Bovine Respiratory Disease
Cinical Diagnosis & Impacts

Food for thoughts

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About this talk

- BRD CLINICAL DIAGNOSIS
  - ✓ Can we rely on clinical observations?
  - ✓ How useful is the monitoring of temperature?
  - ✓ What are clinical scoring used for?
  - ✓ Do we need sensitive or specific clinical diagnosis tests?
  - ✓ Can practitioners trust their ears (thoracic auscultation)?

- CONSEQUENCES OF BRD
  - ✓ What are the immediate impacts of BRD on calves?
  - ✓ What do we know about the long-term impacts of BRD?

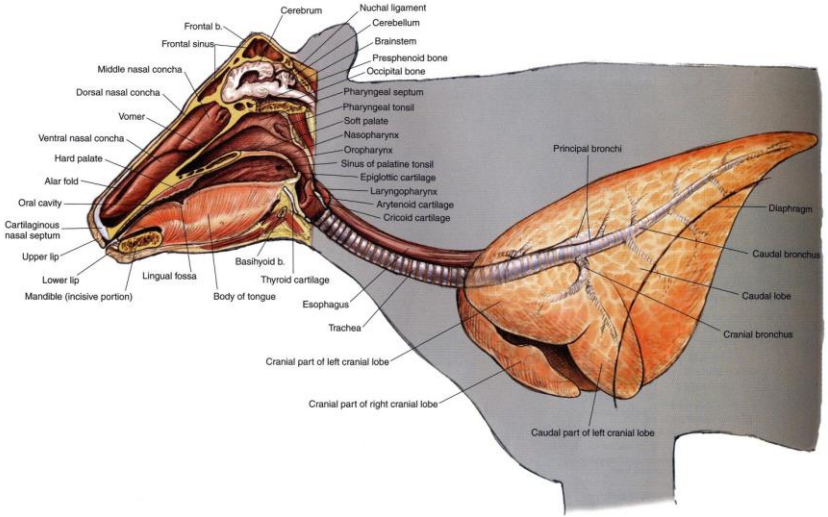
Background

Raising young stock is a real challenge.

Failure to manage adequately calfhood diseases can be costly.

Terminology

- What is BRD?
  - ✓ In the broadest sense, BRD refers to any disease of the upper or lower respiratory tracts
  - ✓ In many situations, BRD in cattle refers to a disease of the lower respiratory tract *(pneumonia)*
  - ✓ The most frequent situation being bronchopneumonia



Broncho-pneumonia | Interstitial | Metastatic/ Embolic

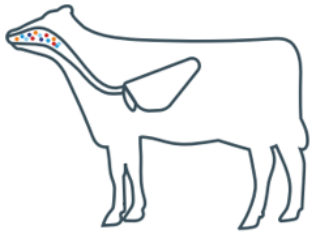
Pathophysiology

- What characterize bronchopneumonia?
  - ✓ Invasion of pathogenic organisms that gain access to the lung through the pulmonary tree

Cranio-ventral distribution of lung lesions

1

Nasal bacterial buildup



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Lung bacterial challenge

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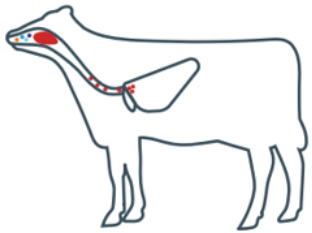
Impaired pulmonary bacterial clearance



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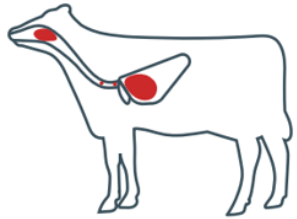
Bacterial bronchopneumonia

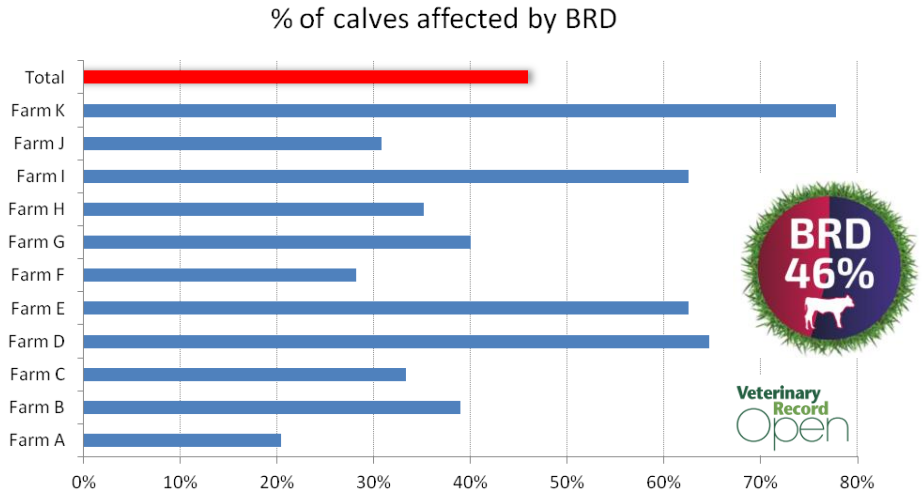


Importance of BRD in dairy calves

Table 10. Main postmortem diagnosis in 65 calves that died in 37 Norwegian dairy herds participating to 2008

Diagnosis	Calves (n)	Proportional rate
Bronchopneumonia	18	27.7
Enteritis	10	15.4
Chronic indigestion	8	12.3
Omphalophlebitis with pyemia, peritonitis, or multifocal hepatitis	4	6.2
Bacteremia/septicemia	4	6.2
Ruminal bloat	2	3.1
Weakborn with bronchopneumonia or bacteremia	2	3.1
Arthritis, purulent	2	3.1
Mesenteric torsion	2	3.1
Abomasal dilatation and peritonitis	1	1.5
Abscess in parotis region	1	1.5
Peritonitis	1	1.5
Pyelonephritis	1	1.5
Small intestine invagination	1	1.5
Inconclusive	8	12.3
Sum	65	100.0

Gulliksen et al, 2009



Johnson et al, 2017

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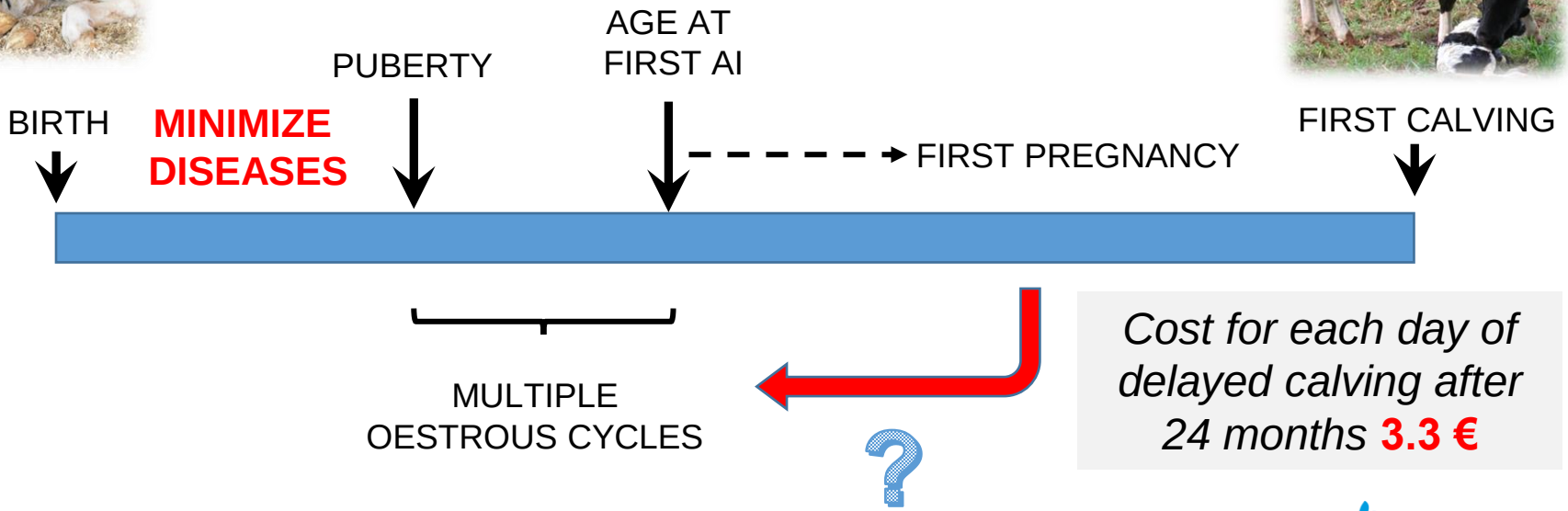
BRD and the lifecycle of heifers

Total costs of heifer rearing
1 700 €



Cost for each day of delayed calving after 24 months **3.3 €**

Pregnancy Loss / Abortion

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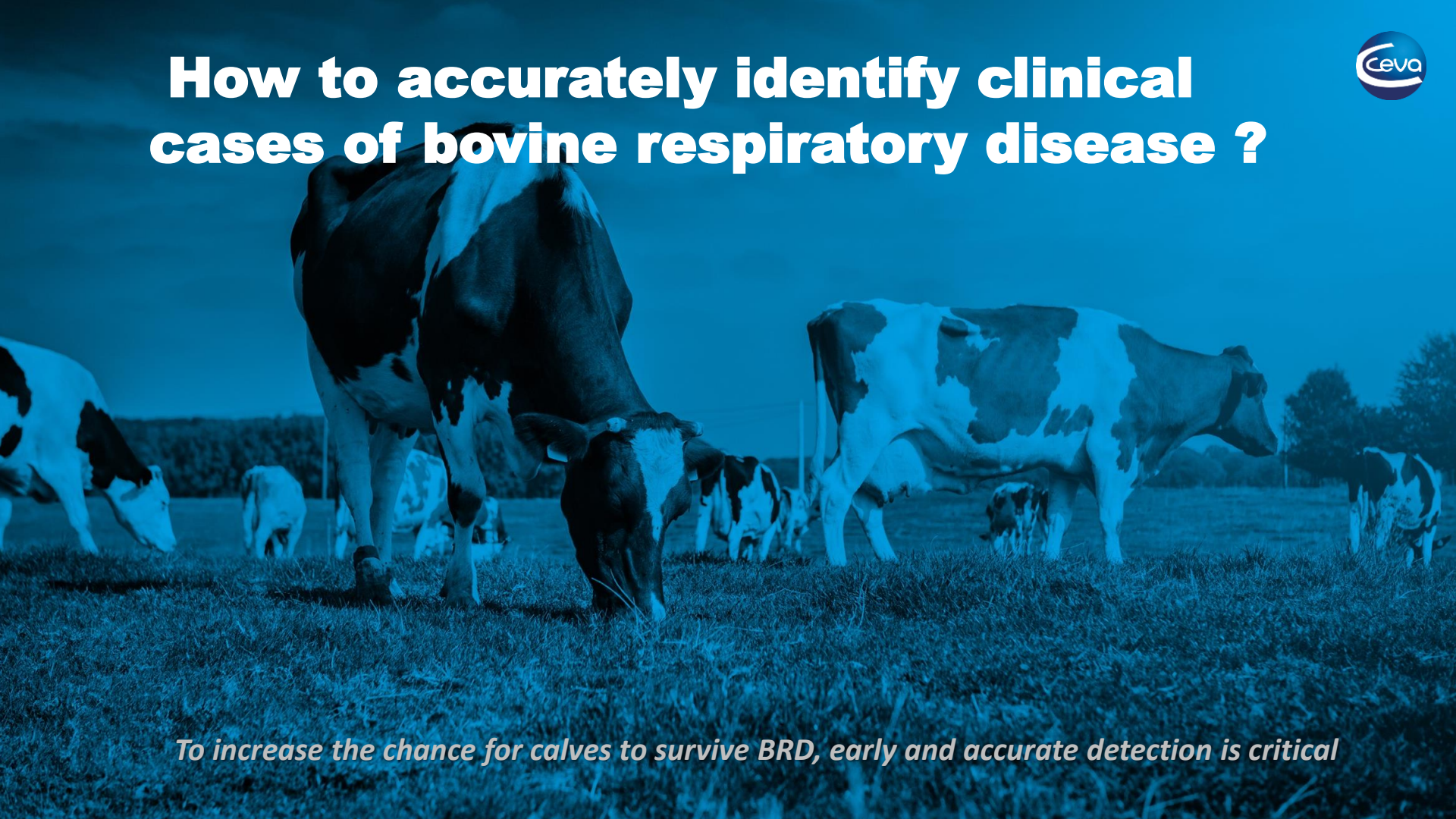
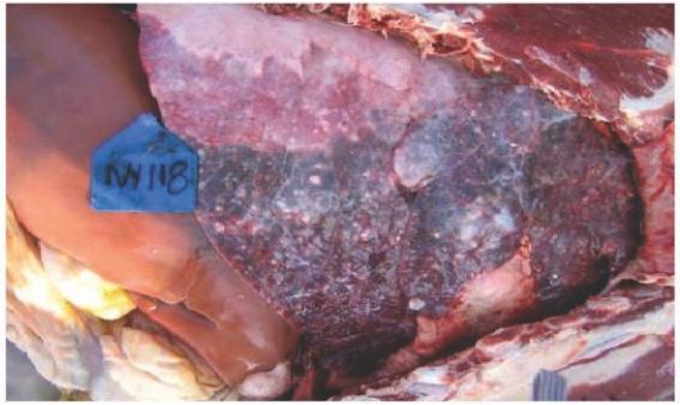
How to accurately identify clinical cases of bovine respiratory disease ?



To increase the chance for calves to survive BRD, early and accurate detection is critical

Why is it critical to detect bronchopneumonia as early as possible

Delay before 1st treatment



Practical consequence
Early detection of BRD is mandatory to avoid untreatable chronic lesions

Hypoxic and necrotic conditions + Abnormal blood flow = Reduced antibiotic distribution

REDUCED EFFICACY WHATEVER THE COMPOUND(S) USED !!!

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Clinical impact

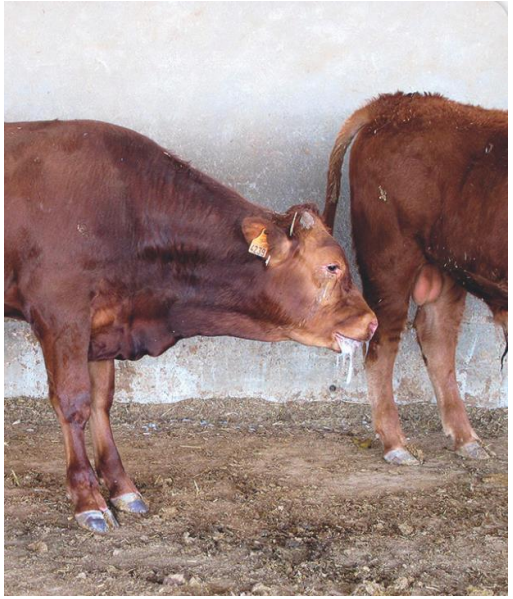
- What characterize bronchopneumonia clinically?

Non specific clinical signs

- Depression
- Fever
- Anorexia

Clinical respiratory signs

- Abnormal or rapid breathing pattern
- Nasal discharge
- Coughing



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Clinical signs can sometimes help to identify the responsible pathogen(s)

VIRUS	BRSV	BHV-1	PI-3	BVDV
CLINICAL SIGNS	Fever, depression, anorexia, tachypnea, nasal discharge (±), coughing, ***expiratory dyspnea, subcutaneous emphysema***	Fever, depression, anorexia, serous to mucopurulent nasal discharge, ***muzzle hyperemia, nasal plaques***, coughing, ***inspiratory stridor*** (conjunctivitis ± keratitis, abortion)	Like BRSV but more mild, ***commonly asymptomatic***	Like BRSV but more mild, ***commonly asymptomatic***

BACTERIA	*M.haemolytica*	*P.multocida*	*H.somni*	*M.bovis*
CLINICAL SIGNS	Fever, depression, anorexia, ***signs of endotoxemia,*** tachypnea, evidence of pleural pain, mucoid to mucopurulent nasal discharge, coughing (not prominent)	Fever, tachypnea, cough, depression, mucoid to mucopurulent nasal discharge	As for *P. multocida*; possibly also evidence of pleural pain (joint effusion, infertility or abortion, otitis, conjunctivitis, neurologic signs)	Fever, anorexia, tachypnea, cough, nasal discharge; ***chronic or ongoing pneumonia that fails to respond as expected to therapy*** (***joint*** or tendon sheath effusion, ***otitis***, conjunctivitis)

What is the accuracy of clinical signs ?

	White et al, 2009	*Timsit et al, 2016*
BRD *Case Definition*	Clinical signs and RT > 40°C	Clinical signs with or without elevated rectal temperature

- ✓ Feedlots in South Africa (N=2) and USA (N=20)
- ✓ Cattle weight from 235 kg to 344 kg at arrival
- ✓ Comparators = Bayesian methods (no gold standard)

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Sensitivity	**55,7 – 68,4 %** (61,8 %)	**1 – 96 %** (27%)
Specificity	**60,0 – 65,7 %** (62,8 %)	**14 – 100 %** (92%)

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Considerable heterogeneity in clinical diagnostic accuracy among studies

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KEY POINTS

Accuracy of clinical signs to identify BRD cases **is limited**

We need **better (standardized)** detection & confirmation tools

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What is the accuracy of clinical signs ?

- Why this lack of accuracy?
  - ✓ Cattle are prey animals and consequently will often mask signs of sickness (false negative)
  - ✓ Clinical signs typically used to diagnose BRD are not always specific to this disease condition (false positive)
  - ✓ Distant evaluation of cattle is highly subjective
  - ✓ Lack of consensus on the definition of a BRD (*vs.* mastitis for example)

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Clinical Scoring System = the solution ?

"Clinical scoring systems compile clinical data into a single value to assess disease more objectively than an unstructured clinical evaluation alone."

Love et al. 2016

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Clinical Scoring System = the solution ?

“ A simple, objective clinical scoring system to improve and standardize BRD identification in dairy calves without the need for expensive equipment would be a useful tool for farm workers, clinicians, and researchers.”

Love et al. 2014

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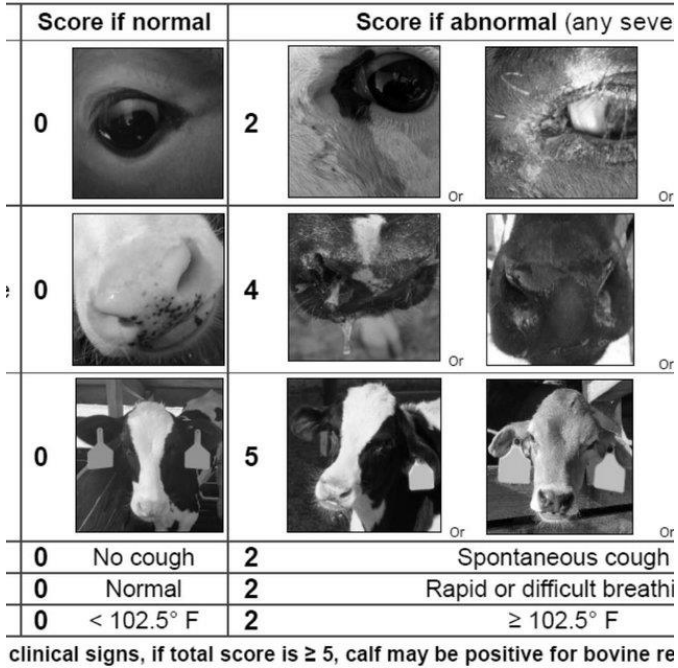
Clinical Scoring System (CSS) = the solution ?

- How does they work?

  - ✓ Scoring systems assign values to clinical signs, which are used to determine a total score
  - ✓ The patient's total score, in turn, should correspond to their risk or likelihood of disease *(e.g. having BRD or not)*
  - ✓ Objective methods should be used to weight scores
  - ✓ Clinical signs that are difficult to measure or require expensive or time-consuming methods to measure should not be included



Clinical Scoring System = the solution ?

- Which one is useful?

  ✓ Clinical scoring systems for BRD are not novel and some can be considered useful to diagnose BRD in cattle

D.A.R.T

- Developed to identify beef cattle for BRD treatment in feedlots *(Depression, Appetite, Respiration, Temperature)*
- Difficult to standardize between locations because the clinical sign weights and decision points are not defined

University of Wisconsin

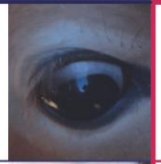
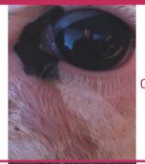
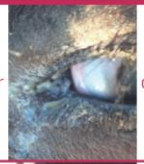
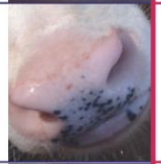
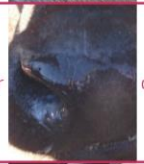
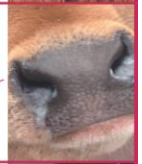
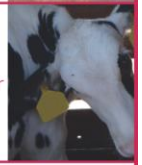
- Based on five clinical signs to identify dairy calves that should be treated for BRD
- Published score weights and a decision rule
- Score subdivided each of its clinical signs into 4 levels can be ambiguous
- Absence of specific weighting between clinical signs

UC Davis

- Simple and validated scoring system
- Each clinical sign is assessed using a dichotomous way *(normal vs. abnormal)*
- Specific chart for pre-weaned and post-weaned dairy calves

Clinical Scoring System = the solution ?

UCDAVIS VETERINARY MEDICINE
International Animal Welfare Training Institute

Clinical sign	Score if normal	Score if abnormal (any severity)*
Eye discharge	0 	2  or  or 
Nasal discharge	0 	4  or  or 
Ear droop or head tilt	0 	5  or  or 
Cough	0 No cough	2 Spontaneous cough
Breathing	0 Normal	2 Rapid or difficult breathing
Temperature	0 <39.2°C	2 ≥39.2°C

- ✓ BRD scoring system for pre-weaned dairy calves
- ✓ Add scores for all clinical signs, if total score is ≥ 5, calf may be positive for BRD
- ✓ Reported performances *(Love et al. 2014)*
  - ✓ Se: 89.4% Sp: 90.8%
  - ✓ Higher performances as a diagnostic *vs.* screening test

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Clinical Scoring System = the solution ?

Clinical sign	Score if normal		Score if abnormal (any severity)[1]	
Sunken eyes	0		4	 Or 
Low body condition	0		5	 Or 
Cough	0	No cough	2	Spontaneous cough
Breathing	0	Normal	1	Rapid or difficult breathing
Diurnal temp fluctuation	0	≤27° F (≤15° C)	1	> 27° F (>15° C)

With diurnal temperature data:
calf is score positive[2] if total score ≥ 2

Without diurnal temperature data:
calf is score positive[2] if total score ≥ 1

Confirmatory step for score positive[3]	Do not treat	Treat
Rectal temperature	< 102.5° F (< 39.2° C)	≥ 102.5° F (≥ 39.2° C)

- ✓ BRD scoring system for weaned dairy calves
- ✓ Does not require handling of calves for preliminary diagnosis (RT done in a second step)
- ✓ Reported performances *(Maier et al. 2019)*
  - ✓ Screening Se: 77%
  - ✓ Diagnostic Se: 100%
  - ✓ Specificity: 61.9%

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Clinical Scoring System = the solution ?

- What is positive
  - ✓ First-line diagnostic test easy to use by producers
  - ✓ A "solid" frame for BRD screening or diagnostic (less place for subjectivity)
  - ✓ Stimulate the implementation of a treatment protocol (rationalization of the treatment)
  - ✓ Useful to monitor within-herd prevalence of BRD

- Some weaknesses
  - ✓ Learning process (training necessary)
  - ✓ Performances not perfect

What about rectal temperature ? Is it useful ?

- **Data from experimental challenges** *Grissett et al. 2015*

✓ Fever is a nonspecific sign of infectious bronchopneumonia that is observed secondary to experimental challenges for all major respiratory pathogens

✓ Onset and duration of increased body temperature is variable depending on the settings and challenges

		VIRUS				BACTERIA		
		BVDV	**BHV-1**	**PI-3**	**BRSV**	***M.h***	***P.m***	***M.b***
FEVER (RT>40°C)	**Onset**	Day 4 *(2-8)*	Day 2 *(1-10)*	Day 7	Day 5 *(1-7)*	Day 1	Day 1	Day 1 *(1-8)*
	Peak	Day 7 *(7-8)*	Day 4 *(3-10)*	NR	Day 6 *(5-8)*	Day 1	Day 1	Day 4.5 *(1-8)*
	Resolution	Day 10	Day 8	NR	Day 8 *(7-10)*	Day 2 *(2-6)*	Day 2	Day 8 *(5-13)*

What about rectal temperature ? Is it useful ?

- **Data from experimental challenges** *Grissett et al. 2015*

✓ Resolution of pyrexia before all CS resolve : for most of BRD pathogens, clinical signs resolved 4–6 days after RT have returned to less than 40°C

✓ CS and fever occur generally concomitantly except for BHV-1 *(peak of fever before peak of CS)* and *M.bovis (peak of fever after peak of CS)*

		VIRUS				BACTERIA		
		BVDV	**BHV-1**	**PI-3**	**BRSV**	***M.h***	***P.m***	***M.b***
FEVER (RT>40°C)	**Onset**	Day 4 *(2-8)*	Day 2 *(1-10)*	Day 7	Day 5 *(1-7)*	Day 1	Day 1	Day 1 *(1-8)*
	Peak	Day 7 *(7-8)*	Day 4 *(3-10)*	NR	Day 6 *(5-8)*	Day 1	Day 1	Day 4.5 *(1-8)*
	Resolution	Day 10	Day 8	NR	Day 8 *(7-10)*	Day 2 *(2-6)*	Day 2	Day 8 *(5-13)*

What about rectal temperature ? Is it useful ?

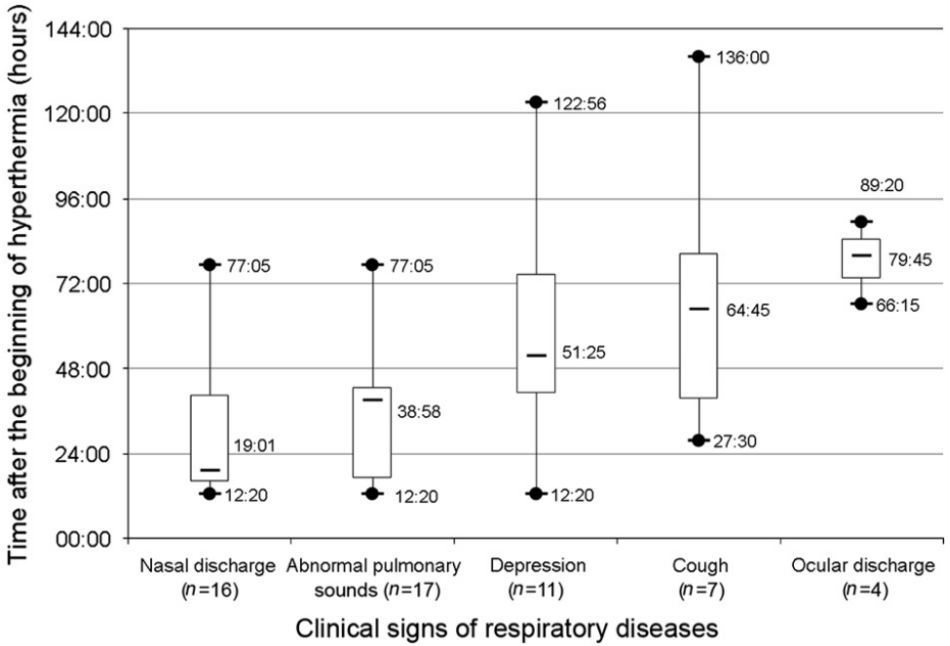
- Data from the field

✓ The accuracy of rectal temperature measurement depends on the thermometer used as well as on the technique used by the operator *(Naylor et al. 2012)*

✓ The onset of BRD signs always occurred after the onset of RH episodes, with a time-lag from 12 to 136 h, depending on BRD signs

Le ThermoBolus®

Timsit et al. 2011



What about rectal temperature ? Is it useful ?

- Bottom line

✓ May allow early detection of BRD cases (reticulo-rumen temperature)

✓ No real consensus on the threshold (39.5°C - 39.7°C - 40.0°C ?)

✓ Not specific enough (clinical examination required to confirm BRD)

- Not all animals with high RT are sick from BRD
- Not in line with rational use of antimicrobials even though better than mass medication

The rectal temperature value of 39.7°C is commonly used as the threshold value for diagnosis of abnormal temperature in young bulls

Lhermie et al., 2017

Is thoracic auscultation a good confirmatory test ?

- Diagnostic performances of TA

  ✓ Most of veterinarians base their diagnosis of BP on thoracic auscultation which is rapid and easy to perform

  - Examination usually focus on the middle and ventral parts of the thorax
  - Abnormal lung sounds includes *increased bronchial sounds*, crackles, wheezes, pleural friction rubs and the absence of respiratory noises

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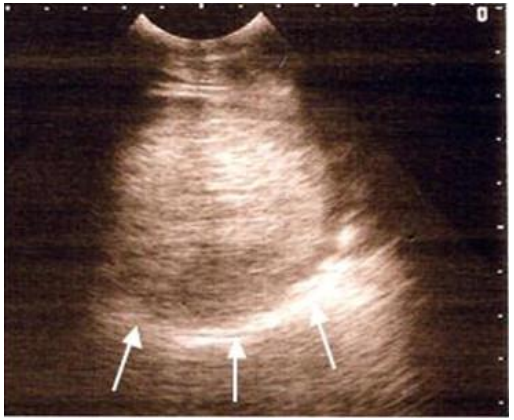
Is thoracic auscultation a good confirmatory test ?

- Diagnostic performances of TA
  - ✓ In sheep, thoracic auscultation has been shown to have limitations because it can be relatively normal despite extensive lung lesions *(Scott et al. 2010)*
    - ➢ Auscultation could not detect focal pleural abscesses (up to 10 cm diameter)
  - ✓ In adult cattle with chronic suppurative pneumonia, auscultation failed to identify the nature and extent of lung pathology (Scott, 2013)



Is thoracic auscultation a good confirmatory test ?

- Diagnostic performances of TA
  - ✓ The sensitivity of auscultation was found to be poor to detect lung consolidation in young dairy calves *(Buczinski et al., 2014)*
  - ✓ In a subsequent field study, TA was found sensitive (72.9%), but not specific (53.3%) to diagnose BP *(Buczinski et al., 2016)*
  - ✓ This apparent discrepancy was attributed to bronchial sounds (included in the latter study)
  - ✓ Thoracic auscultation can improve the accuracy of a clinical examination score alone

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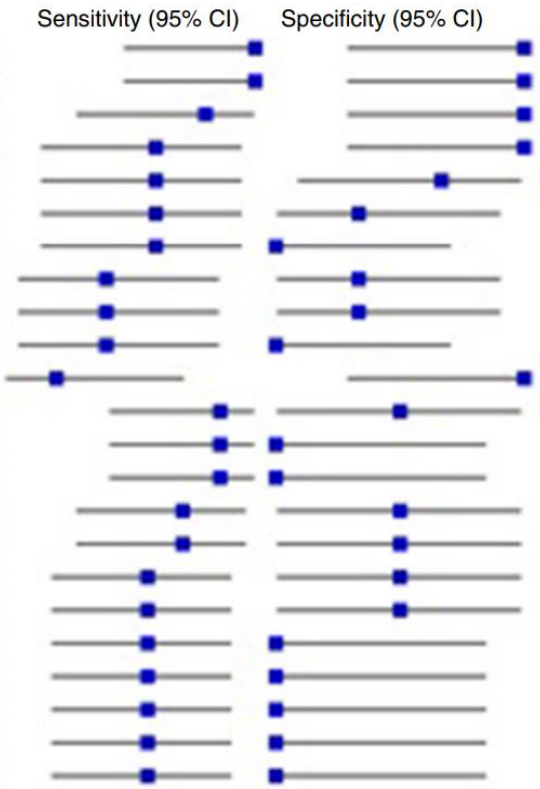
Is thoracic auscultation a good confirmatory test ?

- To what extent diagnostic accuracy of lung auscultation varies between different practitioners?
  - ✓ 49 Dutch veterinarians each auscultated between 8 and 10 calves and make their decision to treat the animal with antimicrobials or not
  - ✓ Their decisions were compared with lung ultrasonography findings
  - ✓ The average sensitivity and specificity of lung auscultation were 0.63 and 0.46 respectively (poor)
  - ✓ Very poor reliability between multiple raters was found (Kalpha = 0.18)



Pardon et al. 2019

Thoracic auscultation is of limited value to identify the responsible pathogen(s)

VIRUS	BRSV	BHV-1	PI-3	BVDV
CLINICAL SIGNS	Harsh bronchovesicular sounds over cranioventral lung, crackles and wheezes rarely, ***quiet lung sounds caused by pneumothorax***	Not specifically described	Not specifically described	Not specifically described

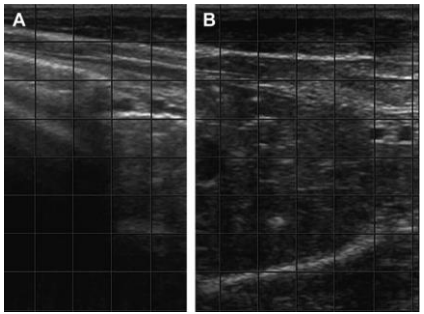
BACTERIA	*M.haemolytica*	*P.multocida*	*H.somni*	*M.bovis*
CLINICAL SIGNS	Harsh bronchovesicular sounds over cranioventral lung ± crackles	Harsh bronchovesicular sounds over cranioventral lung ± crackles	Not specifically described	Not specifically described

Is thoracic ultrasound (TUS) a good confirmatory test ?

- Diagnostic performances of TUS

✓ TUS is able to detect BRD-induced lung lesions more specifically *consolidation*

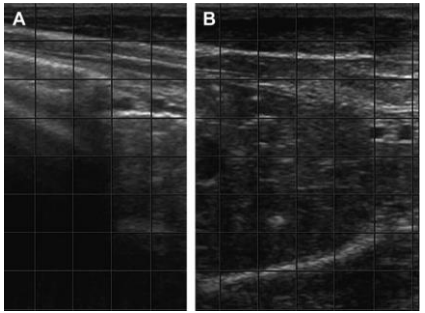
✓ The presence of *lung consolidation* is a reliable parameter to monitor even if the operator does not have a strong expertise on medical ultrasonography



✓ With expertise, time-to-results = 2 min per calf

Is thoracic ultrasound (TUS) a good confirmatory test ?

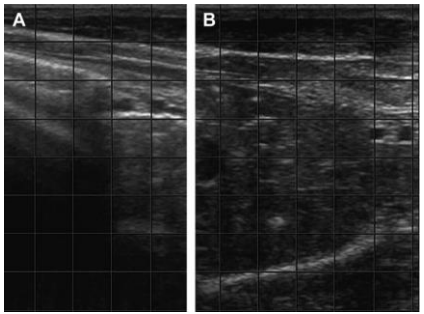
Study	Study Summary	Test Under Investigation	Reference Standard Test	Were Possible Misclassifications of the Reference Standard Test Accounted For?	Sensitivity: 95% CI or BCI (%)	Specificity: 95% CI or BCI (%)	Comments
Ollivett et al,[43] 2015	25 dairy calves (1–12 wk old) with normal WRSC <5	TUS positive if any nonaerated lung visible	Necropsy	No	94 (69–100)	100 (64–100)	2-gate design calves were selected if normal WRSC and stratified by ultrasonography findings to be compared with necropsy
Zeineldin et al,[42] 2016	Feedlot calves 6–8 mo old, 24 cases and 24 matched control calves	TUS (7th-11th ICS) positive if heterogenous hyperechoic or echoic area	Pen-rider examination	No	70.8	87.5	2-gate design
Berman et al,[16] 2019	209 veal calves and 301 preweaned dairy calves	TUS positive if consolidation depth ≥3 cm not considering site cranial to the heart	WRSC and serum haptoglobin	Reference standards uncertainty was accounted for using a bayesian latent class model	89 (55–100)	95 (92–98)	1-gate design Other ultrasonographic thresholds including or not cranial sites accuracy are also mentioned



Buczinski and Pardon, 2020

Is thoracic ultrasound (TUS) a good confirmatory test ?

- Animal's performance with consolidated lungs
  - ✓ Lung consolidation (using TUS) at weaning has been associated with increased risk of being culled before calving *(Adams et al., 2016)*
  - ✓ Lung consolidation at weaning has also been associated with decreased reproductive performances *(Teixera et al. 2017)*
  - ✓ Milk production has been found to be decreased in the 1st lactation of Holstein dairy calves with consolidated lungs *(Dunn et al., 2018)*

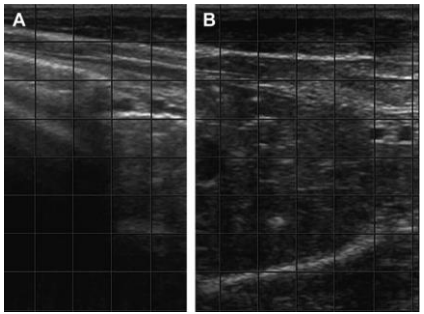


Is thoracic ultrasound (TUS) a good confirmatory test ?

- Drawbacks of TUS

  - ✓ Training and equipment needed

  - ✓ It is not currently possible to distinguish active lung infection lesions that would benefit from treatment from lesions that are a sequela of previous disease for which treatment would not be beneficial



Se vs Sp: what should drive the diagnostic performances ?

- Why this debate?
  - ✓ From a welfare perspective, sensitivity is important because delay in detection can be associated with animal suffering and increased risks of treatment failure
  - ✓ In feedlot calves, increasing diagnostic specificity created more rapid, positive change in net returns than increasing sensitivity *(Theurer et al., 2015)*
  - ✓ The specificity is also important for avoiding unnecessary antimicrobial treatment

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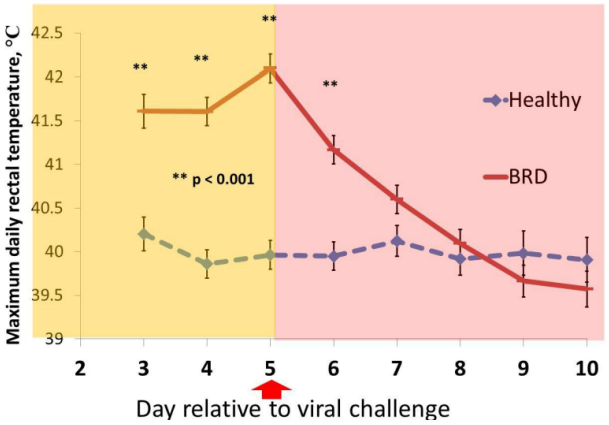
Short & long-term impacts of BRD in dairy calves

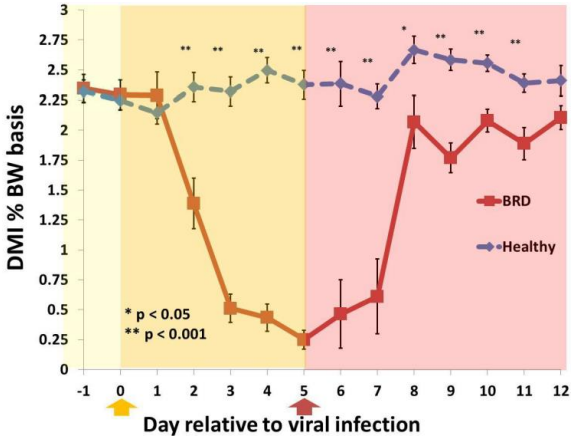
BRD is a major disease in dairy heifers. Recent data highlight the impact BRD has for the whole life of affected animals.

BRD has an immediate impact on calves

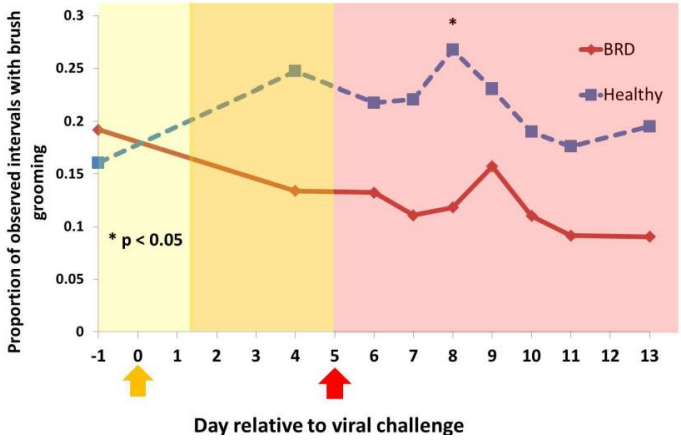
RECTAL TEMPERATURE



FEEDING BEHAVIOR



GROOMING
(brush contact, self-licking)



Sickness response in beef steers

Toaff-Rosenstein et al, 2016

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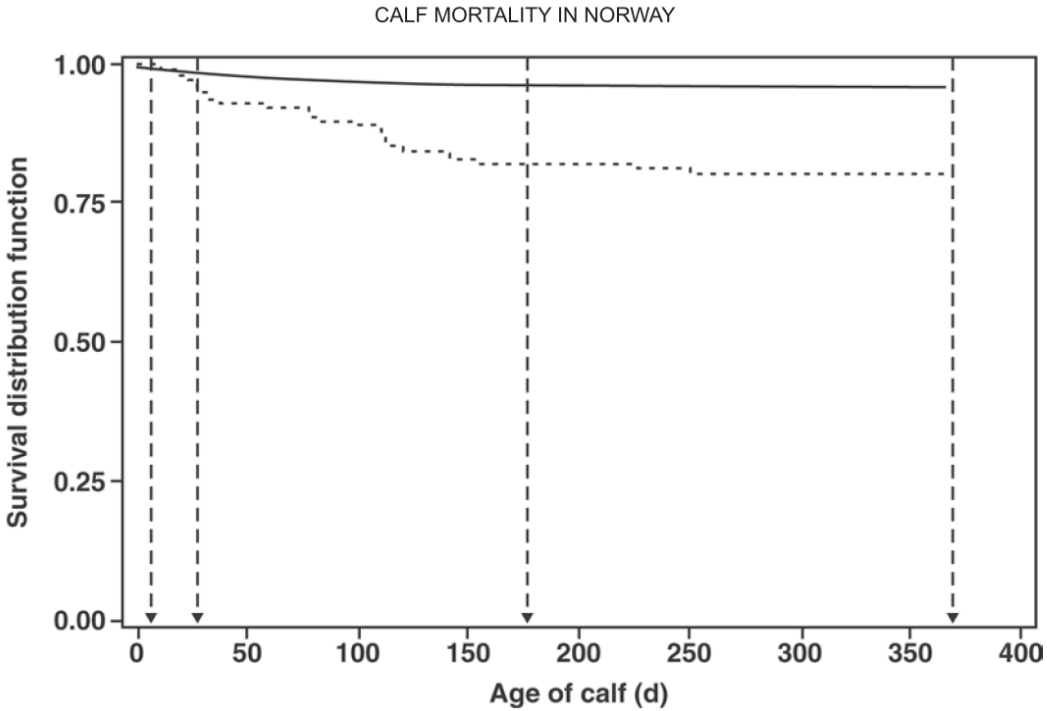
BRD & Survival

Calves with BRD have a higher risk of mortality



Survival distribution for calf mortality in 125 Norwegian dairy herds including calves (n = 5104) previously registered with (…) or without (---) respiratory disease during their first year of life

Gulliksen et al, 2009

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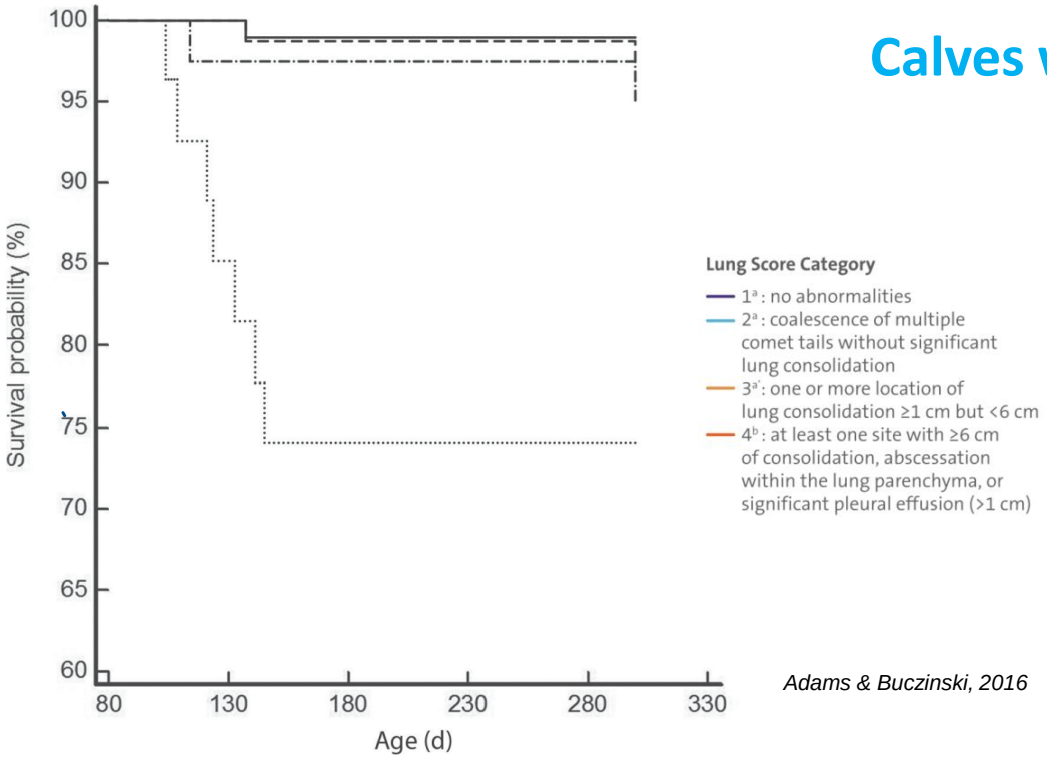
BRD & Survival



Adams & Buczinski, 2016

Calves with BRD have higher culling rates

Dairy calves with extensive lung consolidation, evidence of abscessation or pleural effusion **had significantly greater risk of dying or being culled (26%)** than calves with normal lungs (1%)

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BRD & Growth

Calves with BRD have a decreased growth

Table 2. Linear regression of the ADG of heifers (estimates ± SE; *P*-values in parentheses) from approximately 2 to 13 mo of age recorded during housing in 4 barns with random effects for source farm and weekly enrollment cohort

Variable[1]	Between 2 and 3 mo	Between 3 and 6 mo	Between 6 and 9 mo	Between 9 and 13 mo
Number	1,373	1,332	1,300	1,269
Intercept	0.70 ± 0.11 (<0.001)	0.37 ± 0.11 (0.01)	0.91 ± 0.07 (<0.001)	1.25 ± 0.08 (0.07)
BRD60+ (Referent = BRD60−)	−0.17 ± 0.01 (<0.001)	−0.07 ± 0.02 (<0.001)	−0.04 ± 0.01 (0.001)	(0.83)

BRD was associated with **reduced ADG between 2 and 9 months of age** and resulted in a 14.3 kg decrease in BW for calves with BRD at approximately 13 months of age

Stanton et al, 2012

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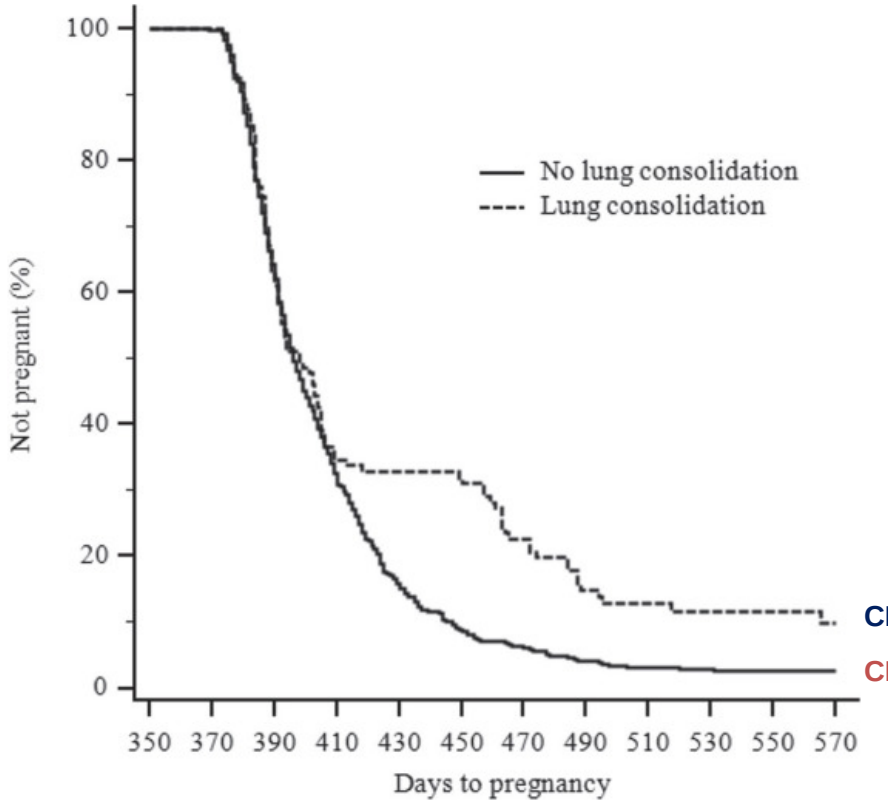
BRD & Reproduction



Calves with BRD have decreased reproductive performances

CR at 1st AI = 52%

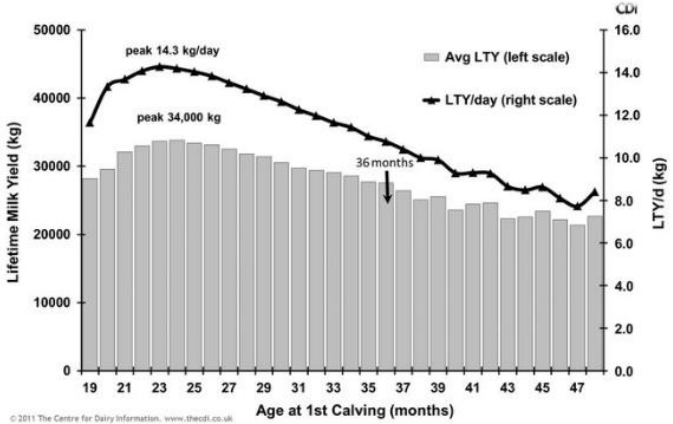
CR at 1st AI = 62%

Teixeira et al., 2017

BRD & Calving

Calves with BRD have a delayed AFC

The median age at first calving for heifers with and without BRD was **714** (95% CI: 705–723) **and 702** (95% CI: 699–705) **days**, respectively



Controlling for source farm, enrollment cohort, and antimicrobial treatment, **the odds of calving by 25 months of age were 0.6** (95% CI: 0.4 to 0.8) **times lower in calves with BRD** (P = 0.01)

Stanton et al, 2012

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BRD & Calving

Calves with BRD have increased risk for dystocia

Heifers with BRD were **1.5 times more likely to have a calving ease score ≥2 at their first calving** (95% CI: 1.1–2.2) compared with heifers without BRD

Stanton et al, 2012

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BRD & Milk production

Calves with BRD can have a reduced milk yield

The presence of lung consolidation (LC), at least once in the first 8 weeks of life did result **in a 525 kg decrease in first-lactation 305-d milk production**

(95% confidence interval: −992.81 to −60.25)

Dunn et al, 2018

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What is important to remember?

BRD & CALVES

- BRD = still the number 1 disease affecting young calves
- To improve the situation = early and accurate detection is critical
- Combine use of several tools is necessary to obtain better results (clinical scores, rectal temperature, lung auscultation, TUS)
- BRD directly impact the well-being of calves and is associated with decrease growth, delayed AFC, increased culling risks, increase risk of dystocia and decrease milk productivity

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Thank you for
your attention !