Epidemiology of swine dysentery in the U.S. and recent research in risk factors, diet, and diagnostic assays

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Outline

- Re-emergence of swine dysentery in the U.S.
- Risk factors for *Brachyspira* infection
- Diagnostic approaches for *Brachyspira* detection: Strengths and limitations
- Treatment and control of swine dysentery
- Summary

RE-EMERGENCE OF SWINE DYSENTERY IN THE UNITED STATES

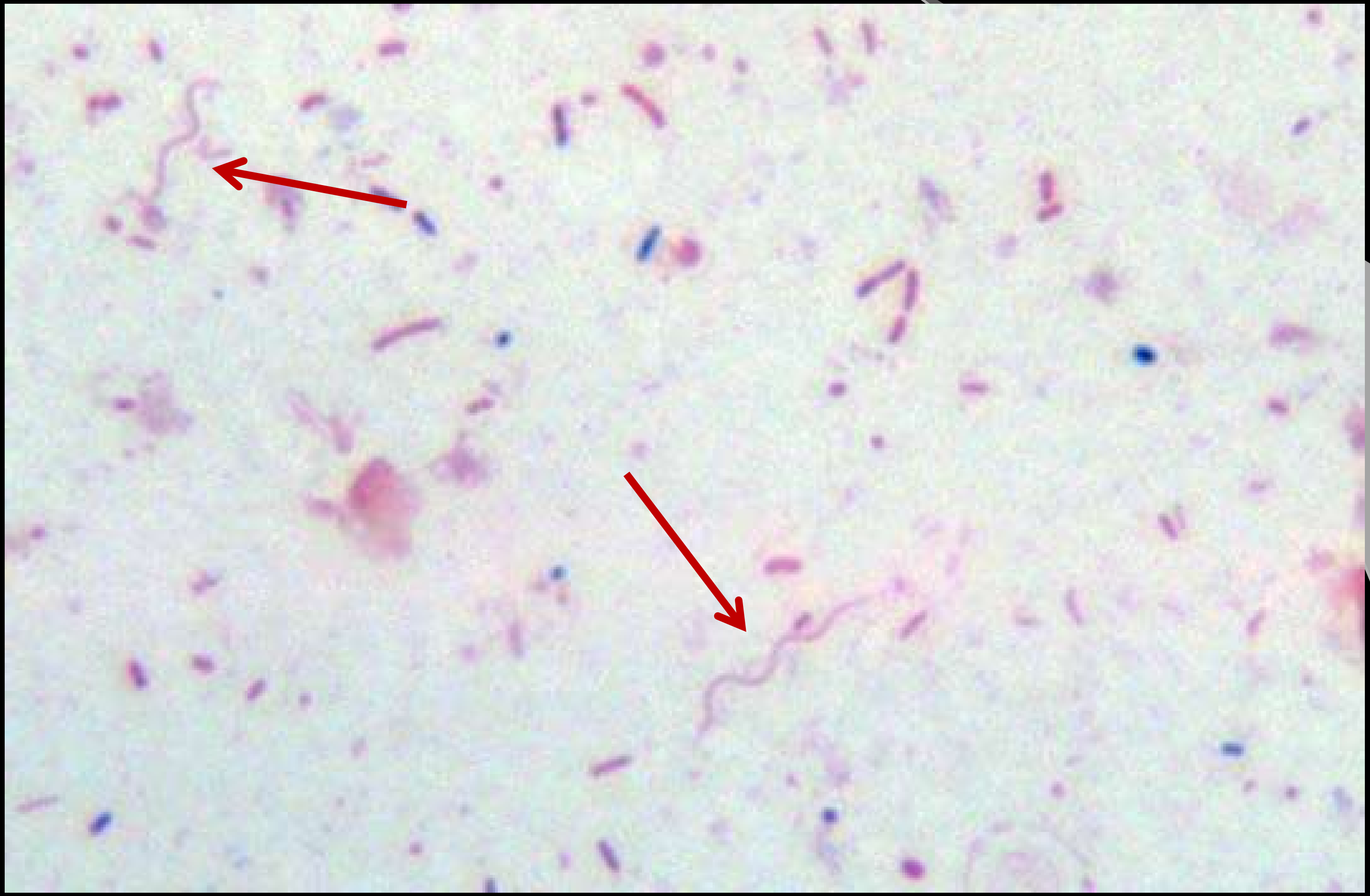
Background

- Swine Dysentery
  - First reported almost 100 years ago (1921) by Whiting *et al.*
    - Slowly progressive disease
    - Beginning 5 – 14 days after arrival on farm
    - Thin feces with mucus and blood
    - Consistent lesions with curved bacteria, spirochetes, and ciliates

Background

- Swine Dysentery
  - Etiologic agent not confirmed until 1970s
    - Taylor and Alexander, 1971
    - Harris *et al.*, 1972
    - *Treponema hyodysenteriae*
      - Then *Serpulina* => *Serpula* =>
    - Currently *Brachyspira hyodysenteriae*

Background



Background

- Swine Dysentery
  - Economically significant disease most often observed in grow-finish pigs
    - Often follows stressors such as feed changes
  - Largely disappeared from U.S. herds by the mid-1990s
    - Improved treatment, control, and elimination methods
  - Sporadic cases were identified at the ISU VDL through the early 2000s
    - Most often from pigs in open-flush gutter systems and lagoon water recycling

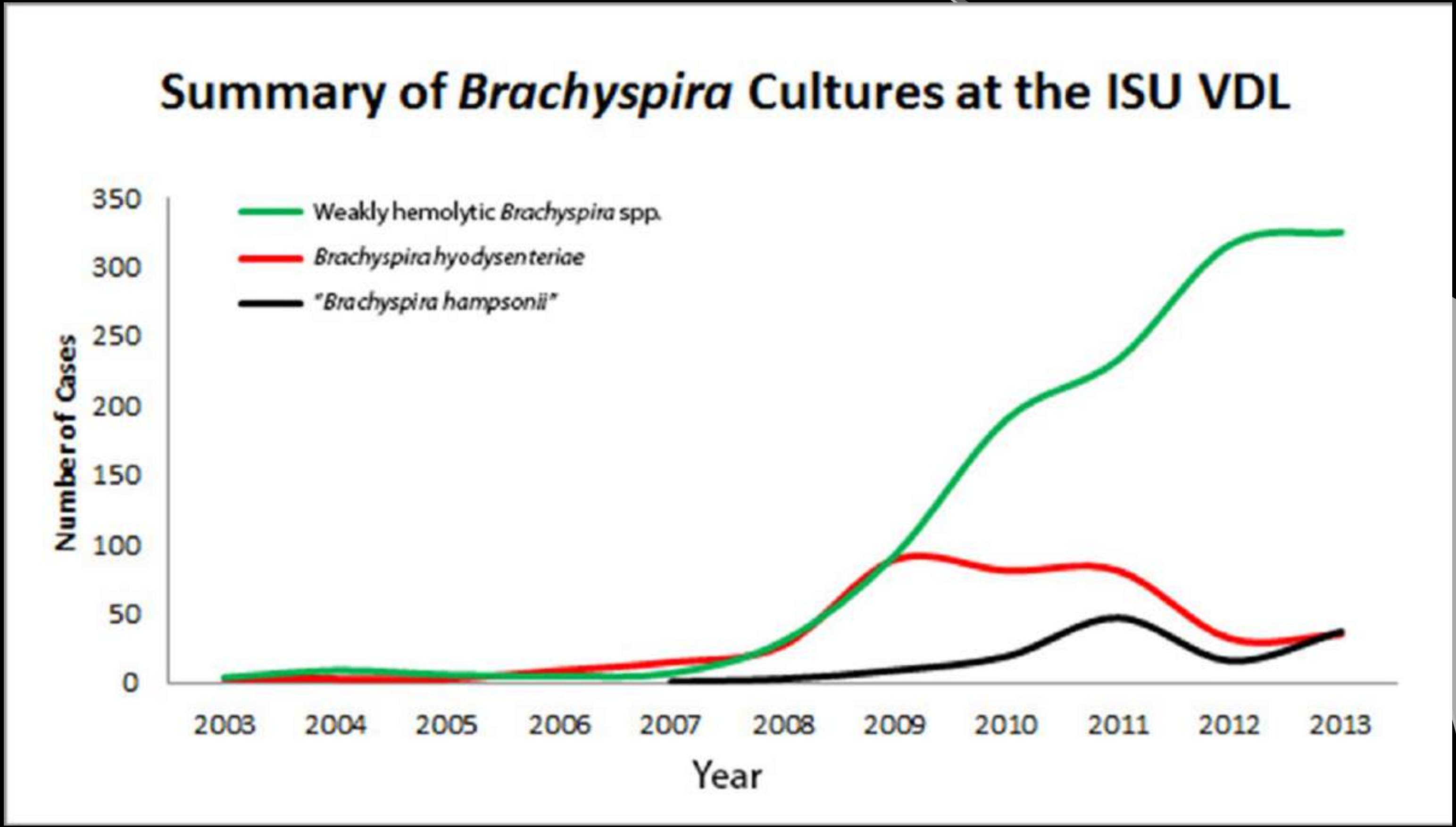
Background

B. hyodysenteriae isolations from 2003 - 2008

Re-emergence of Swine Dysentery in the U.S.

- Beginning in the latter part of 2007, the following trends were observed in submissions to ISU VDL:
  - An increase in the number of cases submitted with clinical signs of swine dysentery (SD)
  - Increased frequency of positive *Brachyspira* culture
  - An increase in the number of SD diagnoses
  - Cases with clinical signs, lesions, and culture results characteristic of SD (strong beta / ring +) where *B. hyodysenteriae* was NOT identified by PCR
    - These untypable and atypical isolates were later confirmed as the recently proposed *"B. hampsonii"* clades I & II

Re-emergence of Swine Dysentery in the U.S.

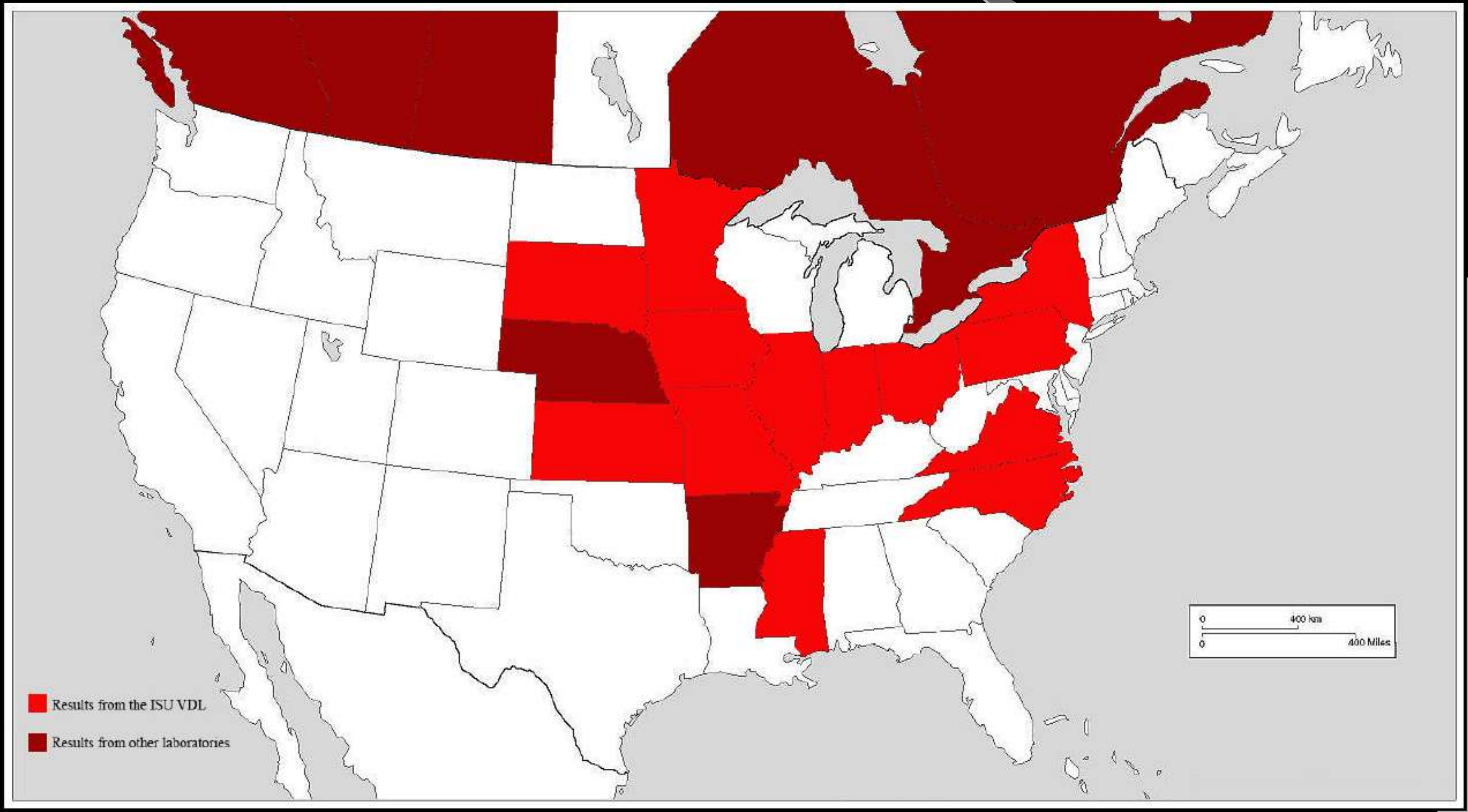


Re-emergence of Swine Dysentery in the U.S.

B. hyodysenteriae isolations from 2003 - 2008

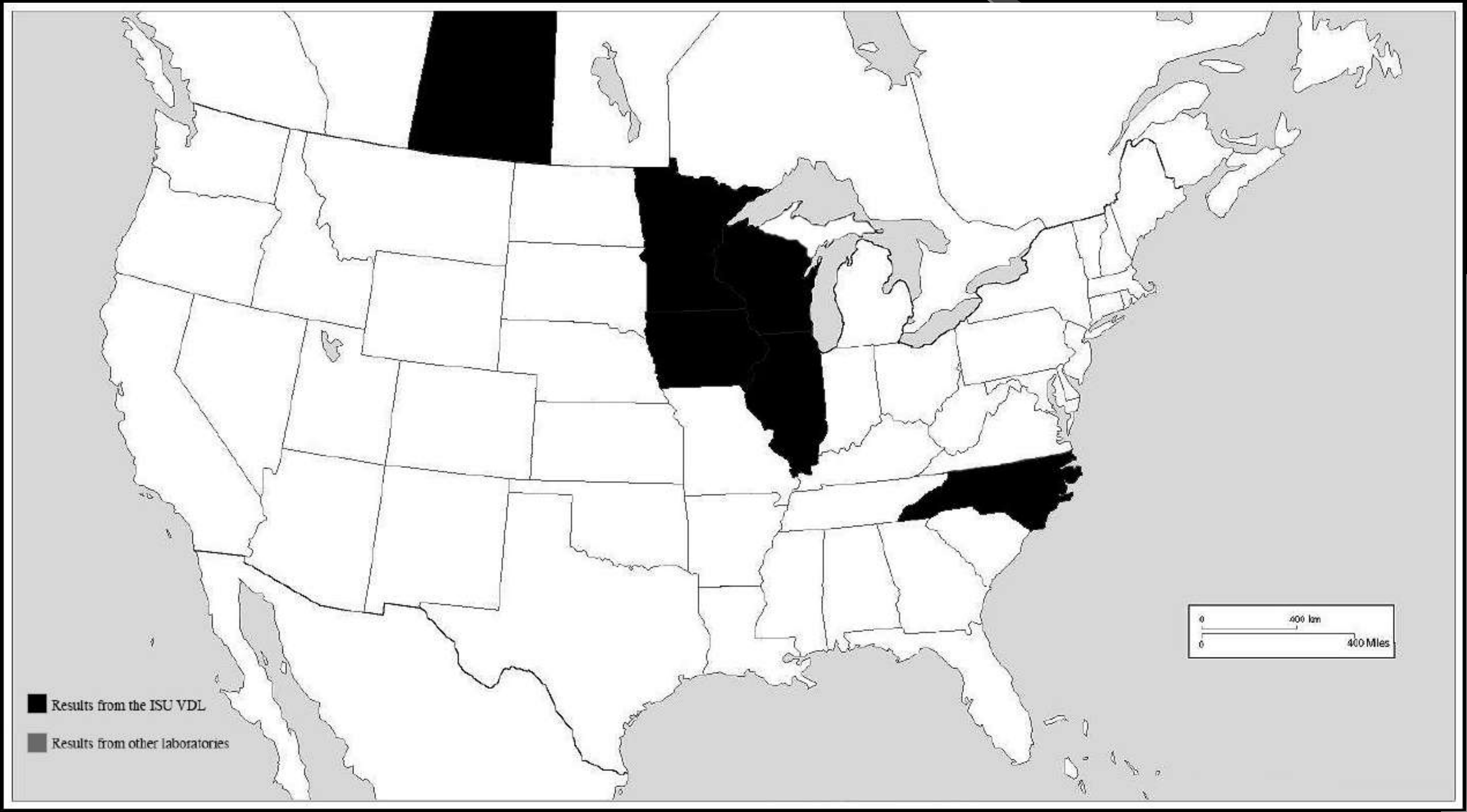
Re-emergence of Swine Dysentery in the U.S.

B. hyodysenteriae isolations from 2009 - 2013



Re-emergence of Swine Dysentery in the U.S.

"B. hampsonii" isolations from 2008 - 2011



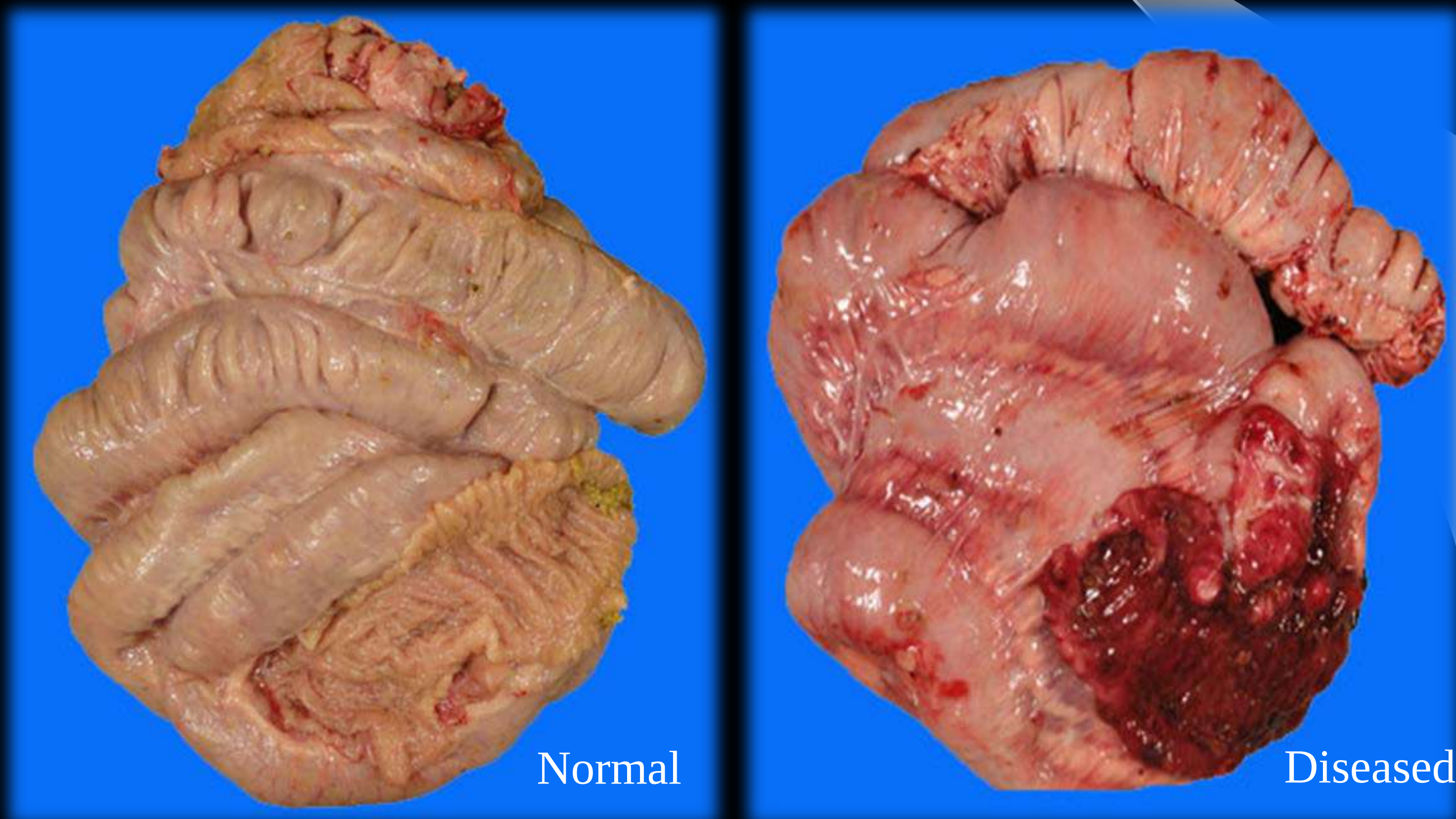
Re-emergence of Swine Dysentery in the U.S.

"B. hampsonii" isolations from 2008 - 2013

Re-emergence of Swine Dysentery in the U.S.

Re-emergence of Swine Dysentery in the U.S.

- Swine Dysentery
  - Gross Lesions



Re-emergence of Swine Dysentery in the U.S.

- Swine Dysentery
  - Classical definition:
    - Severe diarrhea with mucus and blood from which *B. hyodysenteriae* is isolated by culture or detected by PCR.
  - Current definition:
    - Severe diarrhea with mucus and blood from which a strongly beta-hemolytic *Brachyspira* spp. is isolated by culture (or detected by PCR).
      - *"Brachyspira suanatina"*
        - Råsbäck *et al*. 2007
      - *"Brachyspira hampsonii"*
        - Chander *et al*. 2012

Re-emergence of Swine Dysentery in the U.S.

- Swine Dysentery
  - So why did SD re-emerge in the U.S.?

RISK FACTORS FOR *BRACHYSPIRA* INFECTION

Risk Factors for *Brachyspira* Infection

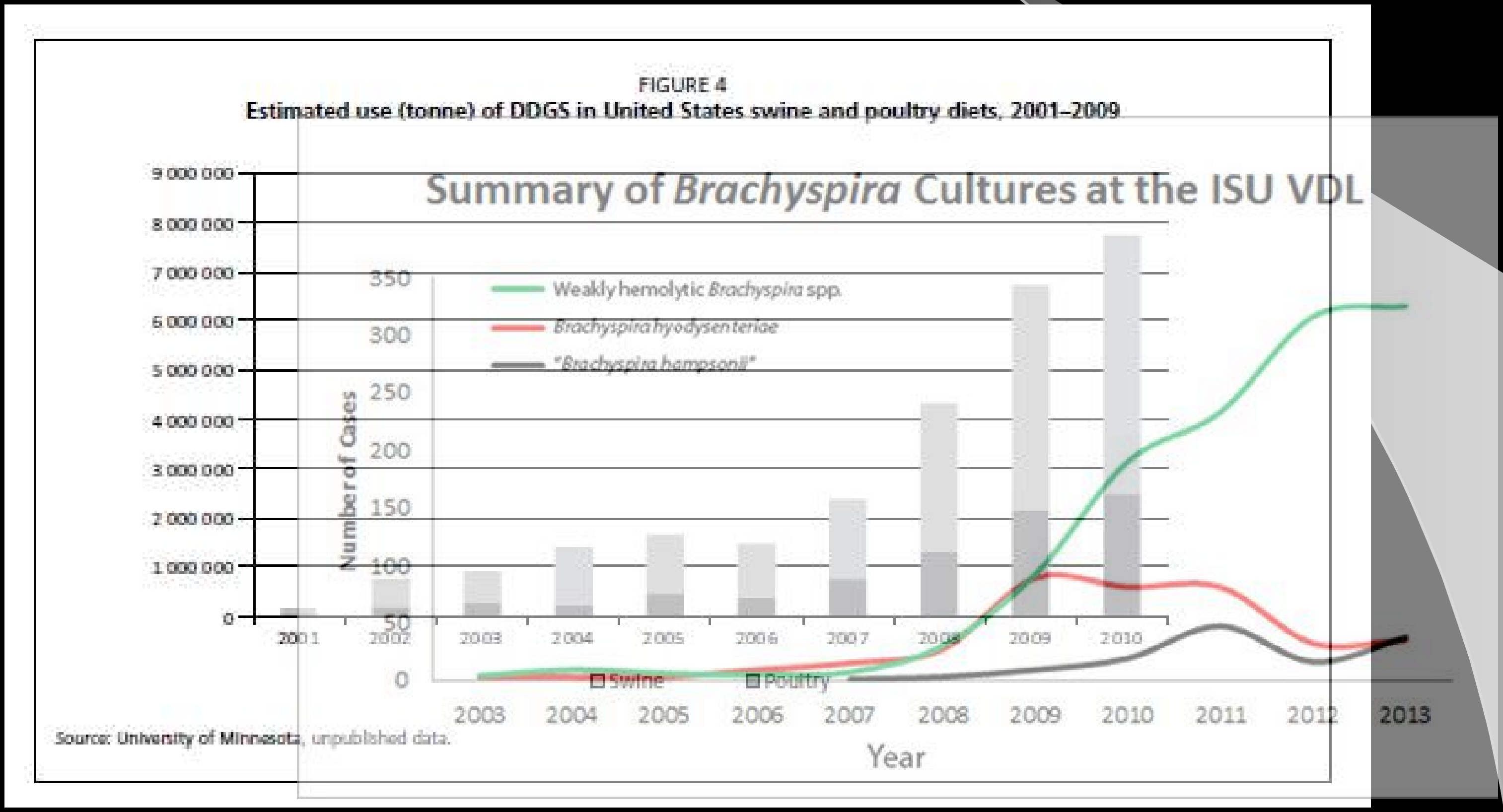
- Diet
  - Research in the late 1990s revealed several generalities:
    - SD expression is typically reduced when pigs are fed highly digestible diets (cooked rice) or inulin
      - Siba *et al*. 1996
    - SD expression is generally enhanced when rapidly fermentable fiber is present in the colon
      - Pluske *et al*. 1998
  - The impact of diet on the colonic microbiota has been postulated to underlie these observations
    - The colonic microbiome is highly dynamic and its composition varies greatly based upon substrates delivered
    - Early work with gnotobiotic pigs revealed a requirement for one or more synergistic bacteria in the pathogenesis of SD
      - Whipp *et al*. 1979

Risk Factors for *Brachyspira* Infection

- Diet
  - This raised the question:
    - Had any changes in feeding and management practices occurred in the US concurrent with the re-emergence of SD?

Risk Factors for *Brachyspira* Infection

- Diet



Biofuel co-products as livestock feed - Opportunities and challenges, Food and Agriculture Organization of the United Nations, Rome, Italy, 2012.

Risk Factors for *Brachyspira* Infection

- Diet
  - What is the impact of feeding distiller's dried grains with solubles (DDGS) on *Brachyspira* spp. infection?
    - One hundred 4-week-old pigs were fed a diet containing either 30% DDGS or no DDGS for 2 weeks and then inoculated as follows:

Table 1: Inoculum	0% DDGS	30% DDGS
Non-inoculated media (control)	n = 10	n = 10
Brachyspira hyodysenteriae (B204)	n = 10	n = 10
"*Brachyspira hampsonii*" (EB107)	n = 10	n = 10
Brachyspira pilosicoli (BR2001)	n = 10	n = 10
Brachyspira intermedia (BR2000)	n = 10	n = 10

Risk Factors for *Brachyspira* Infection

- Diet
  - What is the impact of feeding distiller's dried grains with solubles (DDGS) on *Brachyspira* spp. infection?
    - No significant differences were observed by diet in the control pigs or those inoculated with weakly beta-hemolytic *Brachyspira* spp.
    - Pigs fed DDGS and inoculated with strongly beta-hemolytic *Brachyspira* spp. developed SD nearly twice as fast as those fed no DDGS.

Summary of fecal scores, *Brachyspira* culture results of feces and oral fluids, and timing of euthanasia of B204-inoculated pigs[a,b]

B. hyodysenteriae

Diet / Pig ID	Individual Fecal Scores[c] by Days Post-Inoculation																
	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
0% DDGS[d]																	
88	0^{+}	2^{+}	4^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-	-	-	-	-
83	0^{+}	0^{+}	4^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-	-	-	-	-
85	0	0^{+}	2^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-	-	-	-	-
84	0^{+}	0^{+}	0^{+}	0^{+}	4^{+}	4^{+S}	4^{+}	-	-	-	-	-	-	-	-	-	-
86	0	0	0	1	0	0^{+}	4^{+}	4^{+}	4^{+}	4^{+S}	-	-	-	-	-	-	-
87	0	0	0	0	0^{+}	0^{+}	1^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-
81	0	1^{+}	0	1	0	1	1^{+}	1^{+}	3.5^{+}	4	2.5	2.5	1	1	1	0	1
82	0	1	0^{+}	1	0^{+}	0	0^{+}	0	1	1^{+}	0	0	0	0	0	0	0
89	0	0	0	0	0^{+}	0	0	0	0	0	0	0^{+}	0^{+}	0	0	0	0
90	0	0	0^{+}	0	0	0	0	0	0^{+}	0^{+}	0^{+}	2.5^{+}	1^{+}	4^{+}	4^{+}	3^{+}	4^{+}
Oral Fluids	Neg	Neg	Neg	Pos	Pos	Pos	Pos	Pos	Pos	Pos	Neg	Pos	Neg	Pos	Pos	Neg	Pos
30% DDGS																	
92	3.5^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-	-	-	-	-	-	-
96	0^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-	-	-	-	-	-	-
100	0^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-	-	-	-	-	-	-
91	2^{+}	3.5^{+}	4^{+}	4^{+}	4^{+S}	-	-	-	-	-	-	-	-	-	-	-	-
94	0^{+}	4^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-	-	-	-	-	-
95	0^{+}	4^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-	-	-	-	-	-
98	0^{+}	0^{+}	4^{+}	4	4^{+}	-	-	-	-	-	-	-	-	-	-	-	-
99	0	0^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-	-	-	-	-	-
93	0	0	0	0^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-	-	-	-
97	0	0^{+}	0^{+}	4	4^{+}	4^{+}	4^{+S}	-	-	-	-	-	-	-	-	-	-
Oral Fluids	Neg	Pos	Pos	Pos	Neg	-	-	-	-	-	-	-	-	-	-	-	-

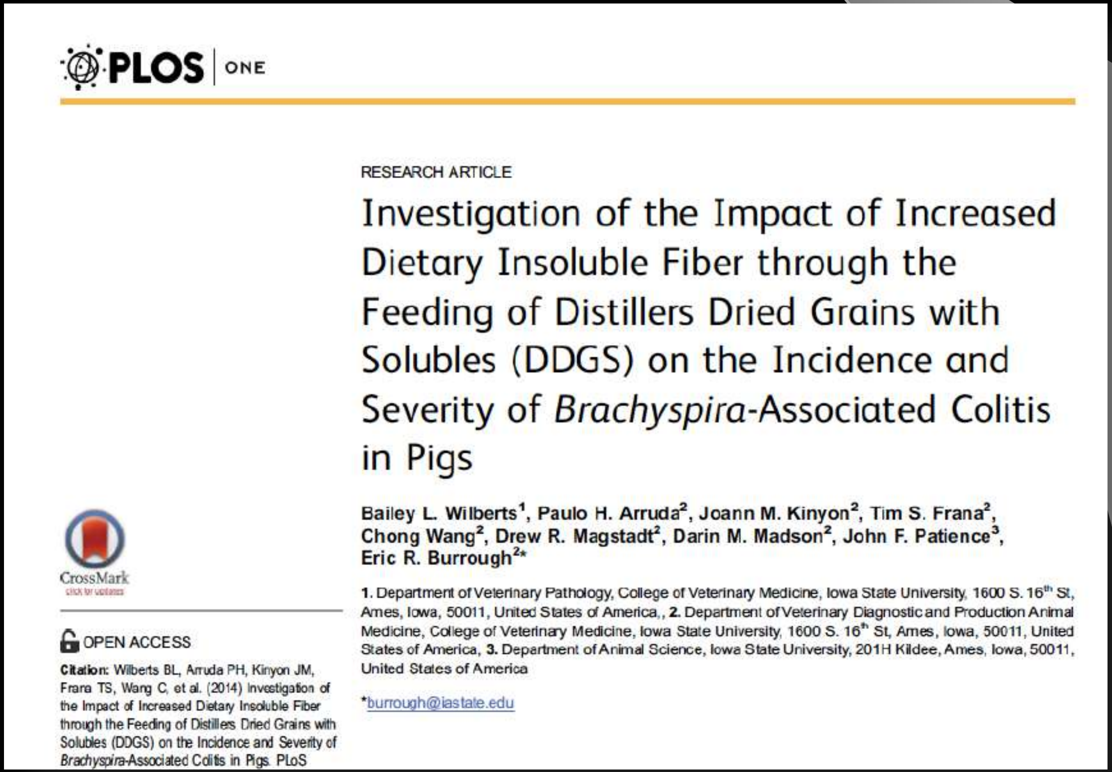
Summary of fecal scores, *Brachyspira* culture results, and timing of euthanasia of EB107-inoculated pigs[a,b]

“B. hampsonii”

Diet / Pig ID	Individual Fecal Scores[c] by Days Post-Inoculation																
	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
0% DDGS[d]																	
70	3.5^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-	-	-	-	-	-	-
69	2^{+}	4^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-	-	-	-	-	-
68	0	0^{+}	1^{+}	2.5^{+}	4^{+}	4^{+}	4^{+S}	-	-	-	-	-	-	-	-	-	-
62	0	0	0^{+}	0^{+}	0^{+}	1^{+}	4^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-
63	1	1^{+}	1	1^{+}	0^{+}	1^{+}	2.5^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-
67	0	0	0^{+}	0^{+}	0^{+}	0^{+}	0^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-
61	0	0^{+}	0^{+}	0	0^{+}	0^{+}	0	0	0	0	0	0	0	0	1	0^{+}	1^{+}
64	0	0	0	0^{+}	0^{+}	1^{+}	0^{+}	0	0^{+}	0	0	0	4^{+}	4^{+}	3^{+}	4^{+}	4^{+}
65	0^{+}	0	0	0	0	0^{+}	0	0^{+}	0^{+}	0	0	0	0	0	0^{+}	0^{+}	0^{+}
66	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0^{+}	0^{+}
Oral fluids	Pos	Pos	Pos	Pos	Pos	Pos	Pos	Pos	Pos	Pos	Neg	Neg	Pos	Pos	Pos	Pos	Pos
30% DDGS																	
76	4^{+}	4^{+}	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
79	0^{+}	4^{+}	4^{+}	4^{+S}	-	-	-	-	-	-	-	-	-	-	-	-	-
78	0^{+}	0^{+}	3.5^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-	-	-	-	-
75	0	0	1^{+}	4^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-	-	-	-
77	0^{+}	0^{+}	1^{+}	4^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-	-	-	-
80	0^{+}	0	0^{+}	1^{+}	4^{+}	4^{+}	4^{+}	-	-	-	-	-	-	-	-	-	-
71	0	0	0	0	0	0^{+}	0	0	0	0	0	0	0	0	0	0	0
72	0	0	0	0^{+}	0	0^{+}	0	0	0	0	0	0	0	0	0	0	0
73	0	0	0^{+}	0^{+}	0	0	0	0	0	0	0	0	0	0	0	0	0^{+}
74	0	0	0^{+}	0^{+}	0^{+}	0	0	0	0	0	0	0	0	0	0	0^{+}	0
Oral fluids	Neg	Neg	Pos	Neg	Pos	Pos	Pos	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg	Neg

Risk Factors for *Brachyspira* Infection

- Diet
  - What is the impact of feeding distiller's dried grains with solubles (DDGS) on *Brachyspira* spp. infection?



PLOS ONE

RESEARCH ARTICLE

Investigation of the Impact of Increased Dietary Insoluble Fiber through the Feeding of Distillers Dried Grains with Solubles (DDGS) on the Incidence and Severity of *Brachyspira*-Associated Colitis in Pigs

Bailey L. Wilberts[1], Paulo H. Arruda[2], Joann M. Kinyon[2], Tim S. Frana[2], Chong Wang[2], Drew R. Magstadt[2], Darin M. Madson[2], John F. Patience[3], Eric R. Burrough[2*]

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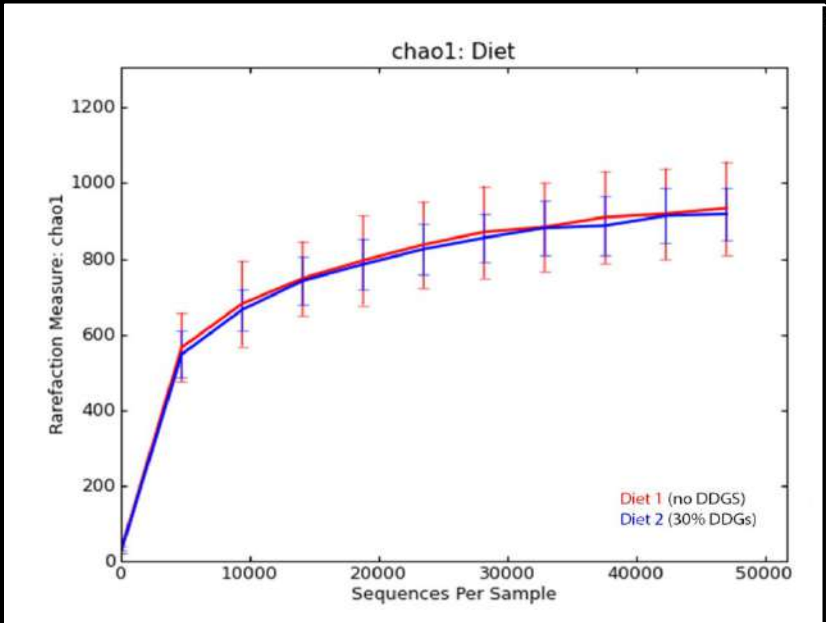
Citation: Wilberts BL, Arruda PH, Kinyon JM, Frana TS, Wang C, et al. (2014) Investigation of the Impact of Increased Dietary Insoluble Fiber through the Feeding of Distillers Dried Grains with Solubles (DDGS) on the Incidence and Severity of *Brachyspira*-Associated Colitis in Pigs. PLoS

Risk Factors for *Brachyspira* Infection

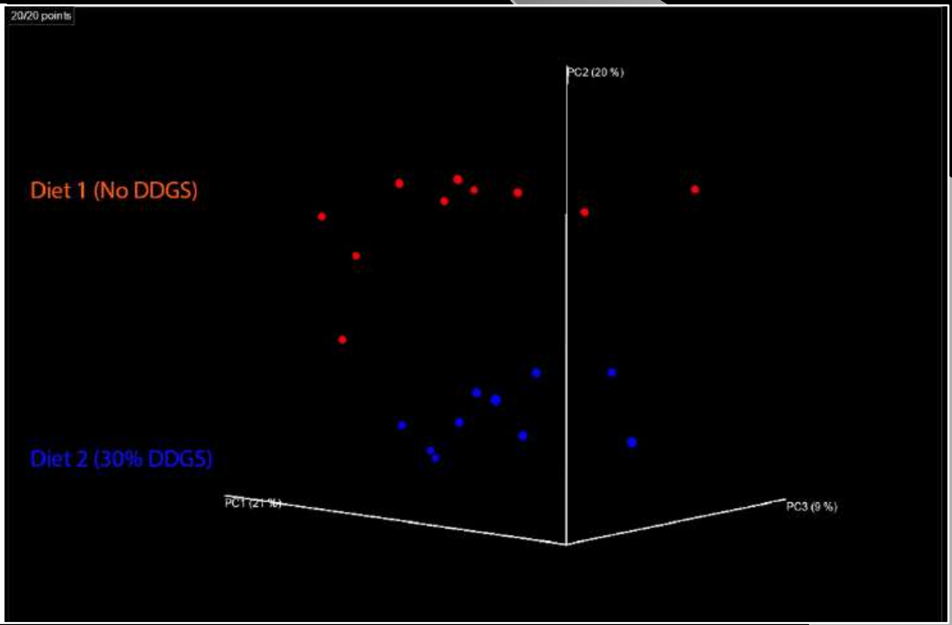
- Diet
  - What is the impact of feeding DDGS on the colonic microbiota of pigs?
    - Feces were collected from the spiral colon of 100 pigs in the previous experiment and flash frozen in liquid nitrogen
    - DNA was purified and extracted
    - Submitted for metagenomic analysis using the 16S rRNA gene

Risk Factors for *Brachyspira* Infection

- Diet
  - What is the impact of feeding DDGS on the colonic microbiota of pigs?



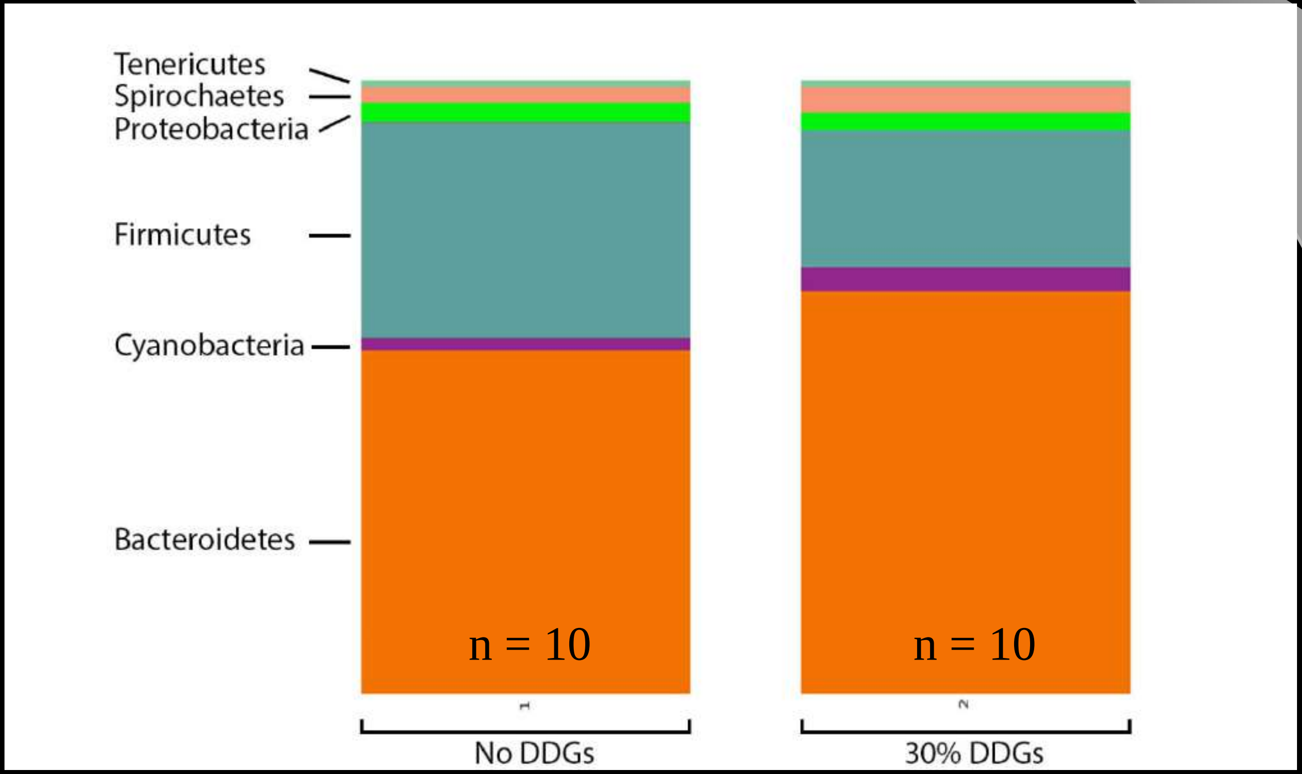
Richness



Diversity

Risk Factors for *Brachyspira* Infection

- Diet
  - What is the impact of feeding DDGS on the colonic microbiota of pigs?

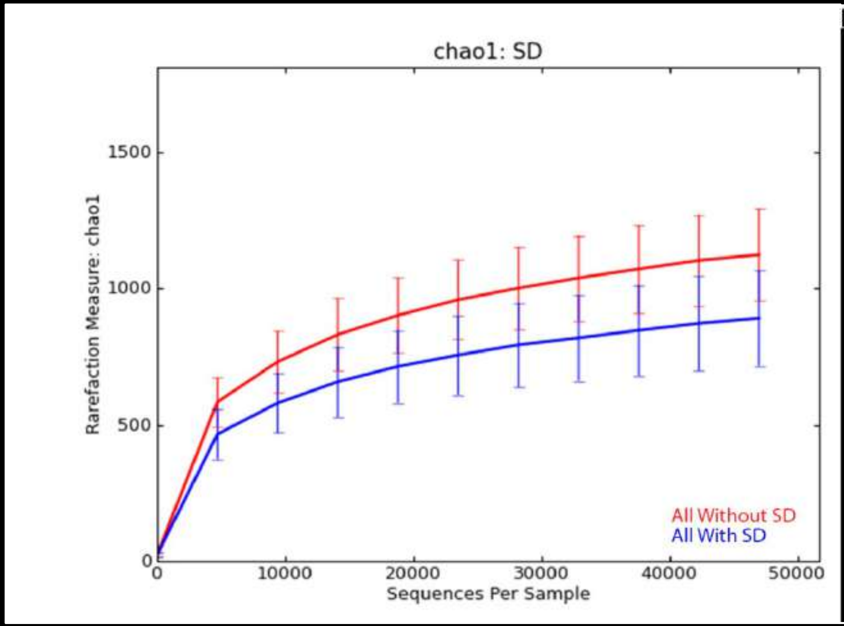


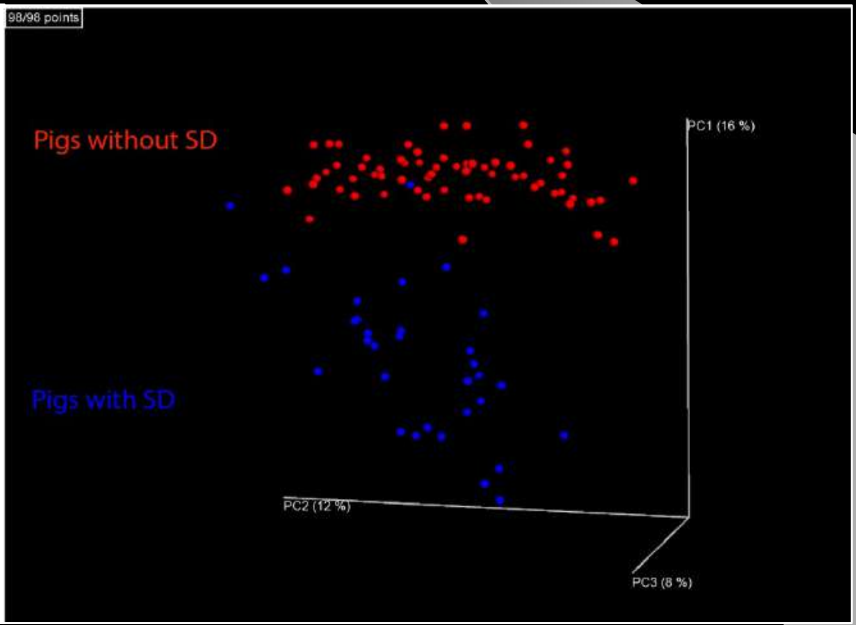
Risk Factors for *Brachyspira* Infection

- Diet
  - What is the impact of feeding DDGS on the colonic microbiota of pigs?
    - Feeding 30% DDGS did not impact alpha diversity (richness), but markedly altered beta diversity ($P < 0.001$).
      - The Bacteroidetes:Firmicutes ratios were significantly higher in pigs fed 30% DDGS (mean 3.555 ± 0.644) relative to pigs fed no DDGS (mean 1.798 ± 0.262) ($P = 0.027$).
      - Spirochaetes were more abundant in pigs fed DDGS (predominantly treponemes)
    - Is the increased susceptibility to SD associated with feeding DDGS due to changes in substrate available, increased presence of synergistic organisms, or the absence of antagonists?

Risk Factors for *Brachyspira* Infection

- SD versus Non-SD
  - What happens to the colonic microbiota of pigs when they develop SD?



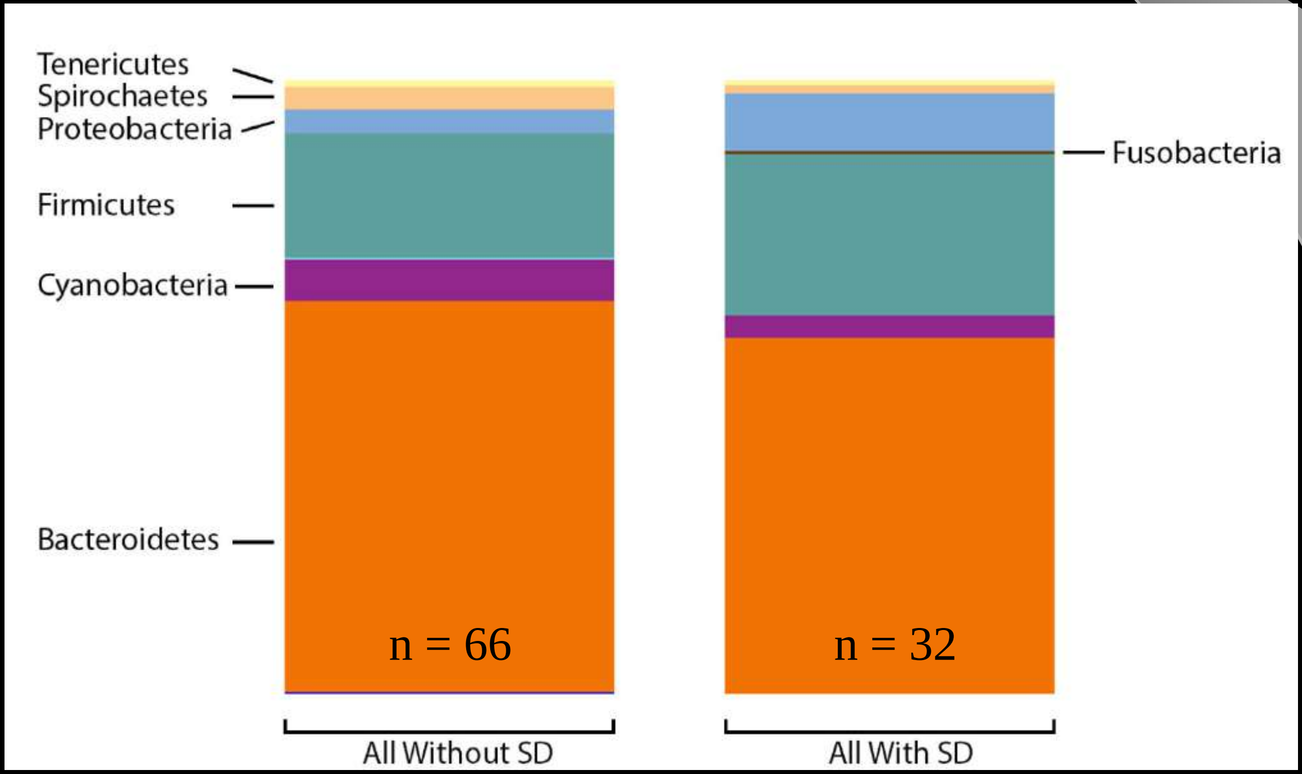


Richness

Diversity

Risk Factors for *Brachyspira* Infection

- SD versus Non-SD
  - What happens to the colonic microbiota of pigs when they develop SD?

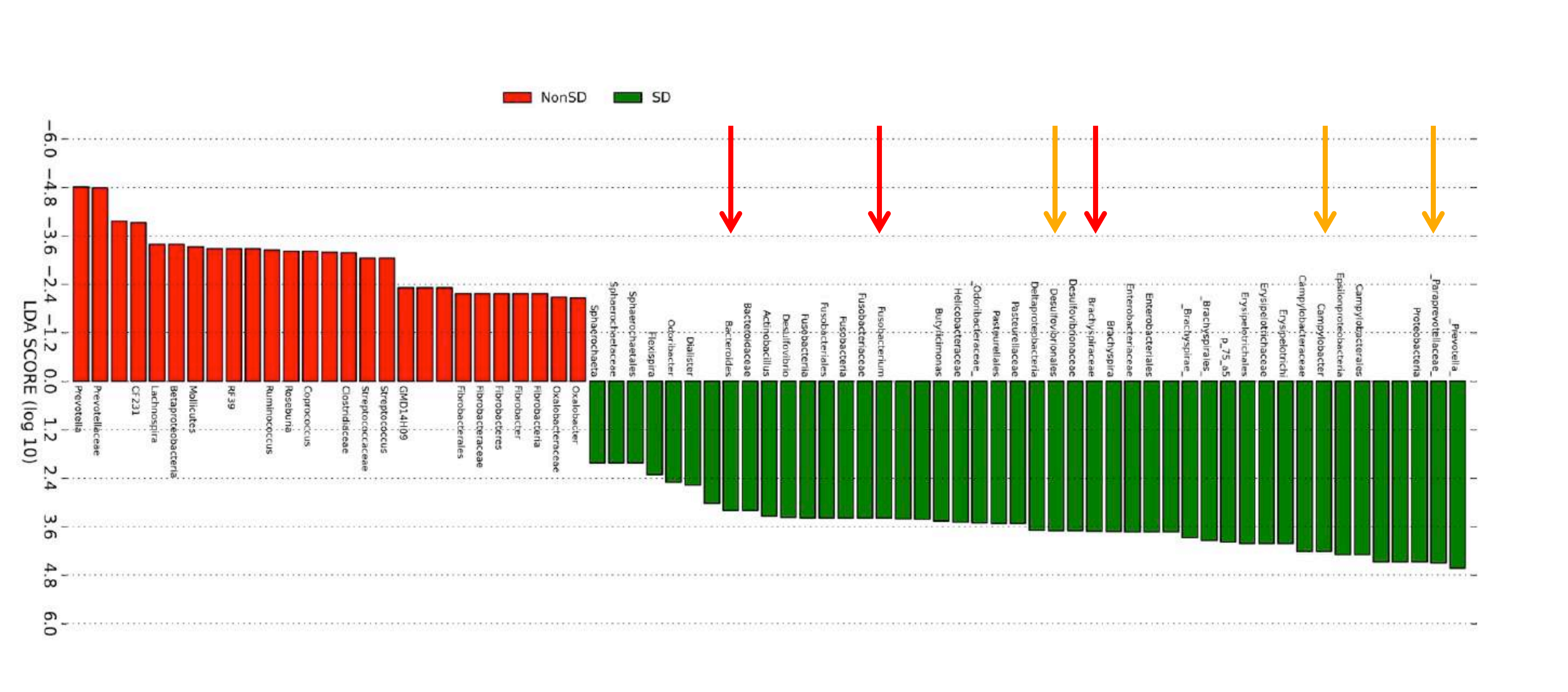


Risk Factors for *Brachyspira* Infection

- SD versus Non-SD
  - What happens to the colonic microbiota of pigs when they develop SD?
    - Pigs with SD had markedly different alpha diversity (richness) and beta diversity relative to pigs without SD ($P \leq 0.001$).
      - The Bacteroidetes:Firmicutes ratios were significantly lower in pigs with SD (mean 2.388 ± 0.174) relative to pigs without (mean 3.645 ± 0.225) ($P < 0.001$).
      - At the phylum level, Fusobacteria and Proteobacteria were significantly more abundant the microbiota of pigs with SD
    - Which specific bacterial species underlie these shifts?

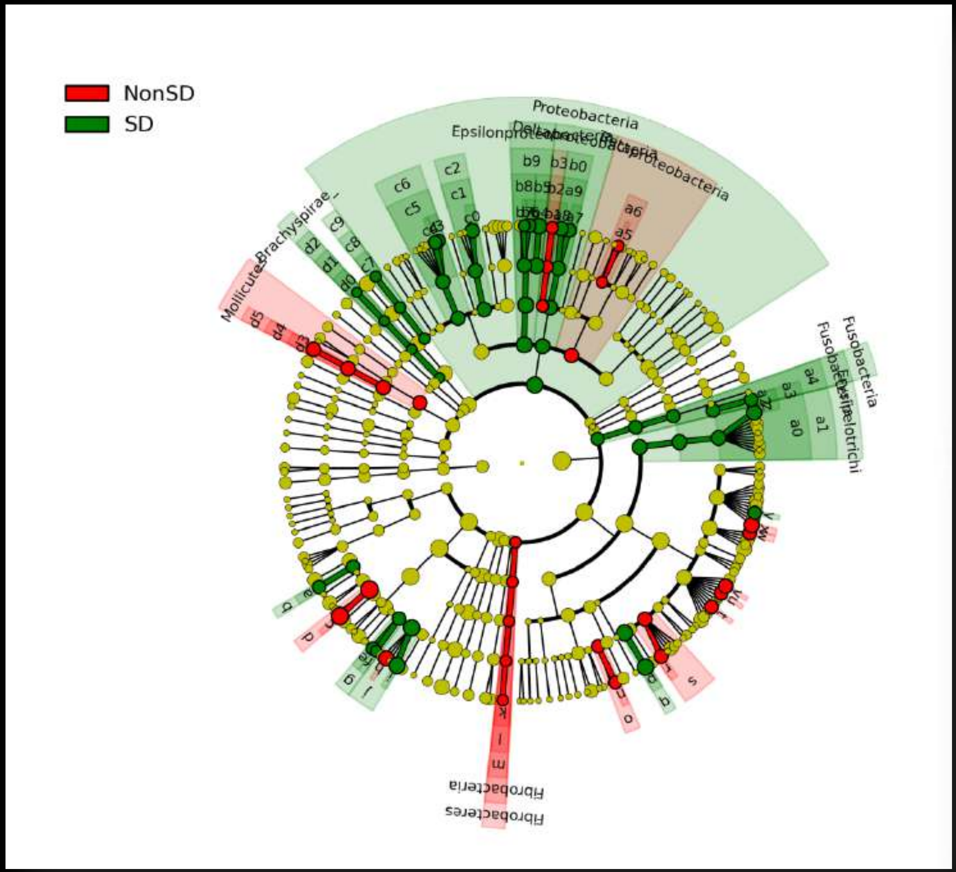
Risk Factors for *Brachyspira* Infection

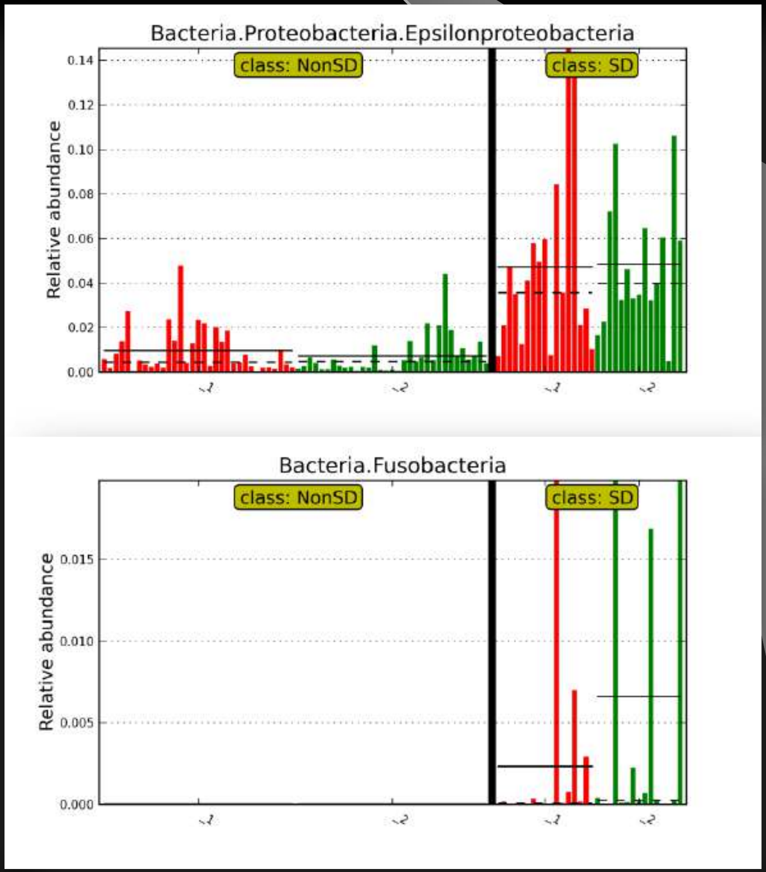
- SD versus Non-SD
  - Which specific bacterial species underlie these shifts?



Risk Factors for *Brachyspira* Infection

- SD versus Non-SD
  - Which specific bacterial species underlie these shifts?





Risk Factors for *Brachyspira* Infection

- Vectors
  - Control of rodents, feral animals, and waterfowl is essential in SD control
    - Recent identification of "*B. hampsonii*" in European waterfowl and geese in the Canadian arctic as well as "*B. suanatina*" from mallards in Sweden

Risk Factors for *Brachyspira* Infection

***Brachyspira* species**	**Common / Potential hosts**	**Clinical disease**
B. hyodysenteriae	Pigs, rodents, poultry, rheas, mallard ducks, geese	**Swine dysentery**; ducks and rodents asymptomatic
B. pilosicoli	Pigs, poultry, humans, nonhuman primates, dogs, rodents, pheasants, mallards, graylag geese	Colonic spirochetosis
B. murdochii	Pigs, rodents, poultry, mallards, graylag geese, lesser snow geese	Non-pathogen; mild catarrhal colitis in swine
B. intermedia	Pigs, poultry	Colonic spirochetosis in poultry; some isolates non-pathogenic in pigs, others reportedly associated with mild clinical disease
B. innocens	Pigs, dogs, poultry, pheasants, mallards, graylag geese, lesser snow geese	Non-pathogen
"*B. hampsonii*"	Pigs, mallard ducks, graylag geese, lesser snow geese	**Swine dysentery**
"*B. suanatina*"	Pigs, mallard ducks	**Dysentery-like disease** in swine; ducks asymptomatic

Risk Factors for *Brachyspira* Infection

- Lagoons
  - Recycling of lagoon effluent is a major risk factor in U.S. systems
    - *Brachyspira* spp. can survive long periods in lagoons
      - Alkalization of lagoons may reduce survivability of *Brachyspira*
  - Rodents and waterfowl may be exposed and then spread

Risk Factors for *Brachyspira* Infection

Risk Factors for *Brachyspira* Infection

DIAGNOSTIC APPROACHES FOR *BRACHYSPIRA* DETECTION: STRENGTHS AND LIMITATIONS

Diagnostic Tests: Strengths and Limitations

- Clinical Signs / Impressions
  – Diagnostic plan based upon observations

Diagnostic Tests: Strengths and Limitations

- Sampling Methodology
  - Index cases:
    - From a system without previous diagnosis
    - Sampling from **non-medicated** pigs (3 – 4):
      - Submission of samples for concurrent culture and histopathology increases value
      - Fix tissues in formalin as soon as possible
    - Feces
      - Swabs of abnormal stools > Random rectal swabs
      - Cecal / colonic contents preferred at necropsy
      - Samples should be fresh and chilled during transit

Diagnostic Tests: Strengths and Limitations

- Sampling Methodology
  - Index cases (continued):
    - Necropsy sampling
      - A thorough gross description is vital for final interpretation
      - Enteric diseases are often segmental
        - Evaluate / open all segments of the large intestine
          - Start with the cecum and open all segments of spiral and descending colon
    - A serial approach will improve **diagnostic specificity**
      - Culture / PCR → Lesion → ISH or silver stain
      - *Increases the predictive value of a positive test*

Diagnostic Tests: Strengths and Limitations

- Sampling Methodology
  - Surveillance:
    - From a system with a previous diagnosis or negative status
    - Sampling from **non-medicated** pigs (15 – 20):
      - Feces
        - Rectal swabs versus swabs of abnormal stools
        - Samples should be fresh and chilled during transit
      - **Oral fluids**
        - *Brachyspira* cultures can be positive when approx. 10% of pigs in a pen are shedding
        - Positive OF cultures may precede clinical disease
      - **A mix of both sample types is ideal to address pen level and individual animal concerns**
        - Parallel testing improves **diagnostic sensitivity**:
          - Concurrent culture, direct PCR, and serology (where available)
          - *Increases the predictive value of a negative test*

Diagnostic Tests: Strengths and Limitations

- Historically, differentiation of *Brachyspira* was based upon phenotypic traits and biochemical testing.

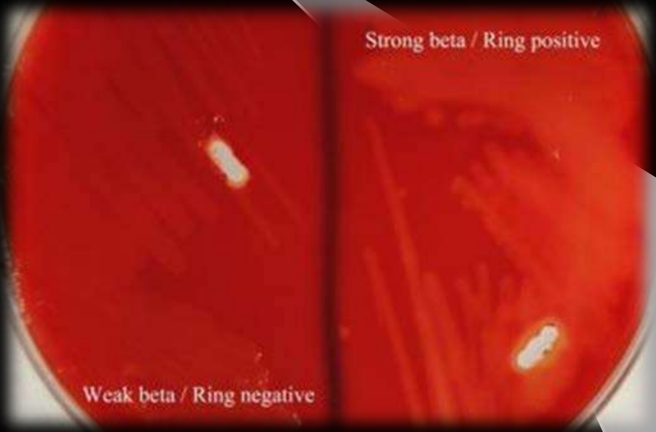
Table 6
Differentiation of porcine *Brachyspira* species by biochemical reactions

Group	Hemo-lysis	Indole production	Hippurate hydrolysis	α-gal[a]	β-glu[b]	Species indicated
I	strong	±[c]	–	–	+	*B. hyodysenteriae*
II	weak	+	–	–	+	*B. intermedia*
IIIa	weak	–	–	–	+	*B. murdochii*
IIIbc	weak	–	–	+	+	*B. innocens*
IV	weak	–	+	±	–	*B. pilosicoli*

[a] α-gal = alpha-galactosidase activity.
[b] β-glu = beta-glucosidase activity.
[c] Negative isolates have only been reported from Belgium, Germany and Canada. **Also the UK in 2000

Diagnostic Tests: Strengths and Limitations

- Phenotypic characteristics of *Brachyspira:*
  - Beta-hemolysis
    - Strong vs. weak
    - **All SD-associated species are strongly hemolytic**
  - Ring phenomenon
    - Enhanced hemolysis around slits in the agar
      - Positive vs. negative



- Speciation by PCR or MALDI-TOF

Diagnostic Tests: Strengths and Limitations

Analytical sensitivity of various detection assays in serially diluted pig feces

"B. hampsonii"

B. hyodysenteriae

Summary of culture, fluorescent *in situ* hybridization (FISH), and real-time polymerase chain reaction (qPCR) results for each isolate and replicate at 0 and 48 hours after sample preparation

Isolate/Count/Time	Assay	Result at indicated dilution: Neat	10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	10^{-7}
EB107[*]	Culture	NA[‡]	TNTC[§]	TNTC	TNTC	76	5	2	0
8.3 X 10^6[†]	FISH	34 (1-6)[‖]	4 (0-2)	0	1	NA	NA	NA	NA
0 hr	qPCR[#]	NA	$\boxed{41.4}$	Negative	Negative	NA	NA	NA	NA
EB107	Culture	NA	4	4	5	0	0	0	0
8.3 X 10^6	FISH	22 (0-6)	3 (0-1)	1	0	NA	NA	NA	NA
48 hr	qPCR	NA	$\boxed{39.7}$[¶]	Negative	Negative	NA	NA	NA	NA
EB107	Culture	NA	TNTC	TNTC	TNTC	106	7	1	1
7.2 X 10^6	FISH	11 (0-3)	3 (0-1)	0	0	NA	NA	NA	NA
0 hr	qPCR	NA	$\boxed{42.4}$[¶]	Negative	Negative	NA	NA	NA	NA
EB107	Culture	NA	TNTC	TNTC	110	7	0	0	0
7.2 X 10^6	FISH	25 (0-7)	3 (0-1)	1	0	NA	NA	NA	NA
48 hr	qPCR	NA	$\boxed{41.6}$	Negative	Negative	NA	NA	NA	NA
B204[**]	Culture	NA	TNTC	TNTC	135	52	5	3	0
5.9 X 10^6	FISH	3 (0-3)	0	0	NA	NA	NA	NA	NA
0 hr	qPCR	NA	$\boxed{44.1}$	Negative	Negative	NA	NA	NA	NA
B204	Culture	NA	5	8	2	0	0	0	0
5.9 X 10^6	FISH	5 (0-2)	0	0	NA	NA	NA	NA	NA
48 hr	qPCR	NA	$\boxed{40.2}$[¶]	Negative	Negative	NA	NA	NA	NA
B204	Culture	NA	TNTC	TNTC	129	6	0	0	0
9.3 X 10^6	FISH	0	0	NA	NA	NA	NA	NA	NA
0 hr	qPCR	NA	$\boxed{41.2}$	Negative	Negative	NA	NA	NA	NA
B204	Culture	NA	7	19	0	0	0	0	0
9.3 X 10^6	FISH	7 (0-4)	0	0	NA	NA	NA	NA	NA
48 hr	qPCR	NA	$\boxed{38.1}$	Negative	Negative	NA	NA	NA	NA

Wilberts BL, Warneke HL, Bower LP, Kinyon JM, Burrough ER: Comparison of culture, PCR, and fluorescent *in situ* hybridization for detection of *Brachyspira hyodysenteriae* and "*Brachyspira hampsonii*" in pig feces. *J Vet Diagn Invest* 2015;27:41-46.

Diagnostic Tests: Strengths and Limitations

Comparison of commonly available diagnostic assays for *Brachyspira* spp.

Assay	Sample types	Options for speciation	Advantages / Disadvantages
Selective anaerobic culture	Fresh colon Mucosal scrapings Feces Swabs Oral fluids*	• PCR assays from primary culture. • MALDI-TOF MS • Biochemical reactions	A: Options exist for speciation at both the genetic (PCR) and protein (MALDI-TOF MS) levels. Novel species detected. D: Requires viable bacteria and often takes more than 6 days to complete.
Polymerase chain reaction	Mucosal scrapings Feces Swabs Oral fluids*	• Many assays are already species-based by design. • Products from genus-level assays can be speciated by sequencing or MLST.	A: Rapid turnaround time and not dependent upon viable bacteria. D: Species-based assays have very defined specificity and are susceptible to false negative results with mutation.

*This sample type has not yet been fully validated for these assays but preliminary results suggest this may be an excellent sample type for *Brachyspira* spp. identification.
MALDI-TOF MS = matrix-assisted laser desorption ionization time-of-flight mass spectrometry
MLST = multilocus sequence typing

Burrough ER: *Brachyspira* infections – diagnostics and clinical considerations. Proceedings of the 21st Annual Swine Disease Conference for Swine Practitioners, Iowa State University, Ames, IA. 2013, pp. 12-15.

TREATMENT AND CONTROL OF SWINE DYSENTERY

Treatment and Control of Swine Dysentery

- Antibiotics
  - Commonly used antimicrobials for SD treatment:
    - Tiamulin, valnemulin, tylosin, and lincomycin
    - For *B. hyodysenteriae*:
      - Resistance to tylosin and lincomycin is common worldwide
      - Resistance to pleuromutilins is increasing regionally, particularly in Europe
        - A recent study of Italian isolates suggests transnational spread of resistance clones

Treatment and Control of Swine Dysentery

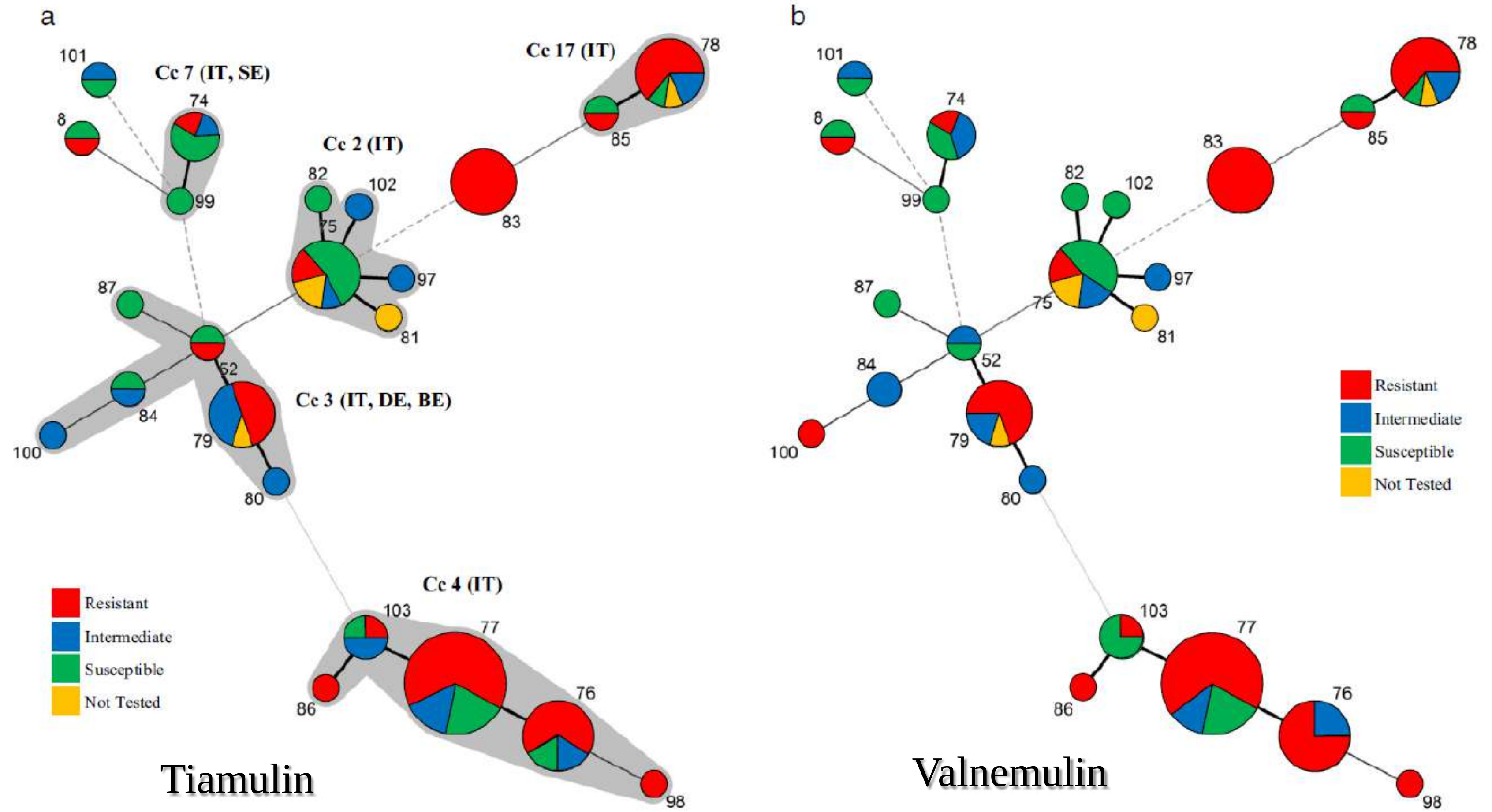


Fig. 2. Minimum spanning tree analysis showing (a) tiamulin and (b) valnemulin susceptibility of 103 isolates of *Brachyspira hyodysenteriae* represented by 23 sequence types (ST). Each node indicates a different ST (labelled), its size indicates the number of isolates in the ST and the colour represents the susceptibility of the isolate to tiamulin. The width of the branches indicates the allelic difference between two STs; heavy lines link single locus variants (SLVs), thin lines link double locus variants (DLVs) and dotted lines link STs differing by more than two loci. The five clonal clusters of STs sharing six or more common loci are indicated by shading in grey. Isolates from other countries that belong in the same ST or Cc are marked: DE, Germany; BE, Belgium; SP, Spain; SE, Sweden; IT, Italy.

Rugna G, Bonilauri P, Carra E, Bergamini F, Luppi A, Gherpelli Y, Magistrali CF, et al.: Sequence types and pleuromutilin susceptibility of *Brachyspira hyodysenteriae* isolates from Italian pigs with swine dysentery: 2003–2012. *Vet J* 2015;203:115-119.

Treatment and Control of Swine Dysentery

- Antibiotics
  - A pleuromutilin-resistant ST has emerged in Italy
    - Recovered from 9 farms between 2011-2012
    - Suggests recent dissemination of this strain

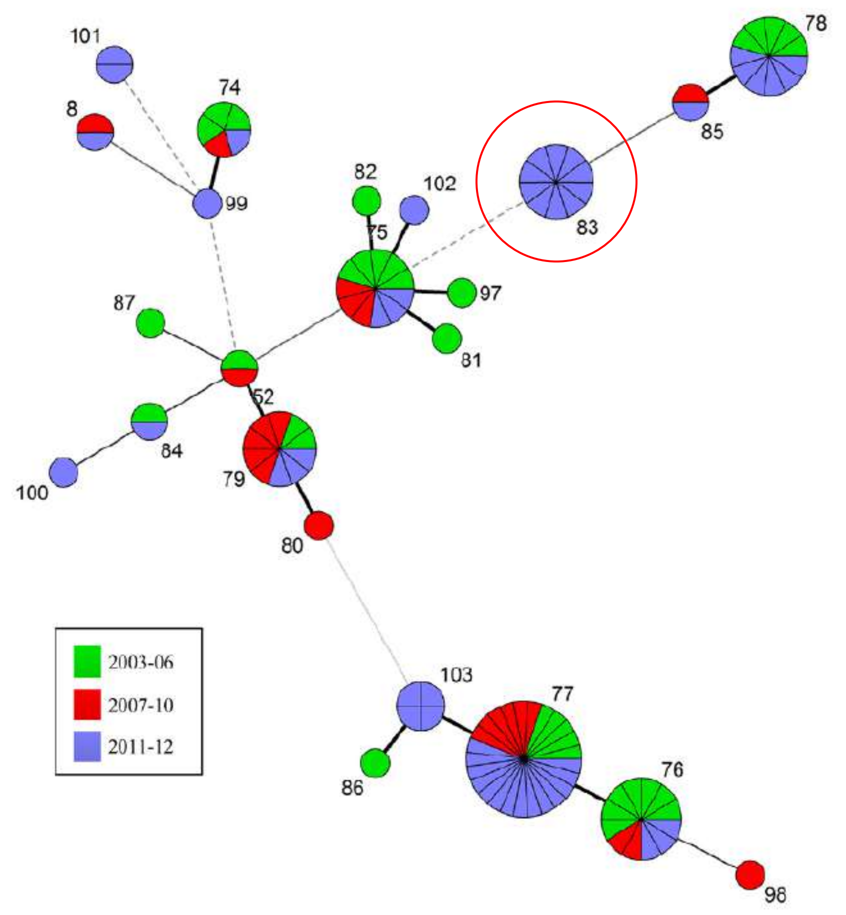


Fig. 3. Minimum spanning tree analysis comparing the year of isolation of 108 Italian isolates with the 23 sequence types (ST) they represent. Year of isolation has been grouped into four-year intervals. Each node of the MST indicates a different ST (labelled), its size reflects the number of isolates and the colour represents the period in which the strain was isolated.

Rugna G, Bonilauri P, Carra E, Bergamini F, Luppi A, Gherpelli Y, Magistrali CF, et al.: Sequence types and pleuromutilin susceptibility of *Brachyspira hyodysenteriae* isolates from Italian pigs with swine dysentery: 2003–2012. *Vet J* 2015;203:115-119.

Treatment and Control of Swine Dysentery

- Antibiotics
  - For "*B. hampsonii*":
    - Recent reports reveal field isolates are generally sensitive to common antibiotics including pleuromutilins
    - A few tylosin and lincomycin resistant isolates have been identified in the US

"*" indicates values with poor susceptibility to antimicrobial (4)		tiamulin	valnemulin	lincomycin	tylosin	tylvalosin	doxycycline	carbadox
MIC_{50}	*B.hyodysenteriae*	≤0.063	≤0.031	16*	>128*	4*	0.5	0.004
	"*B.hampsonii*"	≤0.063	≤0.031	≤0.5	4	0.5	0.5	0.004
	B.pilosicoli	0.5*	0.5*	32*	>128*	32*	2*	0.008
	B.murdochii	0.125	0.125	16*	>128*	8*	1*	0.004
MIC_{90}	*B.hyodysenteriae*	0.5*	0.5*	32*	>128*	16*	2*	0.008
	"*B.hampsonii*"	0.25	≤0.031	16*	>128*	4*	1*	0.004
	B.pilosicoli	>8*	2*	64*	>128*	>32*	4*	0.016
	B.murdochii	1*	0.5*	16*	>128*	32*	1*	0.008

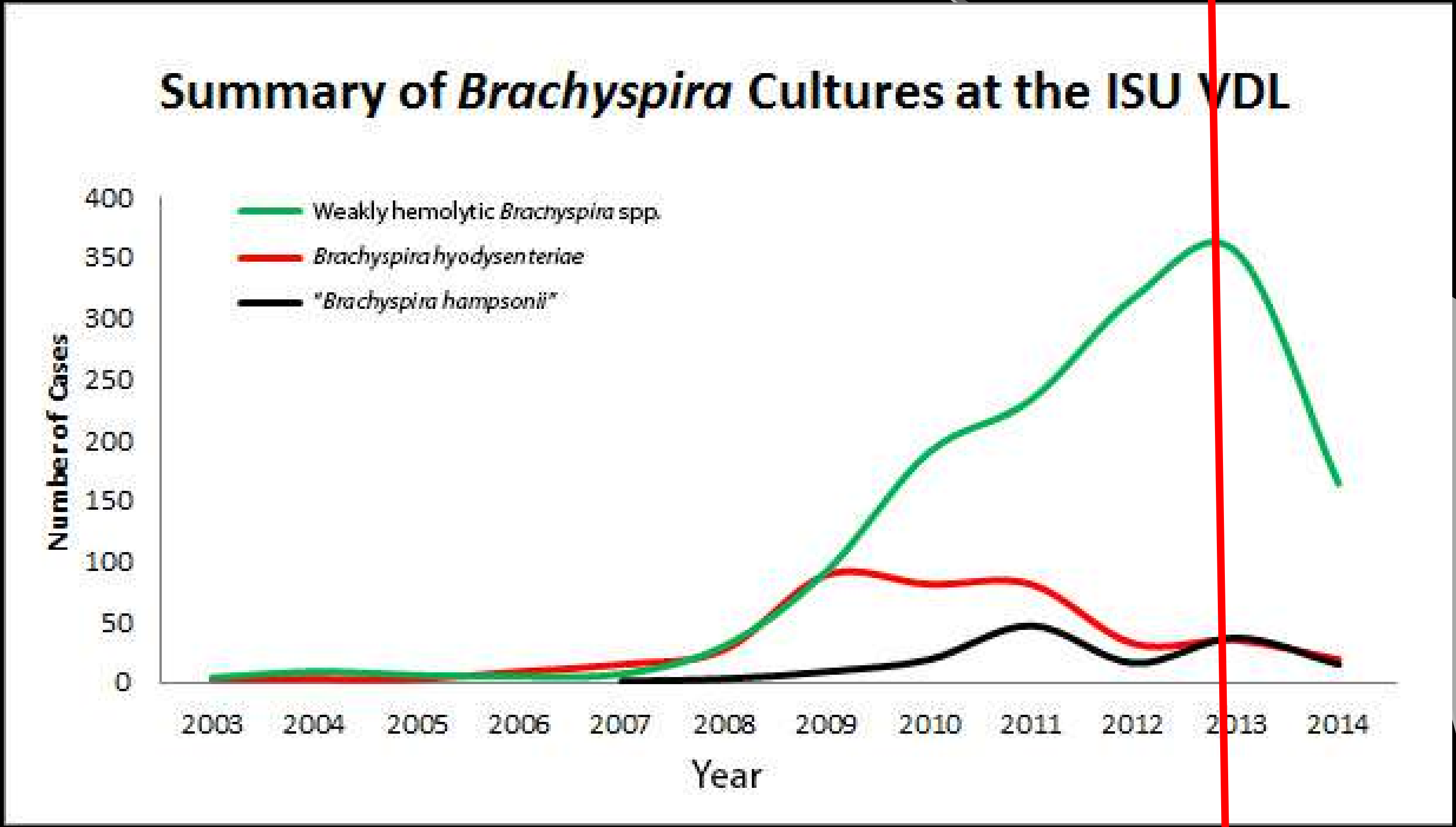
Mirajkar NS and Gebhart CJ. 2013. Antimicrobial susceptibility patterns of *Brachyspira* species in U.S. swine herds. 6th International Conference on Colonic Spirochaetal Infections in Animals and Humans, Guildford, UK, p. 53.

Treatment and Control of Swine Dysentery

- Antibiotics
  - Moving recently medicated pigs into clean, segregated facilities helps break the infection cycle
- Biosecurity
  - Extensive environmental cleaning is essential
    - Removal of all fecal material and disinfection
    - Rodent and waterfowl control
    - All-in/all-out pig flow

Treatment and Control of Swine Dysentery

PEDV identified in the U.S.



Treatment and Control of Swine Dysentery

- Why does SD appear to be declining again in the US?
  - Many potential factors:
    - Increased awareness and elimination efforts
    - PEDV emergence in the US
      - Increased focus on neonatal diarrhea with less grow-finish surveillance (i.e. less detection)
      - Improved biosecurity efforts overall have reduced SD
    - Feeding practices have moved away from DDGS

SUMMARY

Summary

- Swine Dysentery can occur following infection with any of several strongly beta-hemolytic *Brachsypira*:
  - *B. hyodysenteriae*
  - *"B. hampsonii"*
  - *"B. suanatina"*
- Diet plays a major role in the expression of SD
  - Increased colonic fiber alters the microbiota and may increase susceptibility to *Brachyspira* infection
- Rodents and waterfowl are risk factors for on farm persistence and between farm spread

Summary

- For *Brachyspira* spp. detection:
  - For disease confirmation, the diagnostic sensitivity of most assays is similar given the high numbers of bacteria shed
    - Culture = PCR = Histopathology
  - In surveillance situations, the lower threshold of detection (increased analytical sensitivity) makes culture the most appropriate for identifying subclinical infections
    - Culture > PCR > Histopathology
    - Direct PCR may shorten the time to positive results, but *false negatives are a concern*
  - For speciation:
    - A combination of genetic (PCR), biochemical, and protein-based assays (MALDI-TOF) is useful for definitive ID due to genetic variability in these spirochetes

Summary

- For *Brachyspira* spp. detection:
  - Preferred samples
    - Colonic tissue or scrapings > Feces with mucus > Rectal swabs
    - Oral fluids from pens of affected pigs may also be of value
- Treatment and control of SD
  - Efficacious vaccines are not yet commercially available
  - Elimination and prevention efforts are preferred as antibiotic resistant strains are emerging in many countries
    - Improved biosecurity to prevent other diseases may also reduce SD