Martin-Luther-University Halle-Wittenberg
Institute of Agricultural and Nutritional Sciences (IANS)
Animal Breeding

11th WORLD CONGRESS ON GENETICS APPLIED TO LIVESTOCK PRODUCTION
11–16 February 2018
Aotea Centre
Auckland
New Zealand
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Estimation of genomic breeding values for the susceptibility to Digital Dermatitis in Holstein dairy cattle using improved methods for phenotyping

Biology – Disease resistance 1
Feb 12, 2018, 4 pm

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Digital dermatitis (BDD, Mortellaro‘s disease)

= Dermatitis digitalis

= Bovine digital dermatitis (BDD)

= Hairy heel warts

-Increasing problem in Europe (S -> N), also elsewhere

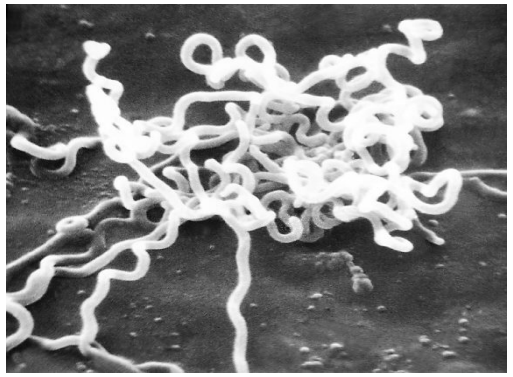
-Proportion of animals affected varies considerably between herds

-Most often spreading at a rapid speed

-infectious

BDD, a multifactorial disease

… a bacterial infection

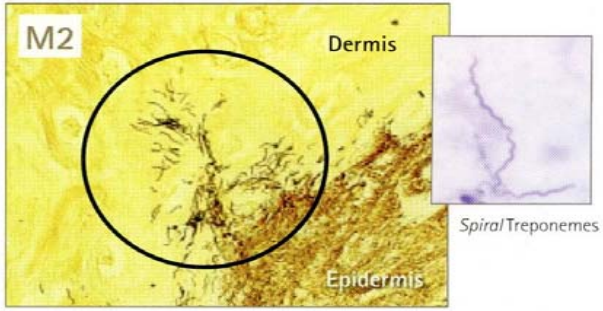


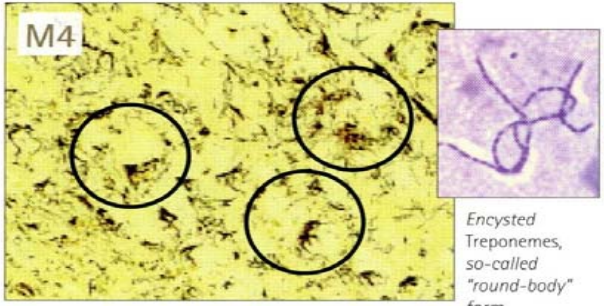
Treponema pallidum

Treponema (*Treponema spp.)*

…ed, actively moving

… deeper tissue laye





BDD: Genetics

J. Dairy Sci. 98:8164–8174
http://dx.doi.org/10.3168/jds.2015-9485

Investigating the genetic background of bovine digital dermatitis using improved definitions of clinical status

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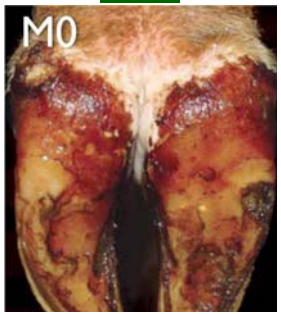
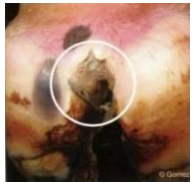
- **Much higher estimates of heritabilities, if developmental stages are considered (0.10 – 0.50; Schöpke et al., 2015)**

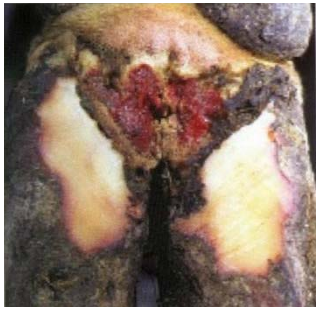
Scoring for BDD using the M-stages system



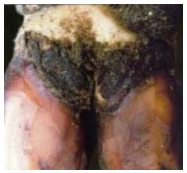
M0



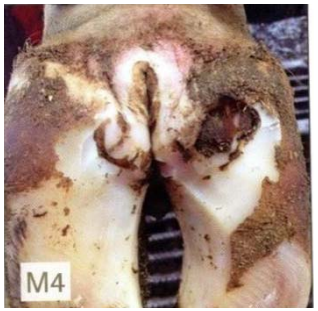
M1



M2

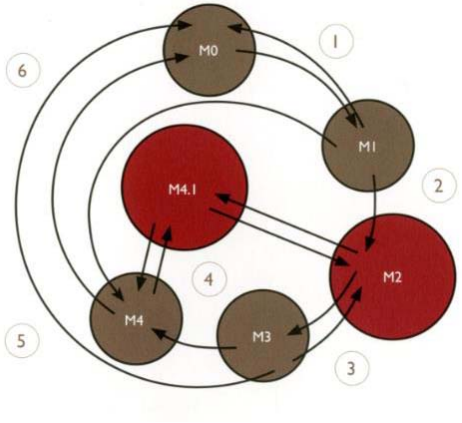


M3

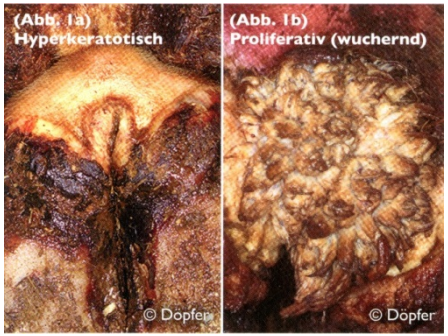


M4

M4.1



BDD-cycle



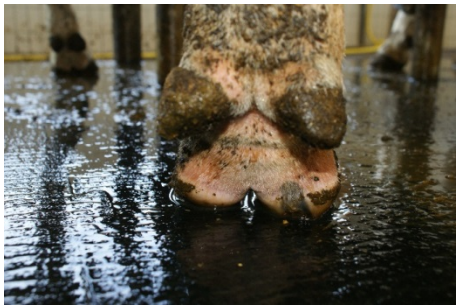
signs of chronicity:
0: none
1: hyperkeratosis
2: proliferation

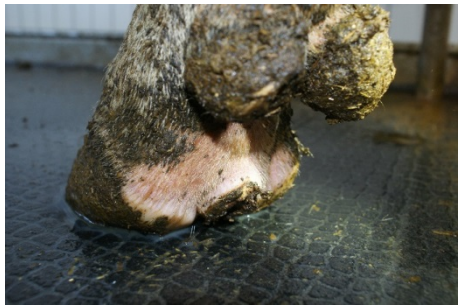
Zinpro corporation 2014
Döpfer *et al.*, 1997, 2012

Phenotyping

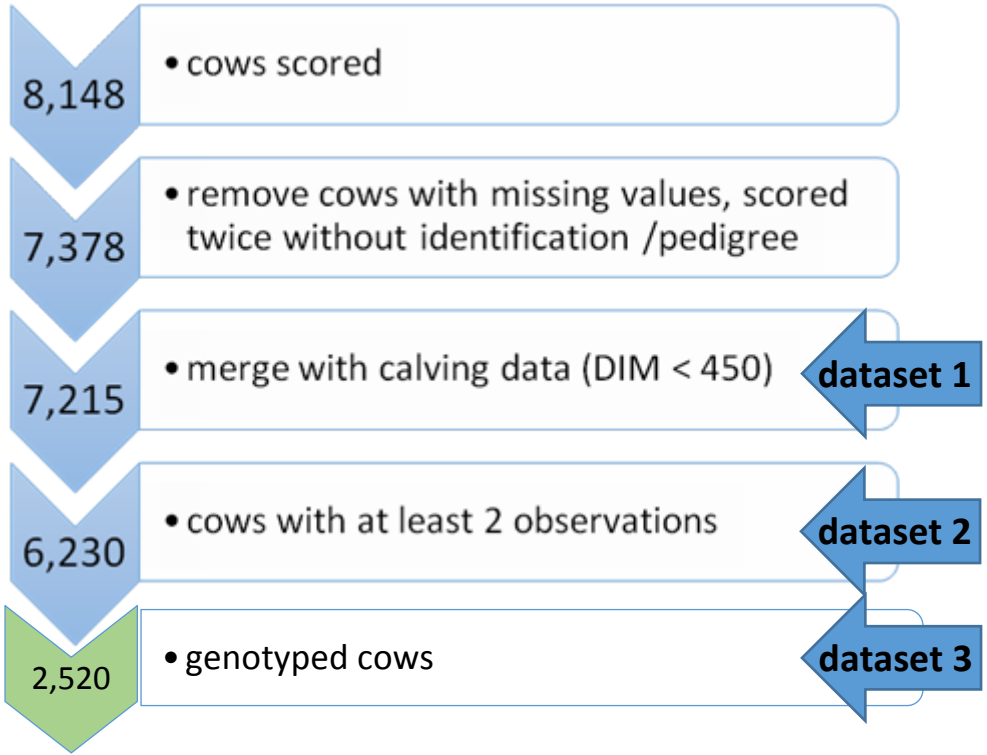
- 7 farms in northeast Germany between October 2015 and April 2016
- > 8,000 cows scored for stages of BDD, 3 times at intervals of 3 weeks

- scoring: - with DD Check App (Zinpro 2015)
  - rotary milking parlour (external rotary, herringbone, side-by-side)
  - 1 score per cow (hind legs)
  - both legs affected → more severe lesion documented





Data; three visits per farm in intervals of three weeks



number of observations per cow (N=7,215)

number of obs.	frequency	percent
1	985	13.7
2	1,353	18.8
3	4,877	67.6

distribution on farms (N=6,230)

farm	N cows	frequency M2
1	1,161	4.2%
2	635	25.1%
3	1,845	2.0%
4	1,147	1.8%
5	528	5.4%
6	348	4.5%
7	566	6.2%

Trait definitions and estimates of heritabilities

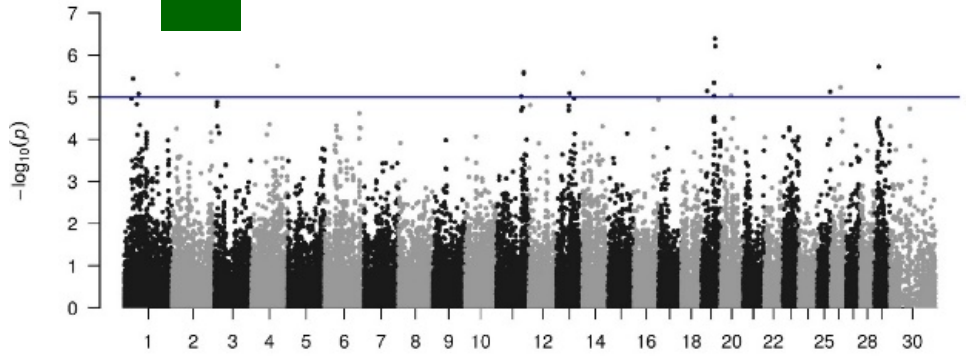
Data set 2, trait definitions across repetitions, linear model

Trait name	Definition	Estimate
TBIN	0 = healthy 1 = M2 or M4	0.28
TBINA	0 = healthy 1 = M2	0.03

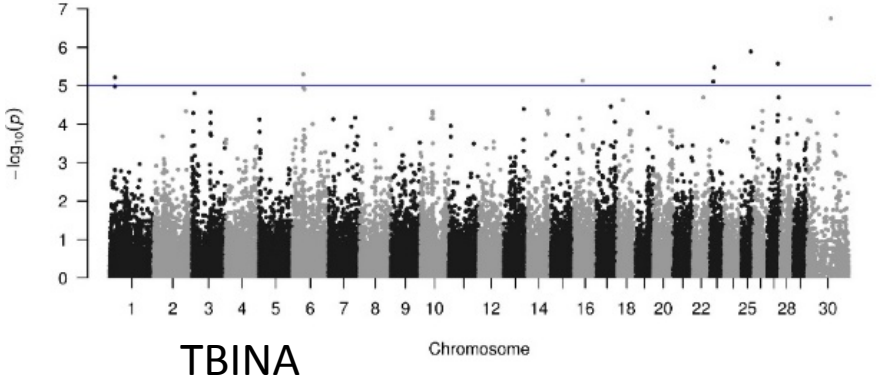
… same, or analogous estimates, if

- linear vs. threshold models
- repeatability model or single value defined across repetitions

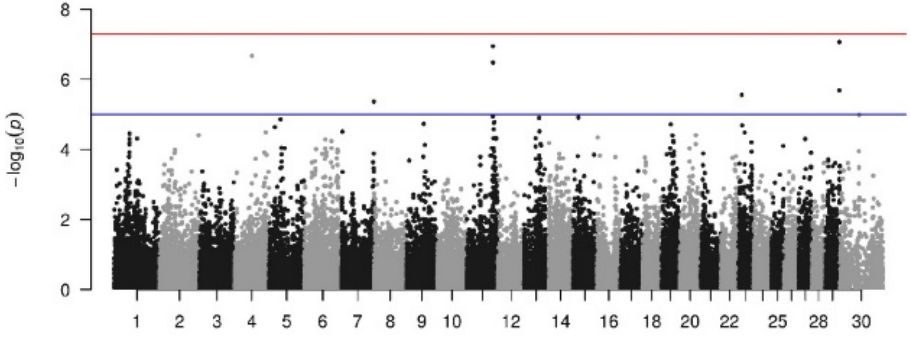
GWAS for TBIN, TCHRONA, TBINA



TBIN



TBINA



TCHRONA

TBIN: 0 vs. M2 or M4

➔ clear signals on various chr.

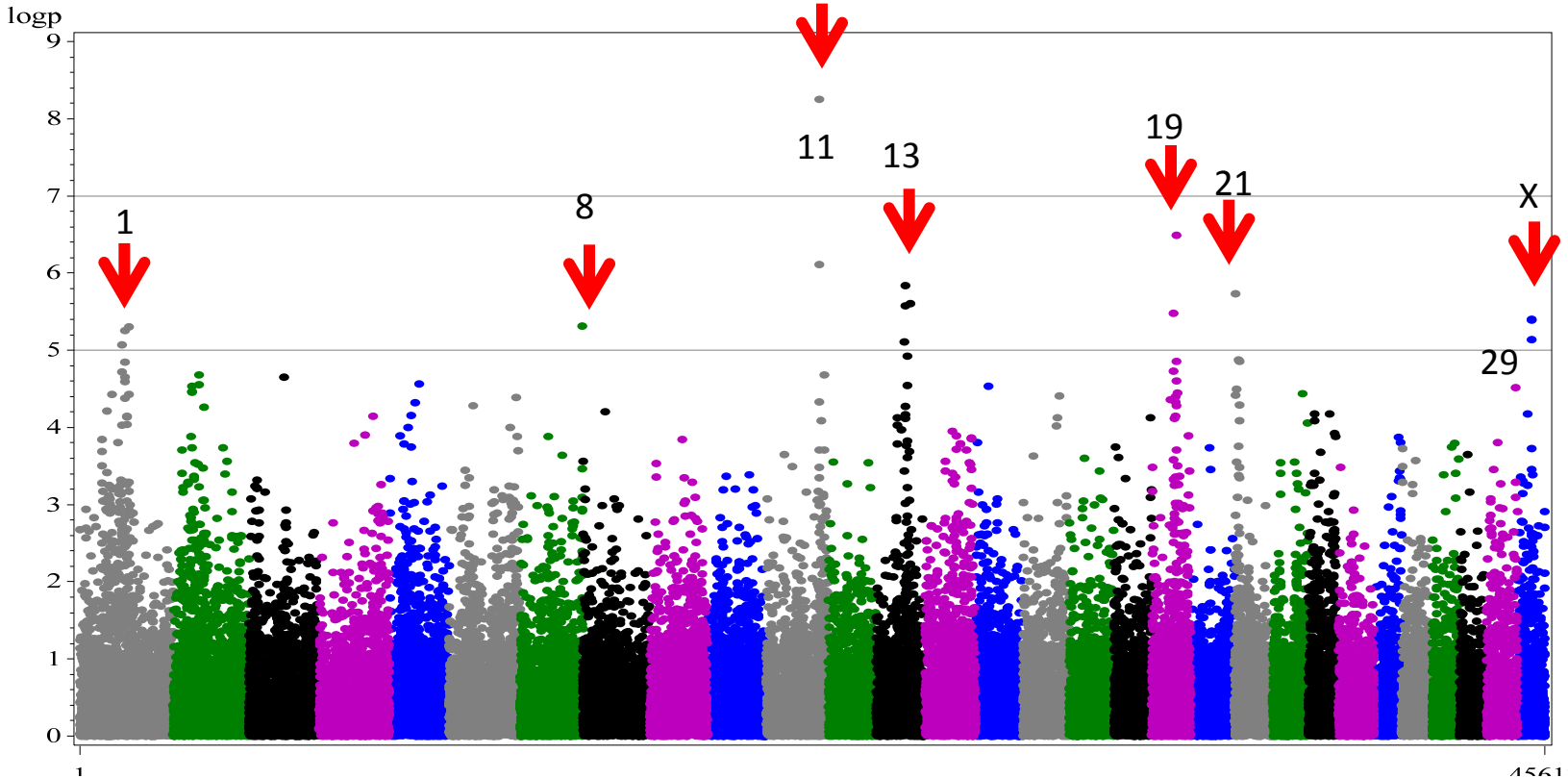
TCHRONA: 0 vs. chronic proliferations

➔ clear signals on some chr.

TBINA: 0 vs. M2

➔ not very clear …

GWAS for TCHRONA



Functional mutations on BTA 11 and BTA 19

- Candidate genes identified on BTA11 and BTA19
- Haplotype analysis for candidate regions
- Candidate regions were sequenced, functional mutations identified
- LSMEANS of incidence rates for TBIN estimated for all genotyped animals, i.e. additional genotyping for the functional and putatively causal mutations (Model: Herd, parity, stage of lactation, genotype)

Genotype	Candidate BTA 11	Candidate BTA 19
WT	0.53 (0.02)	0.77 (0.02)
het	0.64 (0.02)	0.68 (0.02)
MT	0.70 (0.04)	0.54 (0.03)

Genomic selection applying ssGBLUP

- Cows (n = 2,520) with TBIN & sires were included in ssGBLUP (BLUPF90)
- gEBV directly from ssGBLUP; also tested: 2-step
- Sires‘ gEBV grouped in classes from high to low resistance (1 to 5)
- Estimate of h^2: 0.33 (threshold model)
- Validation sample:
  - Hoof trimmer data, 31 contract herds
  - No overlap with herds used for ssGBLUP
  - 259 herd-trimming-date contemporary groups
  - 37,021 1st lactations, 27,961 2nd lactations, 18,293 3rd lactations
- *Model: Herd-event, days in milk, cow (accounting for repeated observations) plus **class of gEBV for sires***

1st validation of gEBV

LSMEAN of frequency of diseased cows for classes of sires‘ resistance

gEBV class (1 = low to 5 = high)	gEBV range	Parity		
		1	2	3
1	< 85	0.196[a]	0.183[a]	0.161[a]
2	86 – 95	0.191[a]	0.187[a]	0.149[ac]
3	96 – 105	0.172[b]	0.157[b]	0.129[bd]
4	106 – 115	0.171[b]	0.154[b]	0.136[bcd]
5	> 115	0.147[c]	0.153[b]	0.125[d]

2nd validation (Reinhardt, Alkhoder, Swalve 2018)

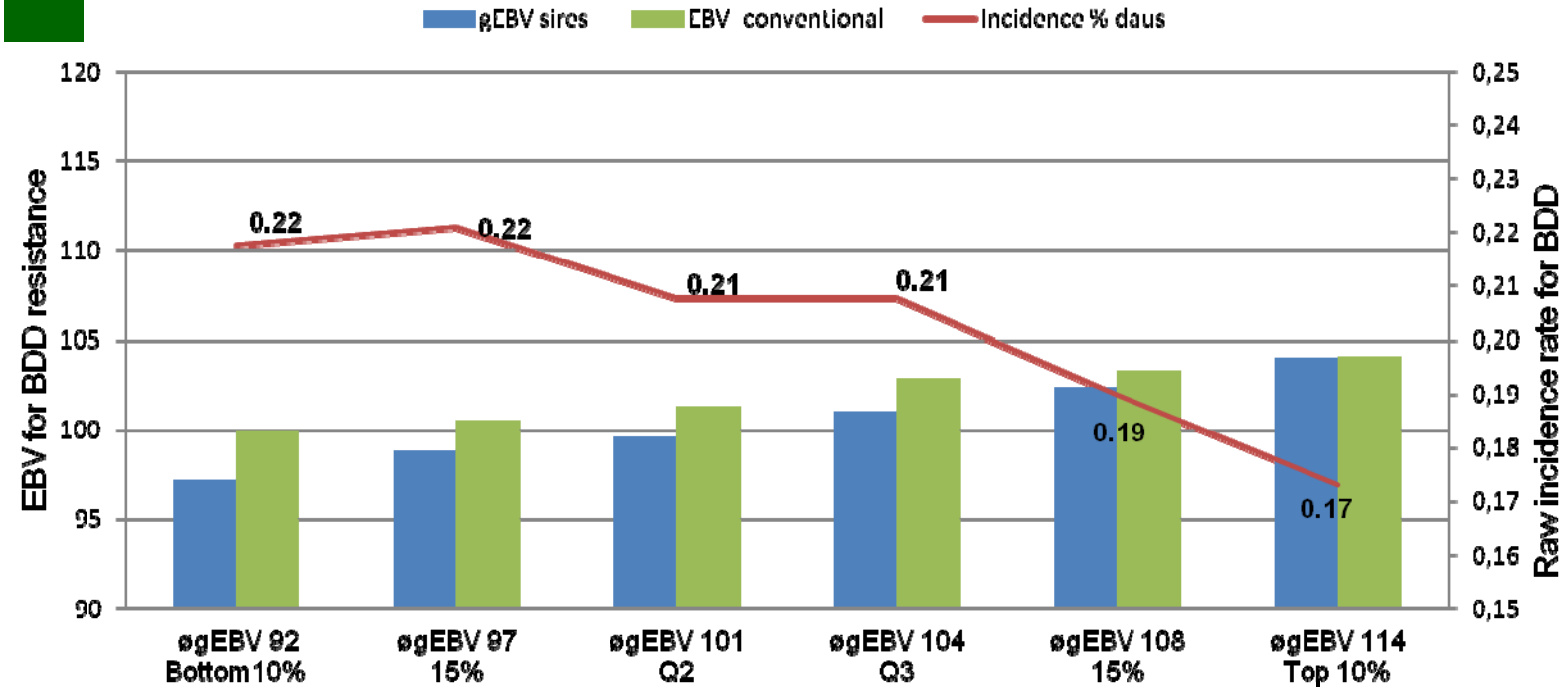
- SNP effects exported from ssGBLUP ➔ vit (National Computing Centre)
- SNP effects used to estimate gEBV for sires on national basis
- Validation data set created using available health data from other projects
- Validation data again hoof trimmer data, scored as 0/1
- 4,180 sires, sires from own experiment excluded; 575 herds, 157,524 daughters

Incidence rate BDD%	0	1-10	10-20	20-30	30-40	40-50	50-60	60-70	70-80	80-90	90-100
No. of herds	178	165	73	54	32	34	12	10	8	5	4

No. daus, 1st lact	1	2	3	4	5	6-10	11-20	21-50	51-100	100-500	>500
No. of sires	593	334	235	188	174	668	629	757	316	243	43

2nd validation (Reinhardt, Alkhoder, Swalve 2018)

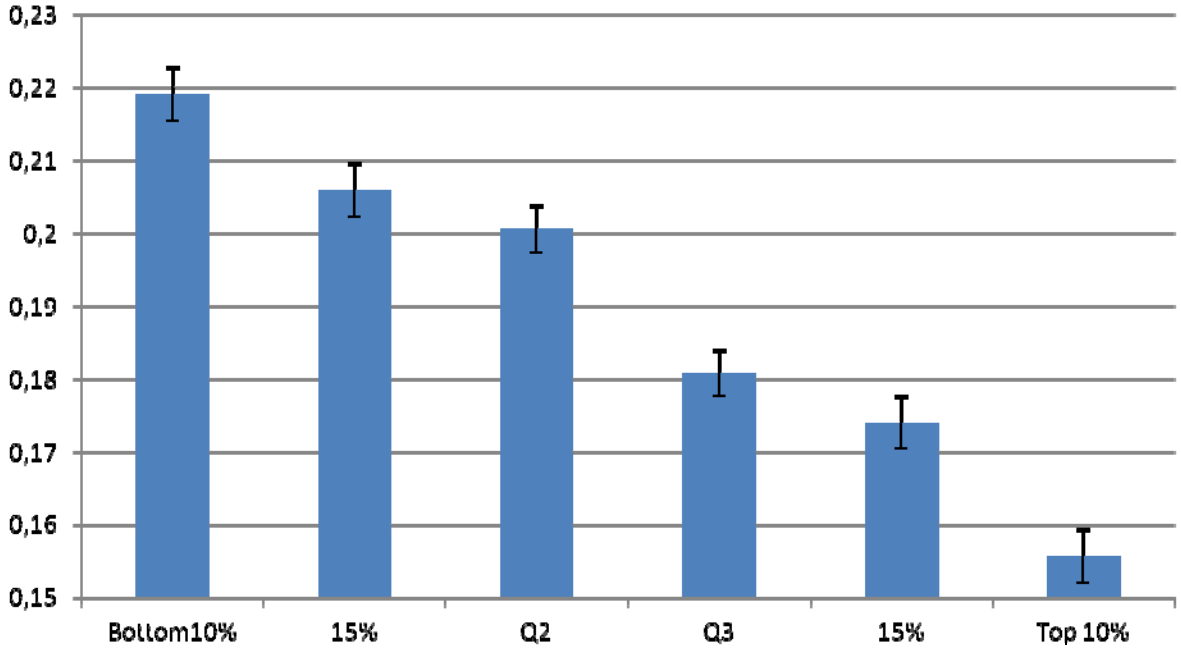
Quartiles of gEBV for sires and cows, raw incidence rates (%)



No. of sires	276	416	692	692	415	278
daus.	21,238	20,468	33,288	36,209	21,477	21,217

2nd validation (Reinhardt, Alkhoder, Swalve)

LSMEANS of incidence rates (%) by quartiles of gEBV (sires)



Incidence rates: BDD (0/1), 1st observation in 1st lactation, herds without BDD =1 excluded

Model: herd, year-season, gEBV-class_sire

Genetics and genomics of bovine digital dermatitis

- New approach: phenotyping based on M-stages
- Drastic differences in heritability estimates between conventional scoring and new approach
- Reference sample of genotyped and phenotyped cows still small (N = 2,520), despite this, GWAS yields clear signals
- ssGBLUP performs very well; two approaches for validation:
  - "Same sires – different set of phenotypes"
  - "Different sires – different set of phenotypes" (exchange SNP effects only)
- gBLUP and GWAS can be meaningful even in small calibration samples if trait has a genetic architecture that is suitable (e.g. several "larger" QTL)

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Thank you for your attention!

Fight it with genetic selection!

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