Attributing Illnesses to Foods Using Data from Outbreaks and Expert Elicitation

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Requisite Disclosure

- Additional affiliation:
  - Executive Director, Food Safety Research Consortium
- Prior employers:
  - University of Maryland School of Medicine
  - Resources for the Future
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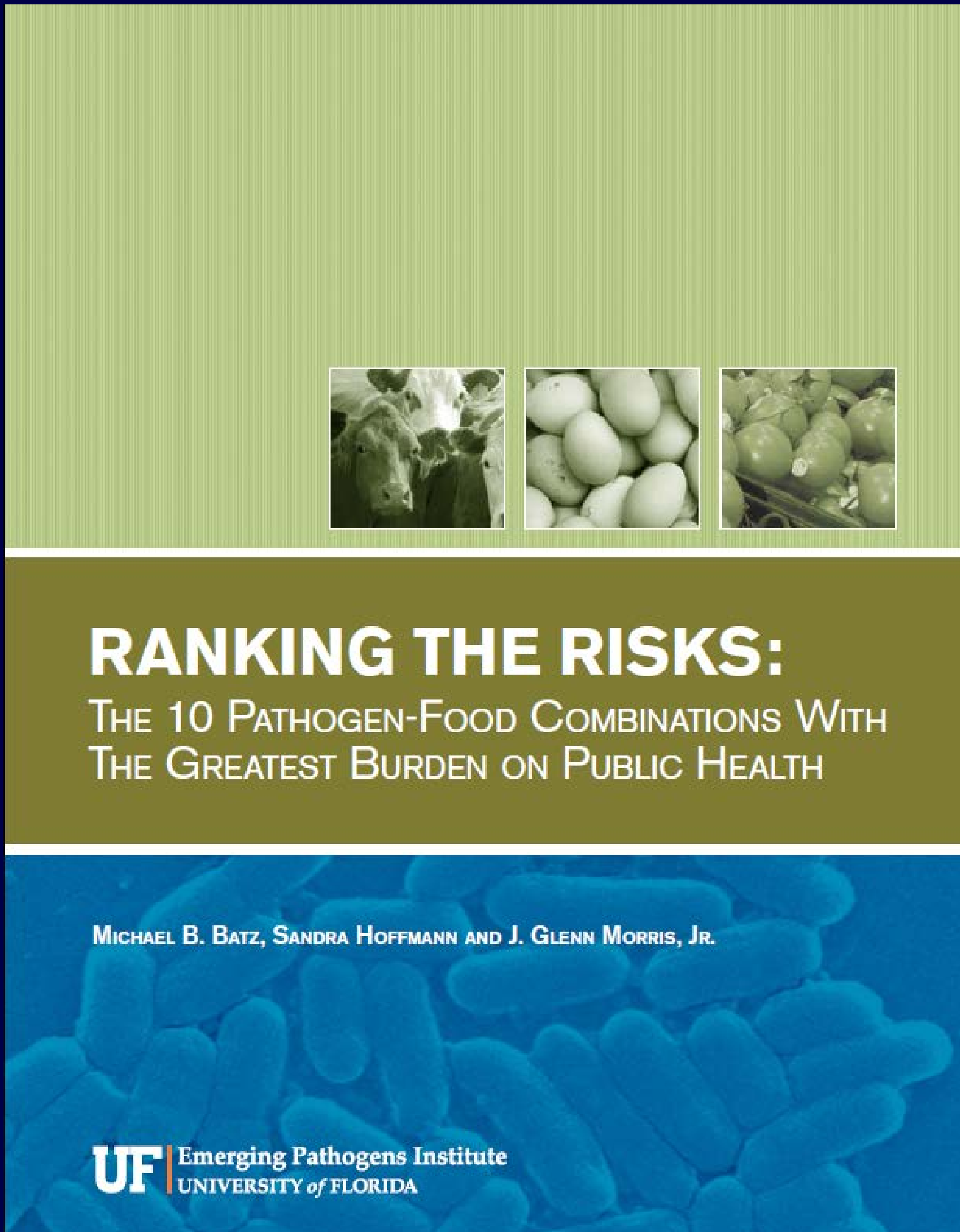

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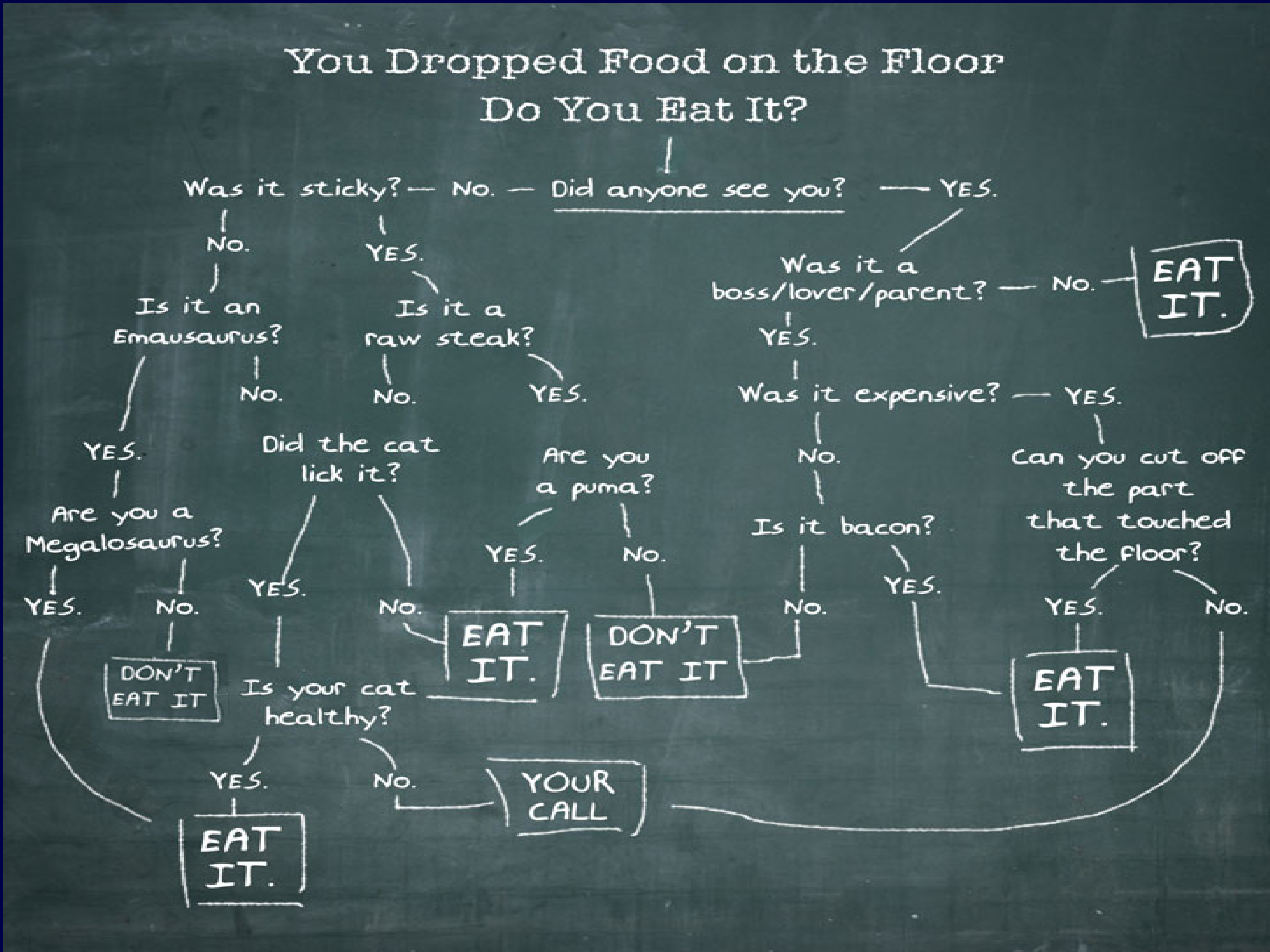
Many of today's results from submitted articles, not report


You Dropped Food on the Floor
Do You Eat It?
Was it sticky?
No.
Did anyone see you?
YES.
No.
YES.
Is it an Emausaurus?
Is it a raw steak?
Was it a boss/lover/parent?
No.
EAT IT.
YES.
No.
No.
YES.
Was it expensive?
YES.
YES.
Did the cat lick it?
Are you a puma?
No.
Can you cut off the part that touched the floor?
Are you a Megalosaurus?
YES.
No.
Is it bacon?
YES.
No.
YES.
No.
EAT IT.
DON'T EAT IT
No.
YES.
YES.
No.
DON'T EAT IT
Is your cat healthy?
EAT IT.
YES.
No.
YOUR CALL
EAT IT.

Risk-Based Food Safety System

NAS. *Enhancing Food Safety*. 2010 (p. 82)

The Analytical Objective

- To target interventions and prioritize effort, we need to understand where the biggest problems lie
- This means estimating the burden of specific etiologic agents (pathogens) and the vehicles (foods) of exposure

Which pathogens in which foods cause the greatest impact on public health?

The Starting Point

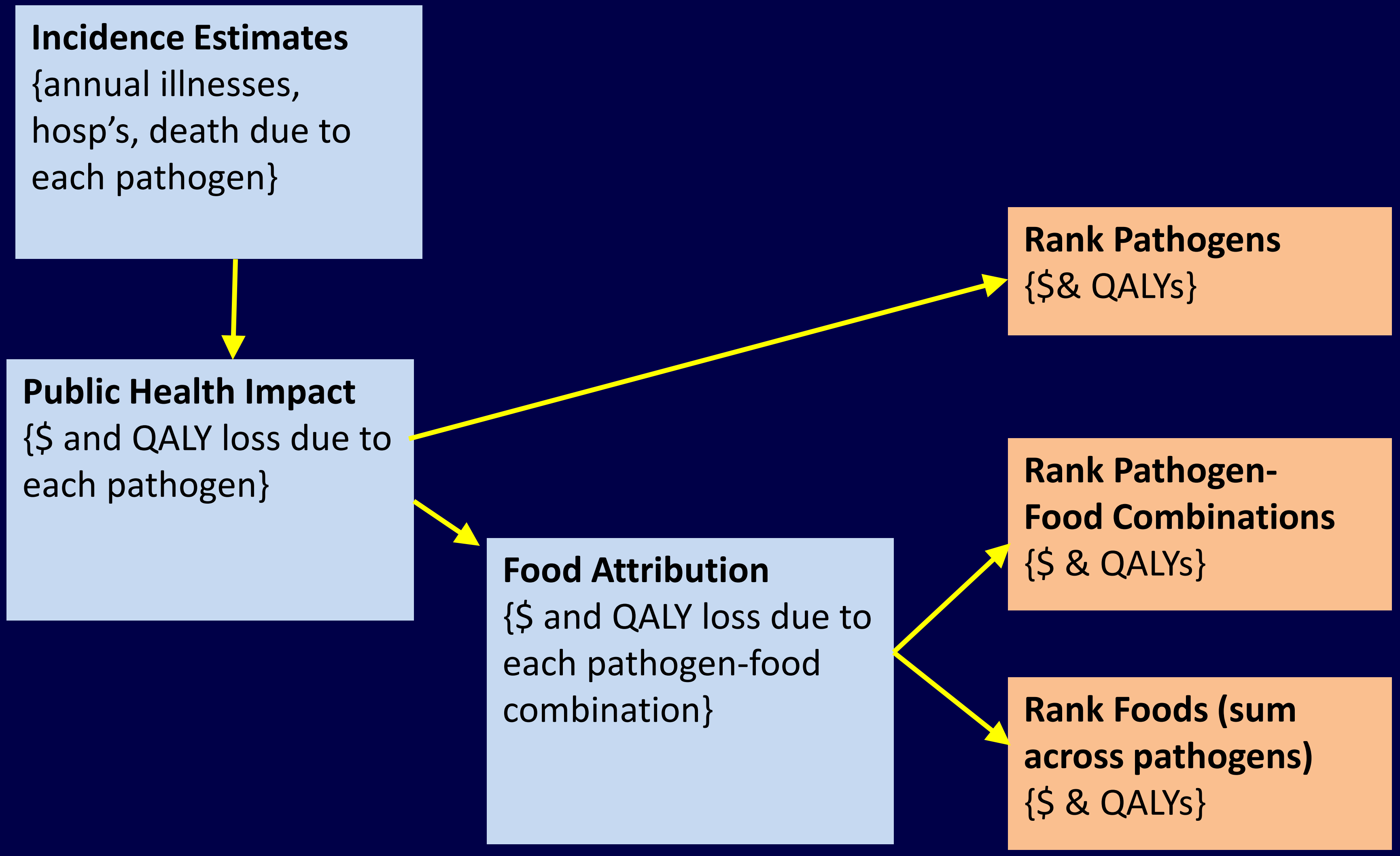
- Scallan et al. (2011):
  - 48 million cases of foodborne illness annually, 128,000 hospitalizations, 3,000 deaths
  - 31 identified pathogens cause 9.4 million cases of illness (20% of total), 56,000 hospitalizations (44%), 1400 deaths (45%)
  - 14 major pathogens cause 95% of illnesses due to known pathogens, 96% of hospitalizations, 98% of deaths

Scallan, E., et al. 2011. Foodborne illness acquired in the United States – major pathogens. *Emerg. Infect. Dis.* 7(1): 7-15.

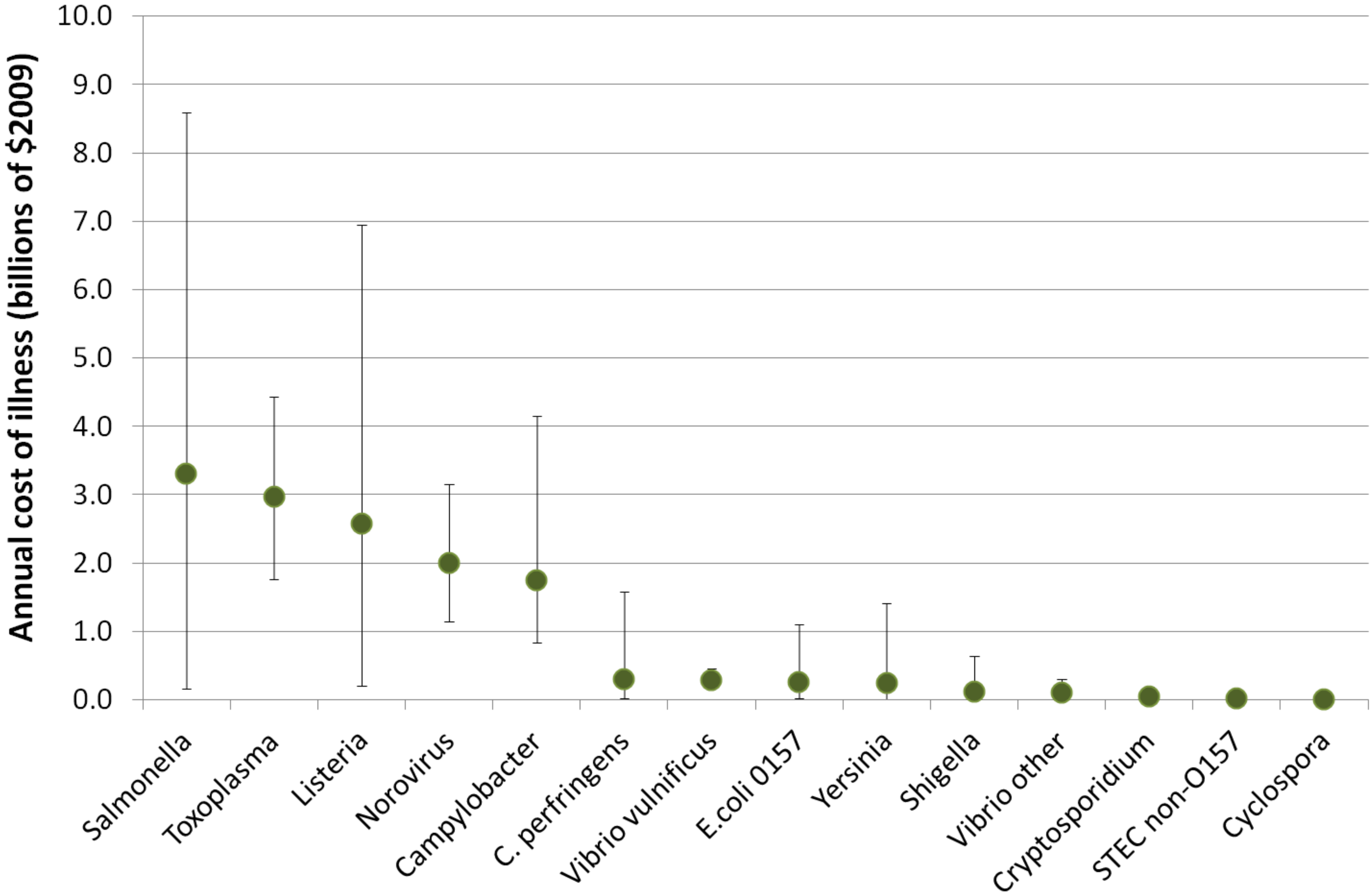
Scallan, E., et al. 2011. Foodborne illness acquired in the United States—unspecified agents. *Emerg. Infect. Dis.* 17(1): 16-22.

Major Steps in Analysis

14 pathogens in 12 food categories

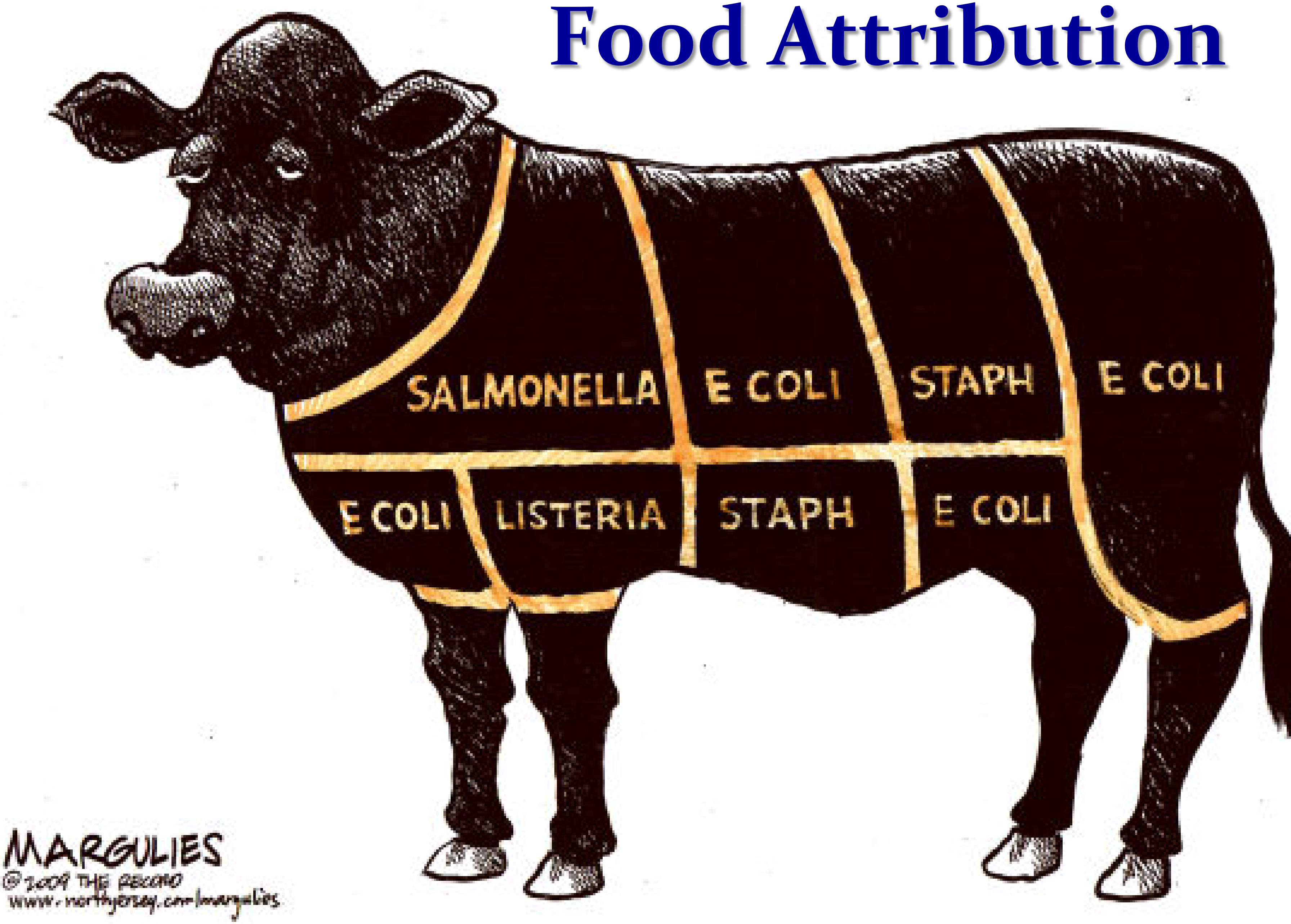


Annual cost of Illness due to 14 major foodborne pathogens



Ranges reflect 90% confidence intervals from Scallan et al.

Food Attribution



Risk Ranking Context

- Approach depends on decision:
  - Targeted risk management: (e.g. on-farm controls for single pathogen)
  - Broad allocation of resources (e.g. many pathogens, many foods)
- Risk ranking is sensitive to methodological differences across risk categories[‡]
  - A mix-and-match approach is problematic
  - Preference is to use same method for all pathogens

‡ Morgan M.G., et al. 2000. Categorizing risks for risk ranking. *Risk Anal.* 20: 49-58.

Attributing Illnesses to Foods
Many Methods, None Perfect

1. Microbial subtyping
2. Outbreak data
3. Case-control studies
4. Intervention studies
5. Comparative exposure assessments
6. Expert elicitation

Data Sources: Outbreaks

- Pulled from predecessor to CDC's database of foodborne outbreak data
  - http://www.cdc.gov/foodborneoutbreaks/
- Ten years (1999-2008)
  - 14 pathogens: 5830 outbreaks (172,495 cases)
  - "Unknown" food: 2636 outbreaks (70,568 cases)
  - Multiple vehicles: 606 outbreaks (22,485 cases)
  - Attributable: <u>2588 outbreaks (79,442 cases)</u>

Food Categories

- Comprehensive across food supply
- Foods as consumed (point of exposure): more akin to menu sections than commodity groups
- Complex foods, baked goods, and deli meat reflect important role of food preparation

Beef	Dairy	Produce
Poultry	Eggs	Beverages
Pork	Seafood	Baked goods
Deli/other meats	Game	Complex foods

Coding Scheme

- Code outbreaks into categories:
  - Single food item or identified ingredient
  - Complex dish with multiple ingredients
    - Ingredients in same category (e.g. green salad)
    - Ingredients in multiple categories
      - Code by primary ingredient (e.g. cheeseburger as beef, quiche as egg)
      - If no obvious primary ingredient (e.g. pizza, macaroni salad), bin as complex foods (776 outbreaks (24,357 cases) as complex foods)
- Tabulate fractions for each pathogen across food categories

Coding Bias?

- Assumptions may bin more in meat categories than other approaches that attribute to constituent ingredients of complex dishes
- But impact likely minimal:
  - Many of these pathogens are zoonotic in origin with known animal reservoirs; sporadic studies repeatedly identify animal pathways as more relevant
  - Outbreaks reflect cross-contamination, which is almost always unidirectional from animal products to non-animal products during preparation

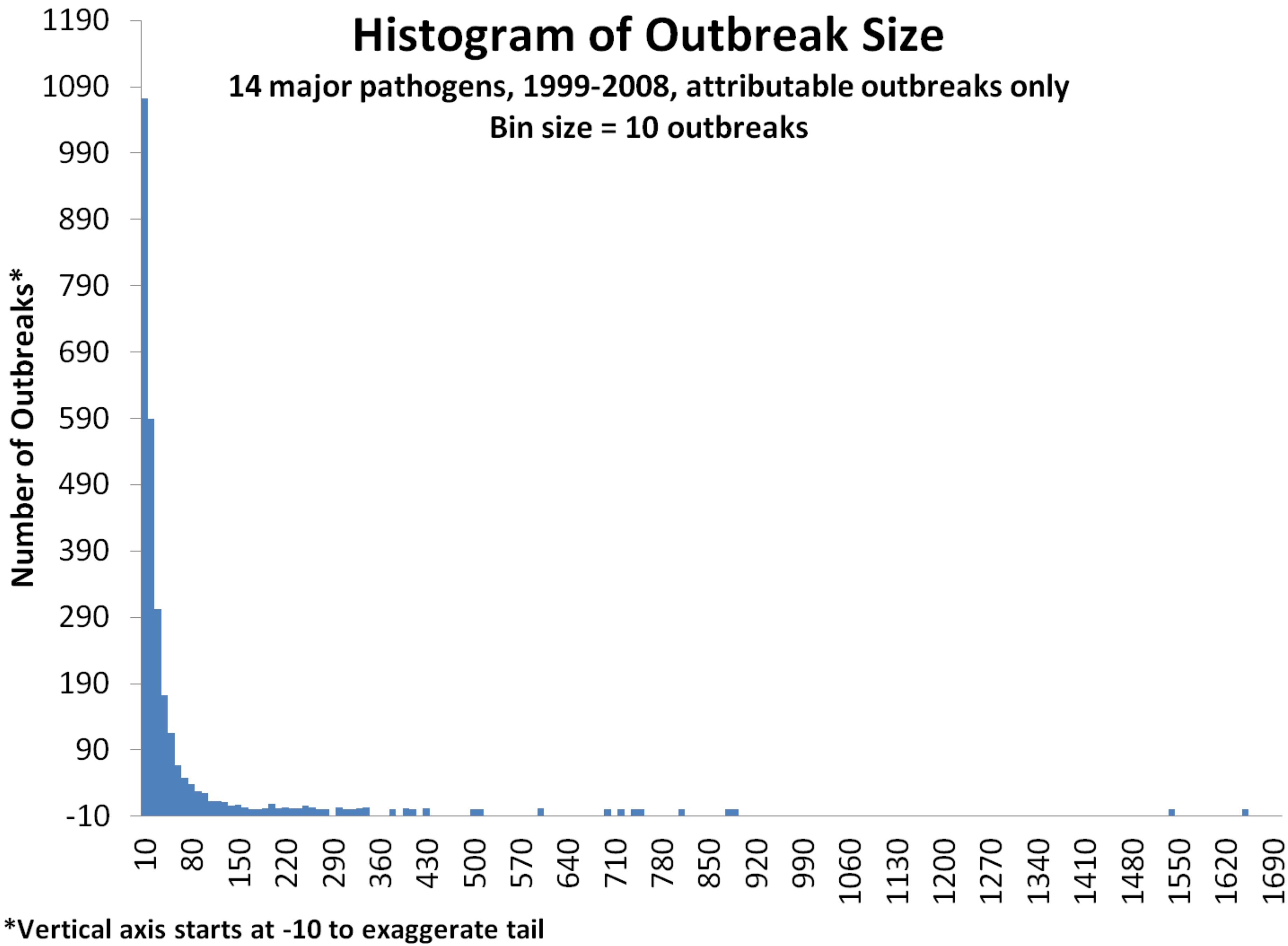
Outbreak Events vs. Cases

- The larger the outbreak….
  - The more likely it is to be reported
  - The more likely it is to be investigated fully
  - The more likely a food vehicle is to be identified
  - The more likely it is to reflect an unusual event caused by a confluence of major failures
- Therefore, large outbreaks are likely over-represented in outbreak data <u>and</u> are more likely to have identified vehicle – this skews attribution towards factors and foods with larger average outbreak size

Likelihood of Identifying Vehicle

Outbreak size	Total number of outbreaks	Percent w/ Known Food (Norovirus)*	Percent w/ Known Food (Non-noro)*
2-5	1252	41%	64%
6-10	1096	42%	60%
11-20	1317	43%	70%
21-50	1346	46%	78%
51-100	485	44%	82%
101-1650	260	44%	84%

Percent of total outbreaks with identified food vehicle(s). Outbreaks include those due to 14 major pathogens from 1999-2008.


Histogram of Outbreak Size
14 major pathogens, 1999-2008, attributable outbreaks only
Bin size = 10 outbreaks
Number of Outbreaks*
1190
1090
990
890
790
690
590
490
390
290
190
90
-10
10
80
150
220
290
360
430
500
570
640
710
780
850
920
990
1060
1130
1200
1270
1340
1410
1480
1550
1620
1690
*Vertical axis starts at -10 to exaggerate tail

Outbreak Size, by Food Category

Food	Average outbreak size
Beef	23
Pork	24
Poultry	28
Deli/Other Meat	26
Game	7
Eggs	25
Dairy	36
Seafood	15
Produce	51
Beverages	56
Breads & Bakery	29
Complex foods	31

Count vs. Case Attribution: *Salmonella*

Salmonella	**Outbreak count attribution**	**Outbreak case attribution**
Beef	7%	4%
Beverages	1%	3%
Breads and Bakery	3%	2%
Dairy	6%	5%
Deli/Other Meats	3%	2%
Eggs	12%	9%
Game	0%	0%
Pork	7%	5%
Poultry	21%	14%
Produce	18%	33%
Seafood	5%	3%
Complex foods	19%	19%
Total	100%	100%

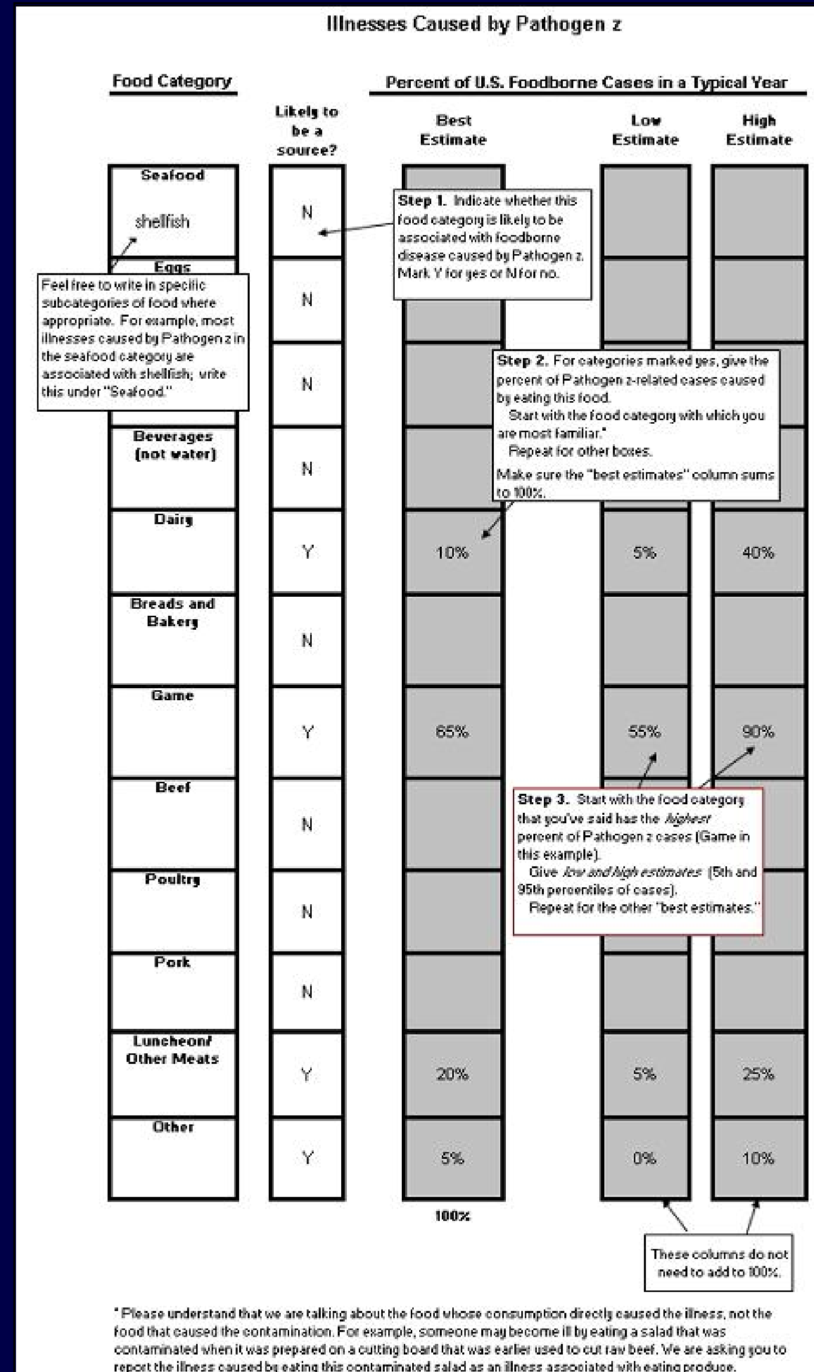
Data Source: Expert Judgment

- Expert elicitation survey (2003)
  - Conducted to evaluate outbreak attribution and fill in gaps
  - 44 finalized surveys (out of about 90)
  - Same food categories as outbreak data with exception of complex foods (removed in pre-tests)
- Published:
  - Hoffmann, et al. 2007. *Dec. Anal.* 4(2):91-109.
  - Hoffmann, et al. 2007. *J. Food Prot.* 70(5):1220-1229.
  - Hoffmann, et al. 2008. *Reliability Eng.and Sys. Safety* 93(5): 687-698.

Elicitation Tool

Hoffmann, et al. 2007. *J. Food Prot.* 70(5):1220-11229.

- Asked to provide:
  - Best estimate
  - 90% confidence intervals
  - Self-assessed certainty
- Intra- and inter-expert measures of uncertainty
- For attribution: mean of best estimates



Can multiple methods be combined?

- Assumption: outbreak data are preferable because they reflect observed data, but are not always adequate
- Approach:
  - Evaluate strength of outbreak data on <u>pathogen-by-pathogen</u> basis
  - Based on totality of evidence, decide where expert attribution should be used as alternative to outbreak attribution

Measuring Reliability (1)

1. Density of outbreak data
   - Number of “attributable” outbreaks reported
   - Some pathogens have too few outbreaks
2. Ratio of estimated incidence (Scallan et al.) to reported outbreak cases
   - Measure of representativeness that reflects number of sporadic, non-outbreak cases for each reported outbreak case
   - High ratios suggest outbreak data captures relatively small fraction of overall illness

Measuring Reliability (2)

3. Sum of mean difference squared between expert and outbreak estimates
   - Use outbreak data from 1993-2002 for data concurrent with 2003 elicitation
   - Large differences show where experts differ from outbreaks considerably
4. Mean standard deviation of expert estimates
   - Signal of agreement among experts
   - High variance → disagreement among experts: scientific knowledge on attribution is low

Attribution reliability measures	**Num of attrib. outbreaks**	**Ratio (Scallan: outbreak cases)**	**Sum of mean diff. squared outbk/expert**	**Mean st dev of experts**
Campylobacter	120	1,712	3,307	0.91
C. perfringens	362	495	--	--
Cryptosporidium	4	1,152	3,622	1.64
Cyclospora	14	87	62	0.42
E. coli 0157	143	132	20	0.76
STEC non-O157	15	745	--	--
L. monocytogenes	20	55	827	0.96
Norovirus	1,125	555	701	1.77
Salmonella	621	296	218	1.02
Shigella	41	256	1,198	1.68
Toxoplasma	0	--	--	2.02
Vibrio spp.	59	780	9	0.25
Yersinia	5	11,909	562	1.38

Expert elicitation did not include *C. perfringens* or STEC non-O157. STEC non-O157 outbreaks include suspected enterohemorrhagic E. coli w/o confirmed etiology. See Hoffmann et al. 2007. *Dec. Anal.* 4(2): 91-109 for more on expert uncertainty measures.

Measuring Reliability (3)

5. Comparison to case control studies
   - Campylobacter
     Friedman et al. 2004. *Clin. Infect. Dis.* 38(S3): S285-96
     - PAF: chicken in restaurant (24%), non-poultry meat in restaurant (21%), turkey in restaurant (4%), pink chicken (3%), raw seafood (3%), raw milk (1.5%)
     - Supports expert attribution
   - Toxoplasma
     Jones et al. 2009. *Clin. Infect. Dis.* 49(6): 878-84
     - No PAF, but high odds ratios for rare lamb, raw ground beef, raw shellfish, locally cured meats.
     - Experts: pork, beef, and game. High variance.
     - No outbreak data.

Baseline attribution percents (%)	*Campyl.*	*C. Perfring.*	*Crypto.*	*Cyclospora*	*E. coli O157*	*non-O157*	*Listeria*	*Norovirus*	*Salmonella*	*Shigella*	*Toxoplasma*	*Vibrio*	*Yersinia*
Data source:	Exp	Out	Exp	Out	Out	Out	Out	Out	Out	Out	Exp	Out	Exp
Beef	4	33	7	0	55	40	0	4	7	15	23	0	2
Beverages	0	0	9	0	2	13	0	2	1	0	0	0	1
Baked goods	0	0	0	0	1	0	0	8	3	0	0	0	0
Complex foods	0	24	0	21	13	7	15	46	19	49	0	0	0
Dairy	8	1	6	0	6	20	30	2	6	2	2	0	12
Deli meats	1	3	1	0	3	0	35	2	3	5	2	0	2
Eggs	3	0	0	0	0	0	0	1	12	0	0	0	0
Game	2	0	5	0	0	0	0	0	0	0	20	0	2
Pork	4	8	2	0	0	0	5	3	7	0	41	0	72
Poultry	72	27	1	0	1	7	5	8	21	10	4	0	1
Produce	5	3	60	79	18	13	5	16	18	12	7	0	3
Seafood	1	1	8	0	1	0	5	9	5	7	1	100	5

Out=outbreak, Exp=expert. Rounded values may not sum to 100%.

Ranked Pathogen/Food Combinations (Average Rank)

Rank	Pathogen/Food Combination	COI ($ mill)	QALY Loss	Illnesses	Hospitalizations	Deaths
1	Campy/Poultry	1,257 (606–2,988)	9,541 (5,753–18,730)	608,231 (242,588–1,159,624)	6,091 (3,095–10,960)	55 (0–239)
2	Toxoplasma/Pork	1,219 (723–1,819)	4,495 (2,471–6,875)	35,537 (26,590–45,879)	1,815 (1,080–2,736)	134 (82–198)
3	Listeria/Deli Meats	902 (71–2,433)	3,281 (536–8,234)	557 (195–1,106)	509 (182–1,056)	89 (0–257)
4	Salmonella/Poultry	693 (33–1,797)	3,513 (64–9,290)	215,109 (134,979–351,621)	4,048 (1,789–7,848)	79 (0–212)
5	Listeria/Dairy	773 (61–2,086)	2,812 (459–7,058)	477 (167–948)	437 (156–905)	77 (0–220)
5	Norovirus/Complex	911 (519–1,432)	2,288 (1,319–3,565)	2,485,694 (1,468,679–3,781,737)	6,673 (3,685–10,615)	68 (38–108)
7	Salmonella/Complex	618 (30–1,604)	3,135 (57–8,290)	191,944 (120,443–313,754)	3,612 (1,596–7,003)	71 (0–189)
8	Salmonella/Produce	581 (28–1,507)	2,946 (53–7,790)	180,361 (113,175–294,821)	3,394 (1,500–6,580)	66 (0–177)
8	Toxoplasma/Beef	689 (409–1,028)	2,541 (1,396–3,886)	20,086 (15,029–25,931)	1,026 (610–1,546)	76 (46–112)
10	Salmonella/Eggs	389 (19–1,009)	1,973 (36–5,217)	120,792 (75,796–197,449)	2,273 (1,004–4,407)	44 (0–119)

Baseline assumptions. Rank based on average of QALY and COI ranks. Ranges based upon 90% CI from Scallan et al. incidence estimates. Game excluded.

Ranking Results: Sensitivity to Attribution Assumptions

Scenario*	Baseline	1	2	3	4	5	6
Attribution method	Out+Exp	Out+Exp	<u>Out</u>	<u>Out</u>	<u>Exp</u>	Out+Exp	Out+Exp
Outbreak Approach	Events	<u>Cases</u>	Events	<u>Cases</u>	N/A	Events	Events
Complex foods	In	In	In	In	In	In	<u>Out</u>
Multi-source	Out	Out	Out	Out	Out	<u>In</u>	Out
Campylobacter/Poultry	1	1	9	27	1	1	1
Toxoplasma/Pork	2	2	-	-	4	2	2
Listeria/Deli Meats	3	4	3	3	2	4	3
Salmonella/Poultry	4	9	4	8	3	6	4
Listeria/Dairy	5	9	6	8	8	6	5
Norovirus/Complex	5	5	5	5	-	4	-
Salmonella/Complex	7	7	6	5	-	3	-
Salmonella/Produce	8	3	8	3	9	9	6
Toxoplasma/Beef	8	8	-	-	6	8	7
Salmonella/Eggs	10	11	9	10	5	10	8
Listeria/Complex	11	5	11	5	-	10	-
Salmonella/Beef	12	18	14	17	11	12	10
Norovirus/Produce	14	12	15	11	7	17	8
Campylobacter/Dairy	19	16	2	2	19	16	21
Norovirus/Seafood	22	27	21	25	10	27	12
Toxoplasma/Unknown	-	-	1	1	-	-	-

Only rows ranking in top 10 in one of scenarios included. Game excluded.

Take Aways (1)

- Outbreak attribution requires judgment
- Remember that outbreak attribution reflects point of consumption, not production
  - Due to significant role of cross-contamination during preparation, produce estimates won’t reflect risks at the farm level
- Clear need for better data on *Toxoplasma*
  - *Salmonella*, *Campylobacter*, *Listeria*, and *Norovirus* also warrant improved estimates

Take Aways (2)

- Expert elicitation is useful
  - When there are data gaps
  - When care is taken to measure uncertainties
  - Particularly when done in manner that allows for comparison and combination with other data
  - A lot of unexplored potential
- Ranking is sensitive to attribution assumptions and data sources, but top-identified pathogen/food pathways are fairly robust

“I can live with doubt and uncertainty and not knowing. If we will only allow that, as we progress, we remain unsure, we will leave opportunities for alternatives. We will not become enthusiastic for the fact, the knowledge, the absolute truth of the day, but remain always uncertain …

In order to make progress, one must leave the door to the unknown ajar.”

Richard Feynman

Questions?

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Thank You!