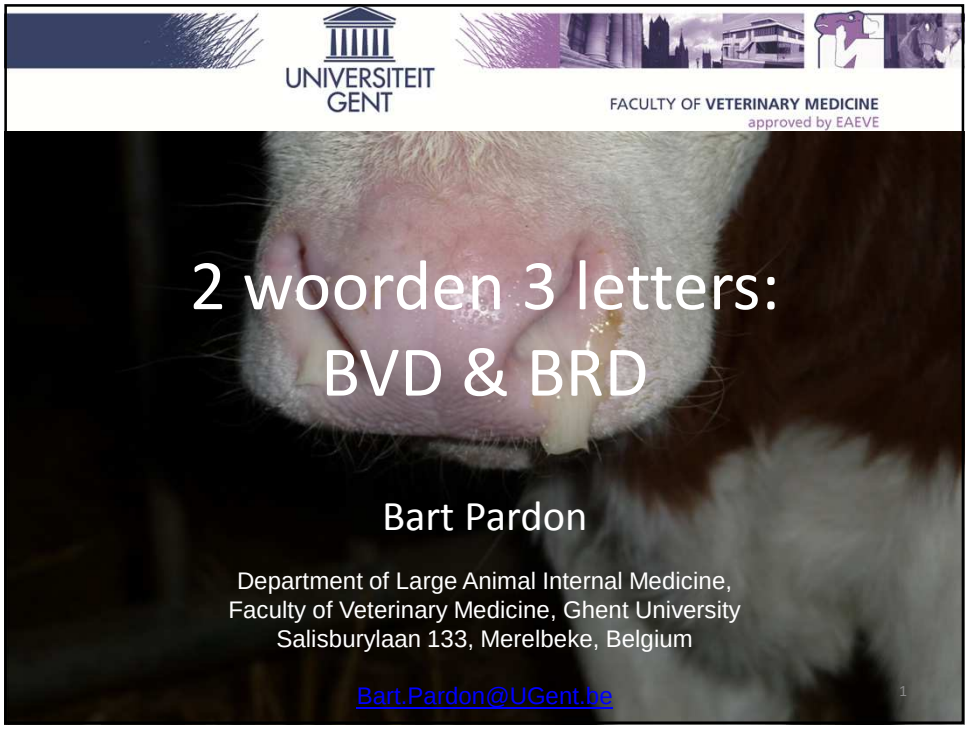
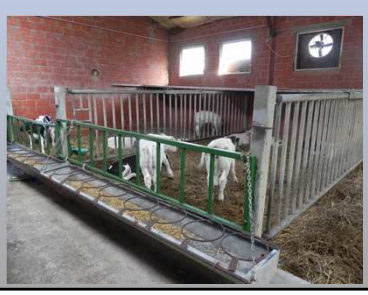
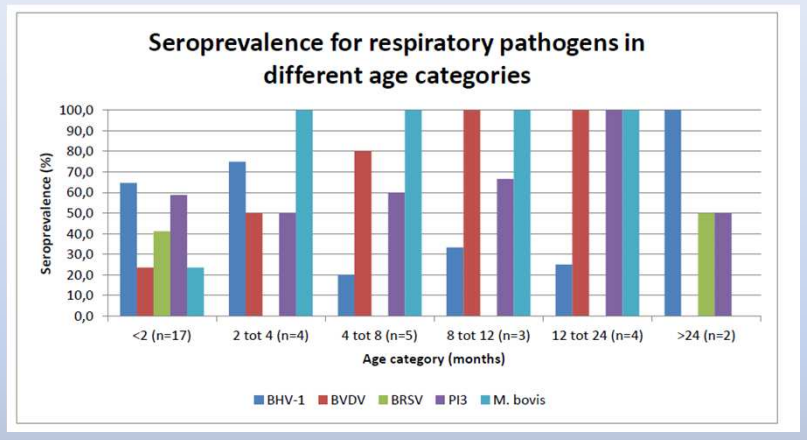
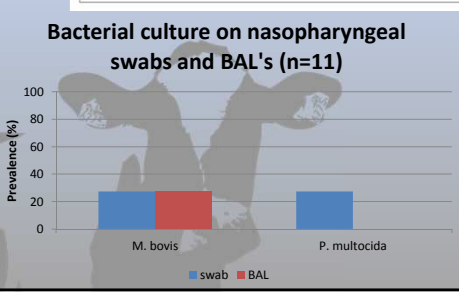


Uit de praktijk… (1)

- 150 dikbillen
- Laatste jaar:
  - Veel hoest bij kalveren <4 maand, weinig respons op therapie
  - 50% moet individueel behandeld worden
  - 10% gestorven
  - (8/12 chronische gevallen)







- Follow-up
  - 1 IPI
  - Maanden aangehouden
  - Uiteindelijk euthanasie
  - Earnotchen gestart
  - 2 dieren moeten injecteren

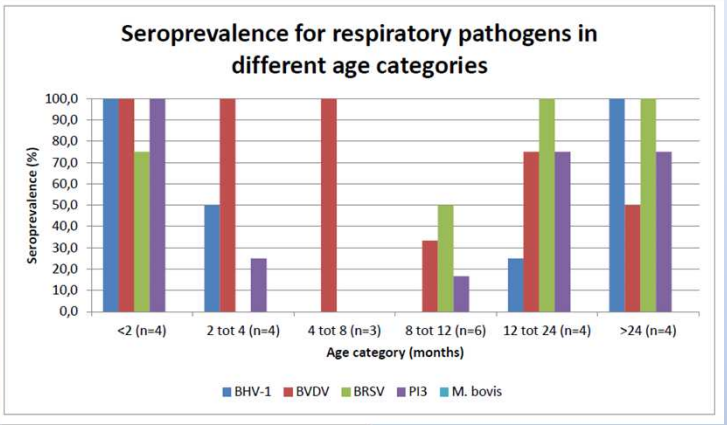
3

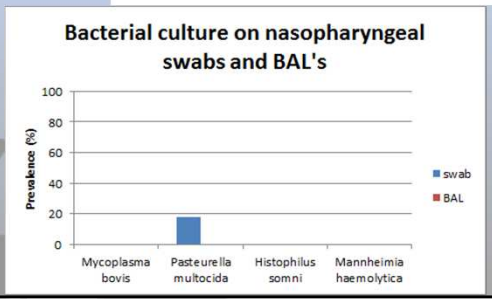
Uit de praktijk…(2)

Rode Holstein, 83 lacterende dieren
Klacht:

- Altijd hoest bij jongvee (< 2 maand)
- Teveel hervallers (100% moeten behandelen)
- Veel diarreeproblemen

4





Evolutie:
- 3 dragers gevonden, onmiddellijk weg

(alles PCR)
- Vaccinatie
- Geen sterfte, geen enkel dieren meer moeten behandelen

5

Praktijktip…dogma?

- “Longproblemen bij kalveren die erger zijn dan normaal? BVDV zit eronder. Haal het weg en het is opgelost”

6

½ TRUTH + ½ TRUT

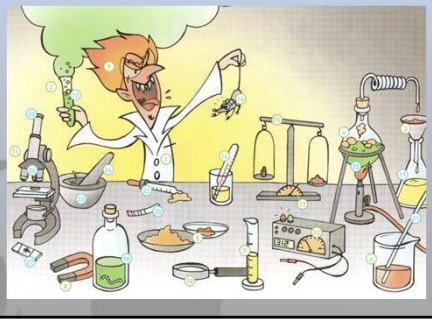
Bedrijf 1:
- Geen koemelk meer
- Individuele huisvesting tot 8 weken
- FPT: meer biest eigen moeder
- Reiniging en desinfectie

Bedrijf 2:
- Individuele huisvesting in iglo's
- Preventie diarree
- Opening inlaat verkleind
- Tochtrisico's weggenomen
- tot 4 weken
- FPT: meer biest eigen moeder
- Reiniging en desinfectie

7

Inhoud

- Welk wetenschappelijke bewijs bestaat er voor de rol van BVDV in het BRD complex??
  - Hoe zit het in het labo? (Fundamenteel)
  - Hoe vertaalt zich dat naar het veld?



Veroorzaakt BVDV BRD?

- Meta-analyse Grissett et al.
- 12 BVDV trials (infectie veld of experimenteel)
- Gemiddeld 15,5 dagen opvolging en 10 kalveren
- BVDV1 en BVDV2 samen
- Infectie= intranasaal of aerosol
- Gemiddeld
  - Na 2 dagen kliniek
  - Symptomen weg binnen 15 dagen
  - (koorts begint tss 2-8 d, gemiddeld 10 dagen)

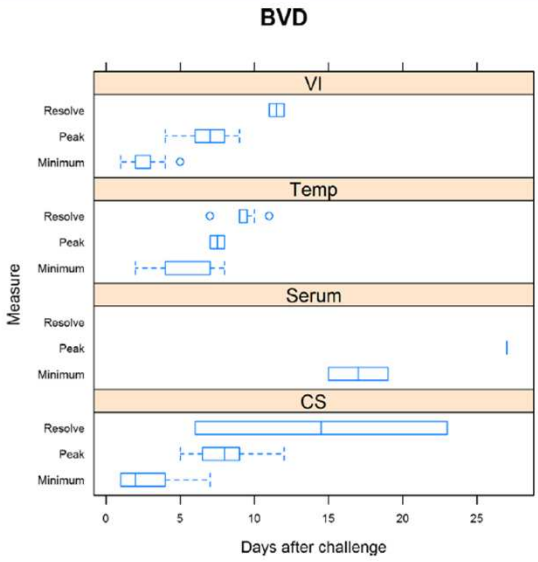


Fig 1. Summary of bovine viral diarrhea trials. For virus isolation, minimum is defined as the day when shedding was first detected, peak is when shedding was at the maximum, and resolution when shedding ceased. For rectal temperature (Temp), minimum is defined as the day when rectal temperature first exceeded 40°C, peak when rectal temperature was highest, and resolution defined as when rectal temperature was less than 40°C. For serum neutralization (Serum), minimum is defined as the day when seroconversion was first detected and peak when serum neutralization was highest. For clinical signs, minimum is defined as the day when clinical signs were first detected, peak being when clinical signs were the most severe, and resolution when clinical signs resumed normal limits.

Hoe veroorzaakt BVDV BRD?

- Infecteert BVDV respiratoire cellen?
- Immunosuppressief effect?
- Synergisme tussen BVDV en andere BRD pathogenen?

"BVDV's role in causing respiratory tract disease is attributable, indirectly, to effects on the host's immune system, not to infection of the lungs."
(Brodersen and Kelling, 1998)

11

Viral Antigen Distribution in the Respiratory Tract of Cattle Persistently Infected with Bovine Viral Diarrhea Virus Subtype 2a

A. W. Confer, R. W. Fulton, D. L. Step, B. J. Johnson, and J. F. Ridpath

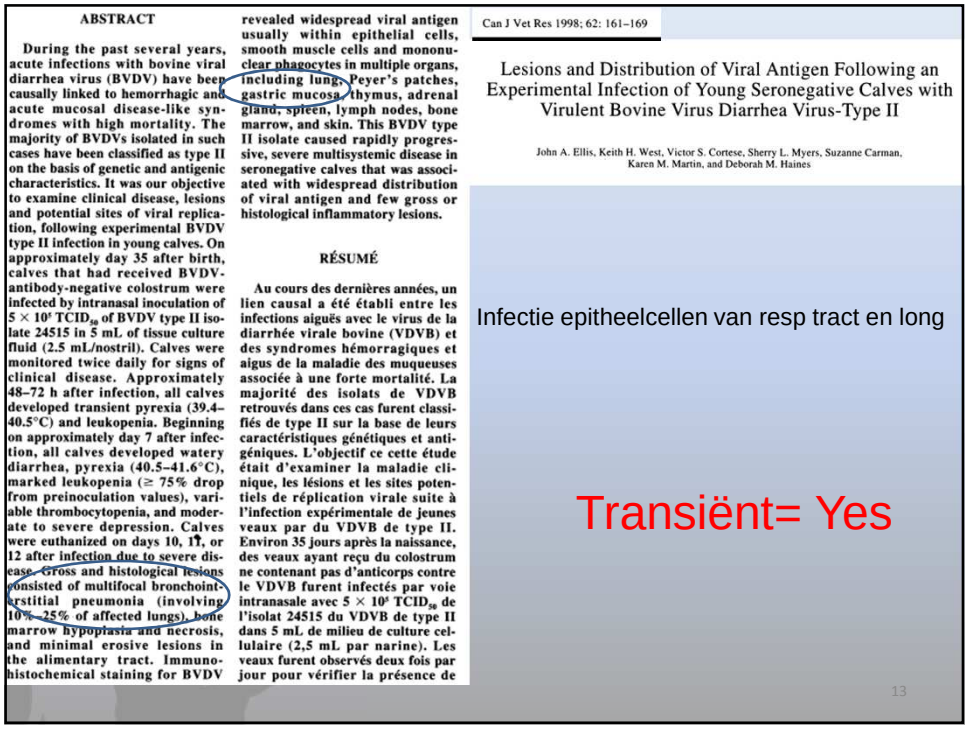
Departments of Veterinary Pathobiology (AWC, RWF) and Clinical Sciences (DLS), and The Oklahoma Animal Disea Diagnostic Laboratory (BJJ), Oklahoma State University, College of Veterinary Medicine, Stillwater, OK; and The National Animal Disease Center, USDA—ARS, Ames, IA (JFR)

Abstract. Tissues were obtained at necropsy from the nasal vestibule, turbinates, nasopharynx, trachea, tracheobronchial bifurcation, and lung from each of 10 clinically healthy calves persistently infected (PI) with bovine viral diarrhea virus (BVDV) serotype 2a. Tissues from the nasal vestibule were obtained by biopsy from five additional PI calves. Formalin-fixed tissues were processed for immunohistochemistry to localize the distribution of BVDV throughout the respiratory tract. Antigen distribution and intensity were subjectively evaluated. Throughout the respiratory tract, mononuclear leukocytes, vascular smooth muscle, and endoneural and perineural cells had BVDV immunoreactivity (BVDV-IR). Multifocally, squamous and ciliated columnar epithelium throughout the respiratory tract contained weak to moderate BVDV antigen. Viral antigen was not seen in goblet cells. BVDV-IR in mixed tubuloalveolar glands of the nasal cavity was weak to strong in serous secretory cells and ductular epithelium. Chondrocytes of the concha often contained BVDV antigen diffusely. Nasal mucus-secreting and tracheobronchial glands multifocally contained weak viral signal. In all cases, alveolar macrophages had moderate to strong BVDV-IR, whereas BVDV-IR in alveolar epithelial cells was weak to moderate. BVDV was present in ~~interalveolar leukocytes and mesenchymal~~ cells. Results indicate that serous secretions of the nasal cavity, productive viral infection of epithelium, and infected leukocytes in respiratory secretions are likely major sources of infectious BVDV from PI calves. The presence of BVDV antigen in respiratory epithelium is, at least, indirect support for the notion that this virus predisposes PI cattle to secondary microbial infections.

Vet Pathol 42:192–199 (2005)

IPI= yes!

12



ABSTRACT

During the past several years, acute infections with bovine viral diarrhea virus (BVDV) have been causally linked to hemorrhagic and acute mucosal disease-like syndromes with high mortality. The majority of BVDVs isolated in such cases have been classified as type II on the basis of genetic and antigenic characteristics. It was our objective to examine clinical disease, lesions and potential sites of viral replication, following experimental BVDV type II infection in young calves. On approximately day 35 after birth, calves that had received BVDV-antibody-negative colostrum were infected by intranasal inoculation of 5×10^5 $TCID_{50}$ of BVDV type II isolate 24515 in 5 mL of tissue culture fluid (2.5 mL/nostril). Calves were monitored twice daily for signs of clinical disease. Approximately 48–72 h after infection, all calves developed transient pyrexia (39.4–40.5°C) and leukopenia. Beginning on approximately day 7 after infection, all calves developed watery diarrhea, pyrexia (40.5–41.6°C), marked leukopenia (≥ 75% drop from preinoculation values), variable thrombocytopenia, and moderate to severe depression. Calves were euthanized on days 10, 11, or 12 after infection due to severe disease. Gross and histological lesions consisted of multifocal bronchointerstitial pneumonia (involving 10%–25% of affected lungs), bone marrow hypoplasia and necrosis, and minimal erosive lesions in the alimentary tract. Immunohistochemical staining for BVDV revealed widespread viral antigen usually within epithelial cells, smooth muscle cells and mononuclear phagocytes in multiple organs, including lung, Peyer's patches, gastric mucosa, thymus, adrenal gland, spleen, lymph nodes, bone marrow, and skin. This BVDV type II isolate caused rapidly progressive, severe multisystemic disease in seronegative calves that was associated with widespread distribution of viral antigen and few gross or histological inflammatory lesions.

RÉSUMÉ

Au cours des dernières années, un lien causal a été établi entre les infections aiguës avec le virus de la diarrhée virale bovine (VDVB) et des syndromes hémorragiques et aigus de la maladie des muqueuses associée à une forte mortalité. La majorité des isolats de VDVB retrouvés dans ces cas furent classifiés de type II sur la base de leurs caractéristiques génétiques et antigéniques. L'objectif ce cette étude était d'examiner la maladie clinique, les lésions et les sites potentiels de réplication virale suite à l'infection expérimentale de jeunes veaux par du VDVB de type II. Environ 35 jours après la naissance, des veaux ayant reçu du colostrum ne contenant pas d'anticorps contre le VDVB furent infectés par voie intranasale avec 5×10^5 $TCID_{50}$ de l'isolat 24515 du VDVB de type II dans 5 mL de milieu de culture cellulaire (2,5 mL par narine). Les veaux furent observés deux fois par jour pour vérifier la présence de

Can J Vet Res 1998; 62: 161–169

Lesions and Distribution of Viral Antigen Following an Experimental Infection of Young Seronegative Calves with Virulent Bovine Virus Diarrhea Virus-Type II

John A. Ellis, Keith H. West, Victor S. Cortese, Sherry L. Myers, Suzanne Carman, Karen M. Martin, and Deborah M. Haines

Infectie epitheelcellen van resp tract en long

Transiënt= Yes

13

Synergisme

- BVDV en BRSV:
  - Ergere symptomen (Brodersen en Kelling, 1998)
- BVDV en Mycoplasma: NS (Prsyliak et al. 2011)
- …

14

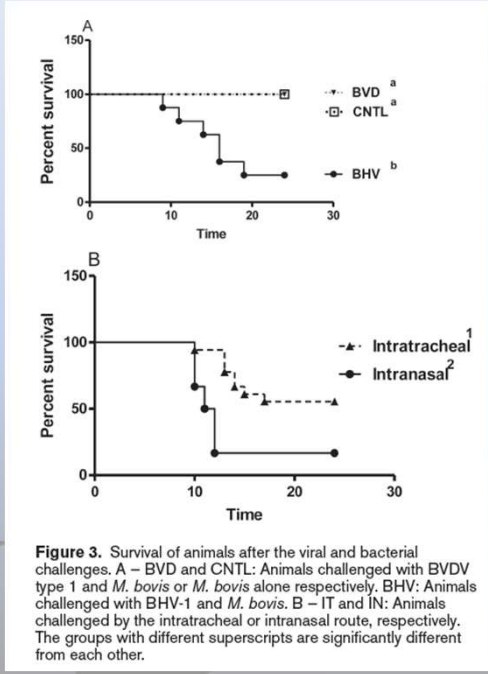


Figure 3. Survival of animals after the viral and bacterial challenges. A – BVD and CNTL: Animals challenged with BVDV type 1 and *M. bovis* or *M. bovis* alone respectively. BHV: Animals challenged with BHV-1 and *M. bovis*. B – IT and IN: Animals challenged by the intratracheal or intranasal route, respectively. The groups with different superscripts are significantly different from each other.

Prsyliak et al. 2011

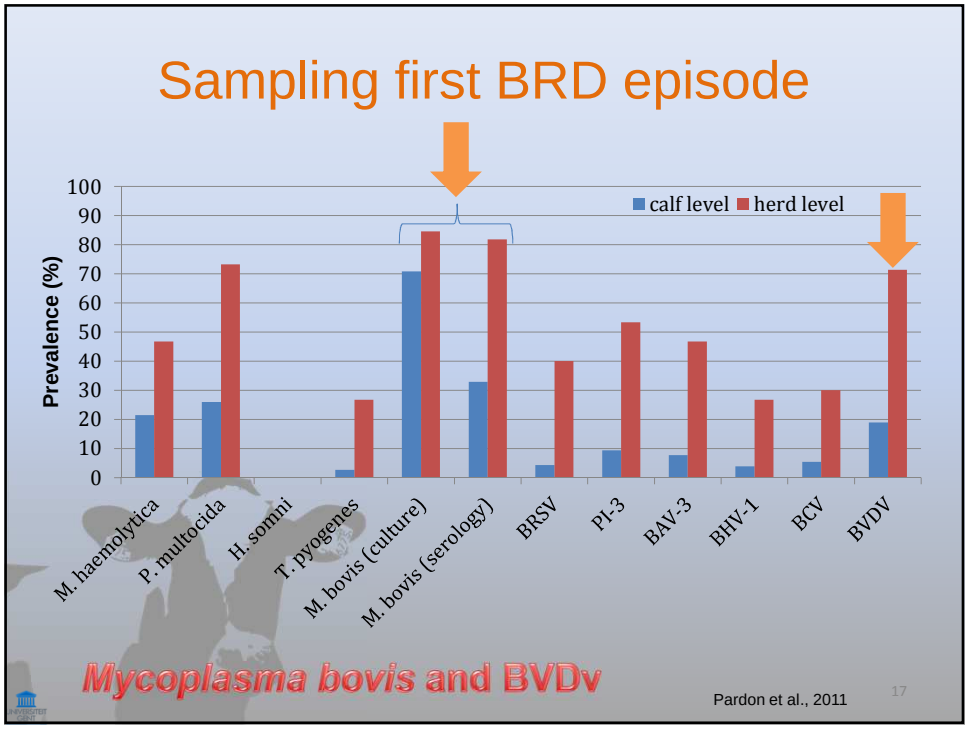
- *M. bovis* wel met BHV-1 niet met BVDV

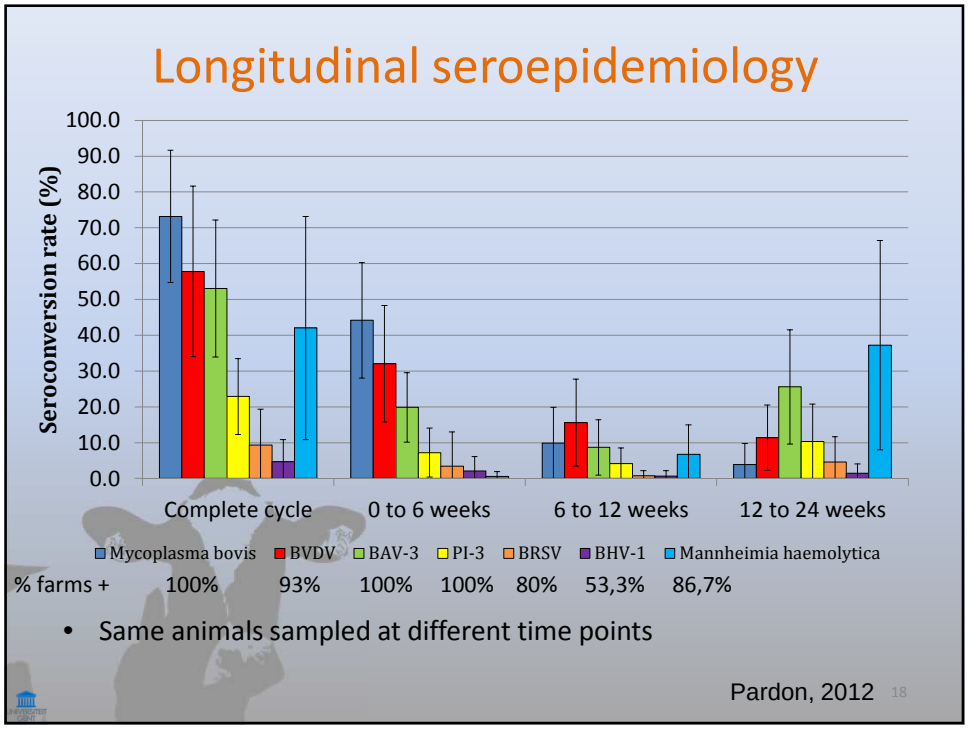
15

In het veld?

- Hoe loopt het met IPI's af?
- Welk effect heeft transiënte infectie op:
  - BRD-risico
  - Dagelijkse groei (ADG)
  - Slachtgewicht (BW)
  - Mortaliteit

16


Sampling first BRD episode
Prevalence (%)
100
90
80
70
60
50
40
30
20
10
0
calf level
herd level
M. haemolytica
P. multocida
H. somni
T. pyogenes
M. bovis (culture)
M. bovis (serology)
BRSV
PI-3
BAV-3
BHV-1
BCV
BVDV
Mycoplasma bovis and BVDv
Pardon et al., 2011
17


Longitudinal seroepidemiology
Seroconversion rate (%)
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
Complete cycle
0 to 6 weeks
6 to 12 weeks
12 to 24 weeks
Mycoplasma bovis
BVDV
BAV-3
PI-3
BRSV
BHV-1
Mannheimia haemolytica
% farms +
100%
93%
100%
100%
80%
53,3%
86,7%
• Same animals sampled at different time points
Pardon, 2012
18

BVDV

- 2,1% is BVDV positive at arrival
- 0,6% is persistently infected (IPI)
- 2/3 IPI's dies
- BVDV positive at necropsy
  - Higher odds for pneumonia (OR= 21,6 (5,7-81,9))
  - Higher odds for pleuritis (OR= 4,9 (1,5-16,3)).

Feedlots: same story (Shahriar et al., 2002)

Pardon et al., 2012; Pardon, 2012

19

In het veld?

- Hoe loopt het met IPI's af?
- Welk effect heeft transiënte infectie op:
  - BRD-risico
  - Dagelijkse groei (ADG)
  - Slachtgewicht (BW)
  - Mortaliteit

20

BRD-risico

- Feedlot: BRD van 18,8→29,6% (Stevens et al., 2007)
- Feedlot: BVDV exposure→ higher morbidity 56-63% vs. 42%(*P*<0,001) (Grooms et al., 2014)
- Feedlot: meer relapse (*P*=0,04) (Richeson et al., 2012)
- Beef (cow-calf) (n= 1782) (Waldner et al. 2008)

21

BRD risk

Table 3. Effects of weaning management and persistently infected bovine viral diarrhea virus (PI-BVDV) exposure on health of newly received beef calves

	Auction market		Preconditioned			Contrasts,[1] *P* =		
Item	Control	PI-exposed	Control	PI-exposed	SEM	Management	Exposure	Interaction
No. pens[2]	14	14	12	11				
Total BRD morbidity[3], %	67.2	73.7	7.7	5.7	4.30	<0.001	0.50	0.22
Treated once, %	33.1	30.2	3.2	0	4.00	<0.001	0.40	0.96
Day of first treatment	3.0	2.7	2.5	0.9	1.47	0.23	0.33	0.49
Treated twice, %	26.0	25.9	1.1	0.6	3.78	<0.001	0.94	0.95
Day of second treatment	7.3	6.2	4.0	2.6	1.65	0.007	0.30	0.92
Treated thrice, %	8.0	17.5	3.2	4.9	3.08	0.002	0.04	0.15
Day of third treatment	10.7	11.1	7.1	6.1	3.07	0.08	0.90	0.76
Relapse[4], %	50.6	58.5	60.3	100	20.78	0.07	0.09	0.26
Chronically ill[5], %	1.1[b]	7.6[a]	0.4[b]	0.3[b]	2.26	0.03	0.07	0.06
Antibiotic cost, $/calf	18.49	22.55	2.31	2.65	2.01	<0.001	0.10	0.16

[a,b]Means within a row without a common superscript are different ($P < 0.05$).

[1]Management = main effect of weaning management (auction market vs. preconditioned); Exposure = main effect of PI-BVDV exposure (control vs. PI-BVDV exposure); Interaction = management × exposure.

[2]Each pen consisted of 8 to 11 animals depending on block.

[3]Percentage of calves clinically diagnosed with bovine respiratory disease (BRD) and administered antibiotic 1 or more times.

[4]Relapse percentage calculated by dividing the number of calves within each experimental treatment treated with a second antibiotic by the total number of calves in each experimental treatment treated for BRD.

[5]Cattle were classified as chronically ill if 3 antibiotic treatments were administered and ADG ≤ 0.45 kg for the entire 42-d trial.

- Richeson et al., 2012

22

ADG

- Feedlot (n = 5047): Geen effect op ADG (O' Conner et al., 2005)
- Feedlot short or long-term exposure: trend voor eerste 28 dagen (Elam et al., 2008) (vaccinated)
- BRD van 18,8→29,6% (Stevens et al., 2007)
- Feedlot: geen effect (Grooms et al., 2014)
- Feedlot: 220g/dag minder tussen d28 en 42 (*P*<0,001) (Richeson et al., 2012)
- Trend tot minder ADG bij BVDV infectie in *M. haemolytica* model (*P*= 0,09) (n= 24) (Burciaga-Robles et al., 2014)

23

ADG

Table 2. Effects of weaning management and persistently infected bovine viral diarrhea virus exposure on performance of newly received beef calves

	Auction market		Preconditioned			Contrast,[1] *P* =		
Item	Control	PI-exposed	Control	PI-exposed	SEM	Management	Exposure	Interaction
No. pens[2]	14	14	12	11				
BW, kg								
Initial	249	248	250	249	9.26	0.36	0.43	0.58
d 14	257	258	273	273	9.75	<0.001	0.60	0.72
d 28	270	270	285	286	9.09	<0.001	0.57	0.73
d 42	286	283	301	299	7.51	<0.001	0.19	0.71
ADG, kg								
d 0 to 14	0.54	0.77	1.64	1.66	0.19	<0.001	0.16	0.20
d 0 to 28	0.74	0.81	1.25	1.32	0.15	<0.001	0.10	0.97
d 28 to 42	1.10	0.89	1.13	0.90	0.15	0.77	0.003	0.87
d 0 to 42	0.86	0.84	1.21	1.18	0.10	<0.001	0.29	0.99

[1]Management = main effect of weaning management (auction market vs. preconditioned); Exposure = main effect of PI-BVDV exposure (control vs. persistently infected bovine viral diarrhea virus exposure); Interaction = management × exposure.

[2]Each pen consisted of 8 to 11 animals depending on block.

Richeson et al., 2014

24

Lichaamsgewicht

- Feedlot short or long-term exposure: geen effect BW (Elam et al., 2008) (vaccinated)
- Feedlot: geen effect (vaccinated and non-vaccinated) (Grooms et al., 2014)
- NS (Burciaga-Robles et al., 2014)

25

Table 7—Herd-adjusted association between serum anti-BVDV type 1 antibody titers and fall calf weight (kg) accounting for calf sex, calf age at weighing, cow breed and age, whether the calf was a twin, treatment and vaccination history, and body condition score of the cow for 676 beef calves in 26 herds.

Variable	Regression coefficient (β)	95% CI for β		*P* value
		Lower	Upper	
Sex				0.0001
Male	15.1	9.6	20.7	0.0001
Female	Reference category			
Unknown	–32.7	–57.2	–8.2	0.01
Breed				0.0001
British	Reference category			
Continental	15.4	5.4	25.3	0.002
Other breed	6.1	–8.3	20.4	0.40
Unknown breed	–21.3	–66.8	24.1	0.37
Calf age (d)	0.95	0.87	1.04	0.0001
Cow age				0.0001
Bred heifer	–23.3	–29.9	–16.7	0.0001
First-calf heifer	–11.0	–17.9	–4.1	0.002
Mature cow	Reference category			
> 10 years old	–13.6	–27.3	0.1	0.05
Age unknown	14.0	–5.6	33.6	0.16
Twin	–19.1	–32.1	–6.1	0.004
Cow body condition score < 5 of 9	–5.6	–14.5	3.3	0.22
Calf vaccinated before spring turnout				0.32
No vaccine	Reference category			
Live	–21.9	–53.1	9.3	0.17
Inactivated	–18.1	–59.5	23.2	0.58
Ever treated	–13.5	–22.4	–4.5	0.003
BVDV-positive biopsy result	–73.5	–116	–30.9	0.001
BVDV type 1 titer > 1,000	–13.0	–20.3	–5.8	0.0004

Hessman et al. 2009

26

Mortaliteit?

Associations between health and productivity in cow-calf beef herds and persistent infection with bovine viral diarrhea virus, antibodies against bovine viral diarrhea virus, or antibodies against infectious bovine rhinotracheitis virus in calves

Cheryl L. Waldner, DVM, PhD, and Richard I. Kennedy, DVM, PhD

Objective—To measure associations between health and productivity in cow-calf beef herds and persistent infection with bovine viral diarrhea virus (BVDV), antibodies against BVDV, or antibodies against infectious bovine rhinotracheitis (IBR) virus in calves.

Animals—1,7

Procedures—
and type 2 B
tested immun
records and ir

Results—There was no association between the proportion of calves with antibodies against BVDV or IBR virus and herd prevalence of abortion, stillbirth, calf death, or nonpregnancy. Calf death risk was higher in herds in which a PI calf was detected, and PI calves were more likely to be treated and typically weighed substantially less than herdmates at weaning. Calves with high antibody titers suggesting exposure to BVDV typically weighed less than calves that had no evidence of exposure.

Conclusions and Clinical Relevance—BVDV infection, as indicated by the presence of PI calves and serologic evidence of infection in weaned calves, appeared to have the most substantial effect on productivity because of higher calf death risk and treatment risk and lower calf weaning weight. (*Am J Vet Res* 2008;69:916–927)

tion ($P = 0.81$). The association between the presence of a PI calf detected either in the fall or from postmortem samples and the herd risk of calf death approached significance (OR, 1.45; 95% CI, 0.99 to 2.14; $P = 0.06$).

27

Evaluation of economic effects and the health and performance of the general cattle population after exposure to cattle persistently infected with bovine viral diarrhea virus in a starter feedlot

Bill E. Hessman, DVM; Robert W. Fulton, DVM, PhD; David B. Sjeklocha, DVM; Timothy A. Murphy, PhD; Julia F. Ridpath, PhD; Mark E. Payton, PhD

Objective—To evaluate economic effects and health and performance of the general cattle population after exposure to cattle persistently infected (PI) with bovine viral diarrhea virus (BVDV) in a feedlot.

Animals—21,743 high-risk calves from the southeastern United States.

Procedures—PI status was determined by use of an antigen-capture ELISA (ACE) and confirmed by use of a second ACE, reverse transcriptase–PCR assay of sera, immunohistochemical analysis, and virus isolation from sera. Groups with various amounts of exposure to BVDV PI cattle were used. After being placed in the feedlot, identified PI cattle were removed from 1 section, but PI cattle remained in another section of the feedlot. Exposure groups for cattle lots arriving without PI animals were determined by spatial association to cattle lots, with PI animals remaining or removed from the lot.

Results—15,348 cattle maintained their exposure group. Performance outcomes improved slightly among the 5 exposure groups as the risk for exposure to BVDV PI cattle decreased. Health outcomes had an association with exposure risk that depended on the exposure group. Comparing cattle lots with direct exposure with those without direct exposure revealed significant improvements in all performance outcomes and in first relapse percentage and mortality percentage in the health outcomes. Economic analysis revealed that fatalities accounted for losses of $5.26/animal and performance losses were $88.26/animal.

Conclusions and Clinical Relevance—This study provided evidence that exposure of the general population of feedlot cattle to BVDV PI animals resulted in substantial costs attributable to negative effects on performance and increased fatalities. (*Am J Vet Res* 2009;70:73–85)

Intermezzo

The associations of viral and mycoplasmal antibody titers with respiratory disease and weight gain in feedlot calves

S. Wayne Martin, Éva Nagy, Dale Armstrong, Søren Rosendal

Abstract — Blood samples from 32 groups of calves (n = 700) were taken on arrival and after 28–35 days at the feedlot. Eleven groups were housed in feedlots in Ontario, and 21 groups in feedlots in Alberta. Serum antibody titers to bovine viral diarrhea virus (BVDV), bovine respiratory syncytial virus (BRSV), parainfluenza virus type 3 (PIV-3), infectious bovine rhinotracheitis virus (IBRV), *Mycoplasma dispar* and *M. bovis*, plus data on bovine corona virus (BCV) from a previous study were investigated for their association with the risk of bovine respiratory disease (BRD), and with 28-day weight change, both before and after controlling for titers to *Pasteurella haemolytica* and *Haemophilus somnus*. Exposure to IBRV and *M. bovis* was infrequent, and although exposure to PIV-3 was more common, none of these agents had important associations with BRD. Higher titers to BVDV, BRSV, and BCV on arrival were associated with reduced risks of BRD and increased weight gains. However, there was some variation in these relationships and higher arrival titers to BVDV and BRSV in a subset of the calves were associated with increased risks of BRD. Titer increases to BVDV were associated with a higher risk of BRD and lower weight gains. Titer increases to BRSV were not usually associated with the occurrence of BRD, but titer increases to BRSV in a subset of calves that were vaccinated against BRSV, on arrival, were associated with an elevated risk of BRD. Of all the agents studied, BVDV had the most consistent associations with elevated risk of BRD and lower weight gains. Higher BRSV arrival titers were related to lower risk of BRD and higher weight gains; in some instances titer increases to BRSV were associated with higher BRD risk. Higher titers to BCV on arrival were related to reduced risks of BRD. Practical ways of adequately preventing the negative effects of these agents are still needed.

Nederlandse vleeskalveren?

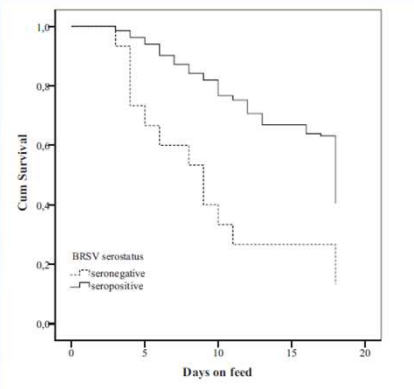


Fig. 3. Survival graph for occurrence of BRD in rosé veal calves in the first weeks after arrival, according to the serostatus for bovine respiratory syncytial virus (BRSV) measured upon arrival (Log Rank test: χ^2 = 13.8, df = 1; P < 0.001)

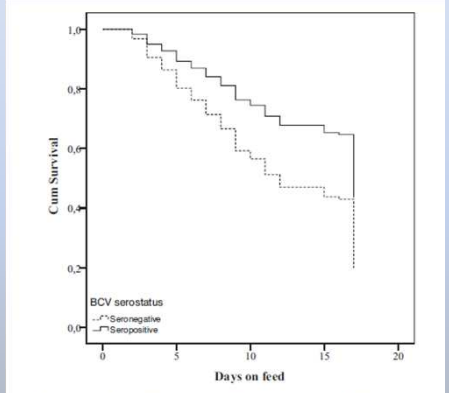
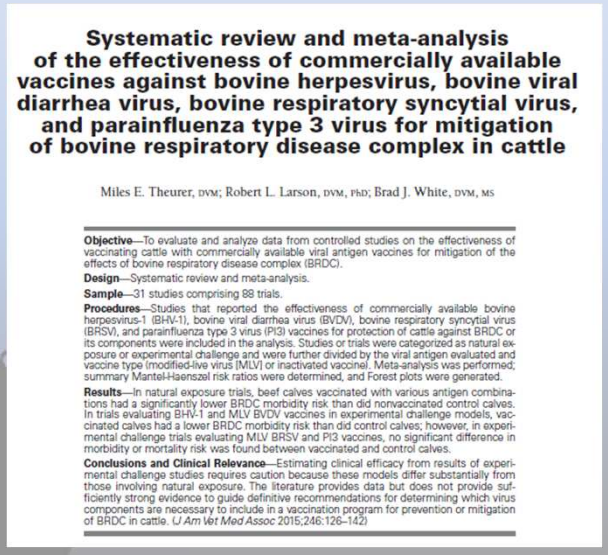


Fig. 4. Survival graph for occurrence of BRD in rosé veal calves in the first weeks after arrival, according to the serostatus for bovine coronavirus (BCV) measured upon arrival (Log Rank test: χ^2 = 10.7, df = 1; P < 0.01).

BVDV niet significant

Pardon et al., 2015

En vaccinatie?



Systematic review and meta-analysis of the effectiveness of commercially available vaccines against bovine herpesvirus, bovine viral diarrhea virus, bovine respiratory syncytial virus, and parainfluenza type 3 virus for mitigation of bovine respiratory disease complex in cattle

Miles E. Theurer, DVM; Robert L. Larson, DVM, PhD; Brad J. White, DVM, MS

Objective—To evaluate and analyze data from controlled studies on the effectiveness of vaccinating cattle with commercially available viral antigen vaccines for mitigation of the effects of bovine respiratory disease complex (BRDC).

Design—Systematic review and meta-analysis.

Sample—31 studies comprising 88 trials.

Procedures—Studies that reported the effectiveness of commercially available bovine herpesvirus-1 (BHV-1), bovine viral diarrhea virus (BVDV), bovine respiratory syncytial virus (BRSV), and parainfluenza type 3 virus (PI3) vaccines for protection of cattle against BRDC or its components were included in the analysis. Studies or trials were categorized as natural exposure or experimental challenge and were further divided by the viral antigen evaluated and vaccine type (modified-live virus [MLV] or inactivated vaccine). Meta-analysis was performed; summary Mantel-Haenszel risk ratios were determined, and Forest plots were generated.

Results—In natural exposure trials, beef calves vaccinated with various antigen combinations had a significantly lower BRDC morbidity risk than did nonvaccinated control calves. In trials evaluating BHV-1 and MLV BVDV vaccines in experimental challenge models, vaccinated calves had a lower BRDC morbidity risk than did control calves; however, in experimental challenge trials evaluating MLV BRSV and PI3 vaccines, no significant difference in morbidity or mortality risk was found between vaccinated and control calves.

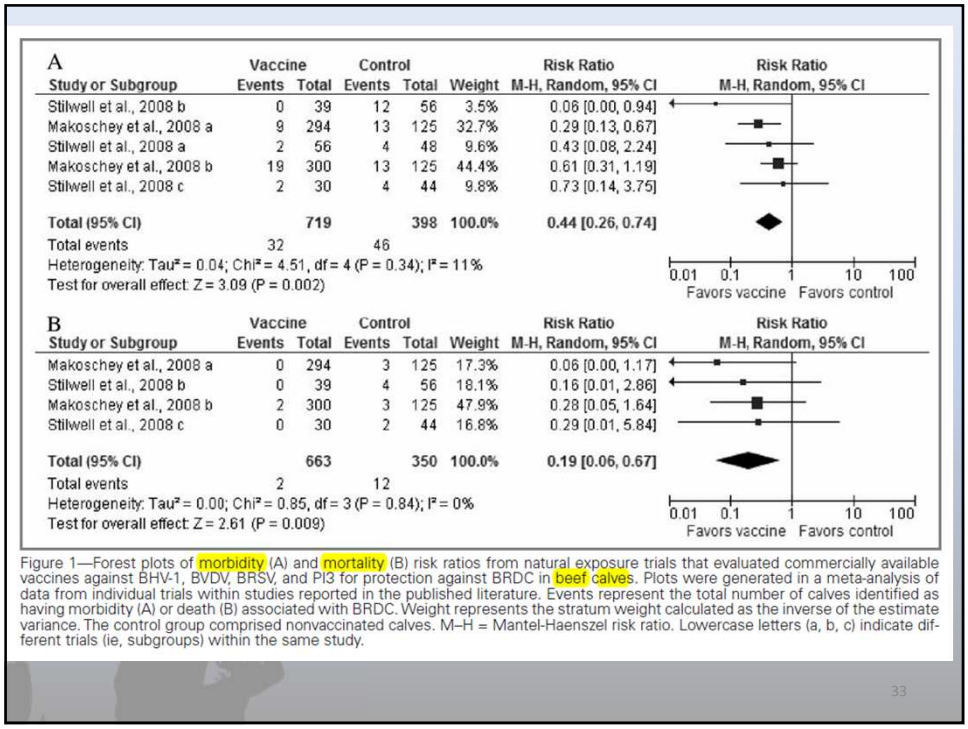
Conclusions and Clinical Relevance—Estimating clinical efficacy from results of experimental challenge studies requires caution because these models differ substantially from those involving natural exposure. The literature provides data but does not provide sufficiently strong evidence to guide definitive recommendations for determining which virus components are necessary to include in a vaccination program for prevention or mitigation of BRDC in cattle. (*J Am Vet Med Assoc* 2015;246:126–142)

31

Achtergrond

- Meta-analyse
- Engelstalige peer-reviewde literatuur
- Virus geïdentificieerd+ levend of inactief type vaccin
- Uitkomsten: ziekte en sterfte
- Ziektedetectie= blinded

32



A

Study or Subgroup	Vaccine Events	Vaccine Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Stilwell et al., 2008 b	0	39	12	56	3.5%	0.06 [0.00, 0.94]
Makoschey et al., 2008 a	9	294	13	125	32.7%	0.29 [0.13, 0.67]
Stilwell et al., 2008 a	2	56	4	48	9.6%	0.43 [0.08, 2.24]
Makoschey et al., 2008 b	19	300	13	125	44.4%	0.61 [0.31, 1.19]
Stilwell et al., 2008 c	2	30	4	44	9.8%	0.73 [0.14, 3.75]
Total (95% CI)		**719**		**398**	**100.0%**	**0.44 [0.26, 0.74]**
Total events	32		46			

Heterogeneity: Tau² = 0.04; Chi² = 4.51, df = 4 (P = 0.34); I² = 11%
Test for overall effect: Z = 3.09 (P = 0.002)

Risk Ratio M-H, Random, 95% CI
0.01 0.1 1 10 100
Favors vaccine Favors control

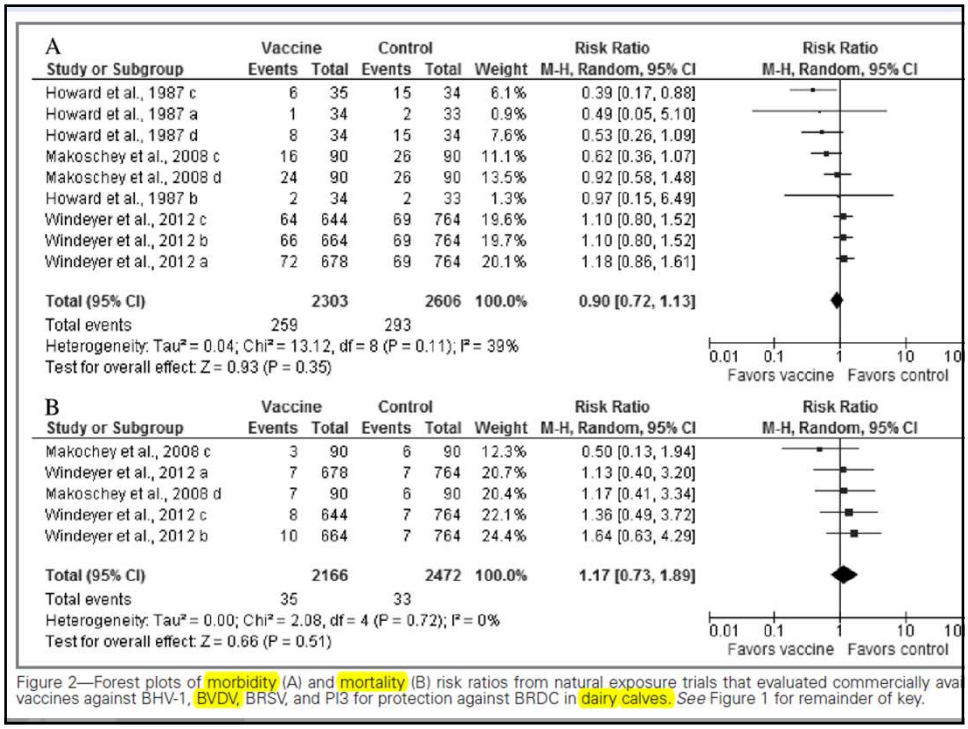
B

Study or Subgroup	Vaccine Events	Vaccine Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Makoschey et al., 2008 a	0	294	3	125	17.3%	0.06 [0.00, 1.17]
Stilwell et al., 2008 b	0	39	4	56	18.1%	0.16 [0.01, 2.86]
Makoschey et al., 2008 b	2	300	3	125	47.9%	0.28 [0.05, 1.64]
Stilwell et al., 2008 c	0	30	2	44	16.8%	0.29 [0.01, 5.84]
Total (95% CI)		**663**		**350**	**100.0%**	**0.19 [0.06, 0.67]**
Total events	2		12			

Heterogeneity: Tau² = 0.00; Chi² = 0.85, df = 3 (P = 0.84); I² = 0%
Test for overall effect: Z = 2.61 (P = 0.009)

Risk Ratio M-H, Random, 95% CI
0.01 0.1 1 10 100
Favors vaccine Favors control

Figure 1—Forest plots of morbidity (A) and mortality (B) risk ratios from natural exposure trials that evaluated commercially available vaccines against BHV-1, BVDV, BRSV, and PI3 for protection against BRDC in beef calves. Plots were generated in a meta-analysis of data from individual trials within studies reported in the published literature. Events represent the total number of calves identified as having morbidity (A) or death (B) associated with BRDC. Weight represents the stratum weight calculated as the inverse of the estimate variance. The control group comprised nonvaccinated calves. M–H = Mantel-Haenszel risk ratio. Lowercase letters (a, b, c) indicate different trials (ie, subgroups) within the same study.



A

Study or Subgroup	Vaccine Events	Vaccine Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Howard et al., 1987 c	6	35	15	34	6.1%	0.39 [0.17, 0.88]
Howard et al., 1987 a	1	34	2	33	0.9%	0.49 [0.05, 5.10]
Howard et al., 1987 d	8	34	15	34	7.6%	0.53 [0.26, 1.09]
Makoschey et al., 2008 c	16	90	26	90	11.1%	0.62 [0.36, 1.07]
Makoschey et al., 2008 d	24	90	26	90	13.5%	0.92 [0.58, 1.48]
Howard et al., 1987 b	2	34	2	33	1.3%	0.97 [0.15, 6.49]
Windeyer et al., 2012 c	64	644	69	764	19.6%	1.10 [0.80, 1.52]
Windeyer et al., 2012 b	66	664	69	764	19.7%	1.10 [0.80, 1.52]
Windeyer et al., 2012 a	72	678	69	764	20.1%	1.18 [0.86, 1.61]
Total (95% CI)		**2303**		**2606**	**100.0%**	**0.90 [0.72, 1.13]**
Total events	259		293			

Heterogeneity: Tau² = 0.04; Chi² = 13.12, df = 8 (P = 0.11); I² = 39%
Test for overall effect: Z = 0.93 (P = 0.35)

Risk Ratio M-H, Random, 95% CI
0.01 0.1 1 10 10
Favors vaccine Favors control

B

Study or Subgroup	Vaccine Events	Vaccine Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Makochey et al., 2008 c	3	90	6	90	12.3%	0.50 [0.13, 1.94]
Windeyer et al., 2012 a	7	678	7	764	20.7%	1.13 [0.40, 3.20]
Makoschey et al., 2008 d	7	90	6	90	20.4%	1.17 [0.41, 3.34]
Windeyer et al., 2012 c	8	644	7	764	22.1%	1.36 [0.49, 3.72]
Windeyer et al., 2012 b	10	664	7	764	24.4%	1.64 [0.63, 4.29]
Total (95% CI)		**2166**		**2472**	**100.0%**	**1.17 [0.73, 1.89]**
Total events	35		33			

Heterogeneity: Tau² = 0.00; Chi² = 2.08, df = 4 (P = 0.72); I² = 0%
Test for overall effect: Z = 0.66 (P = 0.51)

Risk Ratio M-H, Random, 95% CI
0.01 0.1 1 10 10
Favors vaccine Favors control

Figure 2—Forest plots of morbidity (A) and mortality (B) risk ratios from natural exposure trials that evaluated commercially ava vaccines against BHV-1, BVDV, BRSV, and PI3 for protection against BRDC in dairy calves. *See* Figure 1 for remainder of key.

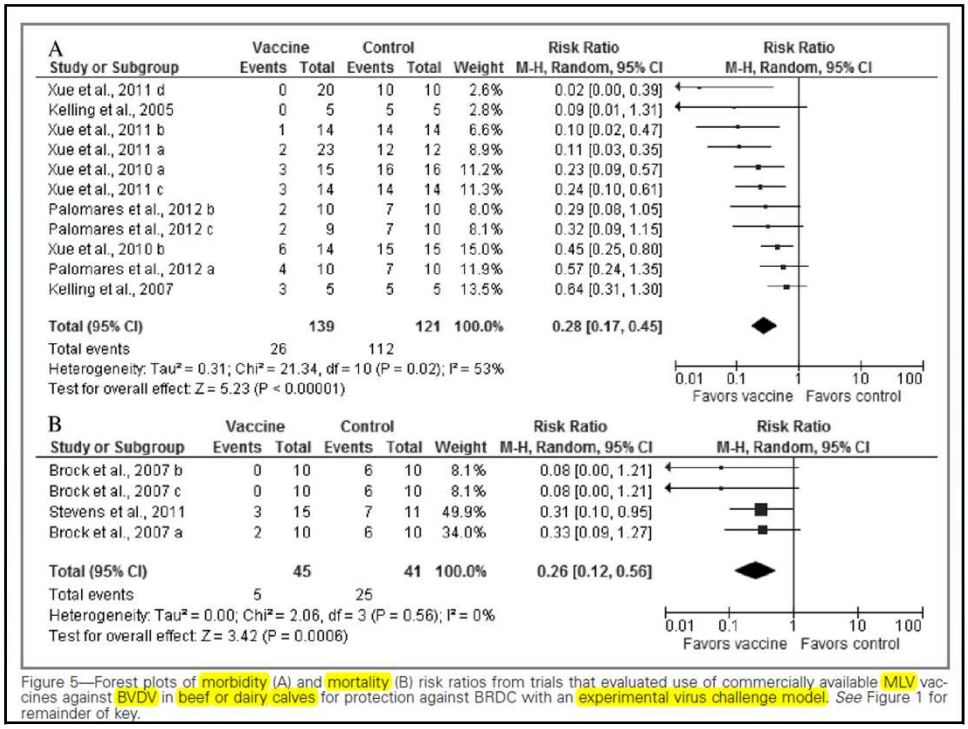


Figure 5—Forest plots of morbidity (A) and mortality (B) risk ratios from trials that evaluated use of commercially available MLV vaccines against BVDV in beef or dairy calves for protection against BRDC with an experimental virus challenge model. *See* Figure 1 for remainder of key.

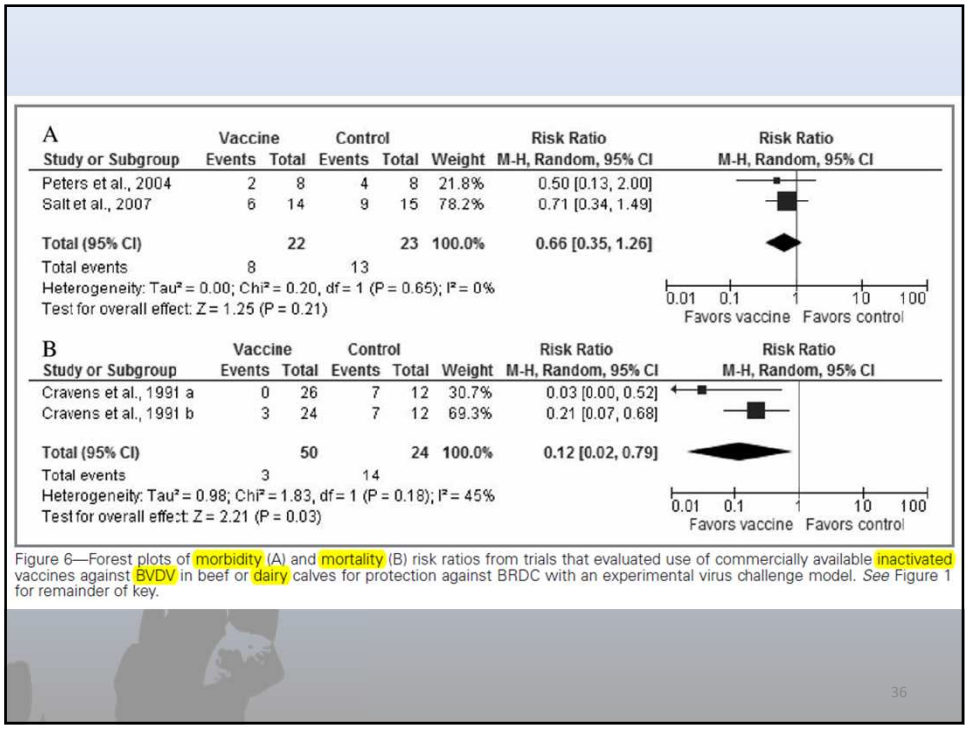


Figure 6—Forest plots of morbidity (A) and mortality (B) risk ratios from trials that evaluated use of commercially available inactivated vaccines against BVDV in beef or dairy calves for protection against BRDC with an experimental virus challenge model. *See* Figure 1 for remainder of key.

Immunisation: basic rules

- Sufficient time before exposure to pathogens and risk factors
- All animals within a herd
- Take maternal immunity into account
  - Injection (inactivated)→ no humoral response, cellular priming?
  - Mucosal vaccination (attenuated/intranasal)→ local immunity for 4 months, possibly blocked by very high levels of maternal immunity

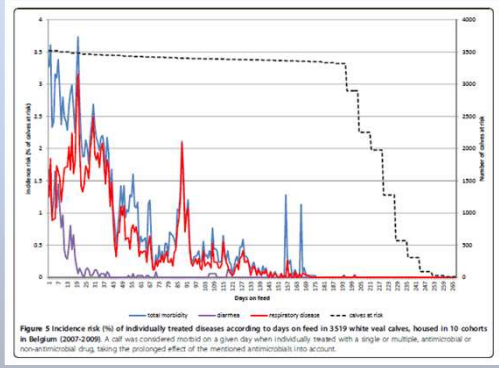
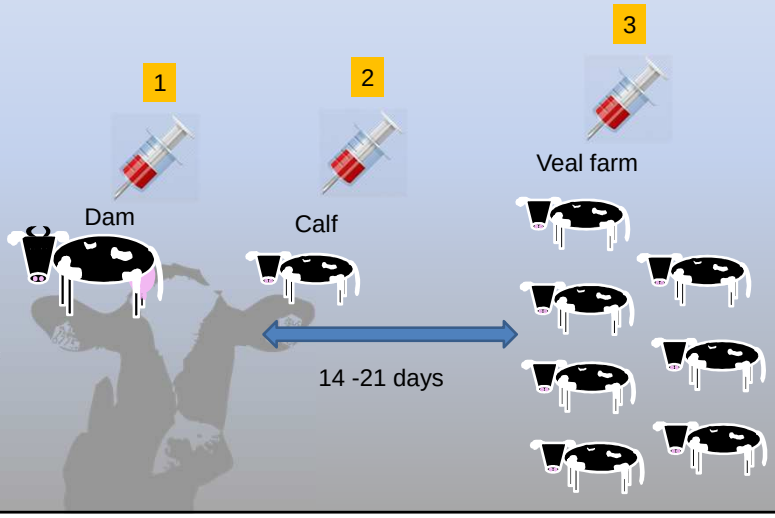


Figure 5 Incidence risk (%) of individually treated diseases according to days on feed in 3519 white veal calves, housed in 10 cohorts in Belgium (2007-2009). A calf was considered morbid on a given day when individually treated with a single or multiple, antimicrobial or non-antimicrobial drug, taking the prolonged effect of the mentioned antimicrobials into account.

37

Immunisation: options



38

A comparison of 2 vaccination programs in feedlot calves at ultra-high risk of developing undifferentiated fever/bovine respiratory disease

Brian K. Wildman, Tye Perrett, Sameeh M. Abutarbush, P. Timothy Guichon, Tom J. Pittman, Calvin W. Booker, Oliver C. Schunicht, R. Kent Fenton, G. Kee Jim

Abstract – The aim of this study was to compare 2 vaccination programs in feedlot calves at ultra-high risk of developing undifferentiated fever (UF)/bovine respiratory disease (BRD). At feedlot arrival, 3882 calves were enrolled in the study and randomly allocated to 2 groups, which were housed by group in 12 pens. At the time of allocation, 1 group (MLV3-BT2) received a multivalent, modified-live viral vaccine containing infectious bovine rhinotracheitis virus (IBRV) and types I and II bovine viral diarrhea virus (BVDV), as well as a *Mannheimia haemolytica* (MH) and *Pasteurella multocida* bacterin-toxoid. The other group (MLV4-BT1) received a vaccine containing IBRV, type I BVDV, bovine respiratory syncytial virus, and parainfluenza-3 virus, as well as a MH bacterin-toxoid. At an average of 69 days post arrival, the groups received their respective viral vaccines. The initial UF treatment, overall chronicity, overall wastage, overall mortality, and BRD mortality rates were significantly ($P < 0.05$) lower in the MLV3-BT2 group than in the MLV4-BT1 group. Average daily gain and the proportions of yield grade Canada 3 and quality grade E carcasses were significantly ($P < 0.05$) higher in the MLV3-BT2 group than in the MLV4-BT1 group. No significant ($P \geq 0.05$) difference in the dry matter intake to gain ratio was detected between the 2 groups. In economic terms, there was a net advantage of $20.86 CDN/animal in the MLV3-BT2 group. This study demonstrates that it is more cost effective to use an MLV3-BT2 vaccination program than a MLV4-BT1 vaccination program in feedlot calves at ultra-high risk of developing UF/BRD.

39

Waarom BVDV vaccineren voor BRD problematiek?

- 1 factor extra uitschakelen van BRD-complex
- Risico op gevolgen hypervirulente stammen inperken
- Bioveiligheid: bedrijfsvaccinatie sluiten (jongvee vroeg mede vaccineren)
- Tip: voor grote groepen→ risk assessment

Do the trial!

40

Conclusies

- Onderzoek toont aan:
  - IPI gaat dood (chronische pneumonie)
  - Transiënte infectie (tegenstrijdigheden)
    - Globaal hoger BRD-risico + hervallen!
    - Verminderde ADG in één periode (weinig effecten op karkas)
  - Immunologisch:
    - Titers bij aankoop zijn gunstig bij oudere dieren vs. geen effect bij NUKA's
  - Vaccinatie…

41

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Take home message

"een multifactoriële ziekte vraagt een multifactoriële aanpak"

"BVDV= 1 factor in het BRD-complex, die meer of minder doorweegt naargelang de andere aanwezige factoren"

42