.4 to 53.7 excess campylobacteriosis illness days for every illness day prevented due to decreased macrolide resistance.
- Translates to an annual increase in the incidence of campylobacteriosis ranging from 0.3 to 8.9%.

- “The public health risk of unhealthy animals is greater than antibiotic resistance concerns”



# Swine Health Impact on Carcass Contamination and Human Foodborne Risk

---

H. SCOTT HURD, DVM, PhD<sup>a</sup>  
JEAN BRUDVIG, DVM, MPH<sup>a</sup>  
JAMES DICKSON, PhD<sup>b</sup>  
JOVAN MIRCETA, DVM<sup>c</sup>  
MIROSLAVA POLOVINSKI<sup>c</sup>  
NEAL MATTHEWS, MS, PhD<sup>d</sup>  
RONALD GRIFFITH, DVM, PhD<sup>a</sup>

## SYNOPSIS

**Objective.** This study measured the relationship between lesions suggestive of subclinical pig illness at harvest to carcass contamination and human foodborne risk.

**Methods.** Over the course of eight visits (December 2005 to January 2006), we swabbed 280 randomly selected carcasses, during normal slaughter operations, at three points in the slaughter line: skin pre-scald; the bung or pelvic cavity following removal of the distal colon and rectum; and pleural cavity, immediately before the final carcass rinse. Each swab sponge was used on five

©2008 Association of Schools of Public Health

**Table 4. Regression coefficients (univariate and multivariate with antibiotic use group as a covariate) between percentage of representative health variables and percentage of carcasses positive for *Enterococcus* spp. or *Campylobacter* spp. in the bung or pleural cavities<sup>a,b</sup>**

Health indicator	Bacterial contamination	Location on carcass	Regression coefficient ( $\beta$ ) (univariate)	95% CI	Regression coefficient ( $\beta$ ) (multivariate)	95% CI
Fatigued <sup>c</sup>	<i>Campylobacter</i>	Bung	41.0	(219.0, 102.0)	10.0	(-50.0, 70.0)
Peel-outs <sup>d</sup>	<i>Campylobacter</i>	Pleura	5.7	(20.3, 11.7)	5.1	(0.4, 9.9)
Peel-outs	<i>Enterococcus</i>	Bung	5.1	(21.3, 11.5)	4.4	(1.3, 7.4)
Abscessed heads <sup>e</sup>	<i>Campylobacter</i>	Pleura	-12.7	(231.0, 5.0)	-6.2	(-33.0, 21.0)
Abscessed heads	<i>Enterococcus</i>	Bung	-13.3	(231.0, 0.5)	-2.5	(-24.0, 19.0)

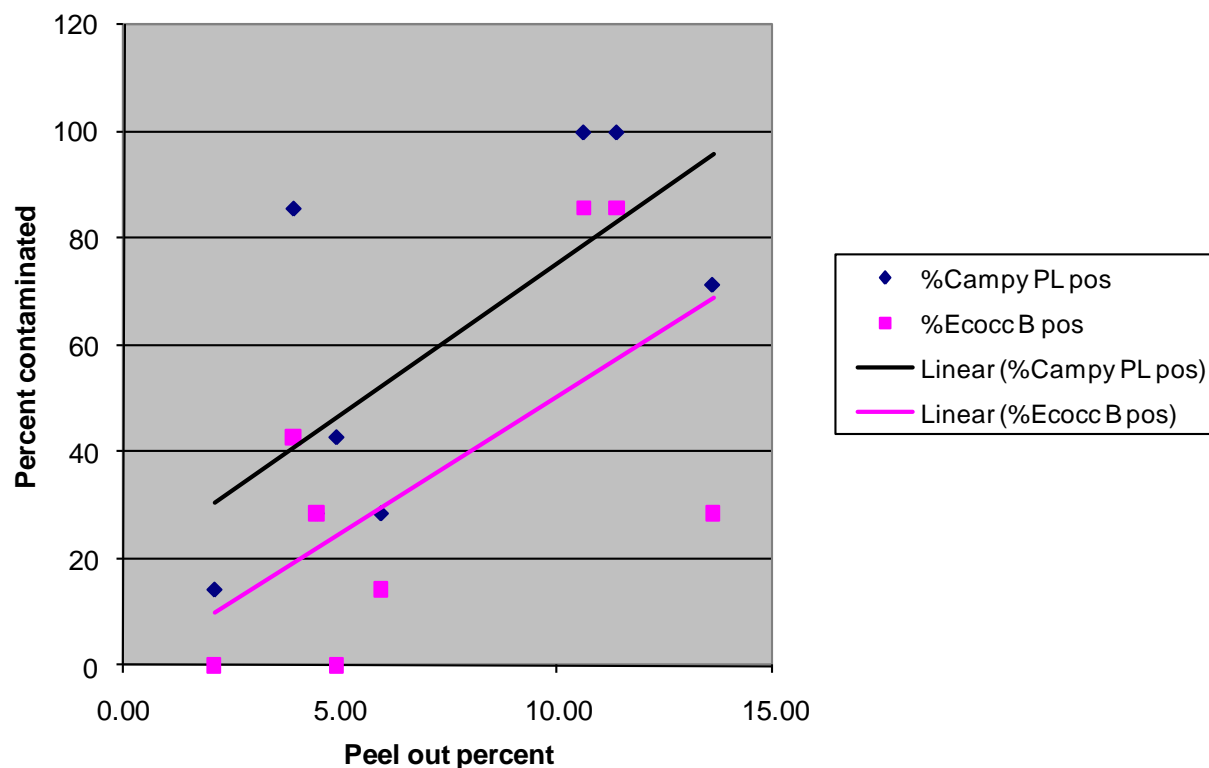
<sup>a</sup>All health and contamination relationships were tested. Only those with  $p < 0.2$  in the univariate comparison are shown.

<sup>b</sup>Conventionally raised animals received antibiotics for growth promotion and disease prevention and treatment; antibiotic-free animals never received antibiotics.

<sup>c</sup>Anaerobic metabolism, respiratory distress, recurrent

<sup>d</sup>Pleuritis and pleural adhesions

<sup>e</sup>Heads condemned due to visible abscess(es)

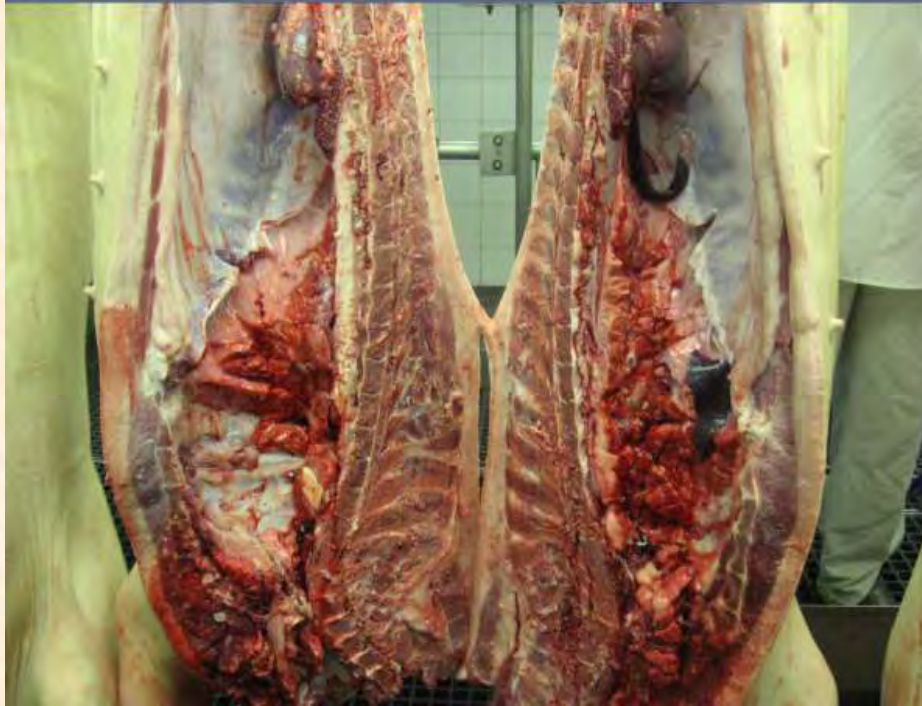


# Recent study

(in press Amer J. of Vet Med Research)

- 358 pork carcasses were selected
  - (four replicates)
  - Antibiotic free and conventional
- Lesioned and non-lesioned carcasses were identified, photographed and swabbed
- Individual carcass swabs cultured for *Salmonella*
- Logistic regression analysis showed the probability of *Salmonella* contamination in lesioned carcasses was 90% higher than in non-lesioned (Odds ratio = 1.9, 95% CI = 0.9-4.0)

# Lesioned and non-lesioned swine carcass



**Pathologist score ~ 6**  
**90% more likely to be**  
**contaminated with**  
**Salmonella** at end of  
slaughter



**Pathologist score ~ 0 to 1**

# Summary

- 1. Concern about antimicrobial resistant bacteria is not equivalent to risk.
- 2. Estimated risk (farm-to-fork) of on-farm antibiotic use is extremely low.
- 3. Alternative risk of sub-optimal animal health may be higher than the risk of on-farm antibiotic use.

# Guidelines for our Deliberations

- Is this a value-based point?
- Where does this fact fit into the causal pathway?
- What is the level of uncertainty about this fact?
- What are potential secondary or unintended consequence of an action