Implementation of genomic evaluation for digital dermatitis in Canada

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Hoof Lesions

- In Canada, around 25-30% of cows have at least one hoof lesion

- Hoof lesions compromise animal welfare
- Economic loss, costs associated with:
  - Treatment of lesions
  - Decreased cow performance

How to Reduce Incidence of Lesions

- Improving management practices at herd level
- Through genetic selection

Improving Hoof Health in Canadian Dairy Herds

- Project funded by the **Dairy Research Cluster 2**
  - Dairy Farmers of Canada, Agriculture and Agri-Food Canada, CDN, Canadian Dairy Commission
- Principal investigator: Dr. Filippo Miglior (Canadian Dairy Network & University of Guelph)
- 2014-2017

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Objectives

Improve hoof health in Canada

1. Centralize data collected by hoof trimmers into a coherent and sustainable national data base
   - Standardize the hoof lesion data
   - Develop a data pipeline: **Hoof trimmers - CDHI - CDN**
2. Develop a DHI management report for producers
3. Develop genomic evaluations for hoof health

Objectives

- **Standardize the hoof lesion data collection**
- Develop a data pipeline

  Hoof trimmers - Canadian DHI - Canadian Dairy Network
- Develop a DHI management report for producers
- Develop genomic evaluations for hoof health

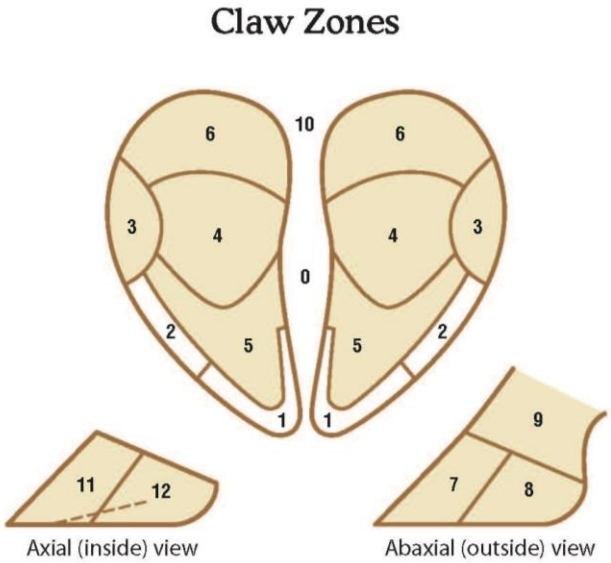
Standardize the hoof lesion data collection

Hoof Supervisor System

- Codes of lesion
- Severity
- Claws
- Zones

Standardize the hoof lesion data collection

Hoof Supervisor System - Codification



Code	Lesion Name	Page	Zones
U	Sole Ulcer	4	4
T	Toe Ulcer	8	1
W	White Line Lesion	12	1,2,3
H	Sole Hemorrhage	16	4,5,6
F	Foot Rot	19	9
D	Digital Dermatitis	22	9,10
E	Heel Erosion	25	6
I	Interdigital Dermatitis	26	0,10
C	Corkscrew Claw	27	7
V	Vertical Fissure	28	7,8
X	Axial Fissure	29	11,12
G	Horizontal Fissure	32	7,8
Z	Thin Sole	35	4,5
K	Interdigital Hyperplasia	37	0
L	Periople Ulcer	39	11

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Participation of Hoof Trimmers

- 54 trimmers across Canada now routinely provide hoof health data to Canadian DHI

- Additional trimmers invited to participate to the data collection

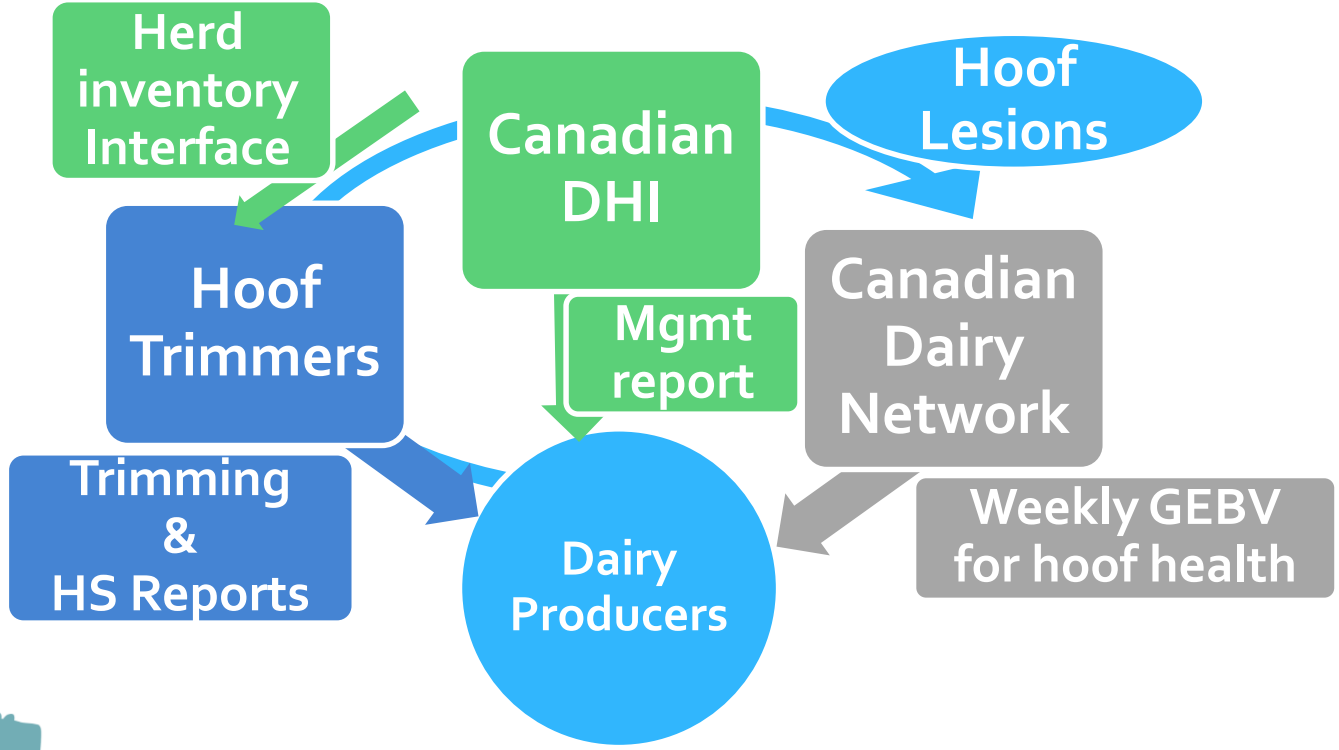
Objectives

- Standardize the hoof lesion data collection
- Develop a data pipeline

  Hoof trimmers - Canadian DHI - Canadian Dairy Network

- Develop a DHI management report for producers
- Develop genomic evaluations for hoof health

Data Pipeline



Objectives

- Standardize the hoof lesion data collection
- Develop a data pipeline

  Hoof trimmers - Canadian DHI - Canadian Dairy Network

- **Develop a DHI management report for producers**
- Develop genomic evaluations for hoof health

DHI Management Report

- Working group with hoof trimmers, dairy advisors, veterinarians and researchers
  - To develop a new DHI management report on hoof health
- This report may include
  - Prevalence of lesions on farm
  - Trends over time
  - Benchmarks with province and national averages
- Added value for trimmers and dairy producers

Objectives

- Standardize the hoof lesion data
- Develop a data pipeline

  Hoof trimmers - Canadian DHI - Canadian Dairy Network

- Develop a DHI management report for producers
- **Develop genomic evaluations for hoof health**

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Data

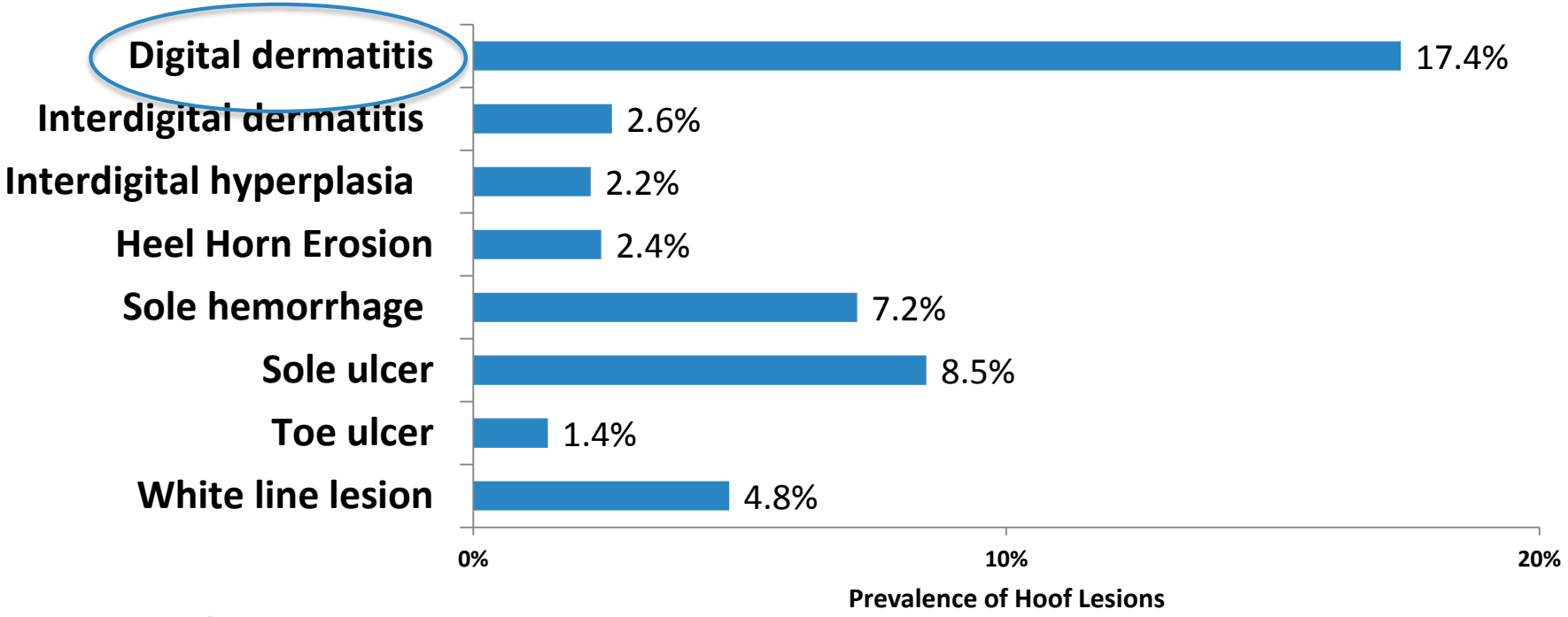
- Historical data from provincial projects up to 2012
- New pipeline data
  - From summer 2015 for Quebec
  - From early 2016 Ontario
  - From mid 2016 for newly recruited trimmers
- Historical data from hoof trimmers

Research Outcomes

- Heritability and Repeatability of hoof lesions
- Effect of pre-selection of cows for trimming
- Correlations with conformation traits
- Severity *vs.* Binary
- Threshold *vs.* Linear Model
- Single-step GBLUP

Genetic Evaluation at CDN

Prevalence of Hoof Lesions



Digital Dermatitis Holsteins

- 307,172 records
- 127,729 cows
- 8,293 sires
- **332,561- animals in pedigree (4 generations)**

Aim is 10-20% of milk recorded cows

Single-step GBLUP

- **Single-trait** (no indicators)
- **Animal linear model with repeated observations (0/1)**
- **Single-step GBLUP using Mix99**
- **Environmental factors:**
  - Herd-Trimming Session
  - Trimmer
  - Days after calving
  - Parity
  - Cow effect (PE)

Single-step Model

- Genetic parameters:
  - Heritability: **0.08**
  - Repeatability: **0.20**
- Reference population (animals):
  - All genotyped sires and cows that are in the pedigree
- Single-step: **19,459** animals
  - 5,268 sires
  - 7,178 cows
  - 7,013 cows with data

Genetic Evaluation

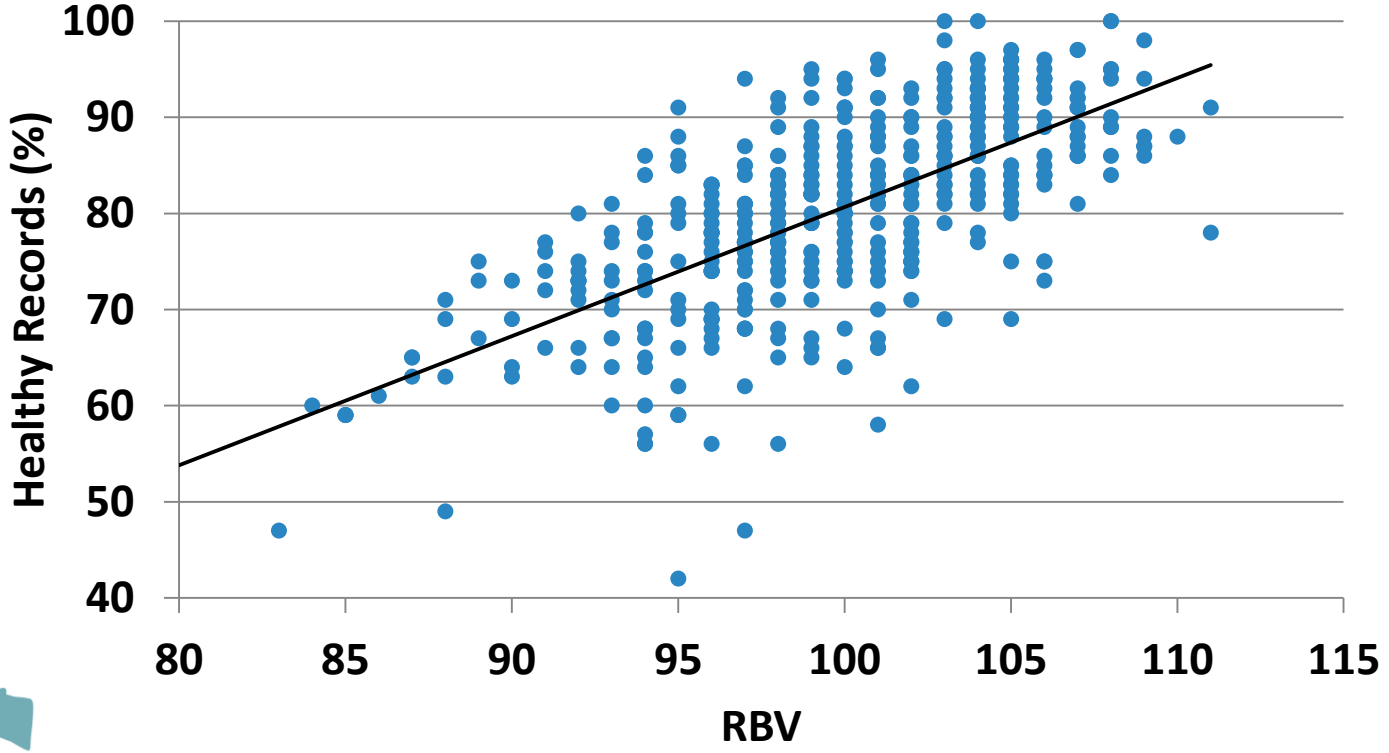
For bulls only:

- Genomic Estimated Breeding Values and Reliabilities
- Like all CDN functional traits, evaluations expressed as Relative Breeding Values (**RBV**):
  - mean = 100 SD = 5 for base sires
  - reversed in sign: higher **RBV** indicate better resistance to **Digital Dermatitis**

Publication Criteria

- Digital Dermatitis proof of a sire official when:
  - Minimum 5 herds
  - Minimum reliability of 70%

RBV distribution by % Healthy Records



RBV distribution

Bulls	Proof				% Healthy Records			
	Mean	SD	Min	Max	Mean	SD	Min	Max
Bottom 10	82	2.0	77	84	61	14.1	33	86
Top 10	114	1.7	112	117	93	7.3	80	100

Summary

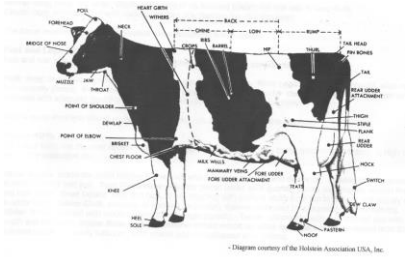
- Hoof trimmers willing to share data and to develop a standard recording protocol identified across Canada
- Routine flow of hoof lesion data from hoof trimmers to Canadian DHI and to Canadian Dairy Network
- Genomic evaluations for Digital Dermatitis from December 2017
- Soon DHI herd management report for Hoof Health

Acknowledgements

Supported by a contribution from the Dairy Research Cluster Initiative (Dairy Farmers of Canada, Agriculture and Agri-Food Canada, the Canadian Dairy Network and the Canadian Dairy Commission) and by Ontario Genomics

Links with Conformation Traits

Traits	Rear side rear view	Feet & Legs	Locomotion
Digital Dermatitis	-0.28	-0.24	-0.45



- Diagram courtesy of the Holstein Association USA, Inc.

CONAFE

UNIVERSIDAD COMPLUTENSE MADRID

Genetic and Genomic Evaluation of Claw Health Traits in Spanish Dairy Cattle

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ICAR THE GLOBAL STANDARD FOR LIVESTOCK DATA

Annual Conference

ICAR2018.NZ

7 – 11 February 2018

Aotea Centre

Auckland,

New Zealand

INTERBULL

Why Claw health?

Claw disorders are one of the main causes of involuntary culling in Spanish dairy herds

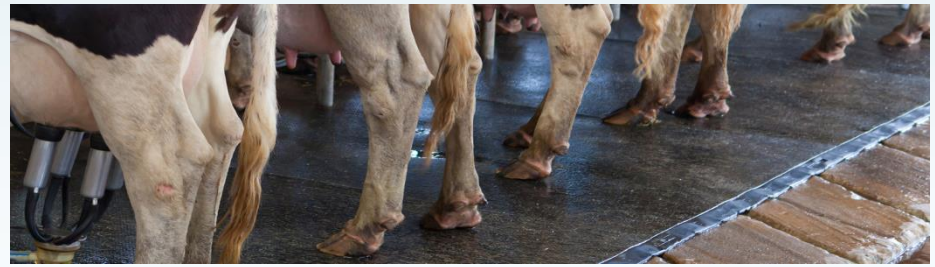
1.- Fertility

2.- Mastitis

3.- Claw lesions

Claw disorders are responsible for most lameness cases which compromise:

Animal Welfare	Productivity	Fertility
↓Feed and water access	↓Yield production	↑Anestrus period
↓Comfort	↓Milk quality	↓Conception rate
↗Pain	↓Productive life	↑Days open



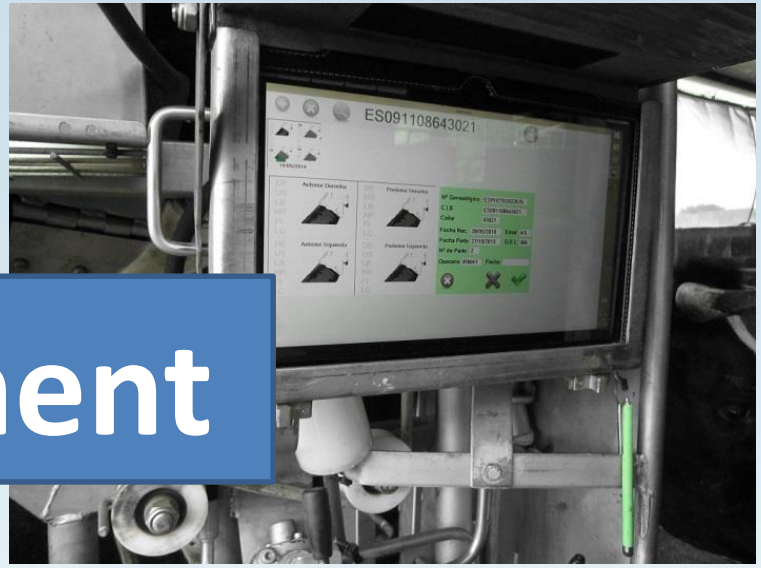
Feet & legs type traits fail in improving claw health

Claw Health Recording

In 2012 was launched the Spanish program for recording claw health data in order to prevent and to control lameness

Win-Win Agreement

- CONAFE provides:
  - A tactile PC-tablet
  - An electronic friendly application called DATPAT
  - An access to the national database
  - Herd reports and animal information
  - Training courses
- Trimmers should:
  - Register at least 2,000 records per year during trimming routine visits.



Objectives

- Implementation of a routine genetic evaluation for claw health traits.
- Assessment of the accuracy of genomic proofs for claw disorders in Spanish dairy cattle.

Recorded claw disorders

Seven claw disorders are recorded:

	Prevalence (%)
Dermatitis (DE)	10.07
Sole ulcer (SU)	11.37
White line disease (WL)	8.03
Interdigital hyperplasia (IH)	0.54
Interdigital phlegmon (IP)	0.95
Concave dorsal wall (CD)	1.50
Overall claw disorders	**29.91**

- Corkscrew claws (CC) has being recorded since 2017

CD and CC are scored as 0/1

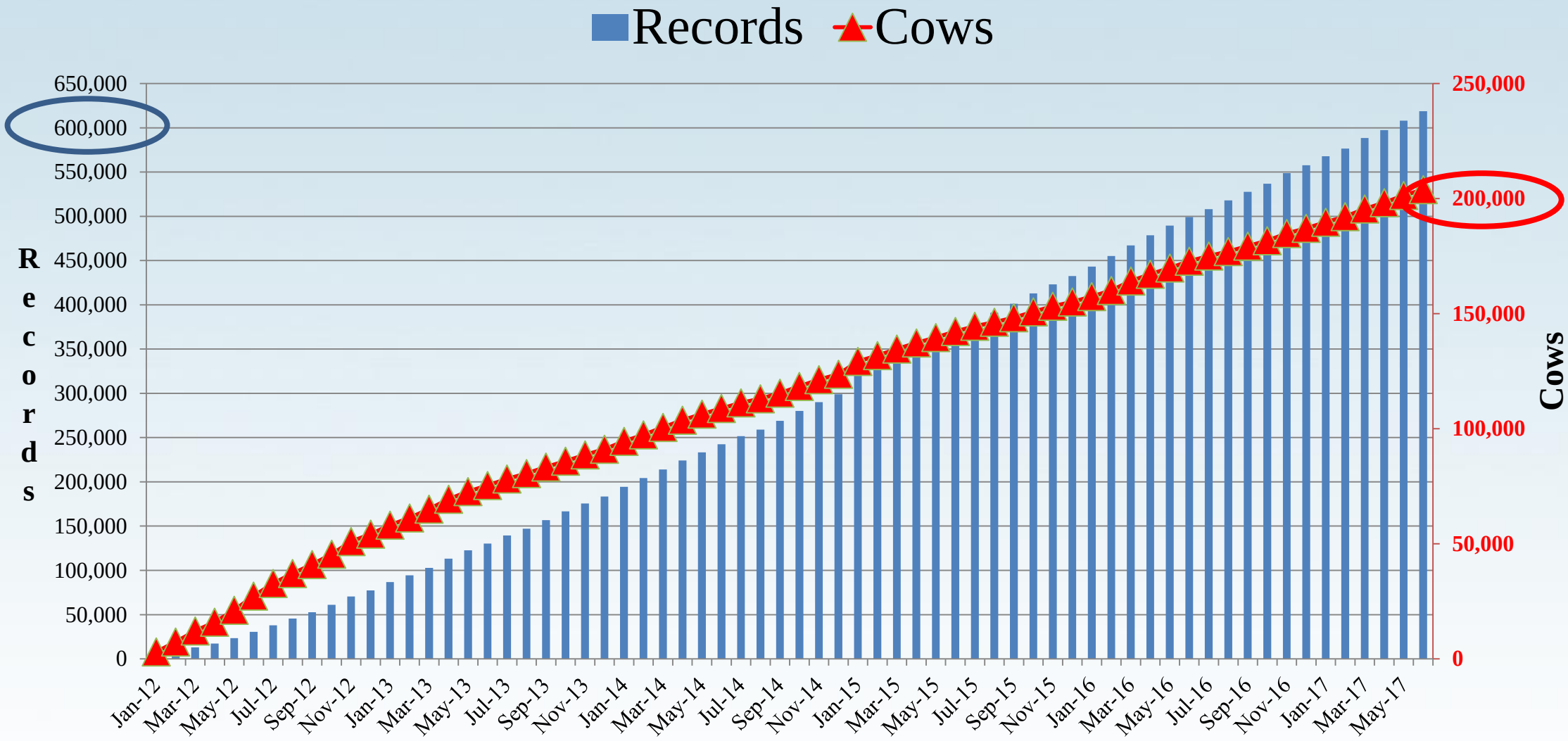
Scoring for each lesion:

0 : Absence

1 : mild

2 : severe

Evolution of Claw data



Data Editing

Initial set of data: 628,228 records from 2012 to 2017

(In 1821 herds by 46 trimmers)

Data selection:

- Records before 2013 were eliminated
- Parity 1 to 5
- Records from day 1 to day 500 after calving
- Only trimmers with at least 2000 records/year
- At herd level: Only herd-year with at least 30% of present cows trimmed

Final set of data: **441,248** records (34 trimmers)

Non trimmed cows were included: **81,228** records

Genetic evaluation: Linear Models

2 multi-trait animal analyses:

- Scenario 1: Only claw disorders
- Scenario 2: Claw disorders and feet and leg type traits

- **Claw disorders**
  - Herd-year-season
  - Lactation-age
  - Lactation stage
  - Trimmer
  - Permanent environmental effect
  - Additive animal effect

- **Type traits**
  - Herd-visit-classifier
  - Lactation-age
  - Lactation stage
  - Additive animal effect

Mix99 Software

Genomic evaluation: GBLUP with polygenic effect

Reference population: 1,317 bulls

- 2-step evaluation
- Polygenic effect: 30%
- 10-fold cross validation
- Mix99 software

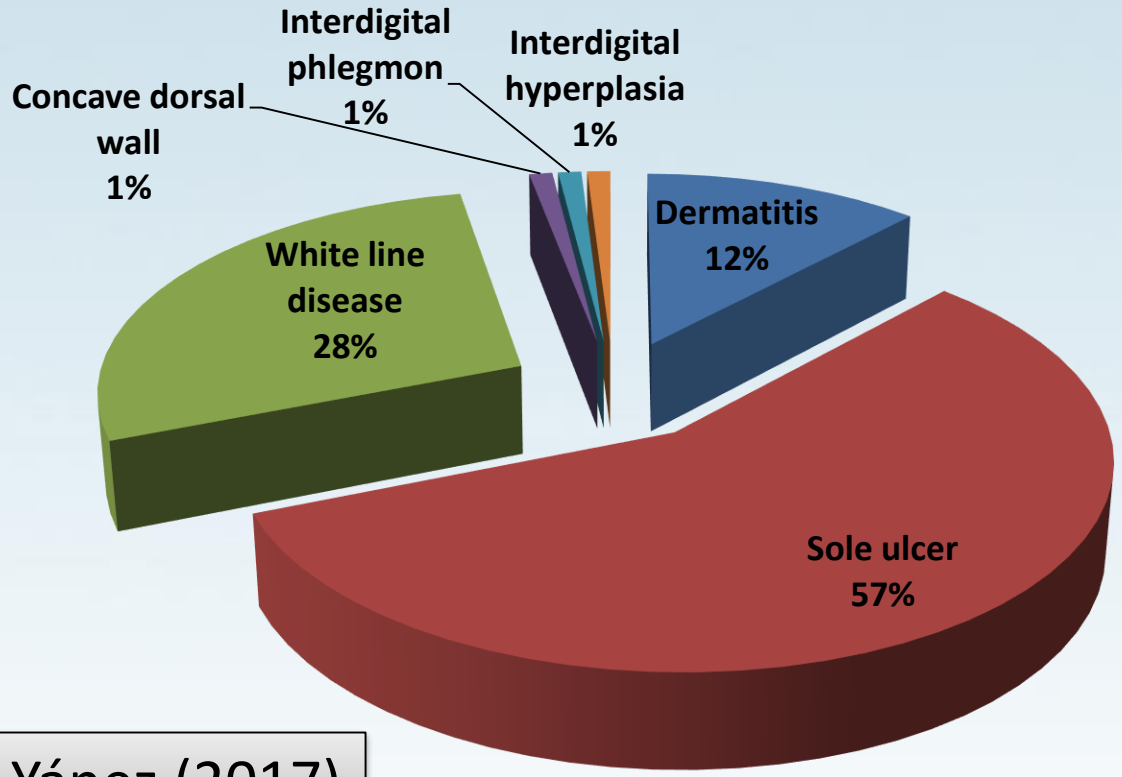
Genetic Parameters

	h^2	r
Dermatitis	0.06	0.11
Sole Ulcer	0.06	0.11
White line disease	0.02	0.07
Concave dorsal wall	0.02	0.22
Interdigital phlegmon	0.01	0.03
Interdigital hyperplasia	0.13	0.07

	h^2
Feet & legs (F&L)	0.15
Rear legs rear view (RLRV)	0.13
Foot angle (FA)	0.09
Bone quality (BQ)	0.26
Locomotion (LOC)	0.12

	F&L	RLRV	FA	BQ	LOC
Dermatitis	-0.18	-0.20	0.23	-0.09	-0.25
Sole Ulcer	-0.30	-0.10	0.15	-0.15	-0.31
White line disease	-0.24	-0.09	-0.16	-0.30	-0.22
Concave dorsal wall	-0.25	-0.12	-0.12	-0.02	-0.35
Interdigital phlegmon	-0.26	-0.23	-0.11	-0.19	-0.32
Interdigital hyperplasia	-0.11	-0.11	-0.04	-0.08	-0.11

Claw health index: ISP*



Economic weights for claw disorders.	
Claw disorders	**€/cow/year**
Dermatitis	- 9.30
Sole Ulcer	- 44.00
White line disease	- 37.40
Concave dorsal wall	- 4.52
Interdigital phlegmon	- 3.55
Interdigital hyperplasia	- 1.45

*Iván Yánez (2017)

ISP net profit: 4.10€/cow/year

Proofs reliabilities

Bull with at least 20 daughters in 10 herds with Reliability ≥ 50%

Average reliabilities (%)	Scenario 1 Without type traits	Scenario 2 With type traits	Rel gain (%)
Dermatitis	68	74	9%
Sole Ulcer	68	75	10%
White line disease	63	72	14%
Concave dorsal wall	63	68	8%
Interdigital phlegmon	50	66	32%
Interdigital hyperplasia	67	81	22%
ISP	**66**	**74**	**12%**

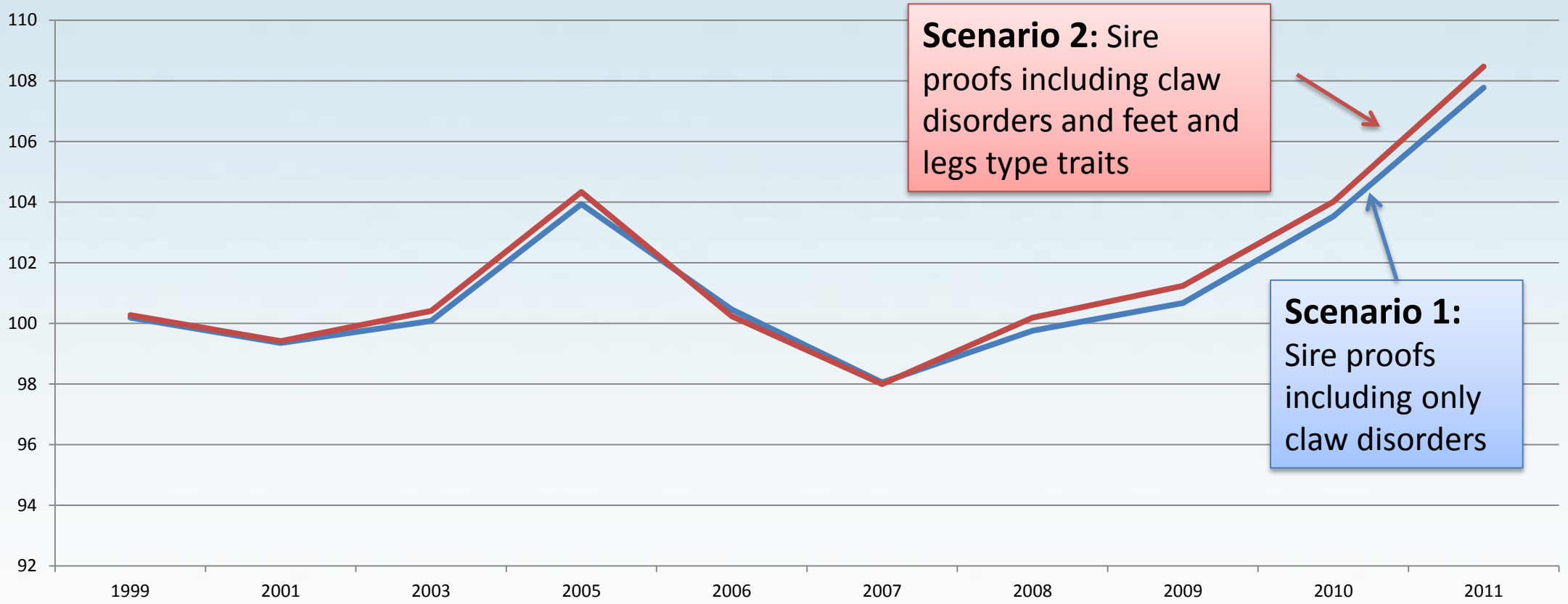
Correlations between EBVs with and without type traits

EBVs were standardized to relative breeding values with a mean of 100 and a standard deviation of 10 and reversed in sign

	Pearson correlations	Spearman correlations
Dermatitis	0.98	0.97
Sole Ulcer	0.96	0.96
White line disease	0.91	0.90
Concave dorsal wall	0.92	0.90
Interdigital phlegmon	0.93	0.94
Interdigital hyperplasia	0.96	0.94
ISP	**0.97**	**0.97**

Genetic Trends

Claw health index: ISP



Validation of Genomic proofs

Results of 10-fold cross-validation

	R^2	b_{VALUE}	(S.E.)
Dermatitis	0.19	0.72	(0.11)
Sole Ulcer	0.34	0.99	(0.08)
White line disease	0.27	0.94	(0.10)
Concave dorsal wall	0.35	0.94	(0.08)
Interdigital phlegmon	0.36	1.03	(0.08)
Interdigital hyperplasia	0.15	0.76	(0.15)

Conclusions and Next steps

- Despite the low heritabilities, large genetic variation between best and worst bulls is observed.
- The inclusion of feet and legs type traits in multi-trait analyses increased reliabilities of claw disorders EBVs.
- Accuracy of genomic proofs are low to moderate.

Next Steps:

- **March 2018**: Interim release for breeding companies
- **June 2018**: first official release


Grant agreements 4156558 and 4159203
Complutense University of Madrid
Spanish Holstein Association
Thanks
FRISONA Española

Estimation of the heritability of a newly developed ketosis risk indicator and the genetic correlations to other traits in three German cattle breeds

H. Hamann[1], A. Werner[2], L. Dale[2], P. Herold[1]

[1] State Office for Spatial Information and Land Development Baden-Württemberg, Germany
[2] Association for Performance and Quality Testing Baden-Württemberg, Germany

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Goal and derivation of the KetoMIR index:

KetoMIR index:

based on logistic regression

numeric range between 0 and 1

partition in three classes

„healthy“:	**0.00**	**-**	**0.50**
„low risk“:	**0.50**	**-**	**0.75**
„high risk“:	**0.75**	**-**	**1.00**

	Calibration set (n=109.479)	**Validation set (n=2.966)**
Sensitivity:	**0.70**	**0.72**
Specificity	**0.86**	**0.84**

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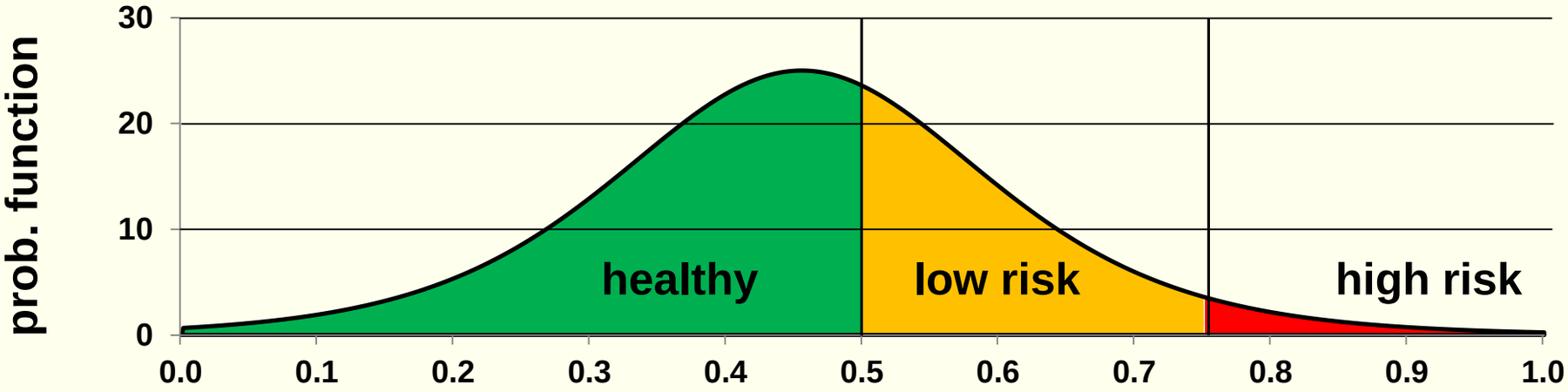
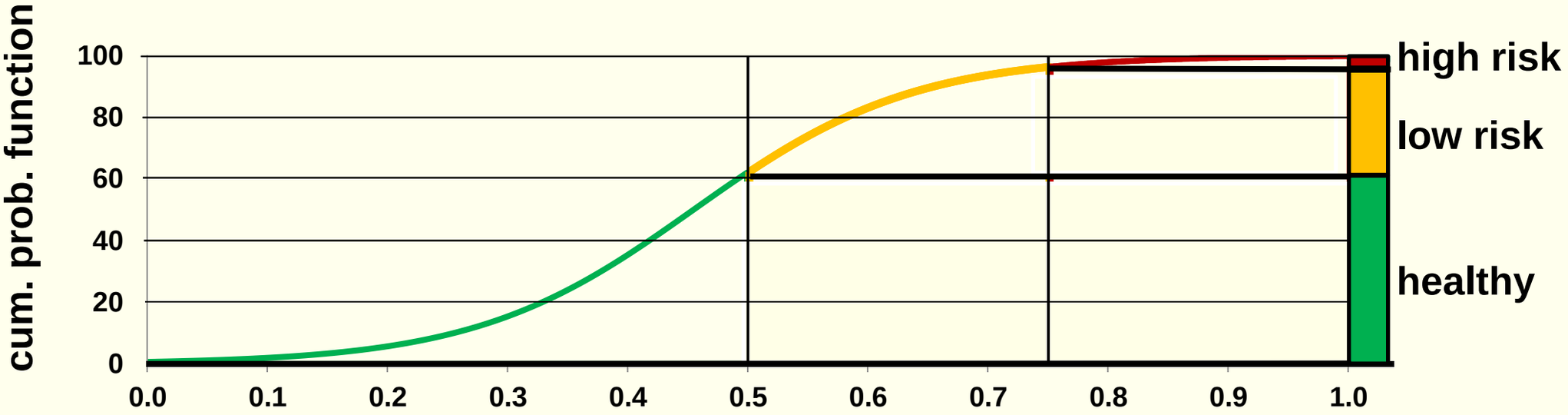
Probability functions of the KetoMIR index and derivaton of KetoMIR classes





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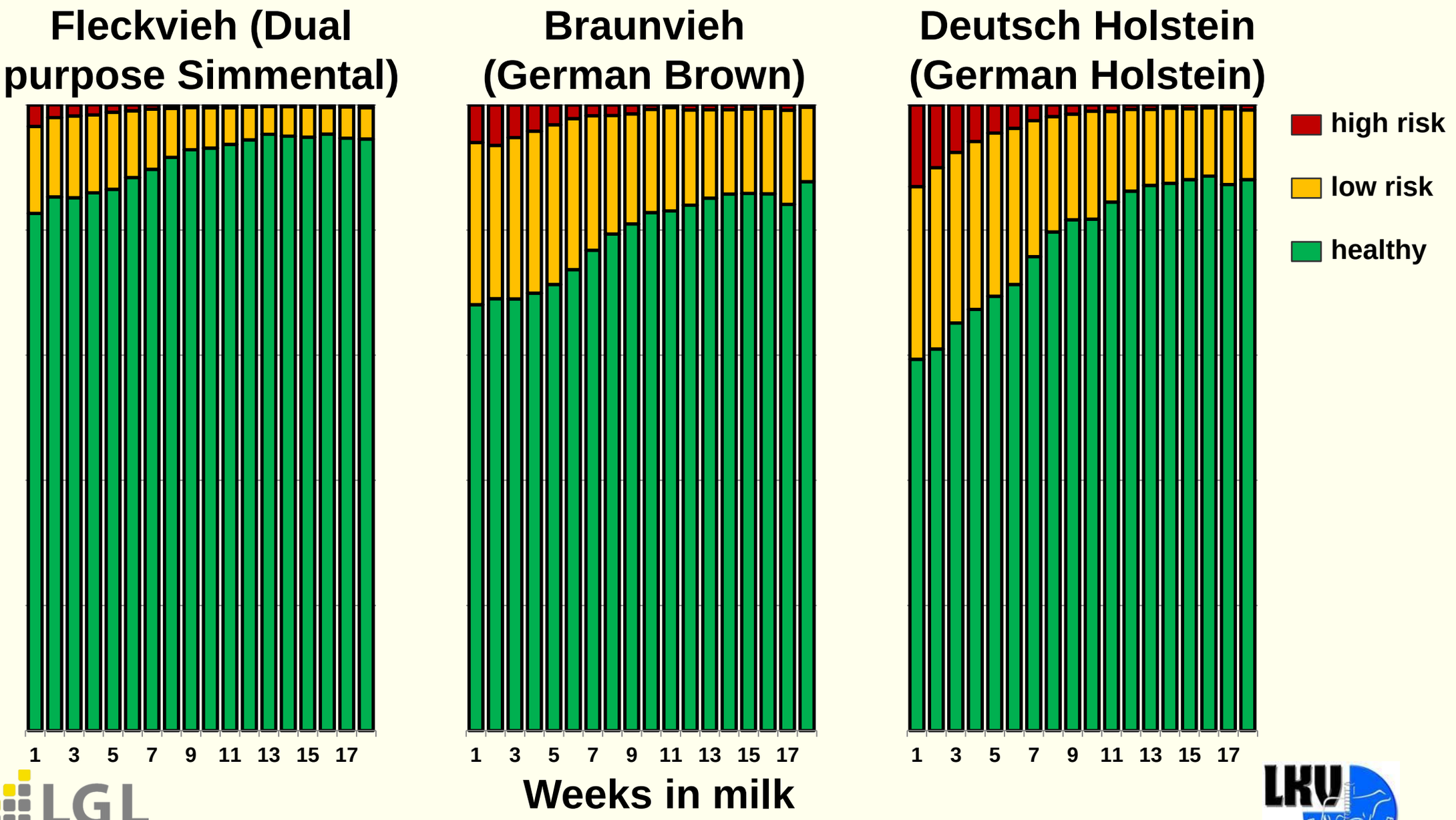
Distribution of KetoMIR classes for breeds and weeks in milk



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Breeding strategies:

Selection against ketosis liability:

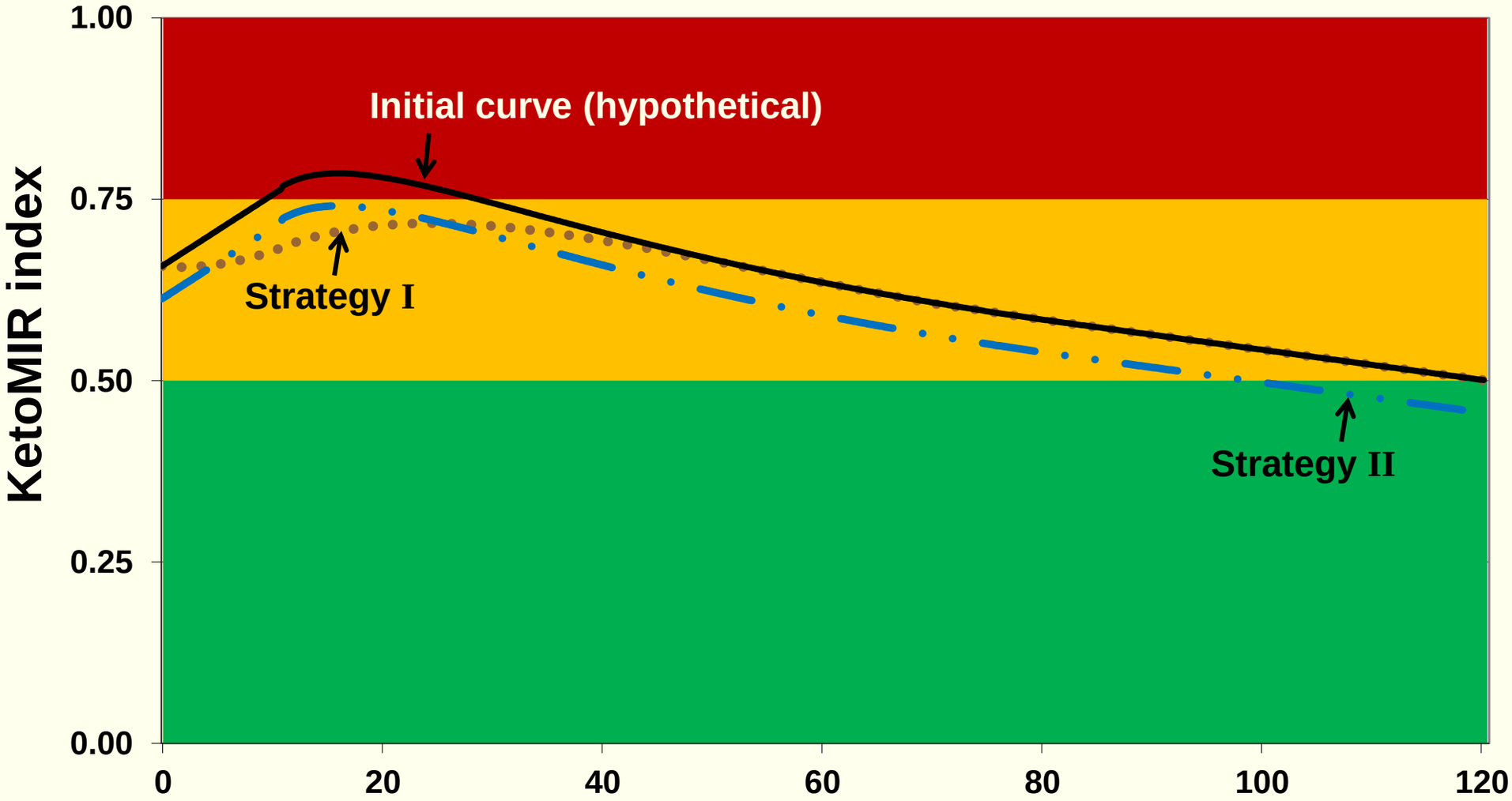
- based on a single (first) test day record (strategy I)

  „breaking“ the peaks in the KetoMIR curve

- based on the average of several test day records (strategy II)

  „lowering“ the general level of the KetoMIR curve

Breeding strategies



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Genetic analyses:

Data:

Fleckvieh:	**37.846**	**lactations with information for the first three test day records (analysed separately or as average)**
Braunvieh:	**15.771**	
Deutsch Holstein:	**31.425**	

<u>Repeatability model (within breed):</u>

HYS, lactation number, days in milk, permanent environmental effect, animal effect

Genetic analyses:

How is the KetoMIR index genetically related to other traits of interest?

Genetic correlations between KetoMIR index and traits for milk components

	TD	Fleckvieh	Braunvieh	Deutsch Holstein
Milk yield	1	0.414	0.525	0.190
	2	0.251	0.354	0.195
	3	0.160	0.207	0.274
	Ø	0.276	0.394	0.200
SCS	1	0.412	0.386	0.391
	2	0.343	0.307	0.279
	3	0.417	0.402	0.266
	Ø	0.401	0.402	0.307

Genetic analyses:

How is the KetoMIR index genetically related to other traits of interest?

Genetic correlations between KetoMIR index and traits for milk components

	TD	Fleckvieh	Braunvieh	Deutsch Holstein
Fat content	1	0.024	-0.077	0.002
	2	-0.280	-0.416	-0.262
	3	-0.294	-0.460	-0.339
	Ø	-0.194	-0.370	-0.190
Protein content	1	-0.661	-0.765	-0.663
	2	-0.665	-0.709	-0.718
	3	-0.557	-0.613	-0.686
	Ø	-0.630	-0.680	-0.655
Fat-protein-ratio	1	0.468	0.463	0.385
	2	0.152	0.108	0.187
	3	0.055	-0.117	0.053
	Ø	0.239	0.143	0.212

Genetic analyses:

Data:

Fleckvieh:	**37.846**	**lactations with information for the first three test day records (analysed separately or as average)**
Braunvieh:	**15.771**	
Deutsch Holstein:	**31.425**	

Repeatability model (within breed):

HYS, lactation number, days in milk, permanent environmental effect, animal effect

Multitrait model (within breed):

HYS, lactation number, days in milk, animal effect

Genetic analyses:

Heritabilities of the KetoMIR index (multitrait model)

	Trait	1. lact. h^2	2. lact. h^2	3. lact. h^2
Fleckvieh	1. TD / x. l	0.256	0.264	0.233
	2. TD / x. l	0.197	0.242	0.308
	3. TD / x. l	0.247	0.358	0.332
	Ø / x. L.	0.278	0.353	0.364
Braunvieh	1. TD / x. l	0.176	0.155	0.171
	2. TD / x. l	0.278	0.272	0.332
	3. TD / x. l	0.246	0.318	0.252
	Ø / x. L.	0.289	0.374	0.348
Deutsch-Holstein	1. TD / x. l	0.292	0.254	0.201
	2. TD / x. l	0.371	0.416	0.415
	3. TD / x. l	0.302	0.298	0.263
	Ø / x. L.	0.385	0.351	0.309

Genetic analyses:

Genetic correlations of the KetoMIR index between lactations (multitrait model)

	Trait	1. to 2. lact. r_g	1. to 3. lact. r_g	2. to 3. lact. r_g
Fleckvieh	1. TD / x. l.	0.790	0.761	0.994
	2. TD / x. l.	0.978	0.967	0.966
	3. TD / x. l.	0.918	0.962	0.992
	Ø / x. L.	0.921	0.908	0.999
Braunvieh	1. TD / x. l.	0.515	0.556	0.877
	2. TD / x. l.	0.655	0.835	0.903
	3. TD / x. l.	0.935	0.932	0.973
	Ø / x. L.	0.742	0.771	0.948
Deutsch-Holstein	1. TD / x. l.	0.819	0.780	0.998
	2. TD / x. l.	0.893	0.944	0.978
	3. TD / x. l.	0.819	0.861	0.935
	Ø / x. L.	0.836	0.858	0.985

Conclusion:

Data collecting as a matter of the routine milk analyses

Genetic background of the KetoMIR index is proven

Mixture of multitrait and repeatability models

Decision of a breeding value evaluation for the KetoMIR index

- **based on a single test day record**
- **based on the average of several test day records**

Applying random regression models to the data

Calculation of economic weights

Thank you for your attention!

LGL
www.lgl-bw.de

LKV Baden-Württemberg

Genetic analyses:

Is the KetoMIR index (classes) heritable?

Heritabilities for the KetoMIR index, catecorical and binary classes

Fleckvieh (Dual purpose Simmental)

TD	Index	C3	B050	B075
1	0.22	0.09	0.09	0.02
2	0.22	0.04	0.05	0.01
3	0.30	0.04	0.05	0.01
Ø	0.30	0.08	0.08	0.01

Braunvieh (German Brown)

TD	Index	C3	B050	B075
1	0.23	0.11	0.09	0.02
2	0.28	0.08	0.09	0.01
3	0.34	0.11	0.11	0.01
Ø	0.33	0.11	0.10	0.00

Deutsch Holstein (German Holstein)

TD	Index	C3	B050	B075
1	0.24	0.13	0.12	0.04
2	0.28	0.12	0.12	0.02
3	0.39	0.13	0.13	0.01
Ø	0.34	0.15	0.14	0.03

Genetic analyses:

How is the KetoMIR index genetically related to ketosis?

Genetic correlations between ketosis (clinical) and the KetoMIR index and categorical classes

TD	Fleckvieh		Braunvieh		Deutsch Holstein	
	Index	C3	Index	C3	Index	C3
1	1.000	1.000	0.749	1.000	0.438	0.522
2	1.000	1.000	0.376	0.368	0.045	0.122
3	1.000	1.000	0.070	-0.194	0.052	-0.065
Ø	1.000	1.000	0.240	0.153	0.319	0.445

Genetic analyses:

Can the KetoMIR index be used as auxiliary trait in breeding programmes?

- **Is the KetoMIR index (classes) heritable?**
- **How is the KetoMIR index genetically related to ketosis?**
- **How is the KetoMIR index genetically related to other traits of interest?**

Genetic parameters of immune response estimated using genetically divergent lines of Holstein-Friesian dairy heifers

M.D. Price, M.D. Camara, J.R. Bryant, T.M. Grala, S. Meier and C.R. Burke

DairyNZ Limited, Private Bag 3221, Hamilton, New Zealand

DairyNZ

Background

- Fertility research herd (Meier *et al.* 2017)
  - ~540 Holstein-Friesian heifers (2015 born)
  - From assortative mating of high or low fertility parents
- Research aims
  - Underlying physiology driving fertility differences
  - New management strategies
  - New traits to predict fertility (h^2 = 0.03)

Immune Response (IR)

- Immunity impacts reproductive function
  - Immune cells key to successful pregnancy (Fair 2015)
  - Post-partum uterine recovery
- Previous IR studies:
  - Heritability (h^2): 0.16 to 0.64
    (Mallard *et al*., 1983; Wagter *et al*., 2000;
    Hernández *et al*., 2006; Thompson-Crispi *et al*., 2012)
  - Genetic Correlation (r_g) with fertility: -0.19 to 0.20
    (Thompson-Crispi *et al*., 2012)

Objectives

- Estimate genetic parameters in NZ Holstein-Friesian dairy cattle:
  - IR (3 traits) h^2 and r_g
  - IR r_g with Breeding Worth (BW) index traits
    - In NZ, BW composed of 8 traits (including fertility)
- Account for bias due to herd structure

Materials & Methods

- 539 Holstein-Friesian heifers
  - Born across 379 herds (June-Sept 2015)
  - From assortative mating of high/low fertility BV parents

    → High & Low fertility heifer lines
- 7 “Contemporary Groups” (CG)
- Pedigree of 10,992 animals
  - 18 generations deep

Materials & Methods

- Immunization protocol (Thompson-Crispi *et al*., 2012)
  - Immunized at ~220 days old
  - Antibody-mediated IR (AMIR)
    - HEWL @ days 0 & 14
    - IgG1 conc. @ days 0, 14 & 21

AMIR0 → Control covariate

AMIR14, **AMIR21** } Response variates

  - Cell-mediated IR (CMIR)
    - *C. albicans*/control @ day 21
    - Log skinfold thickness ratio @ day 23

CMIRc → Control covariate

CMIRt → Response variate

Materials & Methods

- BLUP mixed model:

  $y = CG + control + a + e,$ $y \in$ {AMIR14, AMIR21, CMIRt, nEBV}

  - Univariate model → h^2
  - Bivariate model → r_g
- Estimated Breeding Values (EBV) of BW:
  - De-regressed (dEBV) by ÷ reliability (Garrick *et al*. 2009)
  - Noise added (nEBV) from $N(0,\sigma_e^2)$
  - 100 runs with noise re-sampling → mean r_g ± SE

Materials & Methods

- r_g between nEBV and IR also estimated via a Pearson correlation
  - Simple, and used as validation (no SE though)
- Explored herd divergence in fertility
  - Pedigree determined to be deep enough

Results & Discussion

	AMIR14	AMIR21	CMIRt
AMIR14	**0.44 ± 0.14**	0.67 ± 0.17	-0.44 ± 0.43
AMIR21	0.44 ± 0.04	**0.47 ± 0.15**	-0.07 ± 0.40
CMIRt	-0.03 ± 0.05	0.01 ± 0.05	**0.11 ± 0.10**

r_g

r_p

h^2

Results & Discussion

		AMIR14	AMIR21	CMIRt
BW trait	h^2	r_g ± SE	r_g ± SE	r_g ± SE
Protein	0.31	-0.10 ± 0.22	-0.13 ± 0.21	-0.39 ± 0.31
Fat	0.33	-0.22 ± 0.21	-0.10 ± 0.21	-0.24 ± 0.29
Volume	0.36	-0.12 ± 0.20	-0.08 ± 0.20	-0.40 ± 0.32
Liveweight	0.35	-0.15 ± 0.17	-0.22 ± 0.17	*
Fertility	0.03	0.09 ± 0.22	-0.17 ± 0.21	-0.04 ± 0.32
SCS	0.12	0.05 ± 0.25	0.03 ± 0.25	0.10 ± 0.39
RSv	0.04	0.03 ± 0.62	-0.08 ± 0.41	0.17 ± 0.58
BCS	0.19	0.02 ± 0.19	-0.15 ± 0.18	0.19 ± 0.27

Conclusions

- IR h^2 low/moderate
- AMIR & CMIR antagonistic

} An IR index should have both AMIR & CMIR

- Weak genetic correlations between IR & BW traits
  - IR unlikely helpful as predictor trait ← including for Fertility
  - Selection on IR or BW unlikely to affect each other
    - Caution however, as r_g generally unfavourable still
- Widespread IR recording impractical

→ Genomic selection reference population

Acknowledgements

- Funded by partnership between NZ MBIE and NZ dairy farmers via DairyNZ Inc.
- In-kind support from LIC and CRV Ambreed
- DairyNZ farm & technical staff for data collection
- Dorian Garrick for input to address herd divergence

Q & A

DairyNZ

Materials & Methods

- r_g with EBV verified by Pearson correlation

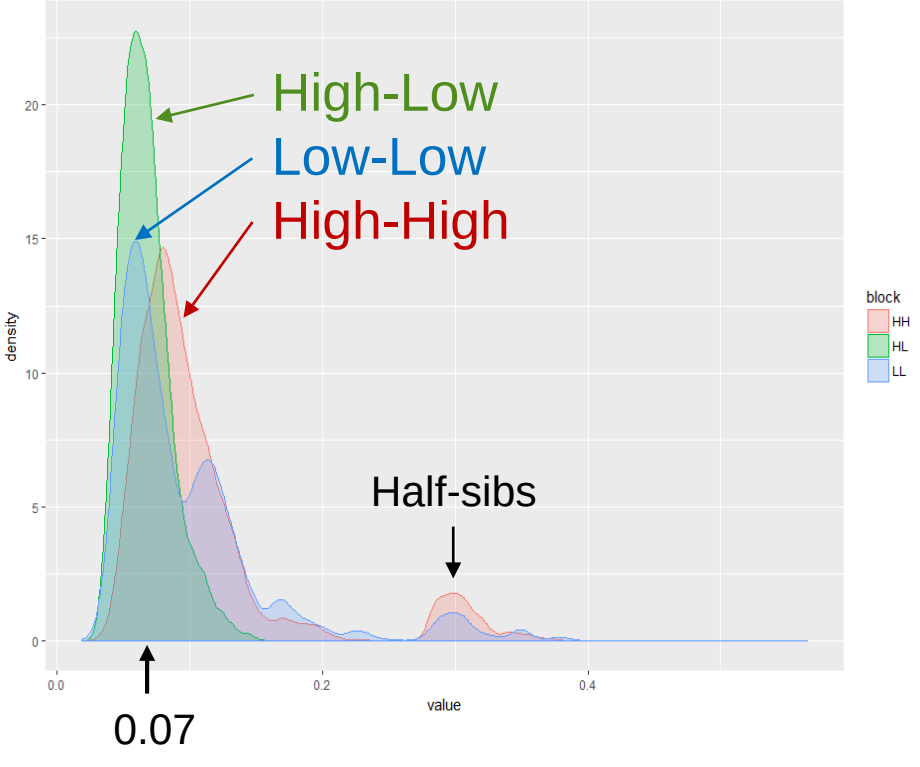
From IR univar →

$$\frac{\sigma^2_{IR} \times \sigma^2_{EBV}}{cov(\sigma^2_{IR}, \sigma^2_{EBV})}$$

← Resid. from bivar. *fixed* model; $\sigma_e^2 \approx \sigma_a^2$ as EBV genetic est.

  - SE not available
- Accounting for fertility divergence
  - If divergence between lines present in founders, and
  - If fertility r_g>0 with trait X, then
  - Model for X req. 2 gen. distributions
    - Fertility line term (GG or fixed effect)

Materials & Methods



- Distribution of A-matrix heifer coefficients
  - Apart from sibs, both within- & between-line ~0.07
  - ∴ pedigree deep enough; 1 genetic distribution ok

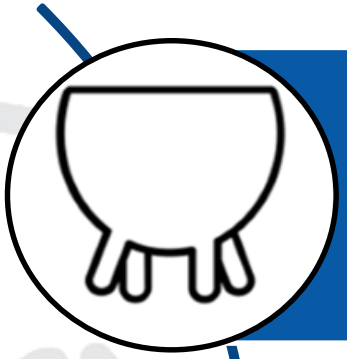
		AMIR14		AMIR21		CMIRt	
BW trait	h^2	Resampling	Pearson	Resampling	Pearson	Resampling	Pearson
Protein	0.31	-0.10 ± 0.22	-0.05	-0.13 ± 0.21	-0.06	-0.39 ± 0.31	-0.05
Fat	0.33	-0.22 ± 0.21	-0.15	-0.10 ± 0.21	-0.03	-0.24 ± 0.29	0.05
Volume	0.36	-0.12 ± 0.20	0.00	-0.08 ± 0.20	0.02	-0.40 ± 0.32	-0.08
Liveweight	0.35	-0.15 ± 0.17	-0.16	-0.22 ± 0.17	-0.18	*	0.33
Fertility	0.03	0.09 ± 0.22	0.10	-0.17 ± 0.21	-0.05	-0.04 ± 0.32	-0.07
SCS	0.12	0.05 ± 0.25	-0.01	0.03 ± 0.25	-0.03	0.10 ± 0.39	0.06
RSv	0.04	0.03 ± 0.62	-0.01	-0.08 ± 0.41	-0.01	0.17 ± 0.58	0.19
BCS	0.19	0.02 ± 0.19	0.05	-0.15 ± 0.18	-0.09	0.19 ± 0.27	0.08

Improved genetic evaluation of health traits using metabolic biomarkers in Nordic dairy cattle

E. Rius-Vilarrasa[1], W.F. Fikse[1], E. Carlén[1], J-Å. Eriksson[1], J. Pöso[2], U.S. Nielsen[3], G. P. Aamand[4]

[1] **Växa Sverige**, Uppsala, Sweden
[2] **Faba co-op,** Vantaa, Finland
[3] **SEGES**, Aarhus N, Denmark
[4] **Nordic Cattle Genetic Evaluation**, Aarhus N, Denmark

Health traits evaluations



UDDER HEALTH

Clinical mastitis , Cell count (indicator trait)

Udder conformation (indicator traits)

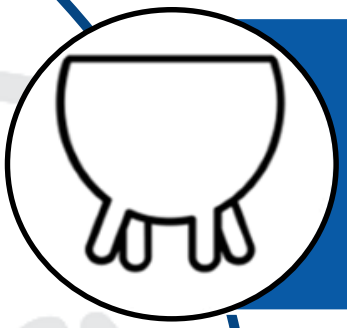
CLAW HEALTH

Claw diseases (trimmers)

GENERAL HEALTH

Reproductive-, Metabolic disorders,
Feet and Leg problems -- Clinical mastitis,
metabolic biomarkers (BHB & Acetone indicator traits)

Health traits evaluations



UDDER HEALTH

Clinical mastitis , Cell count (indicator trait)

Udder conformation (indicator traits)

CLAW HEALTH

Claw diseases (trimmers)

GENERAL HEALTH

Reproductive-, Metabolic disorders,
Feet and Leg problems -- Clinical mastitis,
metabolic biomarkers ***(BHB & Acetone indicator traits)***

General Health index

GH index = Early Reproductive Disorders (**ERP**)

+ Late Reproductive Disorders (**LRP**)

+ Feet & Leg Problems (**FLP**)

+ *Ketosis (**KET**)*

+ *Other Metabolic Disorders (**OMB**)*

General Health index

GH index = Early Reproductive Disorders (**ERP**)

+ Late Reproductive Disorders (**LRP**)

+ Feet & Leg Problems (**FLP**)

Metabolic Disorders	+ *Ketosis (**KET**)* + *Other Metabolic Disorders (**OMB**)*

General Health index

GH index = Early Reproductive Disorders (**ERP**)

+ Late Reproductive Disorders (**LRP**)

+ Feet & Leg Problems (**FLP**)

+ *Ketosis (**KET**)*

+ *Other Metabolic Disorders (**OMB**)*

Metabolic Biomarkers - New indicator traits

Metabolic Biomarkers

Ketone bodies detectable in milk samples:

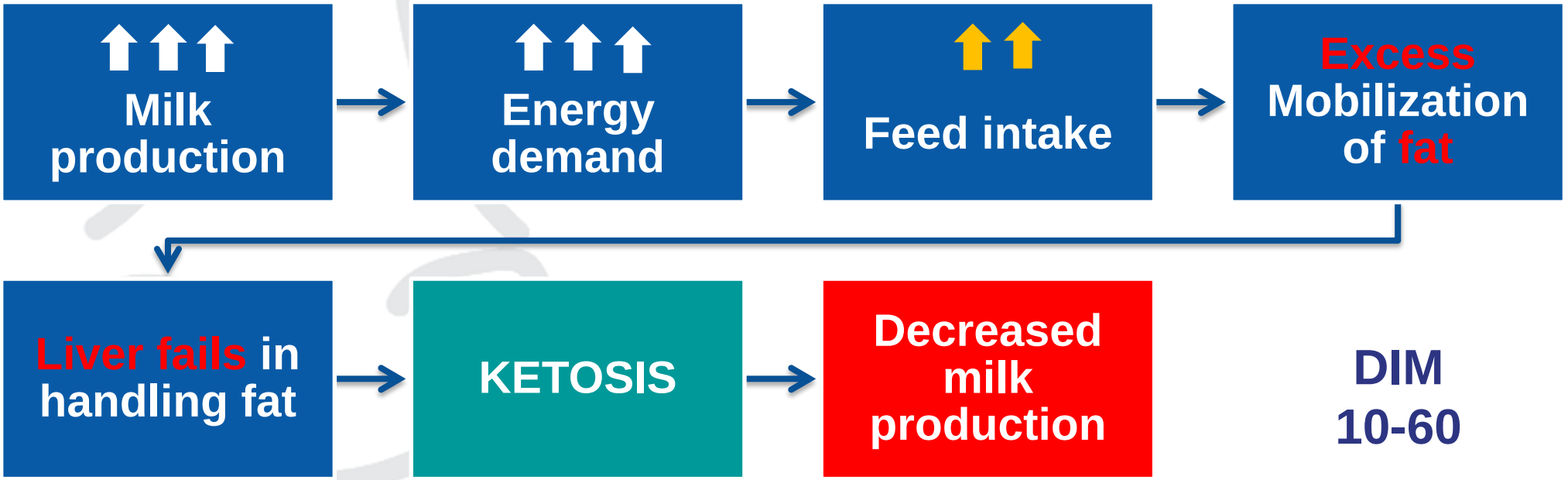
β-hydroxybutyrate (BHB) & Acetone

Metabolic Biomarkers

Ketone bodies detectable in milk samples:

β-hydroxybutyrate (BHB) & Acetone

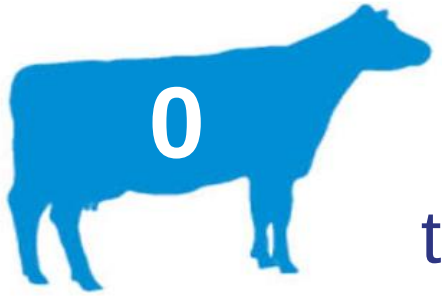
Leading to ketosis:



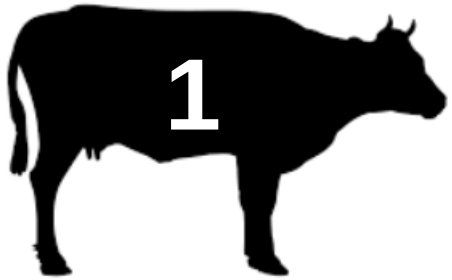
Data – Disease traits

- **Treatment records since the 80's**
- **Veterinarians, AI technicians and Farmers**
- **Breeds:** Holstein, Jersey and Red Dairy Cattle (RDC)
- **Lactations 1-3**
- **Defined as binary 0/1 trait**

Healthy
non-treated

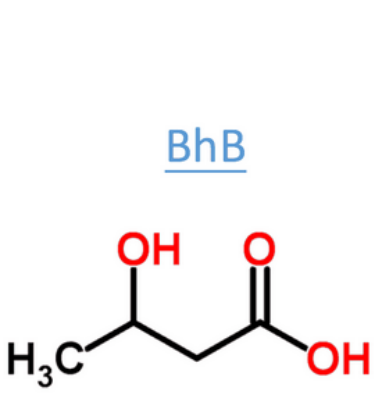


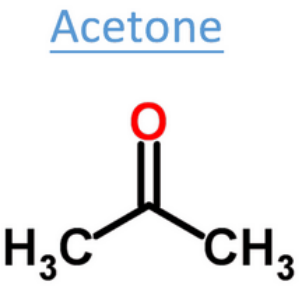
Sick
treated



Data - BHB and Acetone

- **Since 2013 –** Denmark
- **From 2018 –** Finland and Sweden
- **Routine predictions from milk samples collected within the milk recording scheme –** mmol/L
- **Lactations** 1-3





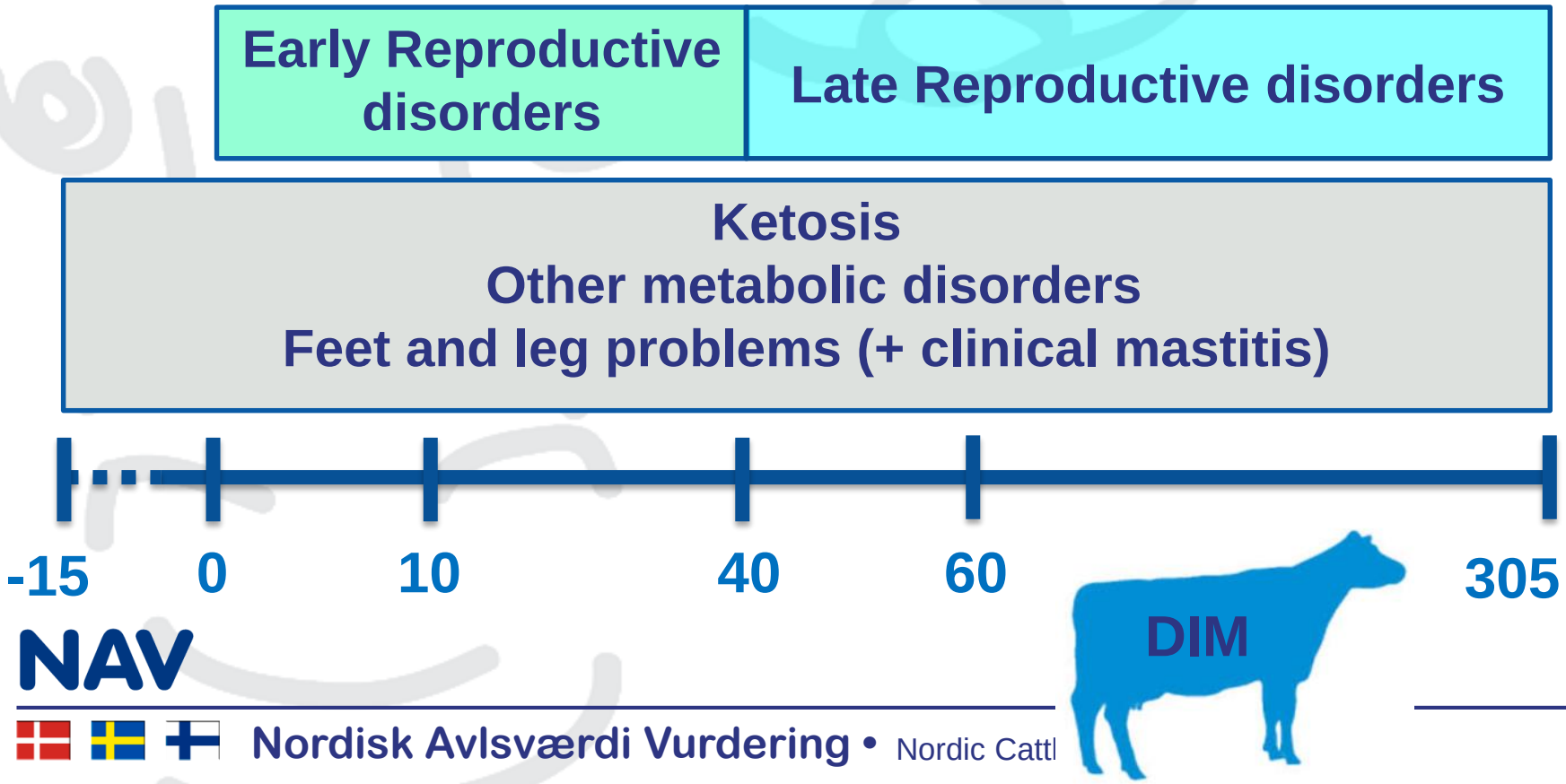
Trait definitions

Ketosis
Other metabolic disorders
Feet and leg problems (+ clinical mastitis)

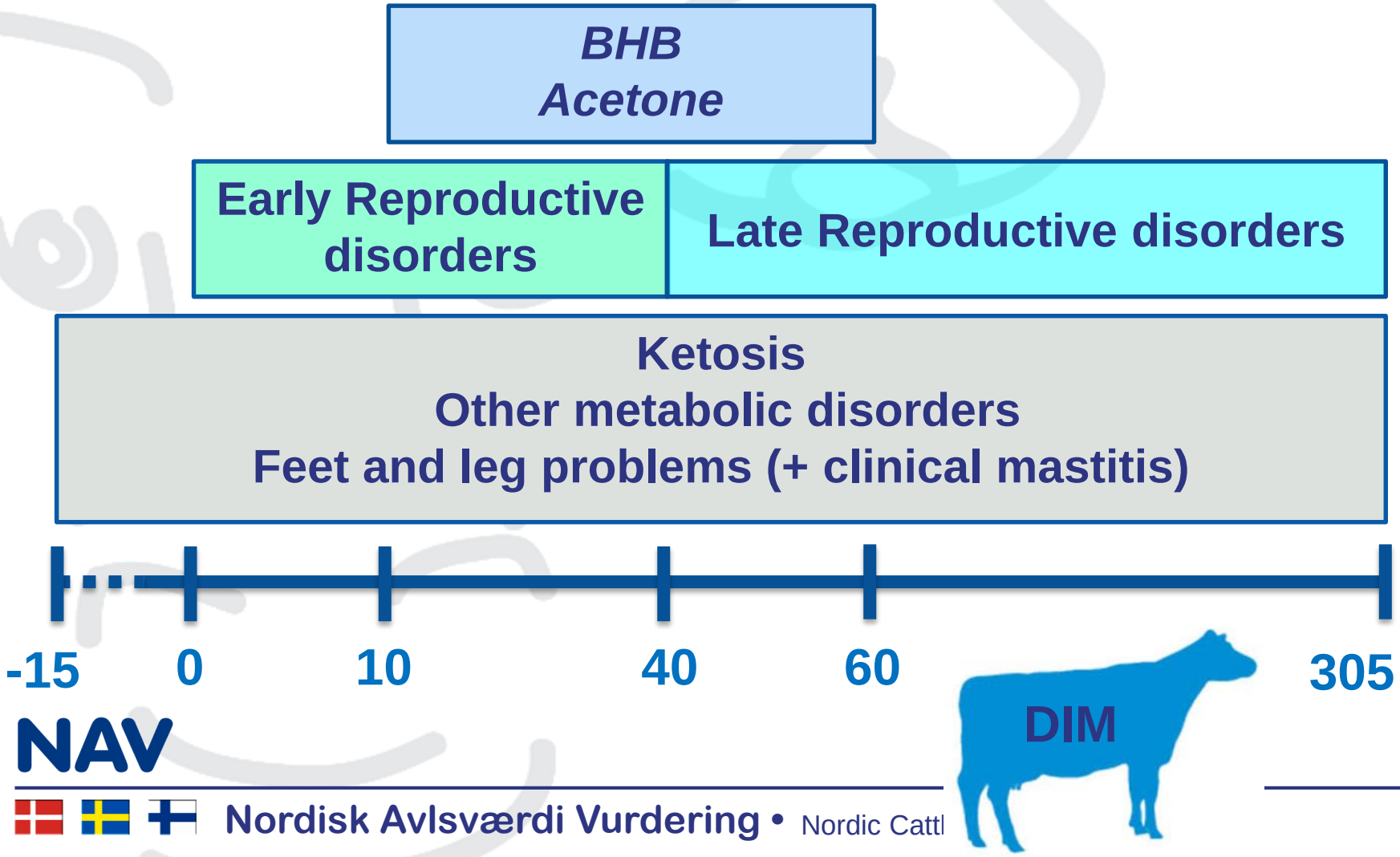
-15 0 10 40 60 305

DIM

Trait definitions



Trait definitions



Model - Multi-trait multi-lactation animal model

Fixed effects

Herd-year * country

Calving age * country

Year-month calving * country

Random effects

Animal

Cow Permanent environmental effect *(only BHB/Acetone)*

(fixed) Regression

Lactation stage *(only BHB/Acetone)*

Breeds and heterosis *(only HOL)*

***Pre-adjustment for heterogeneous variance*

Heritabilities and genetic correlations
Holstein, lactation 1

	Early reproductive disorders	Late reproductive disorders	Other metabolic disorders	Ketosis	Feet and leg problems
Early reproductive disorders	**0.020**	0.40	0.40	0.29	0.35
Late reproductive disorders		**0.010**	0.29	0.21	0.36
Other metabolic disorders			**0.006**	0.74	0.38
Ketosis				**0.012**	0.19
Feet and leg problems					**0.010**

Low heritabilities & low, moderate to high genetic correlations

Heritabilities and genetic correlations
Holstein, lactation 1

	Early reproductive disorders	Late reproductive disorders	Other metabolic disorders	Ketosis	Feet and leg problems
Early reproductive disorders	**0.020**	0.40	0.40	0.29	0.35
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Other metabolic disorders			**0.006**	0.74	0.38
Ketosis				**0.012**	0.19
Feet and leg problems					**0.010**

Low heritabilities & low, moderate to high genetic correlations

Heritabilities and genetic correlations
Holstein, lactation 1

	Other metabolic disorders	Ketosis	BHB	Acetone
Other metabolic disorders	**0.006**	0.74	0.48	0.65
Ketosis		**0.012**	0.65	0.76
BHB			**0.15**	0.88
Acetone				**0.06**

Low to moderate heritabilities & high genetic correlations

Heritabilities and genetic correlations
Holstein, lactation 1

	Other metabolic disorders	Ketosis	BHB	Acetone
Other metabolic disorders	**0.006**	0.74	0.48	0.65
Ketosis		**0.012**	0.65	0.76
BHB			**0.15**	0.88
Acetone				**0.06**

Low to moderate heritabilities & high genetic correlations

Heritabilities and genetic correlations
Holstein, lactation 1

	Other metabolic disorders	Ketosis	BHB	Acetone
Other metabolic disorders	**0.006**	0.74	0.48	0.65
Ketosis		**0.012**	0.65	0.76
BHB			**0.15**	0.88
Acetone				**0.06**

Low to moderate heritabilities & high genetic correlations

Value of including BHB & acetone

Reliabilities for cows with or without BHB and Acetone observations, that have veterinary treatment observations but not own progeny

Breed	BHB & Acetone obs	Other Metabolic disorders		Ketosis		GH index	
HOL	Yes	0.34	15%	0.36	19%	0.32	6%
	No	0.29		0.29		0.30	

Summary

- New objective indicator traits for Ketosis in the General Health evaluation
  - Diagnosis for subclinical and clinical ketosis

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- Higher heritability of BHB and acetone than for Ketosis

Summary

- New objective indicator traits for Ketosis in the General Health evaluation
  - Diagnosis for subclinical and clinical ketosis
- Metabolic biomarkers showed favorable and high genetic correlations with Ketosis
- Higher heritability of BHB and acetone than for Ketosis
- The inclusion of the metabolic biomarkers increases cow EBV reliability, especially for ketosis and metabolic disorders

Summary

- The new General Health evaluation was introduced November 2017 for all breeds (Holstein, RDC and Jersey)

NAV

Nordisk Avlsværdi Vurdering • Nordic Cattle Genetic Evaluation

November 2017

Disease traits and sub-traits used in the GH evaluation

Early reproductive disorders	Late reproductive disorders	Ketosis	Other metabolic diseases	Feet and leg problems
• Retained placenta • Hormonal reproductive disorders • Infective reproductive disorders • Other reproductive disorders	• Hormonal reproductive disorders • Infective reproductive disorders • Other reproductive disorders	• Ketosis • *BHB (β-hydroxybutyrate)* • *Acetone*	• Milk fever • Other metabolic diseases • Other feed related disorders • Other diseases	• Feet and legs disorders

Disease frequencies in % - HOLSTEIN

Traits	DNK	SWE	FIN
ERP	12	2	3
LRP	4	8	13
KET	5	<1	2
OMB	2-9*	1-7	2-8
F&L	8	3	2

***Lactation 1 to lactation 3**

Disease frequencies in % - RDC

Traits	DNK	SWE	FIN
ERP	8	2	3
LRP	2	6	12
KET	1-4*	<1	1
OMB	1-7	1-5	1-6
F&L	7	2	2

***Lactation 1 to lactation 3**

Disease frequencies in % - Jersey

Traits	DNK
ERP	3
LRP	2-3*
KET	2-3
OMB	2-15
F&L	5-7

***Lactation 1 to lactation 3**

ANAFI

ICAR THE GLOBAL STANDARD FOR LIVESTOCK DATA
Annual Conference
ICAR2018.NZ
7 – 11 February 2018
Aotea Centre
Auckland,
New Zealand
INTERBULL

Alternative use of Somatic Cells Counts in genetic selection for mastitis resistance: a new selection index for Italian Holstein breed

R. Finocchiaro[1], G. Visentin[1], M. Penasa[2], J.B.C.H.M. van Kaam[1], M. Marusi[1], G. Civati[1] & M. Cassandro[2]

[1]ANAFI - Italian Holstein Association
[2] DAFNAE - University of Padova

LATTeco

INTERBULL

Interbull Open 3: R&D in (inter)national evaluations: Implementation of new traits in dairy and beef cattle.

CONTEXT

- Mastitis is one of the major diseases in dairy herds

- It induces economic costs for breeders mainly due to worsening of milk yield, milk quality and increase of health care cost

- Somatic cell count (SCC) is an indicator of both resistance and susceptibility of cows to intramammary infections

IDENTIFICATION OF MASTITIS

- ✓ DIRECT MEASURES corresponding to the diagnosis of inflammation with a positive bacteriological examination and observation of clinical cases
  - Accurate
  - Repeated and expensive tests on a large scale

- ✓ INDIRECT MEASURES linked with inflammation of the udder
  - Somatic Cell Count (SCC)
  - Electrical conductivity of milk
  - Cell differentiation (e.g. lymphocyte, macrophages and polymorphonuclear neutrophils)

MASTITIS RECORDING SYSTEM

- Mastitis is not widely implemented in disease-recording systems in many countries
- Lactation-mean SCC or test-day SCC are generally used as indirect mastitis indicators
- Other traits derived from SCC have been suggested as alternatives to improve/implement genetic evaluations for mastitis resistance, such as :
  - maximum SCC
  - standard deviation of SCS
  - SCC peaks pattern

WHAT HAPPENS IN THE WORLD

…INTERBULL DATA…and udder health data

- Two type of EBVs are considered by Interbull:
  - Somatic cell score (SCS)
  - Udder health (MAS) → as trait
    → when missing same as SCS field

- **In total 29 countries send SCS info**
  - **Only 5 countries** provide udder health (MAS) info (Canada, Scandinavian countries, France, The Netherlands and Italy)

WHAT HAPPENS IN THE WORLD

Country	Udder health index	h^2 «Udder health index»	h^2 «Clinical Mastitis»
DFS	$0{,}25*CM_{11}+0{,}25*CM_{12}+0{,}30*CM_{2}+0{,}20*CM_{3}$	6%	3 - 7%
France	0,60*SCS + 0,40*CM	15%	2%
The Netherlands	0,40*SCM+0,60*CM	9%	6%
Canada	$^1/_3\ CM_1 + {}^1/_3 CM_2 + {}^1/_3\ SCS$	15%	3 - 5%
Italy	Predicted traits for CM	15%	3%

CM=clinical mastitis; SCS=Somatic Cell Score; SCM=Sub-Clinical Mastitis

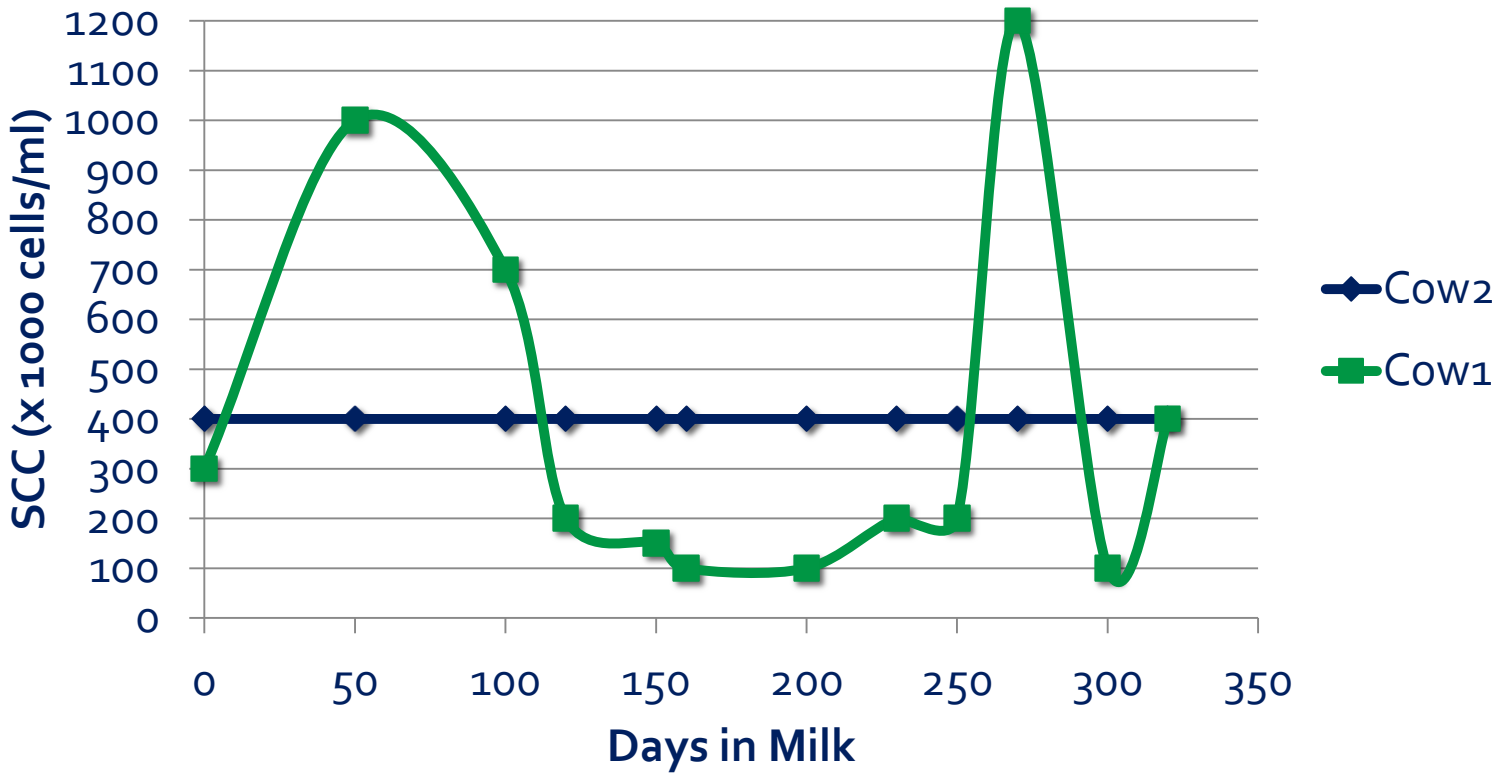
AIM

Setup a new Udder Health Index for Mastitis Resistance using indicators derived from SCC test-day

SCC PATTERN EXAMPLE

……It's important to realize the trend of cells during lactation…

Constant (Cow 2) Fluctuating (Cow 1)



DATA-EDITING

- Only first parity cows (for the moment)
- Cows with at least 3 TDscc records,
- Cows with 1st TD ≤ 60 days after calving
- Cows TDs interval ≤ 70 days

Within lactation SCC patterns have been defined:

- **L** = "Low" (< 100,000 SCC/mL)
- **I** = "Intermediate" (100,000-400,000 SCC/mL)
- **H** = "High" (> 400,000 SCC/mL)

- Several samples distributed in the population were analyzed in order to get an idea of trend repeatability

STEP 1:
NOVEL TRAITS DEFINED TO CAPTURE DIFFERENT ASPECTS OF MASTITIS

TRAIT	Description
SCS_{150}	Average SCS from 5 to 150 days of lactation
$SCS_{151\text{-}305}$	Average SCS from 151 to 305 days of lactation
SCS_{TOTAL}	Average SCS in the entire lactation
INFECTION	(0/1): 1 = cow with at least 1 TD identified as **I** or **H** within lactation
SCS_SD	SCS Standard deviation within lactation
SEVERITY of infection (%)	Ratio between n° TD **H** and the total n° of TD within lactation
PEAK	Presence of peaks **L-H-L** or **L-H-H** within lactation
	0 = no peaks 1 = at least one of the two peaks

STEP 2: VALIDATION ON REAL DATA

- Once indicators traits have been defined, these have been validated on a "robust" sample data-set well distributed in the Italian territory with direct mastitis information

- Those with the strongest genetic correlation with clinical mastitis have been retained.

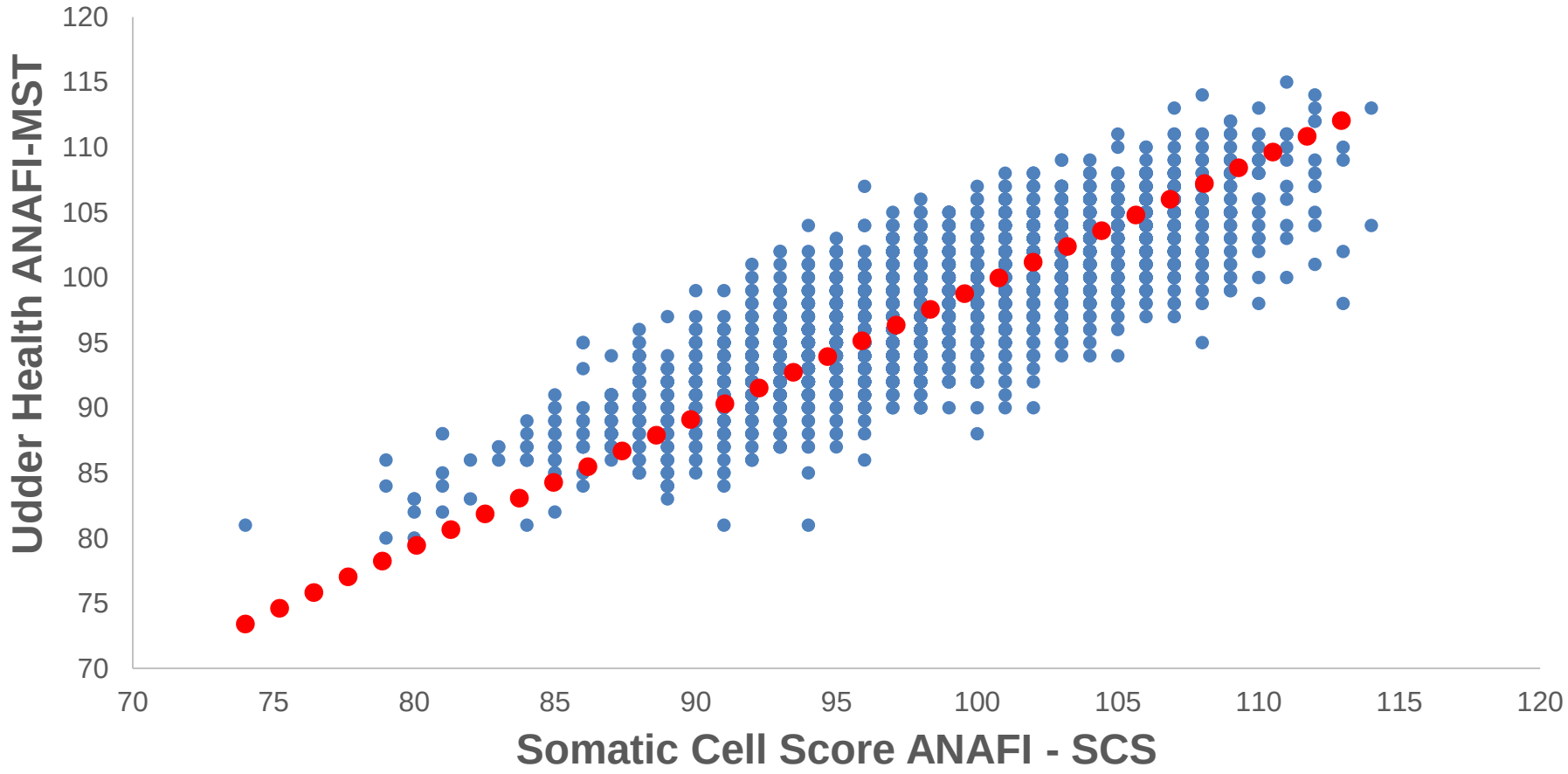
- The new udder health index (MST) was built following selection index theory in order to estimate appropriate weights to combine the alternative traits in the MST aggregate udder health index

RESULTS

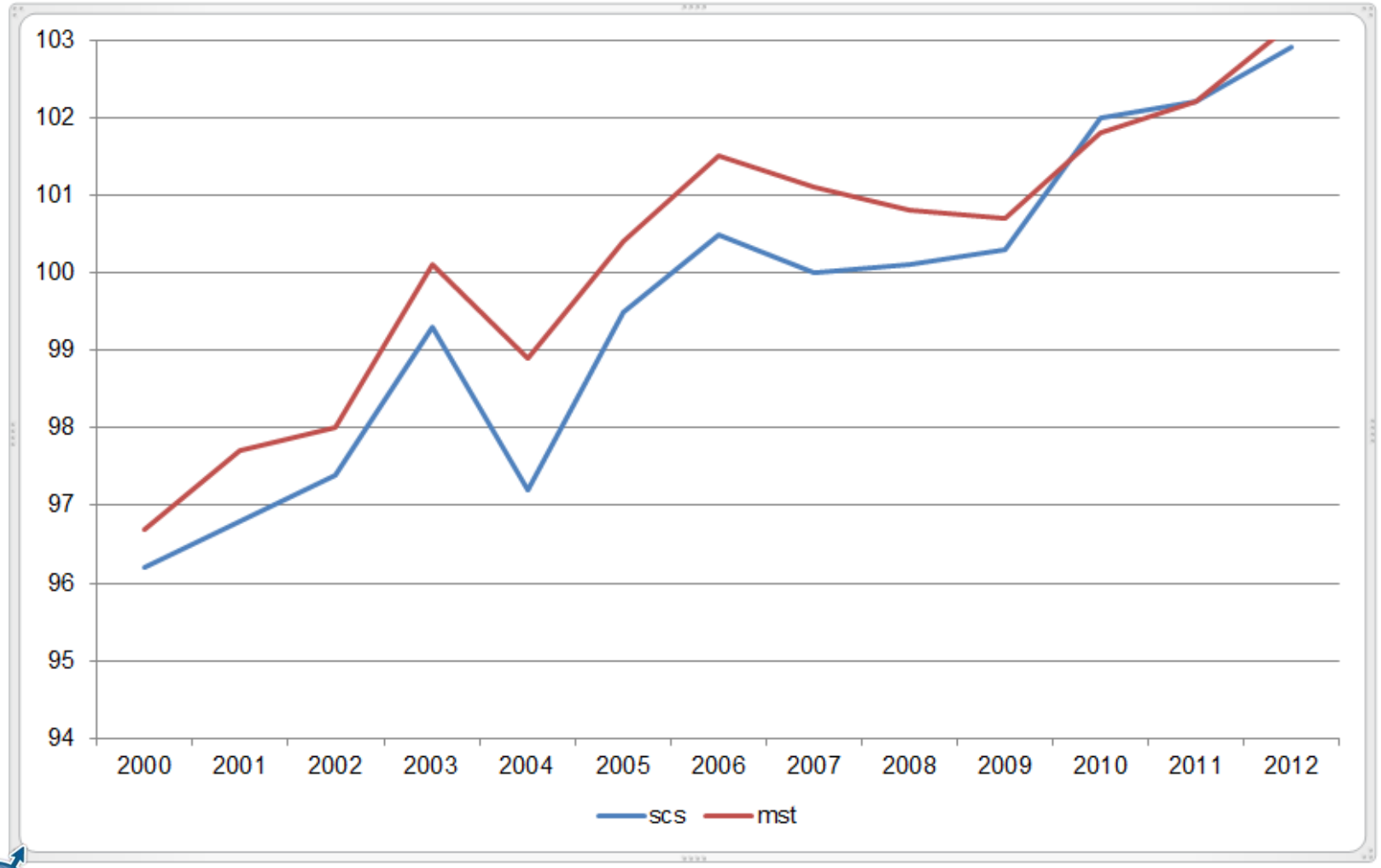
Trait	Mean	SD	h^2	r_g
Clinical mastitis	0,09	0,28	0,03	
SCS150	2,58	1,37	0,06	0,39
SD_SCSt	1,20	0,62	0,02	0,44
Severity of infection	0,11	0,19	0,07	0,41
Peaks pattern	0,10	0,31	0,02	0,51

RESULTS

	Correlation
MST *vs.* SCS	80 %



BULLS GENETIC TREND



CONCLUSIONS

- The new index (MST) **DOES NOT REPLACE** the current SCS Index but it is **a new tool** to select DIRECTLY for clinical mastitis

- This index has been published for the first time during December 2017 evaluation with mean 100 and standard deviation 5.

- Initially this index will be published only for national and international bulls (**no genomics**).

- Currently only first parity cows

FUTURE PERSPECTIVES

- Pluriparous cows and Genomic evaluation → gMace
- Increase mastitis data-set
- Use of differential cells? → Combine all new info

THANKS FOR YOUR ATTENTION!

Breeding for resistance against Paratuberculosis: Genetic relation between antibody response and faecal shedding of MAP in dairy cattle

L.C.M. de Haer, M.F. Weber, G. de Jong

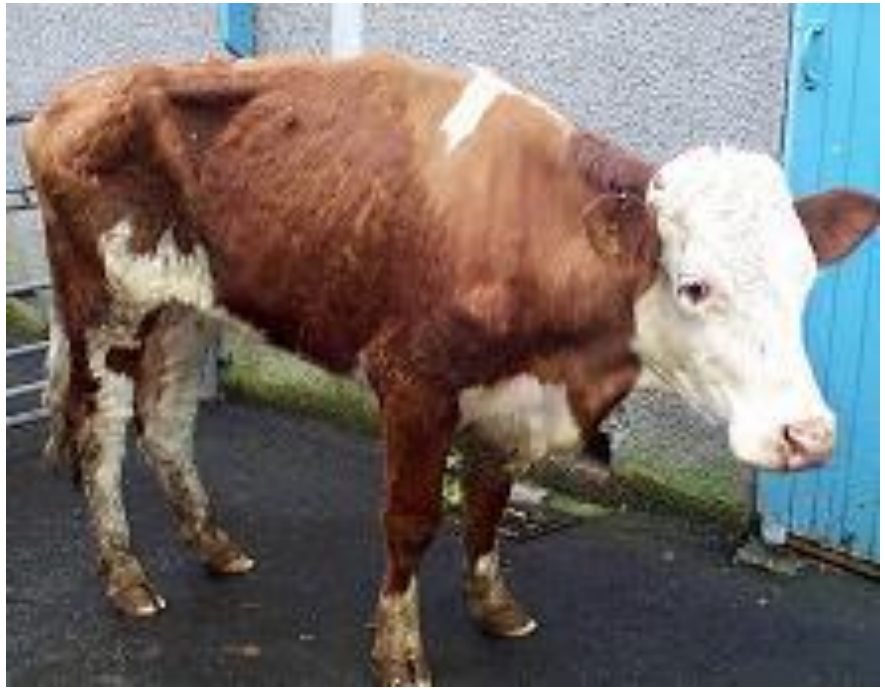
CRV and GD Animal Health; The Netherlands

What is Paratuberculosis?

Paratuberculosis is a chronic intestinal infection of ruminants caused by Mycobacterium avium ssp. Paratuberculosis (MAP).

Infections will develop slowly into:

- chronic intractable diarrhea
- weight loss
- production losses
- low birth weight of calves
- ultimately death since no treatment is available



Economical importance

In The Netherlands in 2008:

47% of farms had at least one positive animal
2.4% of all animals was positive

Economical loss:
770,- euro/year per herd (50 animals) with infected cows

For every animal that develops clinical signs
– there will be 7 to 10 animals excreting
– there will be a further 7 to 10 infected, but not yet excreting (possibly excreting in the future)

Is breeding against Paratbc possible?

- Goal is reduction of faecal shedding of MAP
- Tool is antibody response in milk

-> Are genetic variations of antibody levels and faecal excretion present?

-> Is a lower antibody level in milk related to less faecal shedding?

Data

Causative agent of paratuberculosis:
Mycobacterium avium ssp. Paratuberculosis (MAP)

Two data sets:

1) Individual milk samples tested by Elisa for antibodies against MAP (trait=PA1)

2) Individual faecal samples tested for MAP bacteria (trait=PA2)

Method

- Estimation of genetic parameters for PA1 and PA2
- Estimation of genetic correlation between breeding values for PA1 and PA2

Results: genetic effects

	PA1	PA2
σ^2_g	0.004	0.005
σ^2_{perm}	0.033	0.021
σ^2_p	0.081	0.081
repeatability	0.42 *(0.003)*	0.28 *(0.006)*
h^2	0.05 *(0.003)*	0.06 *(0.008)*

Heritability and genetic variation indicate possibilities for selection.

Genetic correlation

- Genetic correlation between breeding values estimated with milk (PA1) and faecal (PA2) analyses
- Genetic correlation was estimated, accounting for differences in repeatability of breeding values (MACE)
- Sires have at least 15 daughters

- Genetic correlation PA1-PA2: 0.81

Implications

- Genetic standard deviation for ELISA test (antibody levels): 0.063
- *Increase* in breeding value means *decrease* in antibody levels
- Using a bull with 1 genetic standard deviation higher breeding value: 2.8% less daughters tested positive

Economic Development, Jobs, Transport and Resources

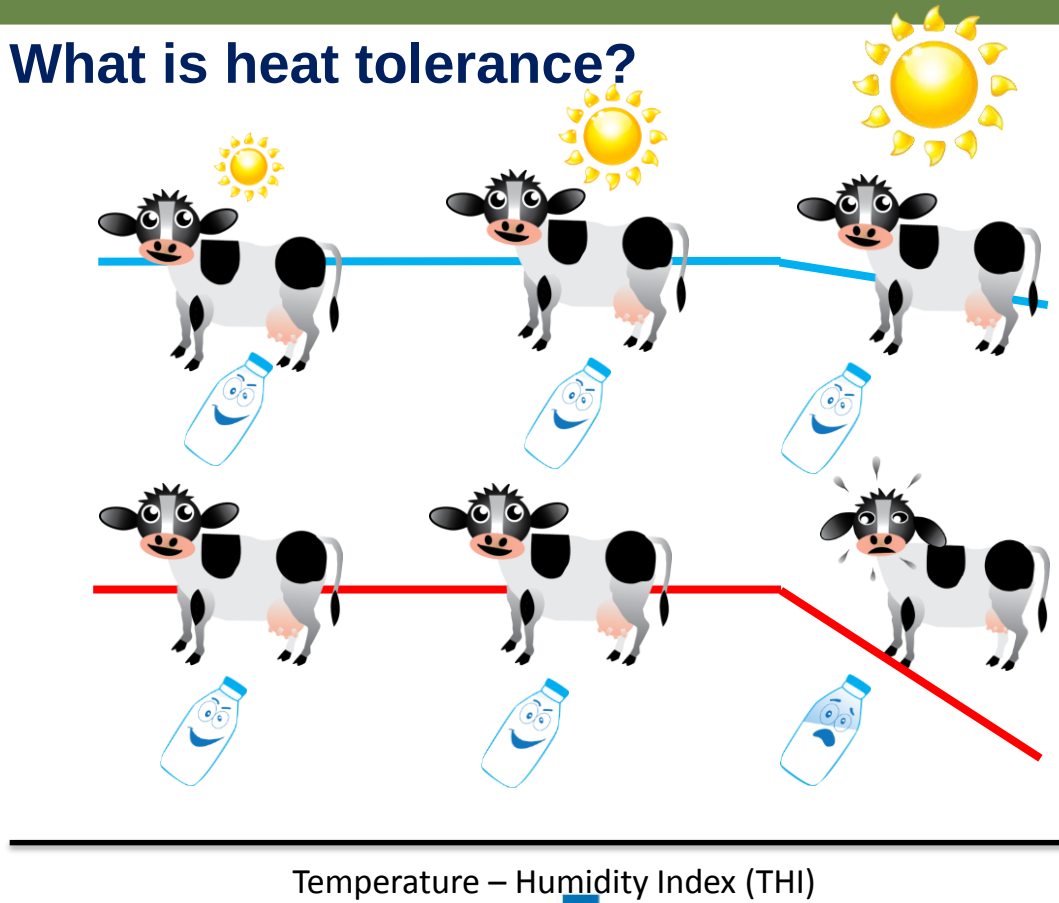
Heat Tolerance ABV

T. Nguyen, J.E. Pryce, LA Monks and M.M Axford

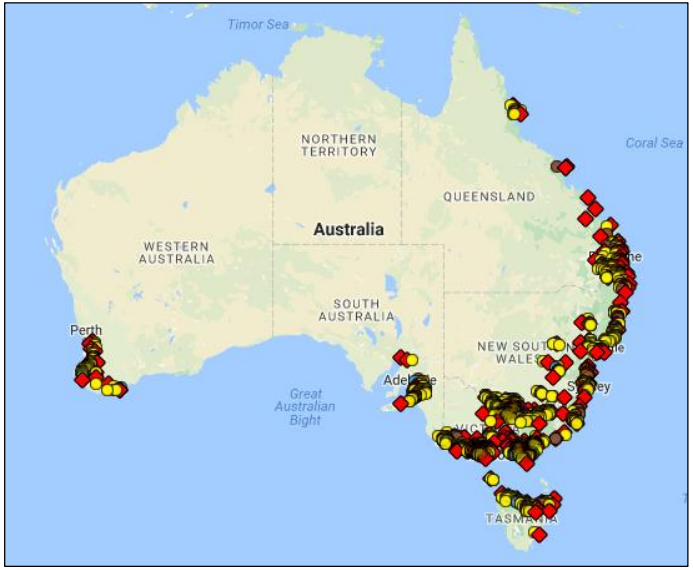
DataGene Solutions for Herd Development

AGRICULTURE VICTORIA

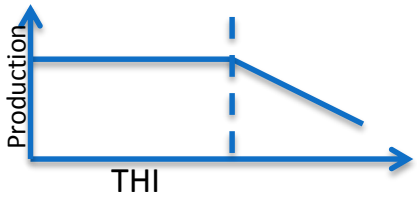
What is heat tolerance?

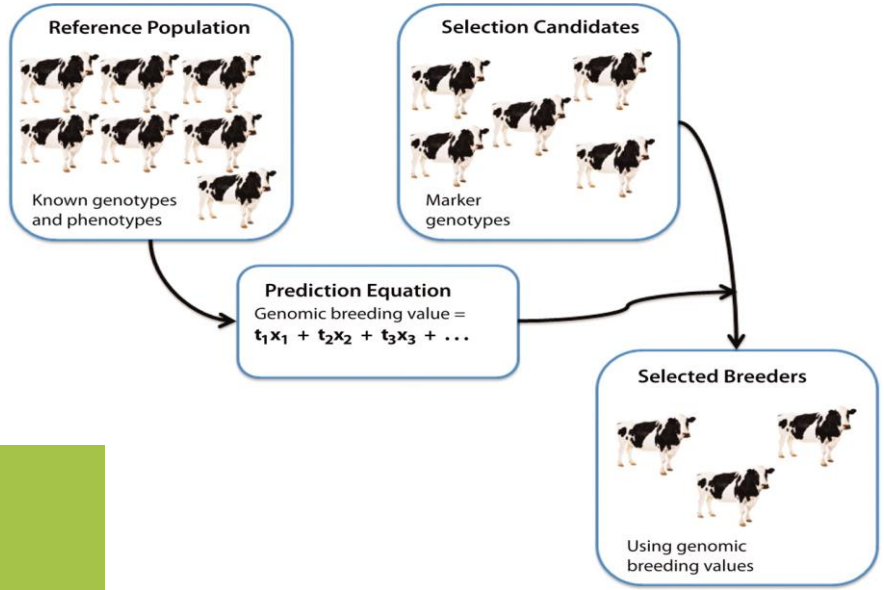


How to estimate genomic breeding value for heat tolerance?



How to estimate genomic breeding value for heat tolerance?





Estimated cow slopes

Decline in milk, fat and protein yields per unit increase in THI

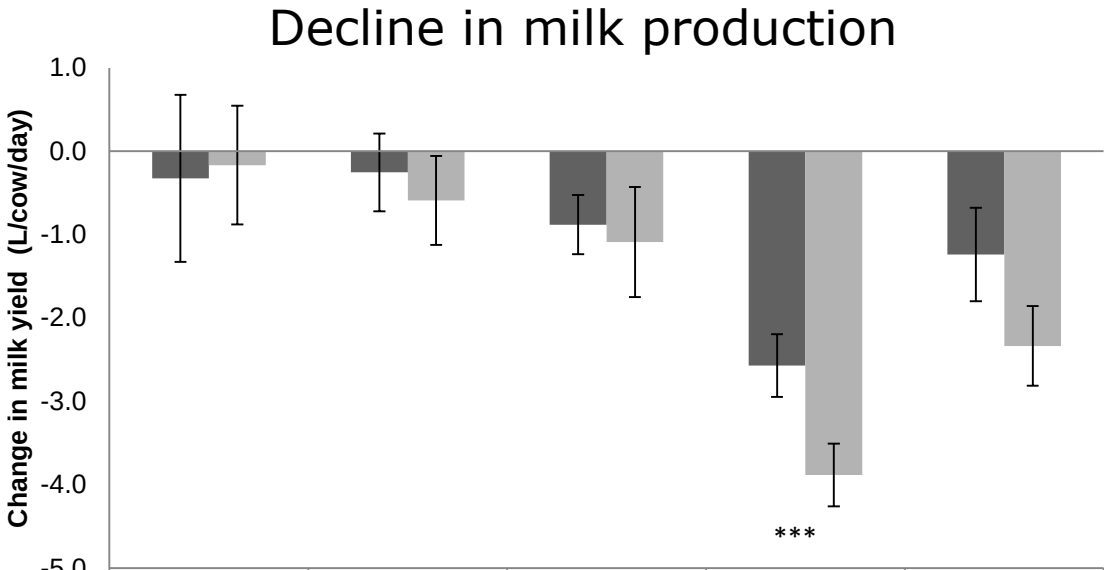
Sire slope = average of daughters

Heat tolerance ABVg reliability:
Average 38%
in Holsteins and Jerseys

Validation experiment

- 400 heifers screened
- 24 predicted most heat tolerant, 24 predicted most susceptible selected on GEBV
- Run through a simulated heat wave event at Ellinbank
- 4 day event, measure milk production, core temperature

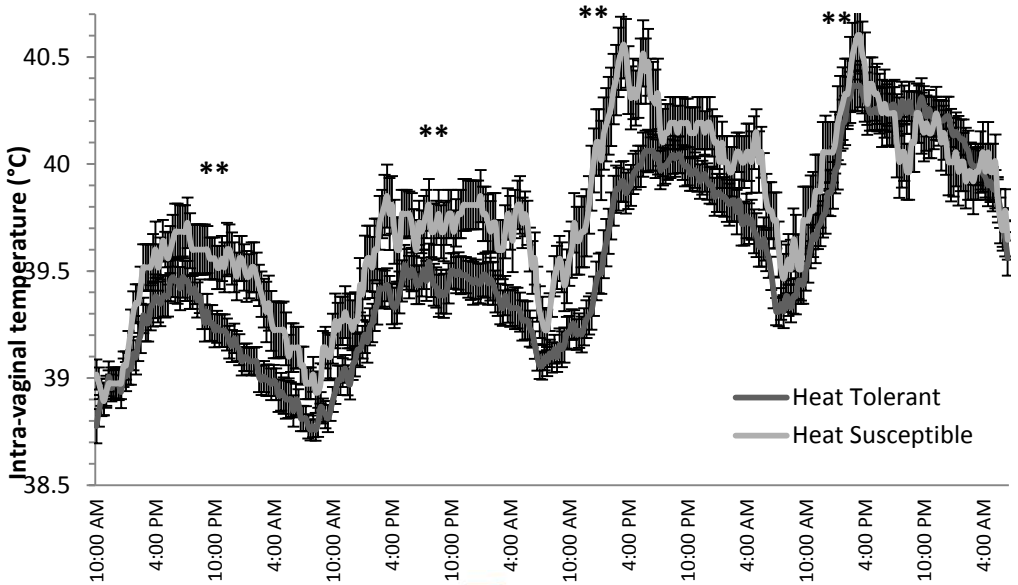
Validation experiment



	Day 1	Day 2	Day 3	Day 4	Recovery
HT	-0.3	-0.3	-0.9	-2.6	-1.2
HS	-0.2	-0.6	-1.1	-3.9	-2.3

Validation experiment

Difference in intra-vaginal temperature



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Expression of heat tolerance ABVg

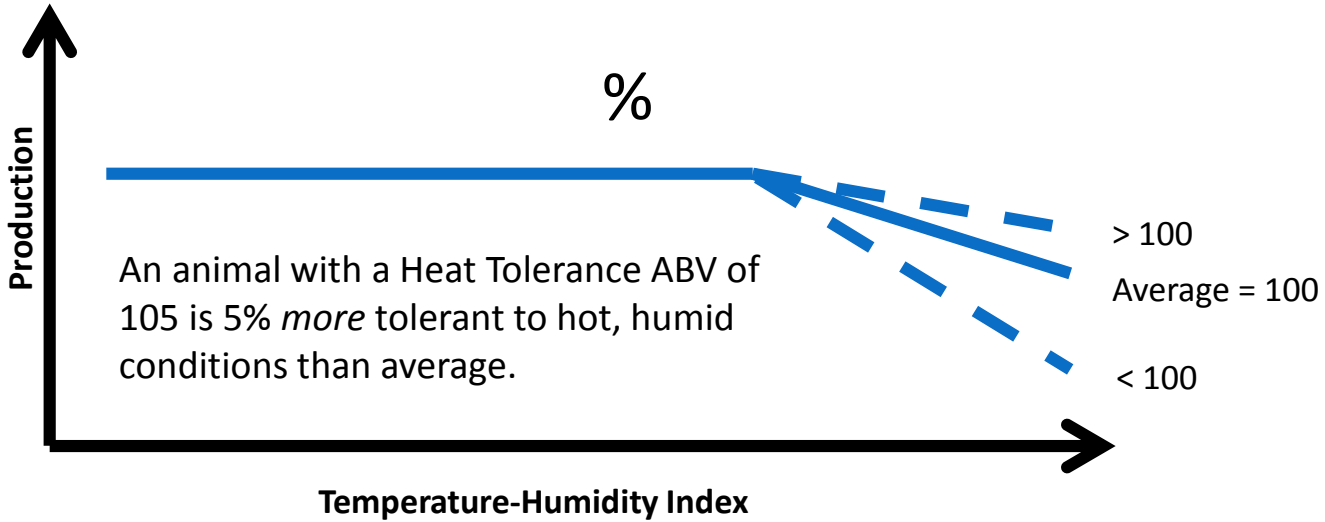
Decline in $

- Using economic weight of milk, fat and protein

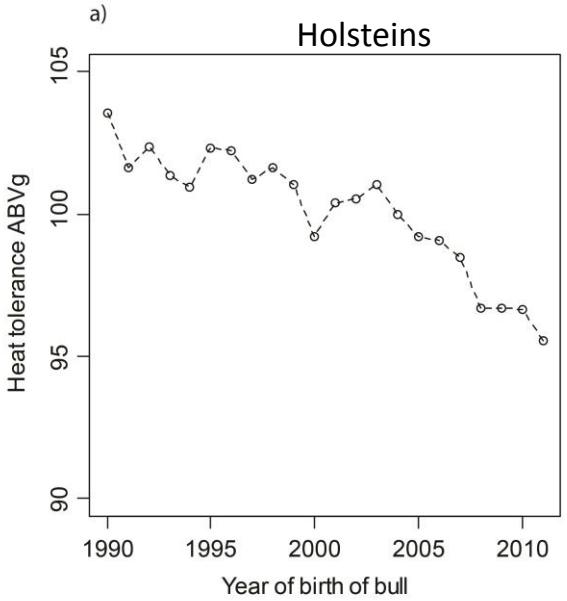
Standardise

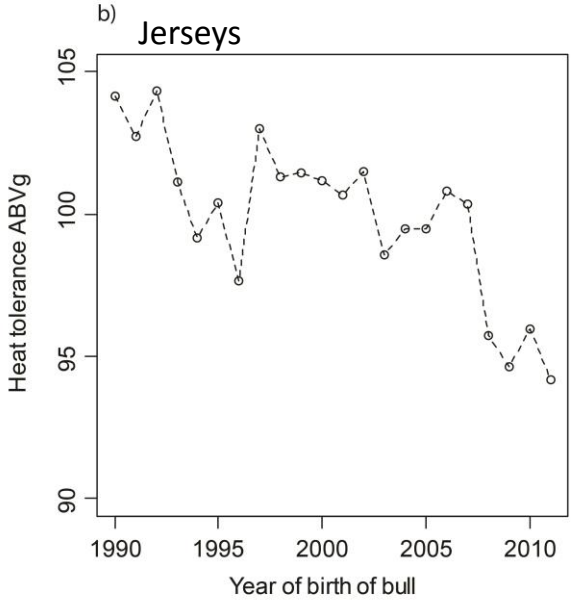
- Mean =100
- Standard deviation = 5

Heat tolerance ABVg



Genetic trend (decline ~1.5 SD in 20 years)





Cool cows toolbox

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Good Bulls

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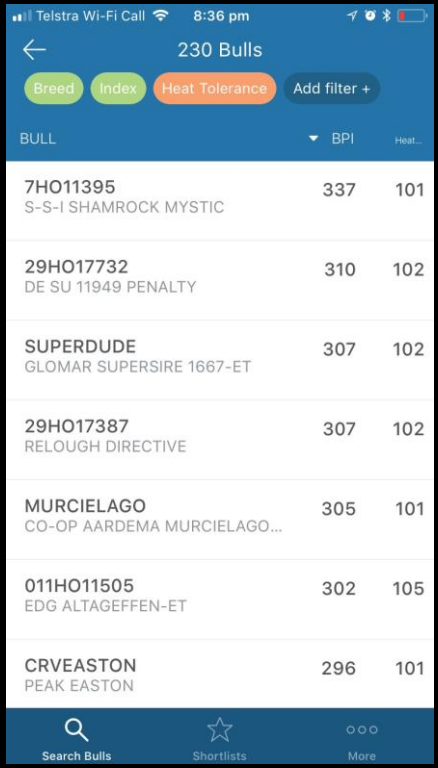
Advice to farmers

- Choose bulls from the Good Bulls Guide
- If Heat Tolerance is important, select above average bulls



What did farmers say?

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Trevor Parrish, New South Wales

“Now when I get a list of bulls I’m going to be looking for bulls which combine increased production and increased heat tolerance – they are going to be the ones who buck the trend.”

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Ray Kitchen, Boyanup, Western Australia

“Having a Heat Tolerance ABV will mean we can breed cows with a greater ability to tolerate hot weather, be better suited to our farming environment.

“ We will be looking for the bulls that pull together production and heat tolerance.”

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Shane Gardiner, Mt Gambier South Australia

“Heat Tolerance is something we can breed in our cows for free so why not? Like all genetic traits, it will be permanent and cumulative.”

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Ross Gordon, Cohuna, Victoria

“If two bulls have the same BPI but one has better heat tolerance than that’s the one we will be selecting”

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Ian Scott, Nanango, Queensland

“We can send a man to the moon but we can’t control the weather so we need to do everything possible to make things better for the cows, which includes breeding cows with good heat tolerance.”

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Key messages

- The Heat Tolerance ABV identifies animals with greater ability to tolerate hot, humid conditions with less impact on milk production
- Released in December 2017
- Validated in research conditions
- The Heat Tolerance ABV is unfavourably correlated with production but there are high Balanced Performance Index bulls that are also above average for Heat Tolerance

Thank you!

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DairyBio

LA TROBE UNIVERSITY

Australian Government
Department of Agriculture

Economic Development, Jobs, Transport and Resources

AGRICULTURE VICTORIA

Effect of heat stress on production traits of Holstein cattle in Japan: parameter estimation using test day records of first parity and genome wide markers

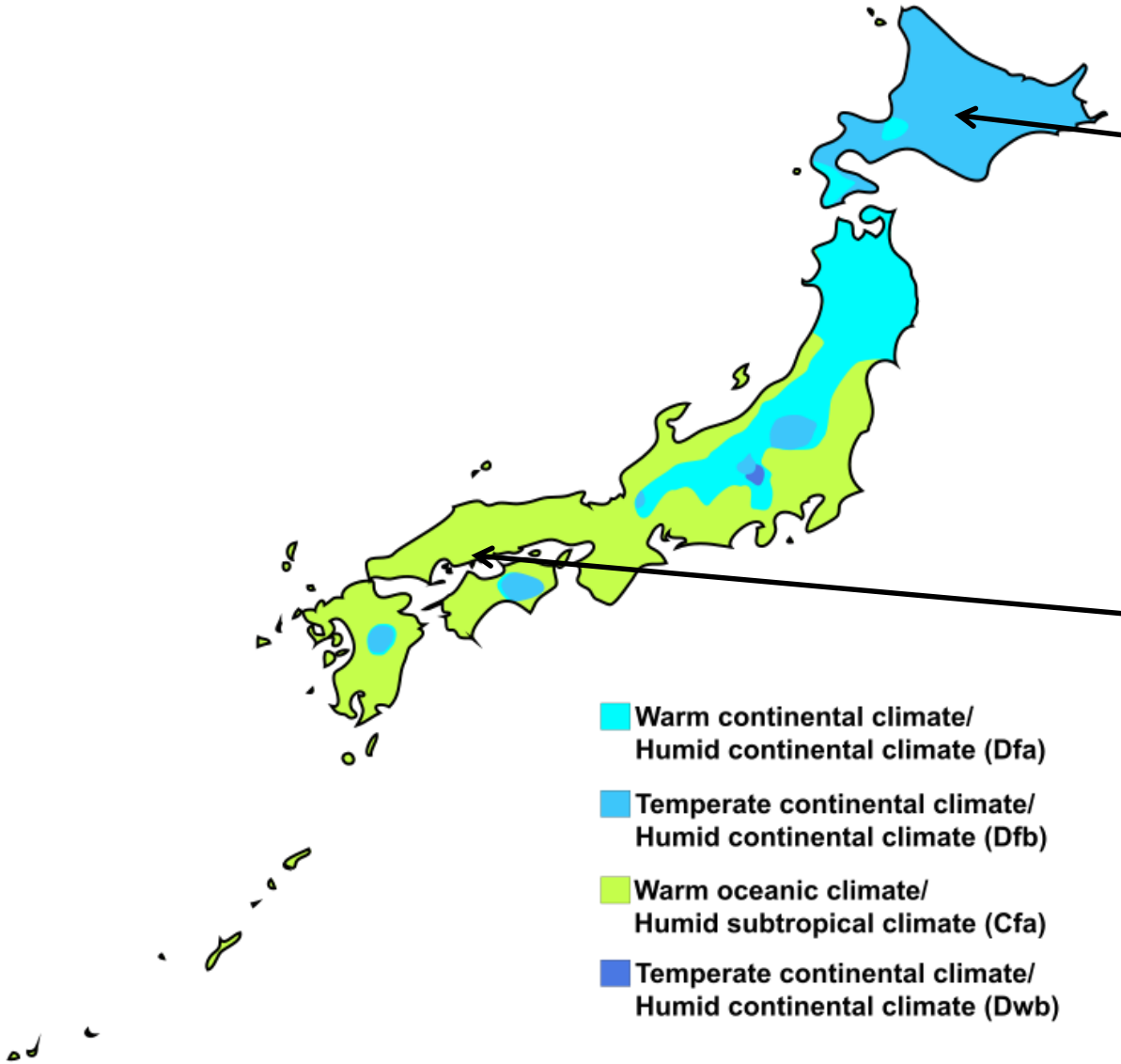
Y. Atagi[1], A. Onogi[1], T. Osawa[2], T. Yasumori[3], K. Adachi[3], S. Yamaguchi[3], M. Aihara[3], H. Goto[3], K. Togashi[3] and H. Iwata[1]

1 The University of Tokyo, Japan

2 National Livestock Breeding Centre, Japan

3 Livestock Improvement Association of Japan, Inc., Japan

Japan map of Köppen climate classification



- Hokkaido, the biggest domestic dairy production area
- Heat stress is minimal

- Heat stress affects dairy production in South west of Japan

From Wikipedia on 8Feb, 2018

Record processing

- phenotypes (Apr1987-Nov2015)
  - in 233 dairy farms with genotyped cows
- genotype
  - impute 20,411 cow LD records using Beagle 3
  - with 50K records (2849 bulls and 2598 cows)
- farms were linked with meteorological offices based on their areas for the announcement of weather forecasts
- calculate Temperature-Humidity Index (THI) at meteorological offices

$$THI = (1.8 \times T_d + 32) - (0.55 - 0.0055 \times RH) \times (1.8 \times T_d - 26)$$

T_d : dry bulb temperature (Celsius), RH : relative humidity (%)

- each phenotype was linked to the average (THI) up to 4 days before test day
- Heat stress
  - defined as decreased production at THI > 60

Summary of records

Traits	Chip used for genotyping	Milk, Fat and Protein	SCS
Test day records, n	-	820,573	752,514
Cows (female with records)	Total	93,725	86,435
	HD	807	
	LD*	363	
	-	92,555	85,265
Bulls (Sire of cows)	HD	3,126	
	-	2,229	
Females with genotypes but without records	HD	1,791	
	LD*	1	
Males other than bulls with genotypes	HD	2,313	
Other animals in a pedigree	-	106,843	101,777

∗LD genotypes: only cows with records and their dams to reduce equation size

Random regression test day model

$$y_{ijklmno} = HTDT_i + M_j w + A_k w + hy_l v + pe_m z + peh_m \cdot f(THI) + u_m z + uh_m \cdot f(THI) + e_{ijklmno}$$

- $y_{ijklmno}$: test day milk, fat, protein (kg), Somatic Cell Score
- $HTDT_i$: fixed effect of herd*test day*milking frequency
- M_j : fixed regression coefficients of calving month
- A_k : fixed regression coefficients of calving age
- hy_l : random regression coefficients of herd*calving year (HY) effects
- pe_m : random regression coefficients of general permanent environment (PE) effects
- peh_m : random linear regression coefficient of PE effect of heat tolerance
- u_m : random regression coefficients of general additive genetic (AG) effects
- uh_m : random linear regression coefficient of AG effects of heat tolerance
- $e_{ijklmno}$: random residuals at DIM: 6-35, 36-65, 66-95, 96-125, 126-215, 216-305
- $w' = \left[\phi_0(t) \quad \phi_1(t) \quad \phi_2(t) \quad \phi_3(t) \quad \phi_4(t) \quad e^{-0.05t}\right], v' = \left[\phi_0(t) \quad \phi_1(t)\right], z' = \left[\phi_0(t) \quad \phi_1(t) \quad \phi_2(t)\right]$
- $\phi_p(t)$: Legendre polynomials

$$f(THI) = \begin{cases} 0 \ if \ THI \le 60 \\ THI - 60 \ if \ THI \ge 60 \end{cases}$$

Covariance components

$$\text{var}\begin{bmatrix} hy \\ pet \\ ut \\ e \end{bmatrix} = \begin{bmatrix} I \otimes Q & 0 & 0 & 0 \\ 0 & I \otimes P & 0 & 0 \\ 0 & 0 & H \otimes G & 0 \\ 0 & 0 & 0 & R \end{bmatrix}$$

- I : identity matrix
- Q : 2×2 matrix of (co)variances for HY effects
- H :a matrix combining additive relationship and genomic relationship
- P, G : 4×4 of (co)variances for total (general + heat tolerance) PE and AG effects
- R : diagonal matrix with residual variance corresponding to DIM category

AG (co)variances and heritability

- General AG (co)variance at DIM t and t’:

$$\mathrm{cov}\left(u(t),u(t')\right)=\mathrm{cov}\left[u_{m0}\phi_0(t)+u_{m1}\phi_1(t)+u_{m2}\phi_2(t),u_{m0}\phi_0(t')+u_{m1}\phi_1(t')+u_{m2}\phi_2(t')\right]$$

$$=\sum_{i,j}\mathrm{cov}\left(u_{mi}\phi_i(t),u_{mj}\phi_j(t')\right)$$

$$=\sum_{i,j}\phi_i(t)\phi_j(t')\mathrm{cov}\left(u_{mi},u_{mj}\right)$$

- AG variance of heat tolerance: $f(THI)^2\sigma^2_{uh}$
- AG covariance and correlation between general and heat tolerance at DIM t:

$$Cov\left(u(t),f(THI)\cdot uh\right)=f(THI)\cdot\mathrm{cov}\left[u_{m0}\phi_0(t)+u_{m1}\phi_1(t)+u_{m2}\phi_2(t),uh_m\right]$$

$$=f(THI)\cdot\sum_i\phi_i(t)\mathrm{cov}\left(u_{mi},uh_m\right)$$

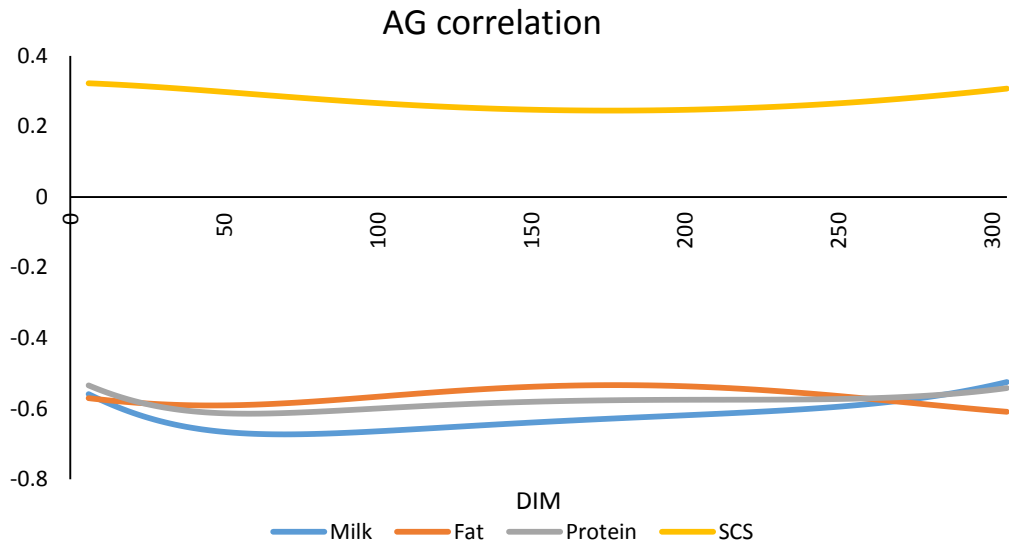
$$Correlation:\frac{\sum_i\phi_i(t)\mathrm{cov}\left(u_{mi},uh_m\right)}{\sqrt{\sum_i\phi_i(t)^2\mathrm{cov}\left(u_{mi},u_{mi}\right)\cdot\sigma^2_{uh}}}$$

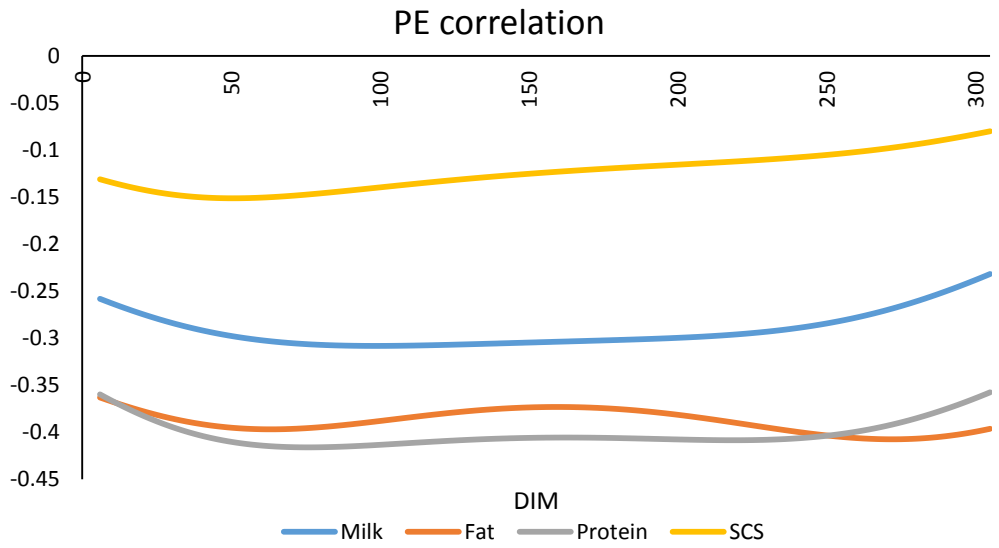
- Total AG variances and heritability at DIM t and THI:

$$\sigma^2_{u_{total}}=\sum_i\phi_i(t)^2\mathrm{cov}\left(u_{mi},u_{mi}\right)+f(THI)^2\sigma^2_{uh}+2f(THI)\sum_i\phi_i(t)\mathrm{cov}\left(u_{mi},uh_m\right)$$

$$h^2=\frac{\sigma^2_{u_{total}}}{\sigma^2_{u_{total}}+\sigma^2_{pe_{total}}+\sigma^2_{hy}+\sigma^2_e}$$

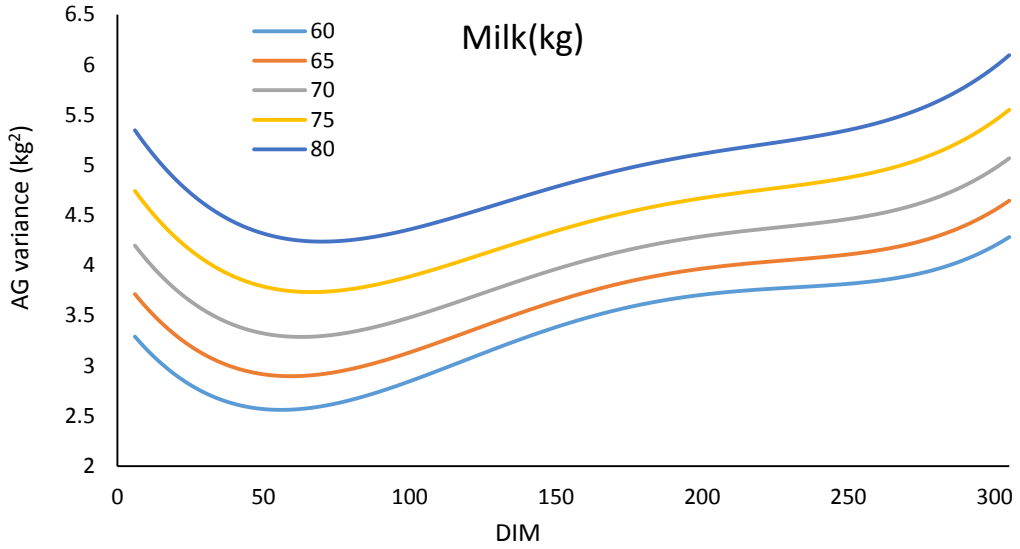
AG / PE correlation

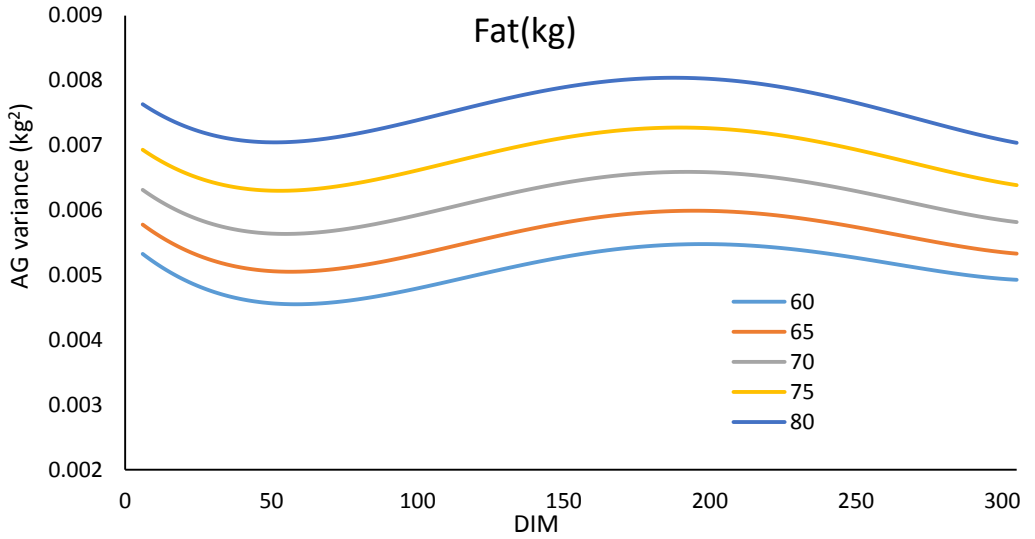


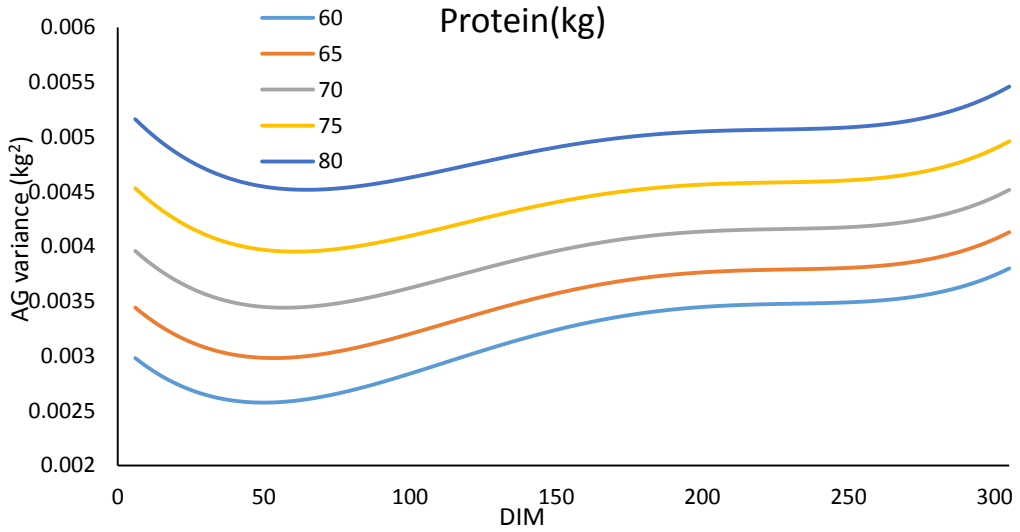


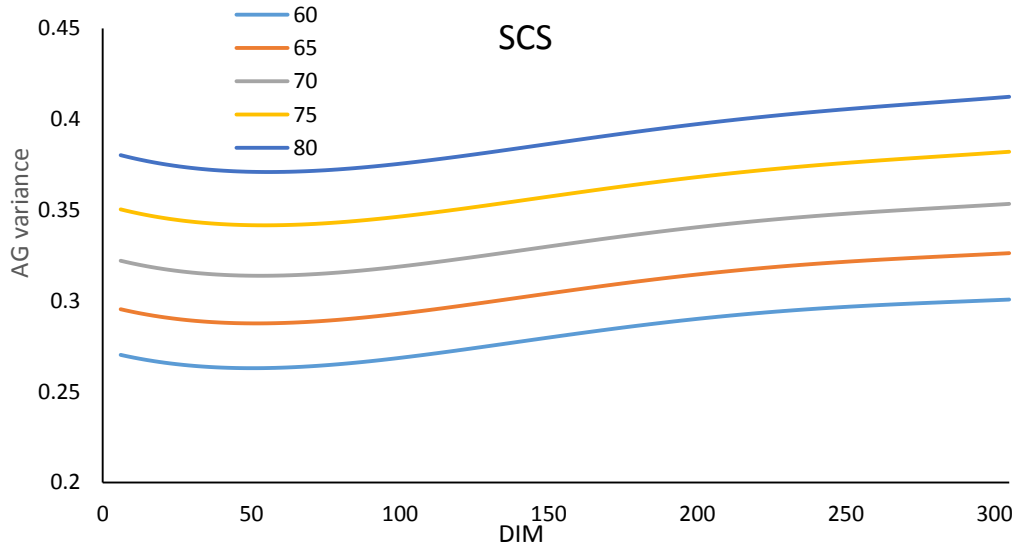
- AG correlations were negative, except for SCS.
- PE correlations were negative and weaker than the AG correlations.

Total AG variance



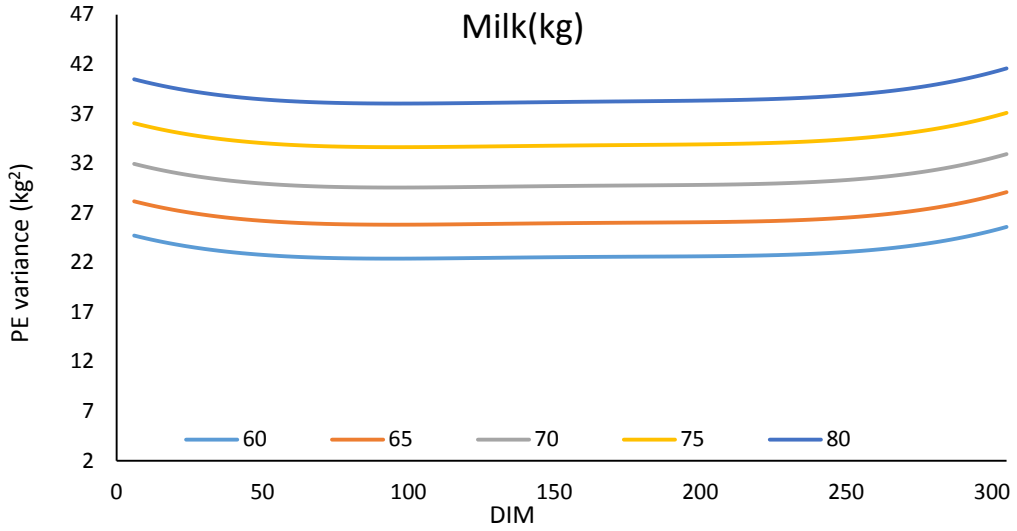


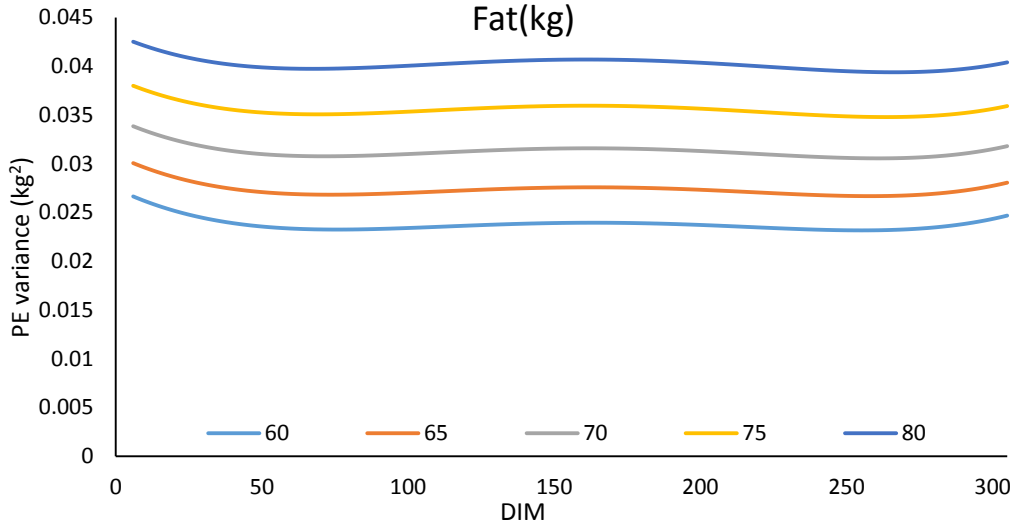


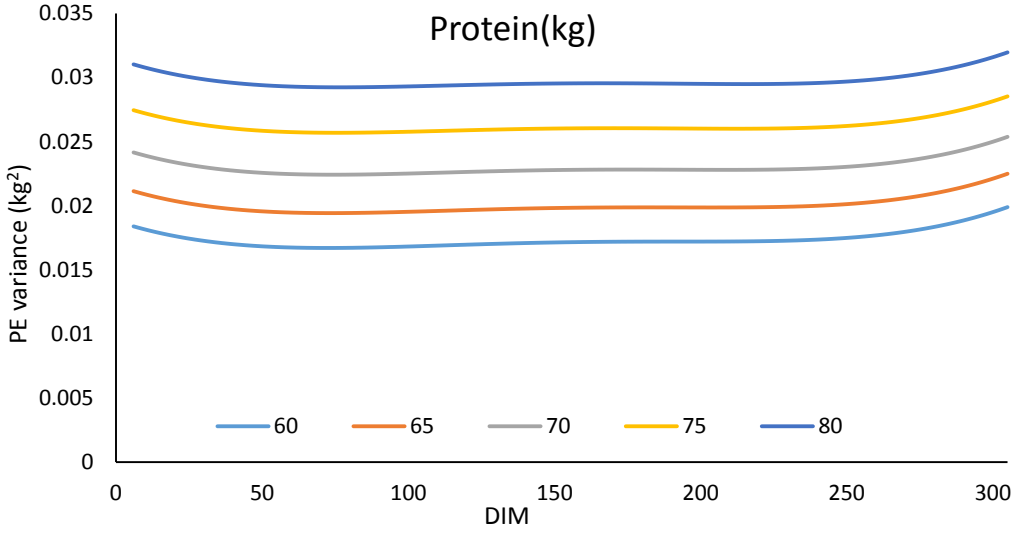


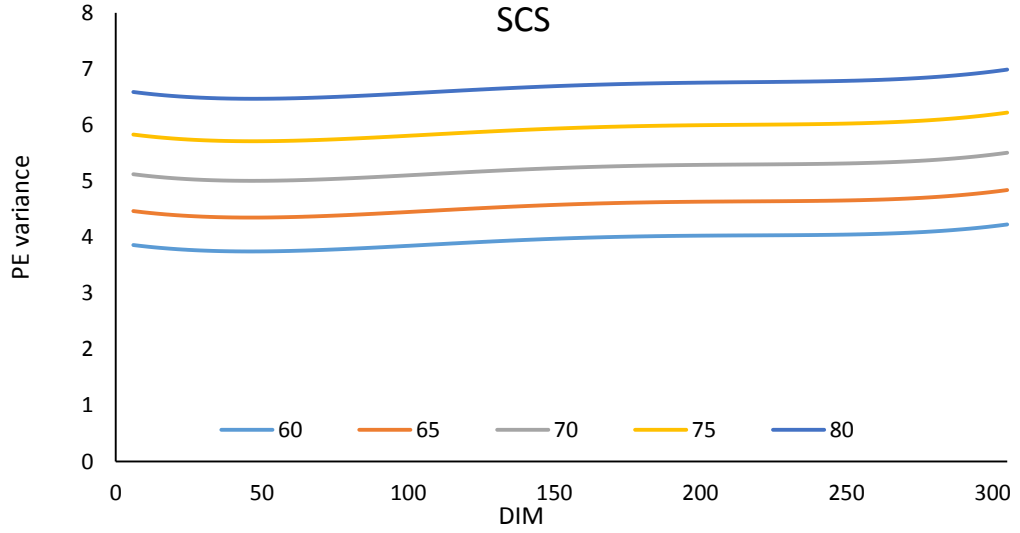
- The higher the THI, the larger the total AG variances.
- Change in Fat looked different at later stage of lactation.

Total PE variance



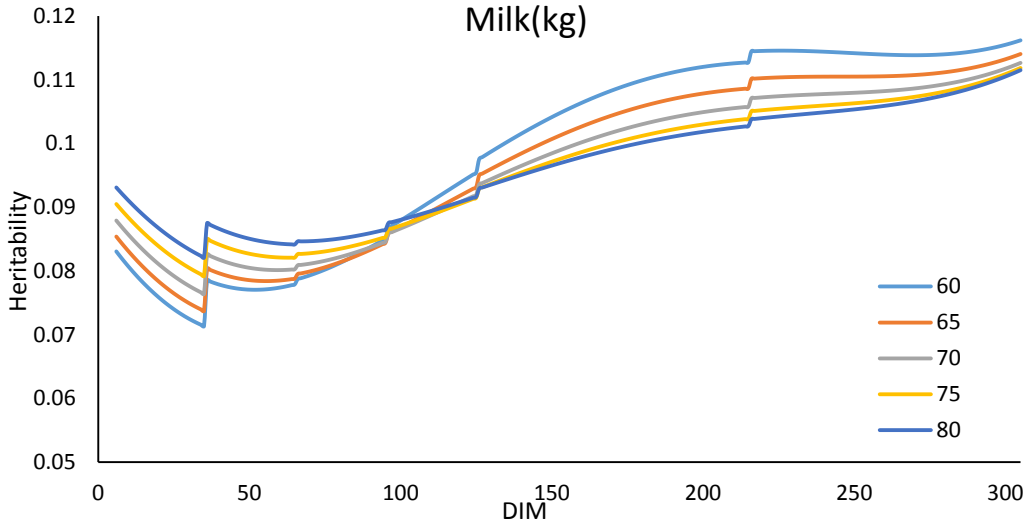


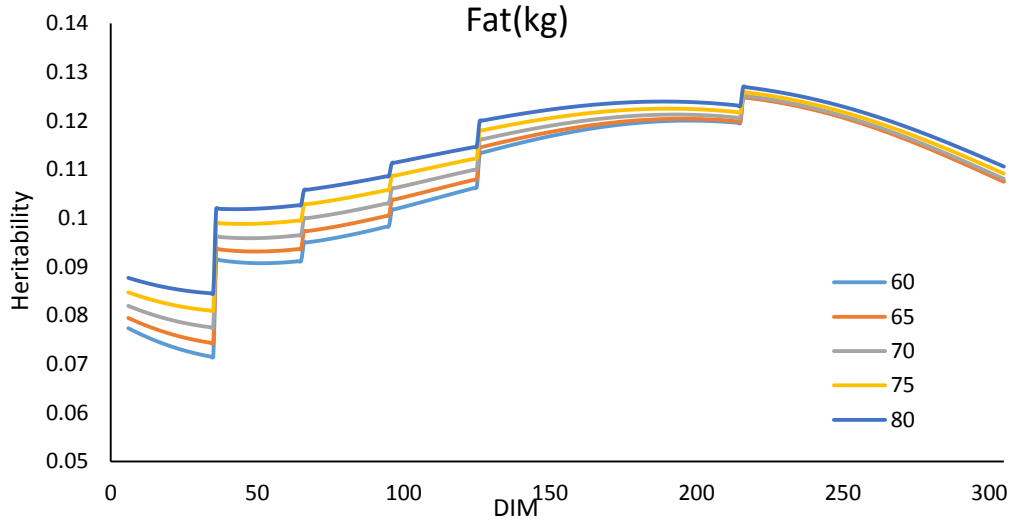


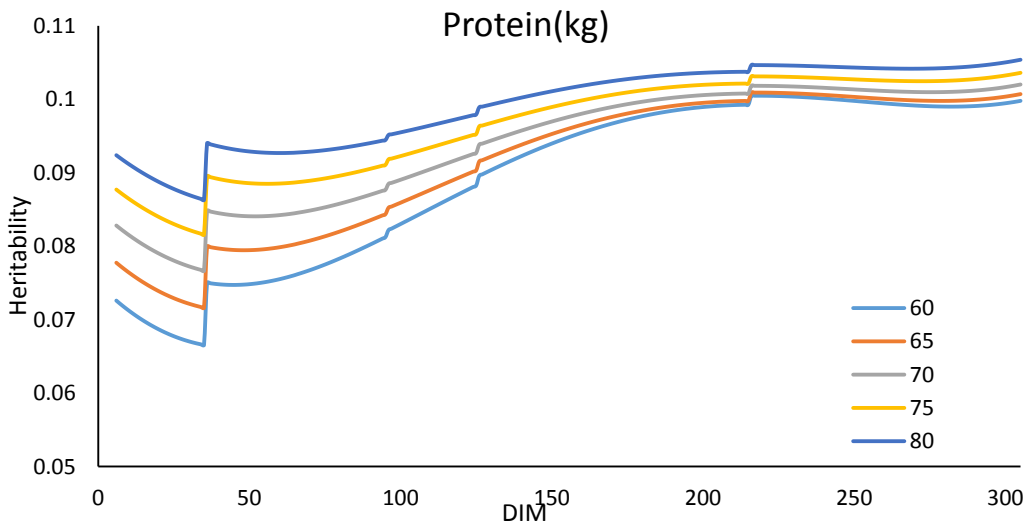


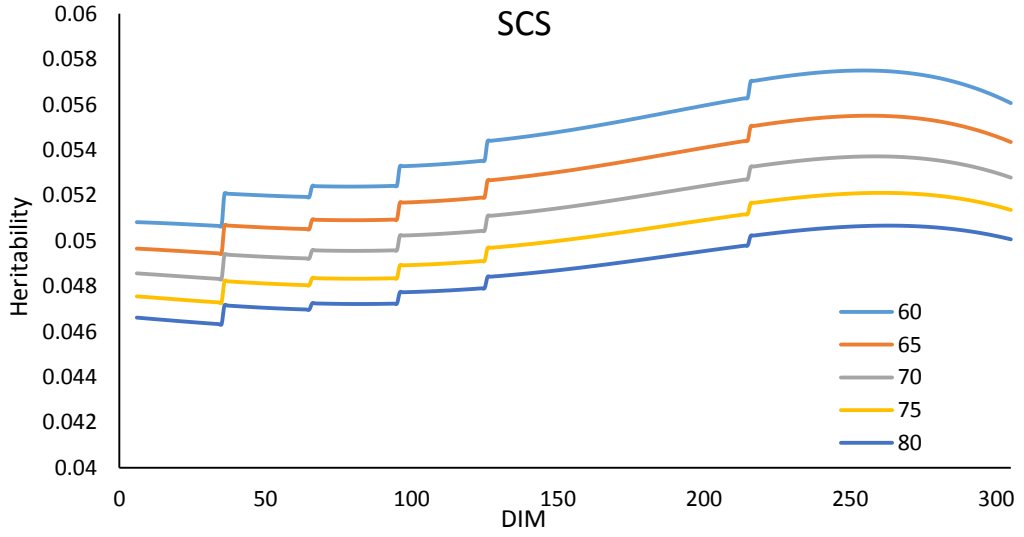
- The higher the THI, the larger the total PE variances.
- PE variances were bigger than AG variances.

Heritability









- h^2 (Fat, Protein) were larger for higher THI.
- h^2 (SCS) was smaller for higher THI due to larger difference of PE variances.

Summary

- PE variances of heat tolerance were larger than AG variances.
  - ➢ Various non-AG factors affect.
- Negative genetic correlation (general effect vs heat tolerance) should be considered carefully.
  - ➢Use total AG effect.
- AG variances were smaller, whereas PE variances were larger than national genetic evaluation.
  - ➢Further study is required.
- Heat stress affects more in later parities.
  - ➢Later parities to be included.
- Variance components were successfully estimated. Genetic evaluation of heat tolerance would be feasible.

Acknowledgement

- JRA Livestock Promotion Funds for financial support.
- Mr. Masaki Oyamada, Holstein Cattle Association of Japan for genotype records.
- Dr Shogo Tsuruta, Yutaka Masuda (University of Georgia), and Dr Koichi Hagiya (Obihiro University of Agriculture and Veterinary Medicine) for their valuable suggestions.

中國農業大學
China Agricultural University

Genetic analysis of skinfold thickness and its association with body condition score, and milk production traits in Chinese Holstein population

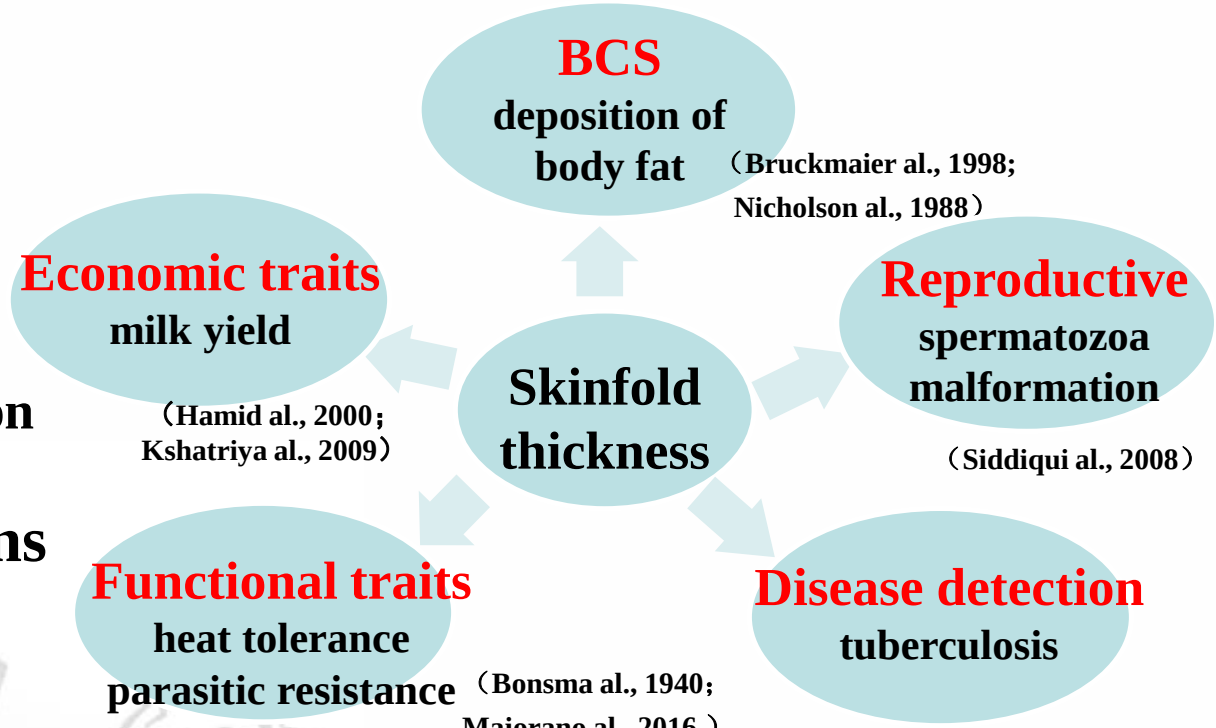
Hailiang Zhang[1], Wei Xu[1], Aoxing Liu[1,2], Xiang Li[1], Hanpeng Luo[1], Yachun Wang[1]

1.China Agricultural University, China
2.Aarhus University, Denmark

Feb 11, 2018
Auckland, NZ

Background

- **Skin: the outermost structure and the largest organ of the mammals' body, undertakes the many important functions**
- **Skinfold thickness:**
  - ✓ **widely used to represent skin thickness**
  - ✓ **measuring method friendly to animal**
  - ✓ **suitable for measurement in large population**
- **The neck and rib are the body regions frequently used in previous studies**
  - ✓ **different repeatability in different regions**
  - ✓ **different measuring difficulty in different regions**



Background

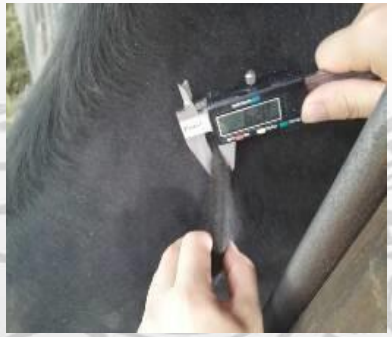
- In previous studies, the factors affecting the skinfold thickness have been explored (Dowling al., 1955; Patel al., 1958; Hayman al., 1966)
  - ✓ breed, body regions, nutrition status, gender, age and measurer
- Skinfold thickness is an important trait, however not been considered seriously in dairy. Very little studies regarding genetic analysis of skinfold thickness

year	author	species	Body region	No. Obs	h^2
2016	Maiorano	Nellore	scapula	17940	0.12 ± 0.02
1991	Slee	Merino Sheep	right mid-side	-	0.35±0.19

- The objectives of this study were to estimate the heritability of skinfold thickness and its genetic association with BCS and milk production traits in Chinese Holstein

Material & method

- Holstein milking cows in 9 scaled farms in Beijing
- Measurement: skinfold thickness, BCS
  - ✓ skinfold thickness at the neck (STN)
  - ✓ skinfold thickness at the last rib (STR)
- Device: Digital Vernier caliper
- Collecting test-day records during measuring period



Measuring skinfold thickness at the neck

Measuring skinfold thickness at the last rib

Body condition score (BCS)

Year-month	No. of farms
2015, July-Aug	6
2016, June-Aug	7

Material & method

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➢ Factor analysis (SAS, GLM)

$$STN_{ijkl} = \mu + FM_i + PARITY_j + STAGE_k + b_1 BCS + e_{ijkl}$$

$$STR_{ijklm} = \mu + FM_i + PARITY_j + STAGE_k + BODYSIDE_l + b_2 BCS + e_{ijklm}$$

➢ Genetic analysis (DMU, animal model)

- bi-variate: STN, STR
- 6-traits: STN, STR, BCS, MY, FP and PP

$$STN = FM + PARITY + STAGE + A + E$$

$$STR = FM + PARITY + STAGE + BODYSIDE + A + E$$

$$BCS = FR + STAGE + A + E$$

$$MY = FY + PARITY + STAGE + A + E$$

$$FP = FY + PARITY + STAGE + A + E$$

$$PP = FY + PARITY + STAGE + A + E$$

Traits

STN: skinfold thickness over the neck
STR: skinfold thickness over the last rib
BCS: body condition score *MY*: milk yield
FP: milk fat percentage *PP*: milk protein percentage

Effects

FM: farm-measurer of skinfold
FR: farm-rater of BCS
FY: farm-year of test-day records
PARITY: parity of the cow
STAGE: milking stage of the cow
BODYSIDE: body side of the measured cow
b_1/b_2: regression coefficient for *BCS*
A: random additive genetic effect
E: random residual effect

Results & discussion

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➢ Descriptive statistics

Traits	No. Obs	MAX	MIN	MEAN	SD	CV
STN/mm	4428	1.00	13.28	7.16	1.30	18.1%
STR/mm	4452	1.07	22.77	11.76	1.97	16.7%
BCS	5810	1.00	5.00	2.90	0.79	27.4%
MY/kg	5646	0.80	90.00	34.58	10.20	29.5%
FP/%	4980	0.68	7.99	3.97	0.88	22.2%
PP/%	5544	1.53	9.33	3.01	0.30	10.1%

- The STN was thinner than STR
- There is a significant body side effect on skin thickness at the last rib!

➢ Factor analysis

Traits	R^2	FM/FS/FY		Stage		Parity		BCS		Body side	
		df	F-value	df	F-value	df	F-value	df	F-value	df	F-value
STN	0.39	13	205.41**	5	6.23**	4	19.49**	1	60.76**		
STR	0.37	12	109.56**	5	3.18**	4	27.78**	1	71.53**	1	149.69**

Results & discussion

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➢Results from bi-variate model

Traits	No. Obs	Additive VC	Error VC	Phenotype VC	Heritability ±SE
STN	4307	0.13	0.90	1.03	0.13±0.03
STR	4331	0.63	1.97	2.60	0.24±0.04

➢Results from 6-traits model

Traits	No. Obs	Additive VC	Error VC	Phenotype VC	Heritability ±SE
STN	4307	0.13	0.90	1.03	0.13±0.03
STR	4331	0.64	1.96	2.61	0.25±0.05
BCS	5585	0.05	0.34	0.39	0.12±0.03
MY	5634	8.34	68.73	77.07	0.11±0.02
FP	4969	0.05	0.66	0.71	0.07±0.02
PP	5533	0.01	0.07	0.08	0.08±0.02

- ✓ Estimated heritabilities for STN was higher than STR: low to moderate
- ✓ Estimated heritability of STN & STR are similar between bi-variate model and 6 traits model
- ✓ The estimated heritability was similar with the previous study on Nellore (Maiorano al., 2016)

Results & discussion

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➢Results from 6-traits model

Genetic (below the diagonal) and phenotypic (above the diagonal) correlations

Traits	STN	STR	BCS	MY	FP	PP
STN		0.33	0.13	-0.01	0.00	-0.01
STR	0.80±0.08		0.15	-0.05	-0.02	-0.02
BCS	0.34±0.15	0.19±0.14		-0.21	0.03	0.09
MY	0.13±0.16	-0.03±0.15	-0.35±0.14		-0.08	-0.16
FP	0.13±0.20	0.04±0.18	0.17±0.19	-0.69±0.15		0.28
PP	0.05±0.19	0.04±0.17	0.30±0.12	-0.58±0.15	0.66±0.17	

- ✓ a high genetic correlation existed between STN and STR
- ✓ a moderate and positive genetic correlation between STN and BCS (0.34)
- ✓ Low genetic correlations existed between skinfold thickness and milk performance. r_g of STN and milk production traits were higher than that between STR and milk production traits

Results & discussion

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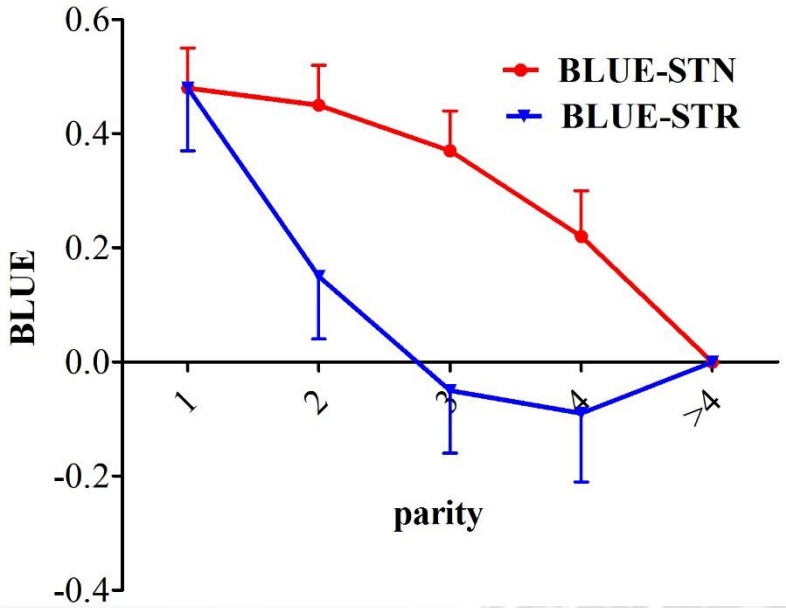
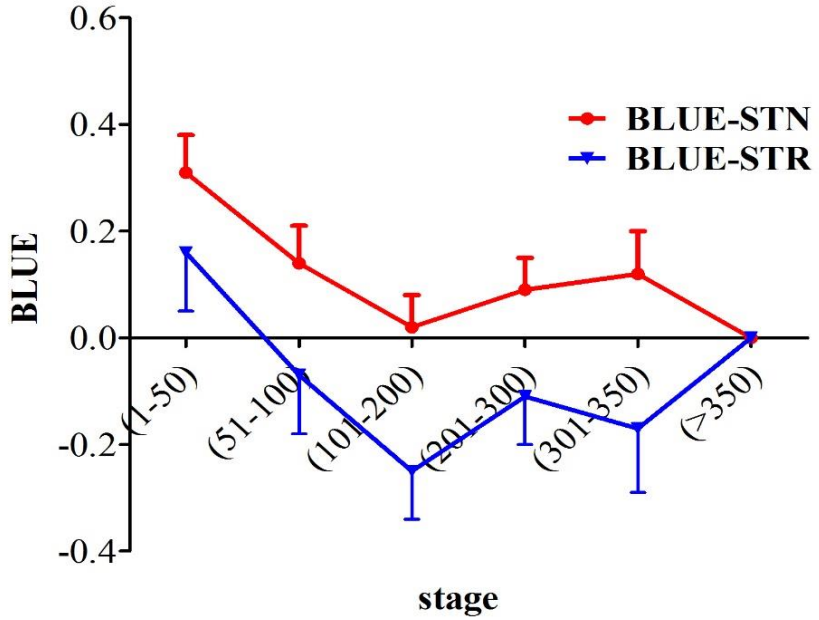
➢BLUE of fixed effects

BLUE：best linear unbiased estimated





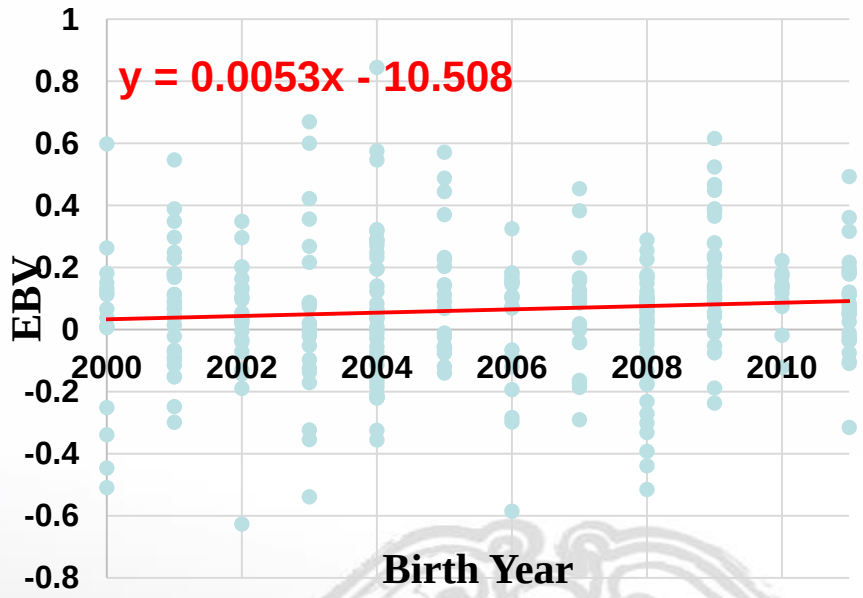
Body side	STR	
	N	BLUE±SE
Left	860	-0.83±0.11
Right	3074	0.00±0.00

- ✓ Roughly, skinfold thickness decreased with the increase of parity, first drop and then rise with the increase of DIM
- ✓ Skinfold thickness is sensitive to change of parity and milking stage in lactating cows

Results & discussion

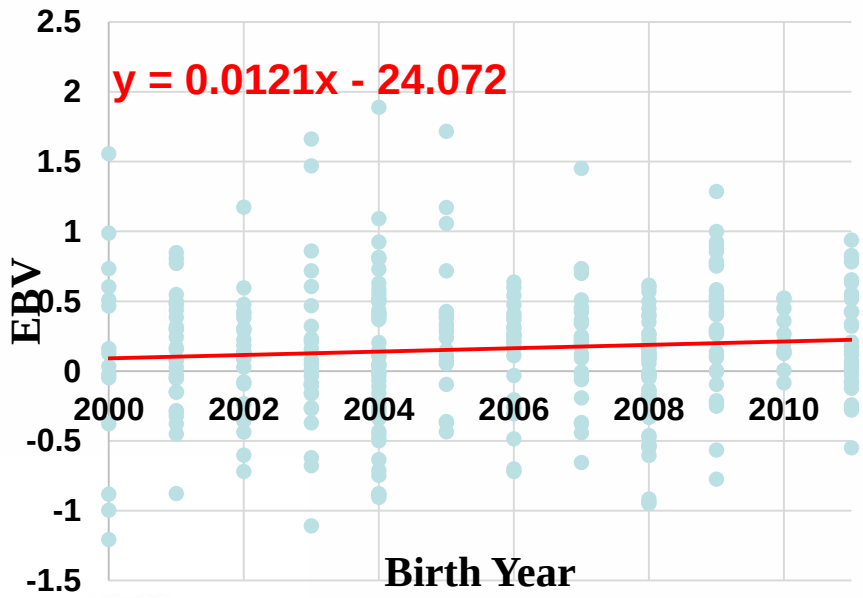
- genetic trend of EBV of skinfold thickness (bulls with Rel. >0.1)

STN



reliability>0.1， N=309

STR



reliability>0.1， N=329

From 2000 to 2011

Change of EBV=0.06 mm=0.17σ_A

Change of EBV=0.14 mm=0.18σ_A

Conclusions

- Skinfold thickness is a trait with a low to moderate heritability, and there is a high genetic correlation between skinfold thicknesses on different body regions in Holstein population
- Skinfold thickness is easy measurable trait and sensitive to change of parity and milking stage in lactating cows
- Skinfold thickness can be considered as an additional information of BCS to evaluate fat deposition
- Selection on skinfold thickness to improve milking cow's ability to fight with the negative energy balance is feasible as only weak genetic correlations existed between skinfold thickness and milk performance

Acknowledgement

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Thanks for listening ☺

Open for questions ☺

Discussions

➢ Genetic correlations with other traits

	Rectal temperature (AM)	Rectal temperature (PM)	longevity	Healthy traits (reproduction)	Healthy traits (digestion)	Healthy traits (udder)	Healthy traits (hoofs)
STN	-0.14	-0.02	0.13	-0.14	0.01	0.03	0.06
STR	-0.11	-0.09	0.20	-0.11	0.00	-0.01	-0.02

$$\hat{r}_{g_{i,j}} = \frac{\sqrt{(\sum RL_i) \times (\sum RL_j)}}{\sum (RL_i \times RL_j)} \times r_{i,j}$$

$$\mathrm{SE} = \sqrt{\frac{1 - \hat{r}_{g_{i,j}}}{n - 2}}$$

(Hickman et al., 1969; Calo et al., 1973)

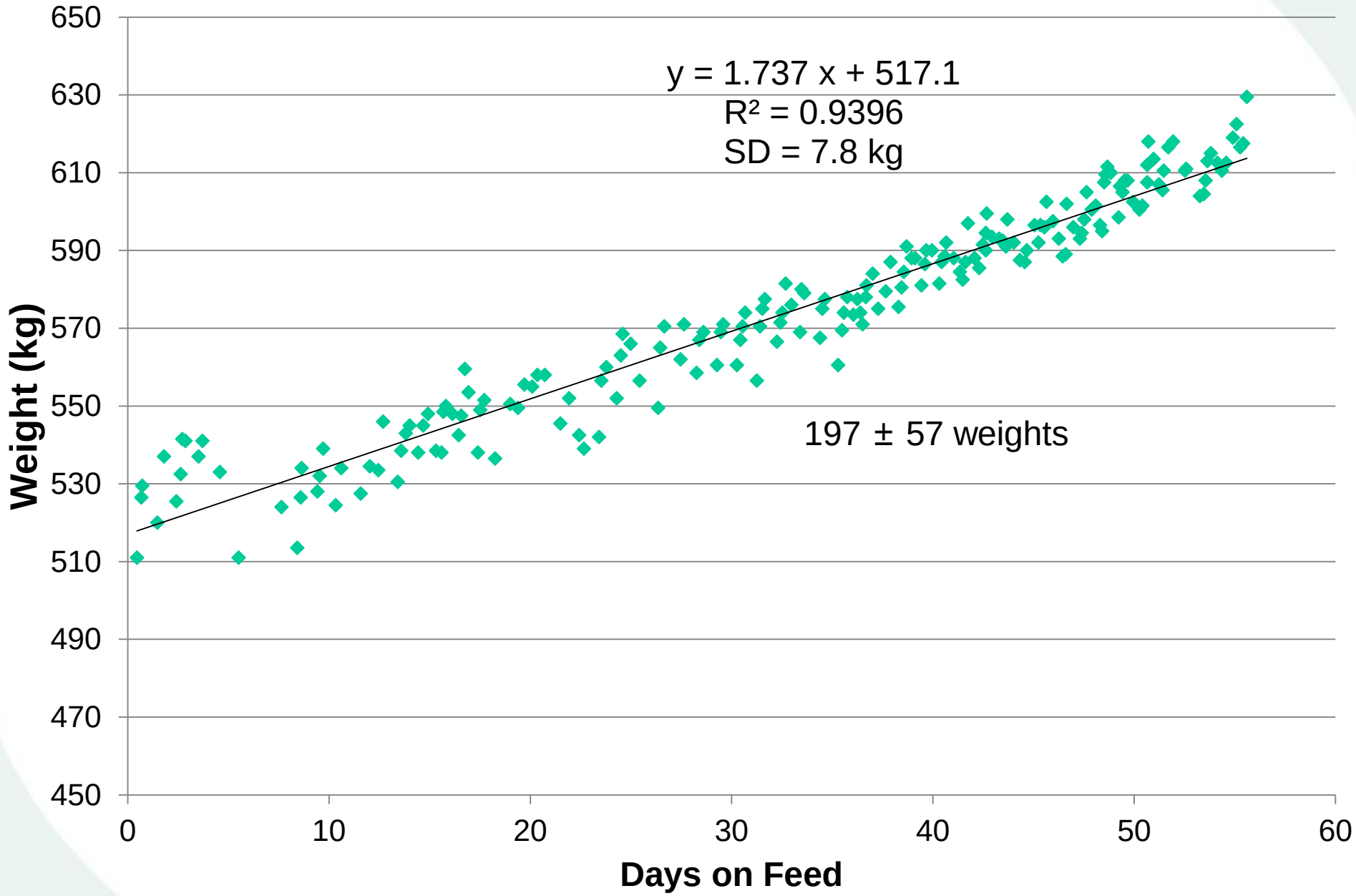
Is a 35-day feeding test with automatic daily weighting good enough for evaluating beef cattle for feed efficiency traits?

R.A.A. Torres Junior, L.O.C. Silva, R. Favero, R.C. Gomes, A. Gondo, S. Tsuruta, M.V. Costa, V. Okamura, G.R.O. Menezes, P.R.C. Nobre, L.M Nieto

Embrapa


Embrapa
Gado de Corte
Empresa Brasileira de Pesquisa Agropecuária
Ministério da Agricultura, Pecuária e Abastecimento


Intergado
ALIMENTADOR INTELIGENTE AF1000M
FAVOR NÃO ENCOSTAR
INTERGADO


y = 1.737 x + 517.1
R² = 0.9396
SD = 7.8 kg
197 ± 57 weights
Weight (kg)
650
630
610
590
570
550
530
510
490
470
450
0
10
20
30
40
50
60
Days on Feed

Standard Error of Computed Gain

- (Final weight – Initial weight)/number days on feed for 70 days

SE of gain = $(2)^{0.5}$ * 7.8/ 70 = **0.157 kg.day^{-1}** (0.098 kg.day^{-1})

- Regression on weekly weights (56 days)

SE of gain = $\frac{7.8}{\sqrt{\sum_{i=0}^{nweeeks}(x_i-\bar{x})^2}} = \frac{7.8}{\sqrt{2444}}$ = **0.158 kg.day^{-1}**

- Regression on multiple daily weights (197 weights in 56 days)

SE of gain = $\frac{7.8}{\sqrt{\sum_{i=1}^{nmeasures}(x_i-\bar{x})^2}} = \frac{7.8}{\sqrt{46{,}630}}$ = **0.036 kg.day^{-1}**

- Regression on multiple daily weights (94 weights in 35 days)

SE of gain = $\frac{7.8}{\sqrt{\sum_{i=1}^{nmeasures}(x_i-\bar{x})^2}} = \frac{7.8}{\sqrt{9{,}460}}$ = **0.080 kg.day^{-1}**

- Regression on daily weights (in 35 days)

SE of gain = $\frac{7.8}{\sqrt{\sum_{x=0}^{ndays}(x-\dot{x})^2}} = \frac{7.8}{\sqrt{3885}}$ = **0.125 kg.day^{-1}**

Material and Methods

- 601 Nelore Bulls from 6 test batches in 2016 and 2017
- Final Weight, Average Metabolic Weight, Average Daily Gain, Average Daily Feed Intake, Residual Feed Intake and Feed Efficiency Ratio
- Total 56 days of test and First 35 days of test.
- Contemporary group included Test Batch and Herd of Origin
- Total Pedigree of 12,785 animals
- Simple animal Model with contemporary group effect and linear effect of age within contemporary group
- Software Gibbs2f90 and Postgibbsf90

Results and Discussion

Table 1. Correlation and their standard-errors between 35-day and 56-day test results for the studied traits.

Trait[1]	Phenotypic Correlation	Genetic Correlation
FW (kg)	0.974	0.976 ± 0.007
AMW (kg)	0.992	0.993 ± 0.002
ADG (kg d^{-1})	0.864	0.904 ± 0.031
ADFI (kg d^{-1})	0.940	0.952 ± 0.021
RFI (kg d^{-1})	0.875	0.937 ± 0.022
FER (g kg^{-1})	0.800	0.879 ± 0.034

[1] FW, final weight; AMW, average metabolic weight; ADG, average daily gain; ADFI, average daily feed intake in dry matter basis; RFI, residual feed intake; FER, feed efficiency ratio.

Results and Discussion

Table 2. Heritability estimates and their standard-error for 35-day and 56-day test results of the studied traits.

Trait[1]	35-day trait	56-day trait
FW (kg)	0.541 ± 0.089	0.538 ± 0.091
AMW (kg)	0.561 ± 0.088	0.557 ± 0.090
ADG (kg d^{-1})	0.583 ± 0.080	0.630 ± 0.075
ADFI (kg d^{-1})	0.508 ± 0.090	0.533 ± 0.094
RFI (kg d^{-1})	0.533 ± 0.088	0.539 ± 0.095
FER (g kg^{-1})	0.603 ± 0.075	0.616 ± 0.079

[1] FW, final weight; AMW, average metabolic weight; ADG, average daily gain; ADFI, average daily feed intake in dry matter basis; RFI, residual feed intake; FER, feed efficiency ratio.

Conclusion

Yes, we can reduce the test to 35 days, as the precision of gain will be high enough to enable small decrease on genetic gain for the feed efficiency measures (around 15%) and even smaller changes on rankings of proven bulls.

Thank you

roberto.torres@embrapa.br

Embrapa

MINISTRY OF AGRICULTURE, LIVESTOCK AND FOOD SUPPLY

BRASIL BRAZILIAN GOVERNMENT

A novel, comprehensive genetic and management initiative to reduce the environmental impact of New Zealand dairy cattle.

Mark Camara, Jeremy Bryant, Peter Amer, Dorian Garrick, Talia Grala, Stewart Ledgard, David Chapman, Eric Kolver, David Burger, Mark Shepherd, Kate Sargeant, Bruce Thorrold

2018 Interbull Meeting, Auckland New Zealand

DairyNZ

New Zealand Animal Evaluation Limited

Government Industry Partnership

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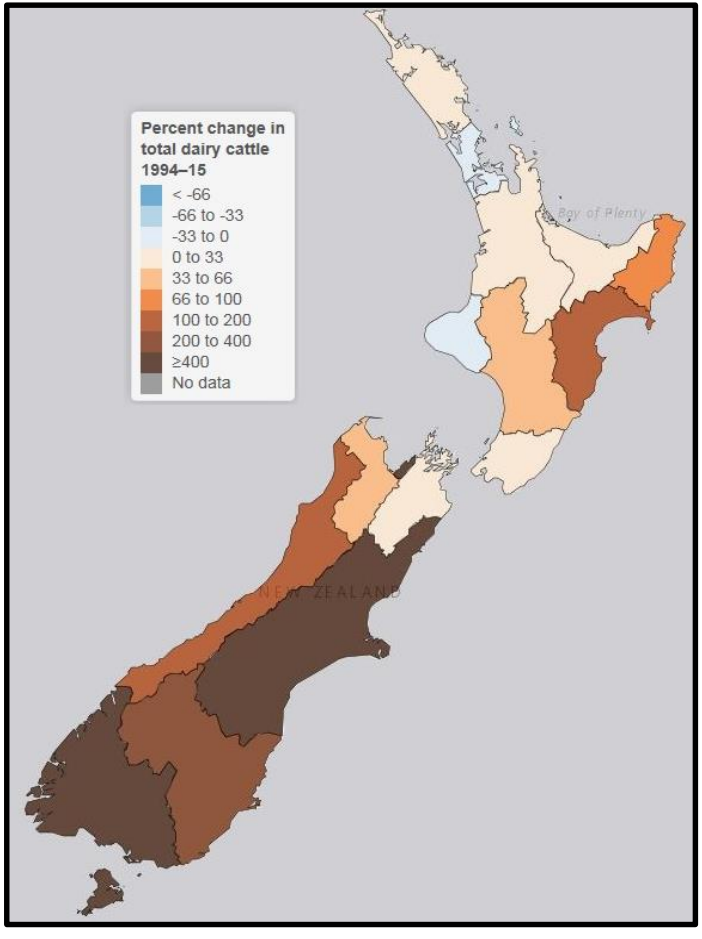
ABACUSBIO LIMITED

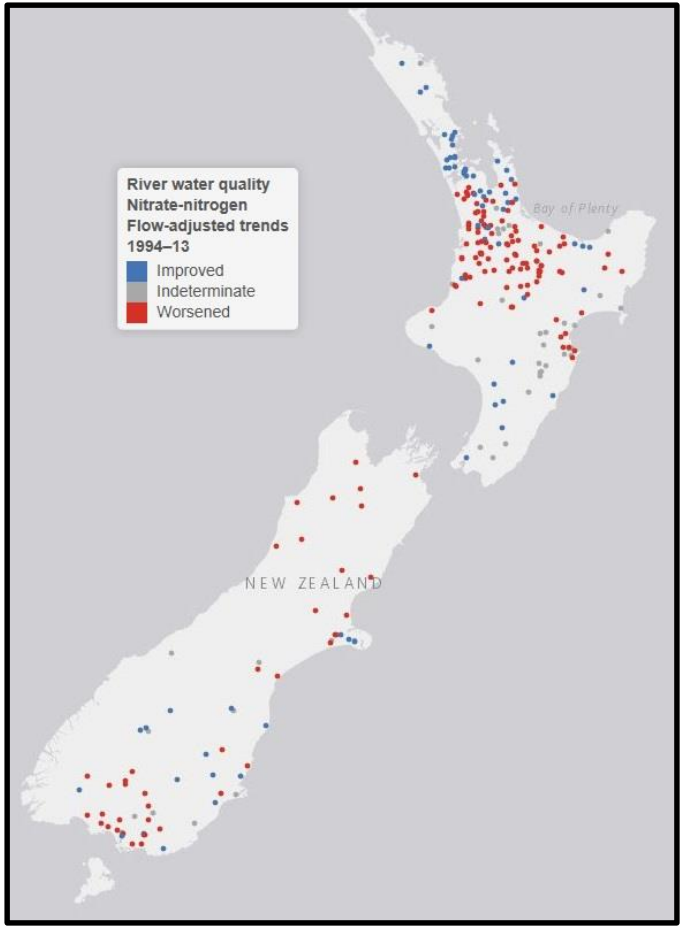
Ministry of Business Innovation & Employment wants impact

This programme will deliver transformational options for dairy and beef farmers to meet environmental targets by:

1. *Developing genetically low nitrogen excreting animals*
2. *Implementing genetic and management strategies to reduce nitrogen leaching*
3. Ultimately, this research partnership will reduce sector-wide nitrate leaching by 20%

Industry growth and water quality





http://archive.stats.govt.nz/browse_for_stats/environment/environmental-reporting-series/environmental-indicators/Home/Fresh%20water/river-water-quality-nitrogen.aspx

DairyNZ

Intense public pressure

The Economist | Topics | Print edition | More | Subscribe | Log in or sign up | Manage subscription

Cows and seep

Dairy farming is polluting New Zealand's water

Government data suggests that 60% of rivers and lakes are unswimmable

Central Government Response

Freshwater National Policy Statement (2014)

- Informs **local governments** about their responsibilities under Resource Management Act
- Directs **regional councils to set objectives** for the state of fresh water bodies and set limits to meet them
- Emphasizes **catchment-level targets** rather than specific on-farm practices
- Full implementation by **31 December 2025**

Regionally variable nitrogen limits

- **Auckland:** N input limits:150kg N/ha/yr on sandy soils, 200kg N/ha/yr other soils
- **Bay of Plenty:** Limits on N and P that can leave a farm property based on a 3 year “benchmark” period (mid-2001 to mid-2004).
- **Horizons:** N limits based on farm’s land use capability (LUC) classification

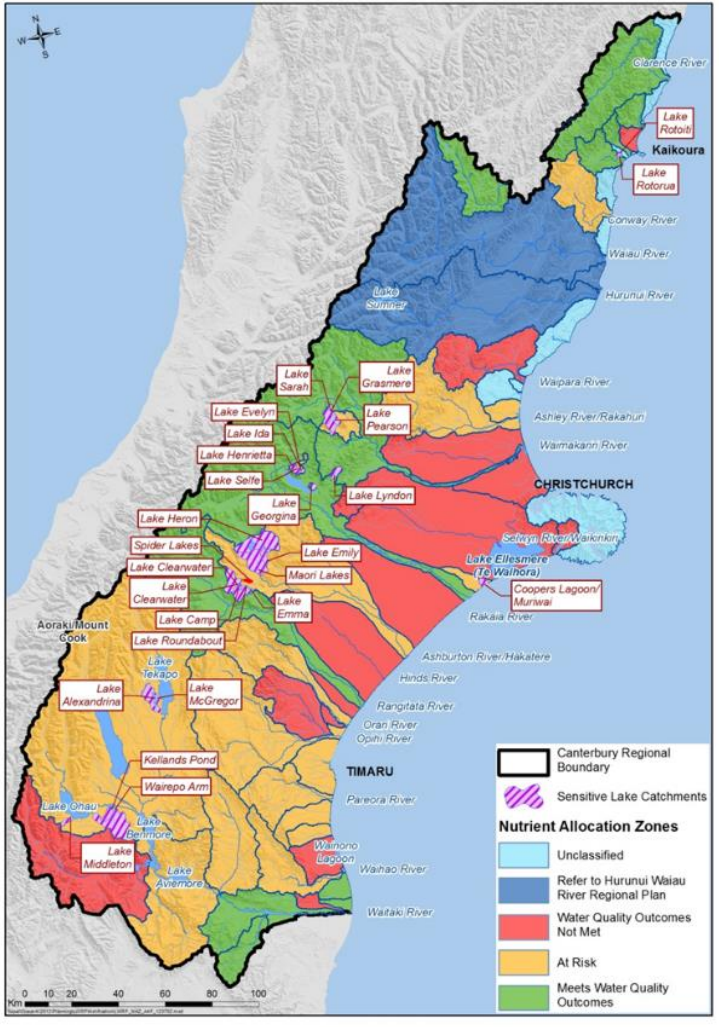
Variation within regions: Canterbury

Nitrogen Baseline 2009-2013 averaged N Loss.

Red - from 2017 need consent and must be at baseline (if over 20kg N/ha/yr).

Orange - Baseline + 5kg N - consent required 2016 (if over 20kg N/ha/yr).

Blue and **Green** – Consent required if increase greater than 5kg N/ha/yr.



Enforcement largely model-based

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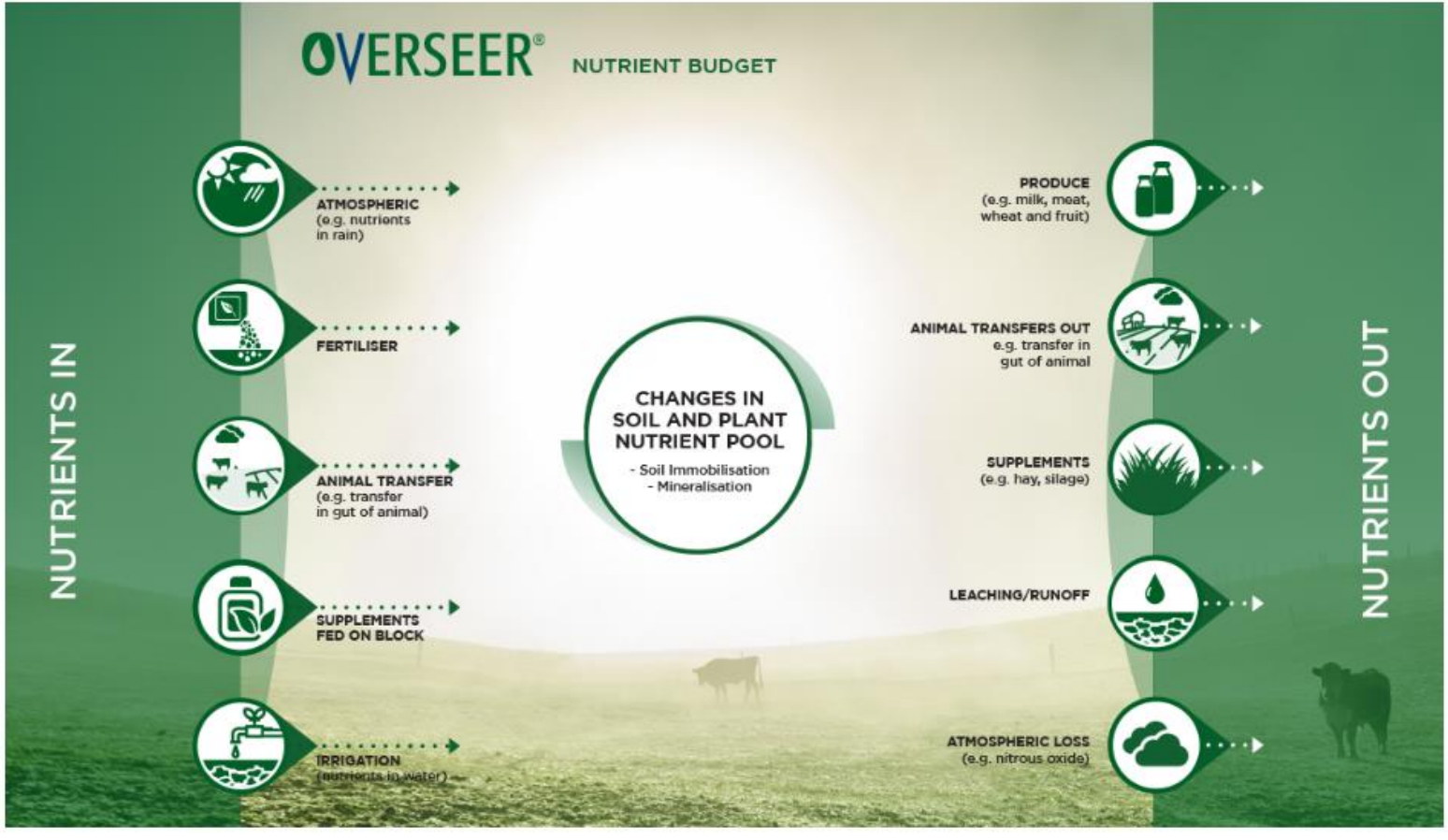
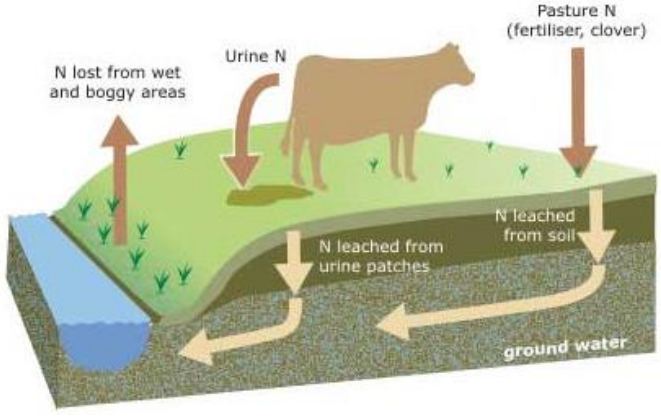
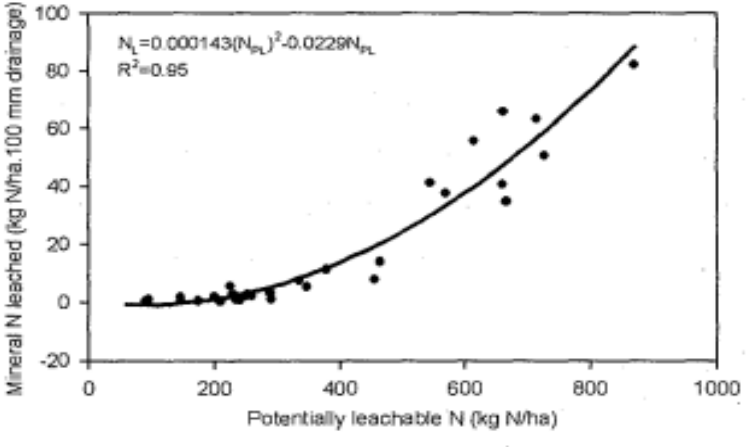


Cow urine important for nitrogen leaching

Urine patches can have1200 kg N per hectare, and plants can't process it all.
(Haynes and Williams, 1993)





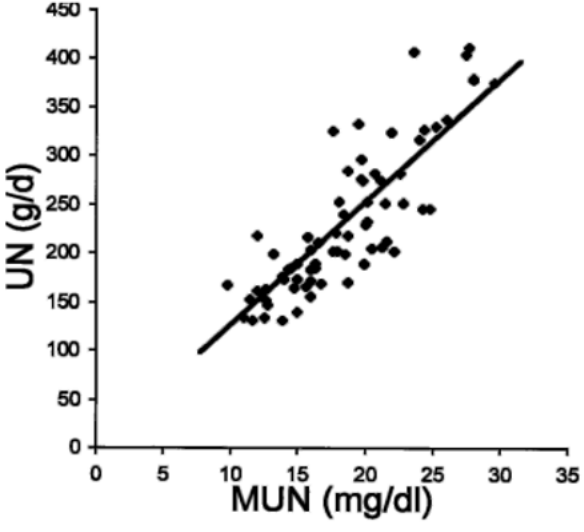
Di HJ, Cameron KC (2000) New Zealand Journal of Agricultural Research 43, 139-147.

Advantages of genetic solutions

- Cumulative and permanent
- Universally applicable (assuming low GxE)
- Infinitely scalable
- No changes to infrastructure or farming practices
- Low cost to farmers once implemented
- Can be “stacked” with management solutions (e.g. alternative pasture plants)

Can milk urea nitrogen (MUN) predict urinary nitrogen (UN)?

1. Ammonia in rumen → b
   passive diffusion to milk
   al., 1993).
2. MUN routinely measure
3. MUN and UN are phenc
   response to dietary [N].
4. MUN is heritable (Beats



Jonker JS, Kohn RA and Erdman RA 1998. Using milk urea nitrogen to predict nitrogen excretion and utilization efficiency in lactating dairy cows. Journal of Dairy Science 81(10), 2681-2692.

Key technology: automated urine sensors

Developed by AgResearch

Continuously-recorded individual-level data for UN, urine volume, and urination frequency in feed stalls or while grazing

M.Shepherd, P.Shorten, D.Costall, K.A.Macdonald (2017) Agriculture, Ecosystems & Environment 236: 285-294

Research Aims

'Knowing is not enough; we must apply. Willing is not enough; we must do.'

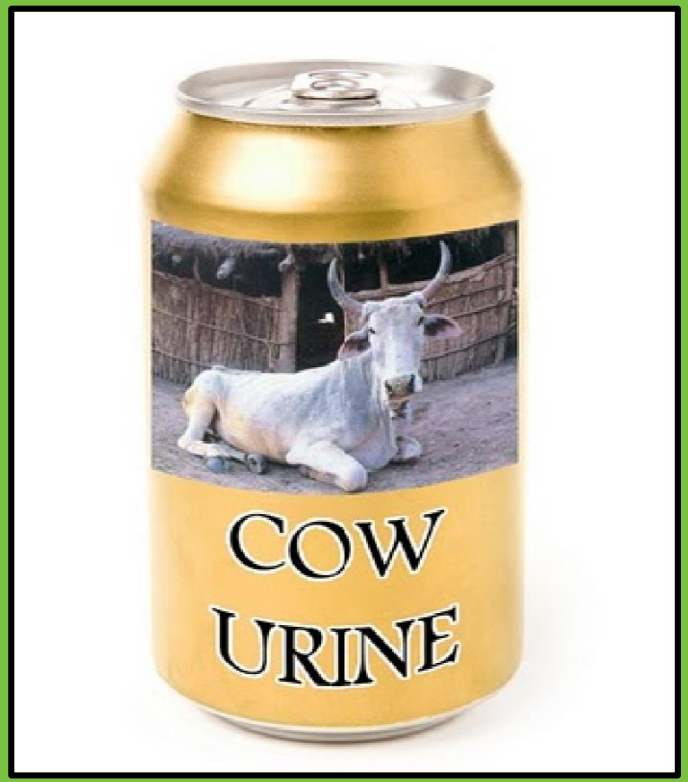
- Johann Wolfgang von Goethe

1. **Genetics, genomics, physiology, and omics to enable selective breeding**
   - Quantitative genetic and genomic analyses in representative "Development Herds"
   - Physiological and -omic comparisons of phenotypically divergent animals
   - Develop new animal evaluation models
2. **Validation, demonstration, and adoption to achieve national water quality outcomes**
   - Develop practical breeding strategies & economic values
   - Validate mitigation strategies at the whole-farm and catchment levels
   - Develop enhanced models for sensible regulation

7-year Programme

Questions?

Mark.Camara@dairynz.co.nz



DairyNZ

New Zealand Animal Evaluation Limited

Methods for discovering and validating relationships among genotyped animals

G.R. Wiggans,[1] P.M. VanRaden,[2] and L.R. Bacheller[2]

[1] Council on Dairy Cattle Breeding, Bowie, Maryland, USA

[2] Animal Genomics and Improvement Laboratory, Agricultural Research Service, USDA, Beltsville, Maryland, USA

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USDA
United States Department of Agriculture

Validation of parents

- Over 2.2 million animals genotyped in U.S. system
- Portion of parents validated
  - 97% of sires
  - 39% of dams
- Each genotype compared with all others to discover identical genotypes and parent-progeny relationships
- Animals with incorrect sire or dam excluded from evaluation

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Validation of grandsires

- If parent not genotyped or not confirmed, grandsire is checked
- Grandsire declared unlikely if animal and grandsire have more opposite homozygotes than threshold, which declines as possible comparisons increase
- Possible grandsires are suggested if low percentage of conflicts and birth date reasonable
- Animals with unlikely grandsires excluded from evaluation

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Detection of chromosomal abnormalities

- Where parent and progeny have more conflicting SNPs than allowed for a true parent-progeny relationship, location of conflicts is checked

- If conflicts are concentrated on a single chromosome, parent-progeny relationship is accepted
  - Large deletion – animal is homozygous in the region
  - Uniparental disomy – heterozygous SNPs in the region
  - 102 cases discovered so far

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Quality control

- Each SNP evaluated for
  - Call rate
  - Portion heterozygous
  - Parent-progeny conflicts
- Parent-progeny conflicts assessed for all SNPs in common between parent and progeny genotypes
- Trio test if both parents genotyped
- 30 chips supported

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Computational burden

- Computer time to compare each genotype with all others steadily increases with number of genotype in database
- 1,000 SNPs that were on all chips used to exclude most unrelated animals
- Further speed-up needed
  - Compare fewer SNPs
  - Exclude some genotypes from comparison
  - Optimize comparison method

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100 SNPs

- Selected based on call rate, MAF, and Mendelian consistency
- Measure: Conflicts/(number of both SNPs homozygous)
- Threshold of 8.4% eliminated 99.7% of genotypes without eliminating any confirmed parent-progeny pairs
- Test with only 50 SNPs eliminated only half the unrelated animal genotypes

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Compare genotypes for fewer animals

- For animals with both parents confirmed, check only recent genotypes (starting with births 500 days before) for identical genotypes
- For animals with 1 parent confirmed, skip genotypes with a different confirmed parent when checking for identical genotypes
- For grandsires, skip comparisons with bulls that have no progeny

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MGS checking with haplotypes

- For animals included in the evaluation, haplotypes are generated during imputation
- These haplotypes can be used to validate or discover MGS more accurately (even MGGS can be discovered)
- For MGS, identify bulls with around 45% of haplotypes in common and at least 15% better than next best bull
- Discovered MGS assigned as dam's sire if unknown

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Use haplotypes for initial MGS discovery

- Remove searching for possible MGS from initial genotype validation program for faster processing
- Include new animals with unknown or unlikely MGS in weekly evaluation calculations (confirmed sire required)
- For genotypes not qualifying for evaluation, blank conflicting pedigree and suppress release of evaluation
- Continue use of current SNP comparison process for PGS

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Timing comparison

- Time to load 1 submission of 1,967 genotypes
  - Current – 51 minutes
  - Eliminate 497 MGS searches – 39 minutes
- Time to run weekly MGS discovery for Holsteins – 9 minutes
- Time to run monthly MGS/MGGS discovery for Holsteins – 7 hours

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Further possible use of discovered MGS

- When dam is unknown, constructed ID necessary to store discovered MGS

Ayrshire	Brown Swiss	Guernsey	Holstein	Jersey
21	245	68	213,704	21,963

- More complete pedigree gives better imputation
- Numerator relationship matrix (A) more similar to genomic relationship matrix (G)

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Conclusions

- Rapid increase in size of genotype database requires periodic modification of procedures
- Checking all genotypes is desirable for correctly assigning animal to genotype and improving pedigree accuracy
- 100 high quality SNPs are effective in excluding most genotypes that are not parents or progeny
- Grandsires (even great-grandsires) can be checked and candidates discovered

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Acknowledgments & disclaimers

- **USDA-ARS project 8042-31000-002-00, “Improving dairy animals by increasing accuracy of genomic prediction, evaluating new traits, and redefining selection goals”**

- **Mention of trade names or commercial products in this presentation is solely for the purpose of providing specific information and does not imply recommendation or endorsement by USDA; USDA is an equal opportunity provider and employer**

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Efficient computation of base generation allele frequencies

11 February; Interbull meeting, Auckland, New Zealand

Michael Aldridge, Jeremie Vandenplas & **Mario Calus**

WAGENINGEN UNIVERSITY & RESEARCH

100years 1918 — 2018

Allele frequencies in genomic prediction

- Genomic prediction requires allele frequencies (AF)
- Commonly, AF are current data averages
- Theoretically, AF should be computed for the base generation

Base generation AF

Base generation = base generation in pedigree!

Base generation AF required for calculation of:

- Genomic relationships in (single-step) GBLUP
- Model-based reliabilities for multi-step genomic evaluations
- Computation of relationships among metafounders[1]

[1]Legarra, A., O. F. Christensen, Z. G. Vitezica, I. Aguilar, and I. Misztal. 2015. *Genetics*. 200:455-468.

Objective

Compare accuracy and efficiency

of different methods to compute

base generation allele frequencies

Methods – overview

- AF: $p = \frac{1}{2}\hat{\mu}$

Method	Mean is estimated:
All	Across all genotypes
Oldest	Across oldest generation genotyped
BLUP	In BLUP model
GLS	General Least Squares (GLS)

Methods - BLUP

- BLUP model; y = genotype (0,1,2)
- h^2=0.99; allowing some genotyping error
- Univariate; or multivariate with zero genetic correlations
- Implemented using MiXBLUP

McPeek, M. S., X. D. Wu, and C. Ober. 2004. Biometrics. 60:359-367.
Gengler, N., P. Mayeres, and M. Szydlowski. 2007. Animal. 1:21-28.

Methods – GLS (dense / sparse)

- GLS: $\hat{\mu}_i = (\mathbf{1}'\mathbf{A}_{22}^{-1}\mathbf{1})^{-1}\mathbf{1}'\mathbf{A}_{22}^{-1}\mathbf{Z}_i$
- Dense: Compute and invert $\mathbf{A}_{22}$ — Calc_grm
- Sparse: $\mathbf{A}_{22}^{-1}\mathbf{1} = \left(\mathbf{A}^{22} - \mathbf{A}^{21}\left(\mathbf{A}^{11}\right)^{-1}\mathbf{A}^{12}\right)\mathbf{1}$ — Own program / Intel MKL-PARDISO

McPeek, M. S., X. D. Wu, and C. Ober. 2004. Biometrics. 60:359-367.
Garcia-Baccino, C.A., Legarra, A., Christensen, O.F., Misztal, I., Pocrnic, I., Vitezica, Z.G., and Cantet, R.J. 2017. Genet. Sel. Evol. 49, 34.

Data (simulation)

- Holstein-like population
- Generations 9 to 12 (after base) fully genotyped
- 325,266 animals in pedigree; 100,078 genotyped
- 1670 SNPs (providing replication)
- Selection: None or Strong

Change in AF across generations (with selection)

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100years
1918 — 2018

Results - accuracy

Method	Without selection	With selection
All	0.99 ± 0.01	0.87 ± 0.01
Oldest	0.99 ± 0.01	0.88 ± 0.01
BLUP	0.99 ± 0.01	0.96 ± 0.01
GLS_dense	0.99 ± 0.01	0.97 ± 0.01
GLS_sparse	0.99 ± 0.01	0.97 ± 0.01

Results - efficiency

Method	Process time	RAM
All	0-00:03:44	7.8 GB
Oldest	0-00:01:19	1.6 GB
BLUP (60 SNPs)	0-13:42:17	49.0 GB
GLS_dense	50-20:12:16	165.9 GB
GLS_sparse	0-00:01:28	2.6 GB

=> Efficiency of GLS_sparse is very competitive!

Discussion

- Few GLS_sparse estimates outside 0-1 range:
  - Only for very low MAF <0.001
  - Swapping allele code solved most of those

- Estimates were not affected when having:
  - 2% genotyping errors
  - 25% of sires unknown

Conclusions

- Base generation AF required for:
  - Genomic relationships in (single-step) GBLUP
  - Model-based reliabilities for multi-step genomic evaluations
  - Computation of relationships among metafounders

- GLS_sparse estimator recommended
  - Accurate & very efficient

Acknowledgements

UNIVERSITY OF GEORGIA

Tuning indirect predictions based on SNP effects from ssGBLUP

Daniela Lourenco

A. Legarra, S. Tsuruta, D. Moser, S. Miller, I. Misztal

Interbull 2018

Why Indirect predictions?

- Interim evaluations
  - Between official runs
- Not all genotyped animals are in the evaluations
  - Animals with incomplete pedigree increase bias and lower R^2
- Commercial products
  - e.g. GeneMax for non-registered animals

Indirect predictions in ssGBLUP

$$\begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}'\mathbf{W} \\ \mathbf{W}'\mathbf{X} & \mathbf{W}'\mathbf{W}+\mathbf{H}^{-1}\lambda \end{bmatrix} \begin{bmatrix} \hat{b} \\ \hat{u} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{y} \\ \mathbf{W}'\mathbf{y} \end{bmatrix}$$

$$\mathbf{DGV} = \mathbf{Z}\hat{\boldsymbol{a}}$$

SNP effects

GEBVs

$$\hat{\boldsymbol{a}} = \lambda \mathbf{D}\,\mathbf{Z}'\mathbf{G}^{-1}\hat{\boldsymbol{u}}$$

$$\mathbf{GEBV}_{\mathbf{young}} = w_1\mathbf{PA} + w_2\mathbf{DGV} - w_3\mathbf{PP}$$

$$\mathbf{GEBV}_{\mathbf{young}} \approx \mathbf{DGV} = \mathbf{Z}\hat{\boldsymbol{a}}$$

$$\mathbf{H}^{-1} = \mathbf{A}^{-1} + \begin{bmatrix} 0 & 0 \\ 0 & \mathbf{G}^{-1} - \mathbf{A}_{22}^{-1} \end{bmatrix}$$

$$\mathbf{G}_{\mathrm{APY}}^{-1}$$

Lourenco et al., 2015

Problems with Indirect predictions

Genetic evaluation using single-step genomic best linear unbiased predictor in American Angus[1]

D. A. L. Lourenco,*[2] S. Tsuruta,* B. O. Fragomeni,* Y. Masuda,* I. Aguilar,[†] A. Legarra,[‡] J. K. Bertrand,* T. S. Amen,[§] L. Wang,[§] D. W. Moser,[§] and I. Misztal*

© 2015 American Society of Animal Science. All rights reserved. J. Anim. Sci. 2015.93:2653–2662
doi:10.2527/jas2014-8836

$$COR(\widehat{GEBV}, \mathbf{Z}\hat{a}) > 0.99$$

$$Avg(\widehat{GEBV}) \approx 100 \quad \neq \quad Avg(\mathbf{Z}\hat{a}) \approx 0$$

Objectives

1) Fine-tune indirect predictions to be compatible with GEBV

2) Investigate whether SNP effects are accurate when APY is used

- Possibly use subset of core animals

Dataset

- American Angus Association
  - 8.2M animals in pedigree
  - 6.2M birth weight (BW)
  - 6.8M weaning weight (WW)
  - 3.4M post-weaning gain (PWG)
  - 81k genotyped
    - born 1977-2012: 66k
    - born 2013-2014: 15k

- Complete
  - Phenotypes up to 2012
  - Genotypes up to 2014 (81k)
- Reduced
  - Phenotypes up to 2012
  - Genotypes up to 2012 (66k)

- 3-trait with mat and mpe
  - Results for PWG

Accuracy of SNP effects from $\mathbf{G}^{-1}_{\mathbf{APY}}$ or $\mathbf{G}^{-1}_{\mathbf{cc}}$

$$\hat{\boldsymbol{a}}_{\mathbf{G}} = \lambda \mathbf{D}\, \mathbf{Z}' \mathbf{G}^{-1} \hat{\boldsymbol{u}}$$

$$\hat{\boldsymbol{a}}_{\mathbf{G}^{-1}_{APY}\mathbf{H}} = \lambda \mathbf{D}\, \mathbf{Z}' \mathbf{G}^{-1}_{\mathrm{APY}\_high\_reliability} \hat{\boldsymbol{u}}_{\mathrm{APY}}$$

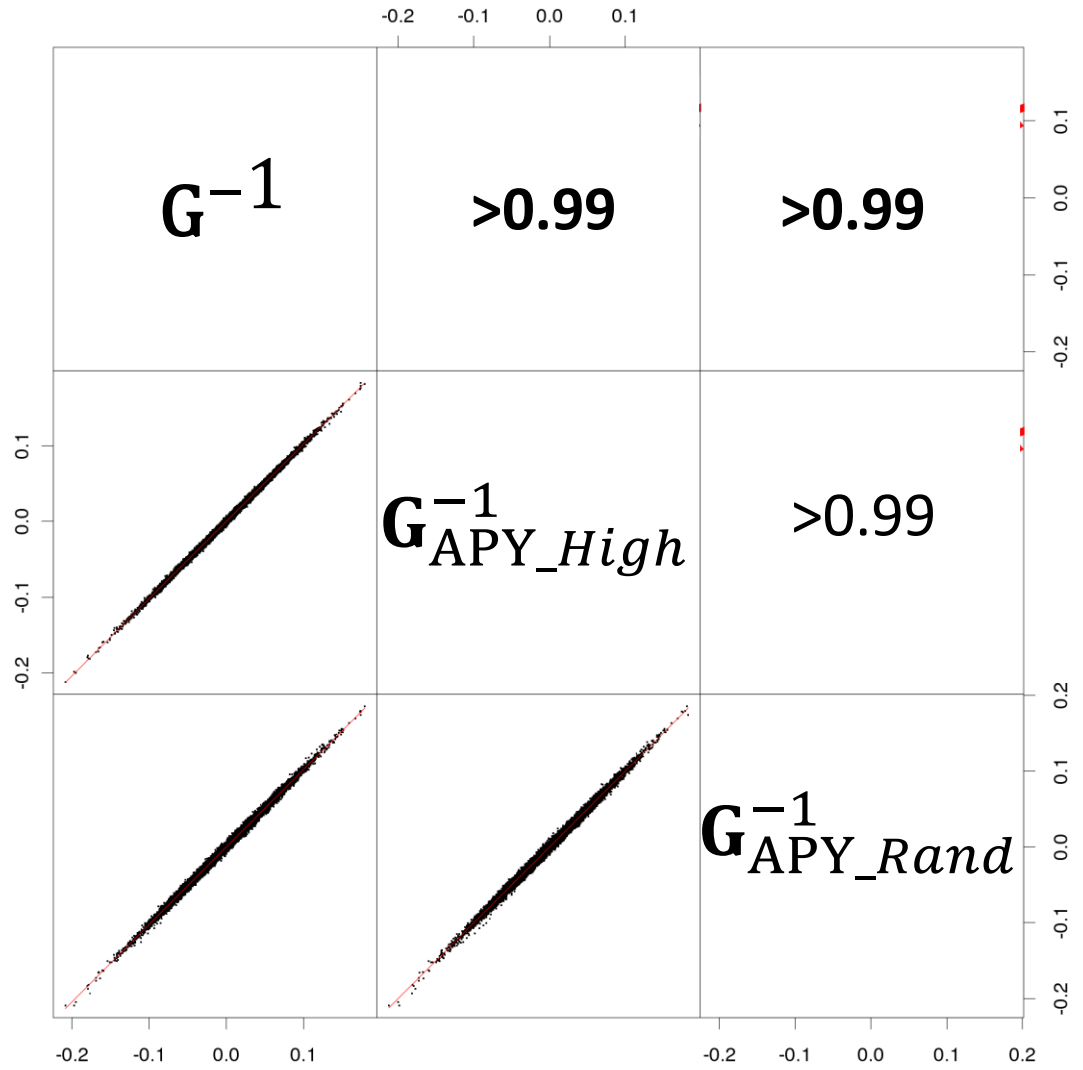
$$\hat{\boldsymbol{a}}_{\mathbf{G}^{-1}_{APY}\mathbf{R}} = \lambda \mathbf{D}\, \mathbf{Z}' \mathbf{G}^{-1}_{\mathrm{APY}\_random} \hat{\boldsymbol{u}}_{\mathrm{APY}}$$

$$\hat{\boldsymbol{a}}_{\mathbf{G}^{-1}_{cc}\mathbf{H}} = \lambda \mathbf{D}\, \mathbf{Z}' \mathbf{G}^{-1}_{CC\_high\_reliability} \hat{\boldsymbol{u}}_{\mathrm{APY}}$$

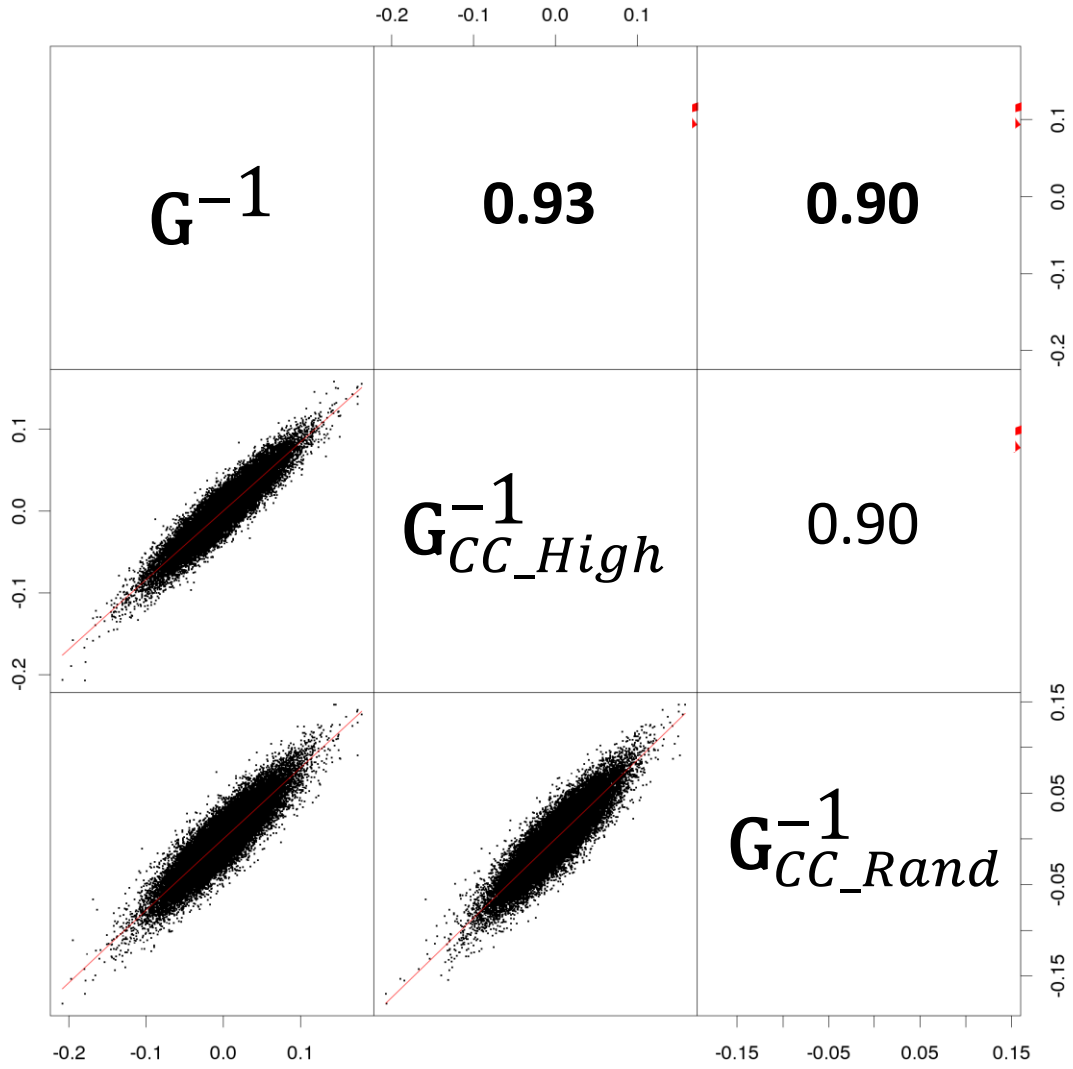
$$\hat{\boldsymbol{a}}_{\mathbf{G}^{-1}_{cc}\mathbf{R}} = \lambda \mathbf{D}\, \mathbf{Z}' \mathbf{G}^{-1}_{CC\_random} \hat{\boldsymbol{u}}_{\mathrm{APY}}$$

- Correlation between SNP effects
- Correlation between $\mathbf{Z}\hat{a}$

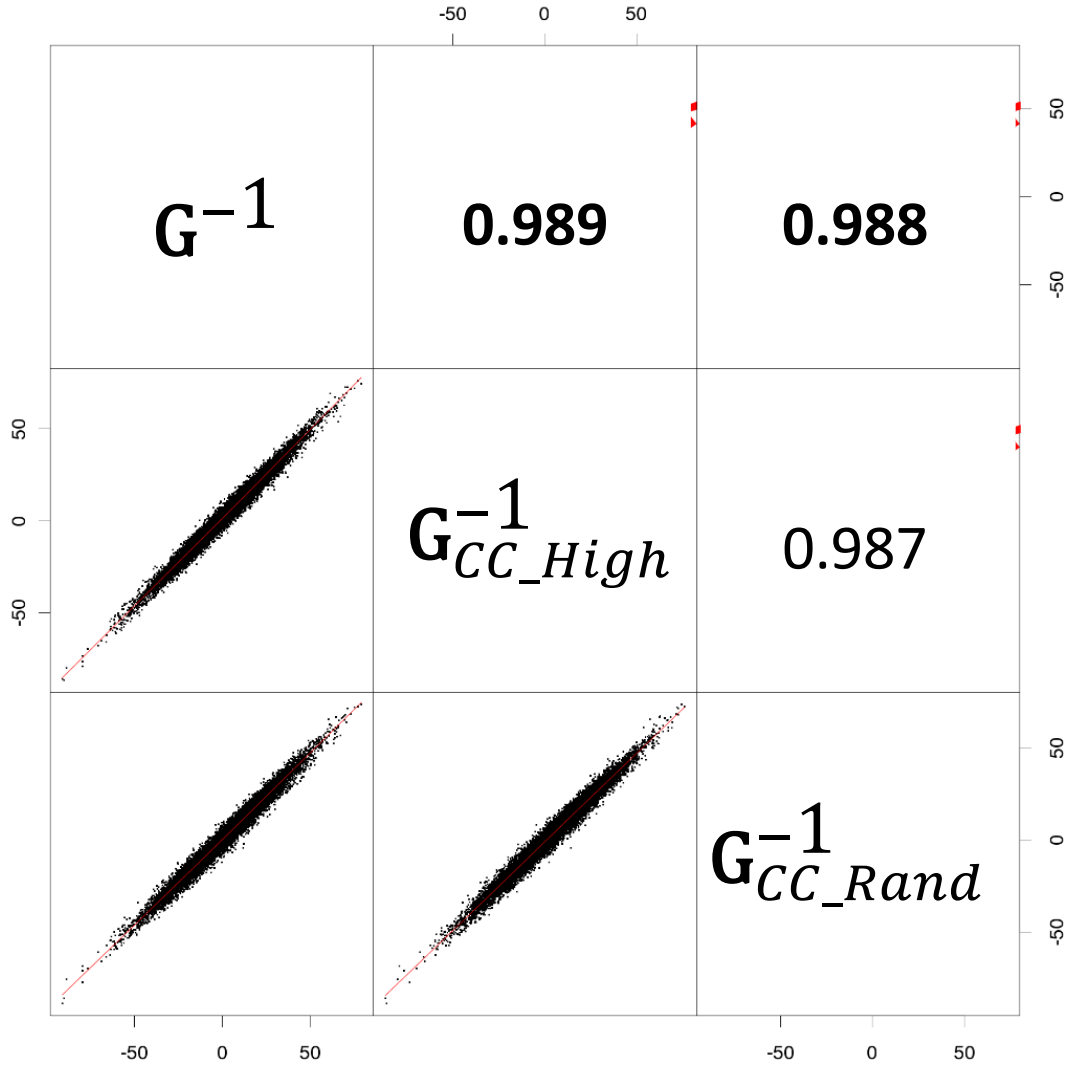
Statistics for SNP effects



Statistics for SNP effects



Statistics for $\mathbf{Z}\hat{a}$



Fine-tuning indirect predictions from ssGBLUP

Understanding genetic and genomic bases

- Base of BLUP: *founders of the pedigree*
- Base of GBLUP: *genotyped* animals
- Base of SSGBLUP: Vitezica et al. (2011) modelled as a mean in genotyped animals
  - $p(\boldsymbol{u}_g) = N(\mathbf{1}\mu, \mathbf{G})$
  - μ = (Pedigree base) – (Genomic base)

Fine-tuning indirect predictions from ssGBLUP

1) Formula in Legarra (2017) $\hat{\boldsymbol{u}}_{ip} = \hat{\mu} + 0.95\mathbf{Z}\hat{a} + 0.05\,\hat{\boldsymbol{u}}_{parents}$

SNP and pedigree fractions

2) Double fitting

a) fit a regression using genotyped animals in the evaluation

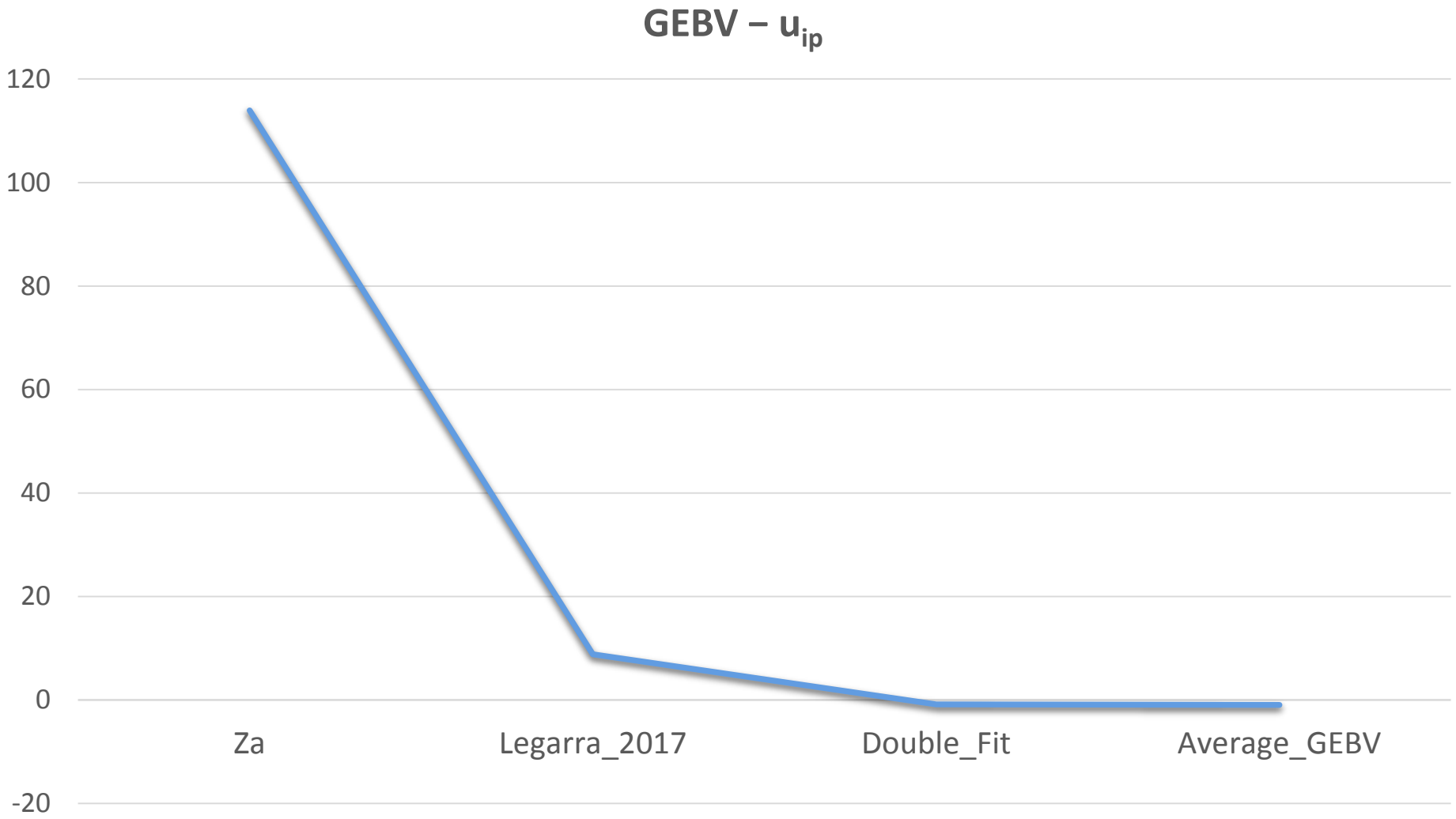
$$\mathrm{DGV}_{eval} = b_0 + b_1\mathbf{Z}\hat{a}$$

b) apply regression for indirectly predicted animals

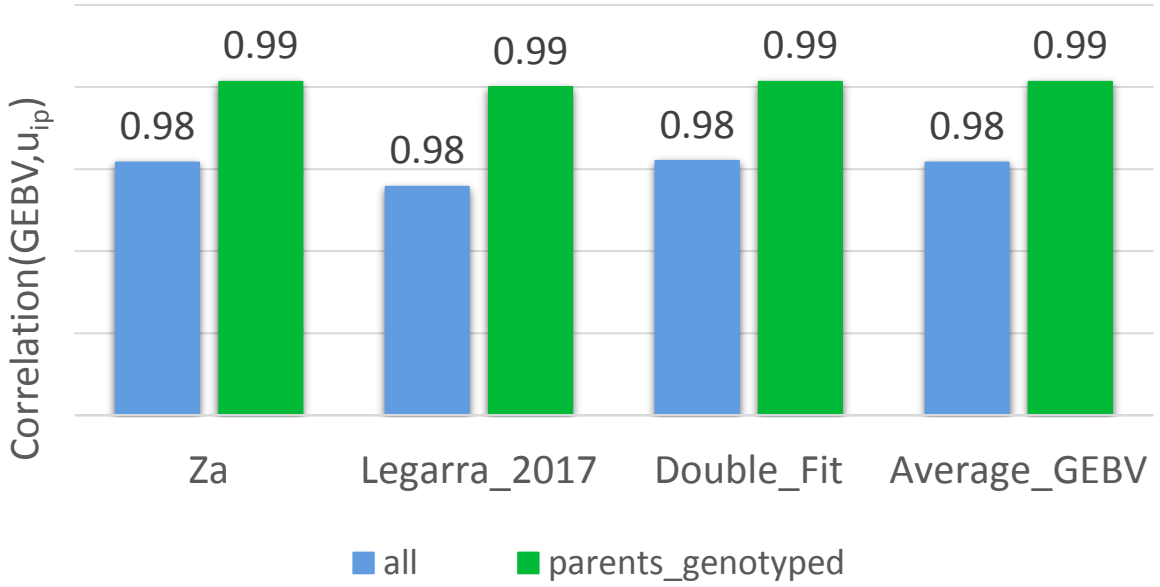
$$\hat{\boldsymbol{u}}_{ip} = b_0 + b_1\mathbf{Z}\hat{a}$$

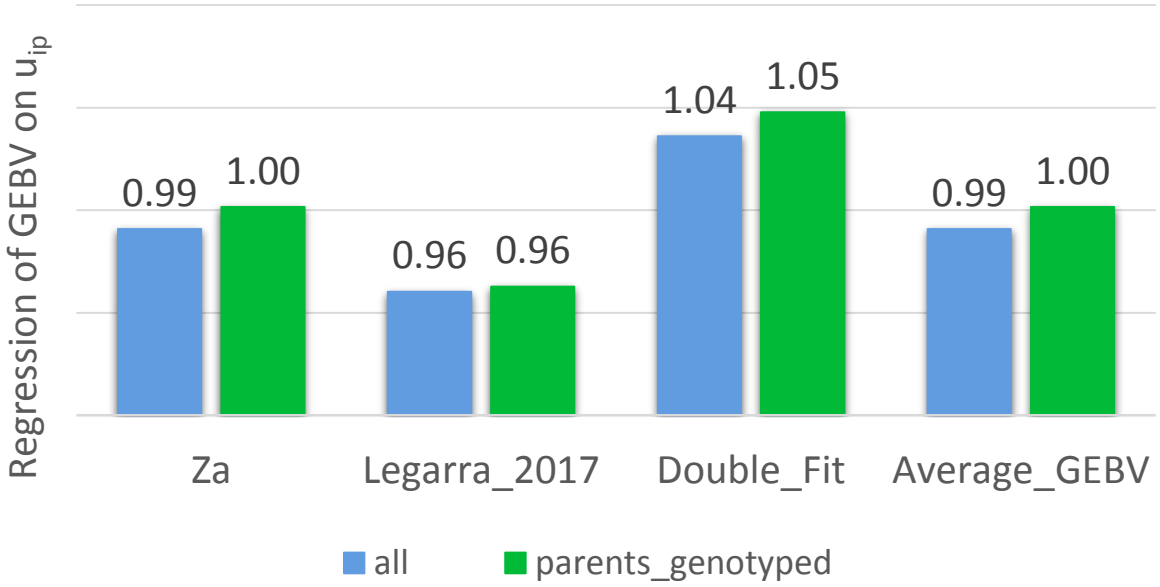
3) Add average GEBV $\hat{\boldsymbol{u}}_{ip} = \overline{GEBV_{eval}} + \mathbf{Z}\hat{a}$

Bias of indirect predictions



Correlation & Regression Coefficient





Fine-tuning indirect predictions in ssGBLUP

$$\mathrm{E}(\boldsymbol{u}|\boldsymbol{a}) = \hat{\boldsymbol{u}}|\hat{\boldsymbol{a}} = \mu + \mathbf{Z}\frac{\mathbf{1}}{\mathbf{2}\sum \boldsymbol{p}(\mathbf{1}-\boldsymbol{p})}\left(\mathbf{I}\frac{\mathbf{1}}{\mathbf{2}\sum \boldsymbol{p}(\mathbf{1}-\boldsymbol{p})}\right)^{-\mathbf{1}}(\hat{\boldsymbol{a}} - 0)$$

$$\hat{\boldsymbol{u}}|\hat{\boldsymbol{a}} = \mu + \mathbf{Z}\hat{\boldsymbol{a}}$$

$$\approx$$

$$\hat{\boldsymbol{u}}|\hat{\boldsymbol{a}} = \overline{GEBV} + \mathbf{Z}\hat{\boldsymbol{a}}$$

Final Remarks

- Indirect predictions are unbiased after corrections
  - Can be used as interim evaluation
- Indirect predictions based on core animals are slightly less accurate
  - Reduction in computing time (no $\mathbf{G}_{nc}^{-1}$ and $\mathbf{G}_{nn}^{-1}$)
- SNP effects from ssGBLUP may be useful for SNP MACE

Acknowledgements

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Validation of genomic reliability and gains from phenotypic updates

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Agricultural Research Service, USDA, Beltsville, MD
***University of Maryland-Baltimore**
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Topics

- Methods to compute genomic reliability
  - Summarized by Liu et al (2017)
  - GREL compared by Sullivan and Jakobsen (2014)
- Simple validation of genomic reliability
  - Do actual EBV changes agree with published REL?
  - Examples from USA and Intergenomics
- Gains in reliability from more frequent updates
  - Similar math can determine the value of re-estimating marker effects more often

REL calculation vs. validation

- REL estimation
  - Adjust theoretical REL such as from SNP-BLUP-REL or from size of reference population
  - Use prediction error variance (PEV) because correlations are biased downward by selection
- REL validation
  - Similar to validating EBVs using truncated data
  - Examine published REL for 6 traits and Net Merit
  - Examine 3 breeds (HOL, JER, BSW) on USA scale

Genomic reliability theory

- Selection reduces variance such that Var(EBV) < REL * Var(BV), but not prediction error variances (PEV):
- PEV = Var(EBV – BV) = (1 – REL) Var(BV)
- Variance of EBV differences are proportional to the difference in reliabilities regardless of selection. If EBV_1 and EBV_2 are earlier and later genomic evaluations with reliabilities REL_1 and REL_2, then
- $Var(EBV_2 – EBV_1) = (REL_2 – REL_1)\ Var(BV)$
- If REL_2 is known, high, and accurate, then solve for
- $REL_1 = REL_2 – Var(EBV_2 – EBV_1) / Var(BV)$

Data to validate genomic reliability

- Published genomic evaluations from April 2014
- Published genomic evaluations from April 2017
- SD of difference in genomic PTAs
- REML estimates of true TA SD from Interbull MACE
- Example for Holstein protein validation bulls:
- Average published REL_1 was 0.76, REL_2 was 0.95, SD of change was 8.4, and REML TA SD was 17.5. The observed REL_1 for protein was calculated as
- Observed $REL_1 = 0.95 - (8.4)^2 / (17.5)^2 = 0.72$

Observed vs. published reliability, 2014

Trait	Observed	Published	Diff	Observed	Published	Diff
	Jerseys			Holsteins		
Milk	73	68	+5	72	76	-4
Fat	72	68	+4	74	76	-2
Protein	71	68	+3	72	76	-4
Longevity	47	55	-8	65	70	-5
SCS	64	62	+2	77	73	+4
Preg Rate	63	52	+11	69	68	+1
NetMerit	68	64	+4	68	73	-5
Average	65	62	+3	71	73	-2

Observed vs. published reliability, BSW

Trait	Observed	Published	Diff	Observed	Published	Diff
	Brown Swiss - USA			BSW - Intergenomics		
Milk	62	63	-1	70	68	+2
Fat	64	63	+1	76	68	+8
Protein	57	63	-6	66	68	-2
Longevity	57	55	+2	63	61	+2
SCS	64	59	+6	71	66	+5
Preg Rate	56	51	+5	67	58	+9
Average	60	59	+1	69	65	+4

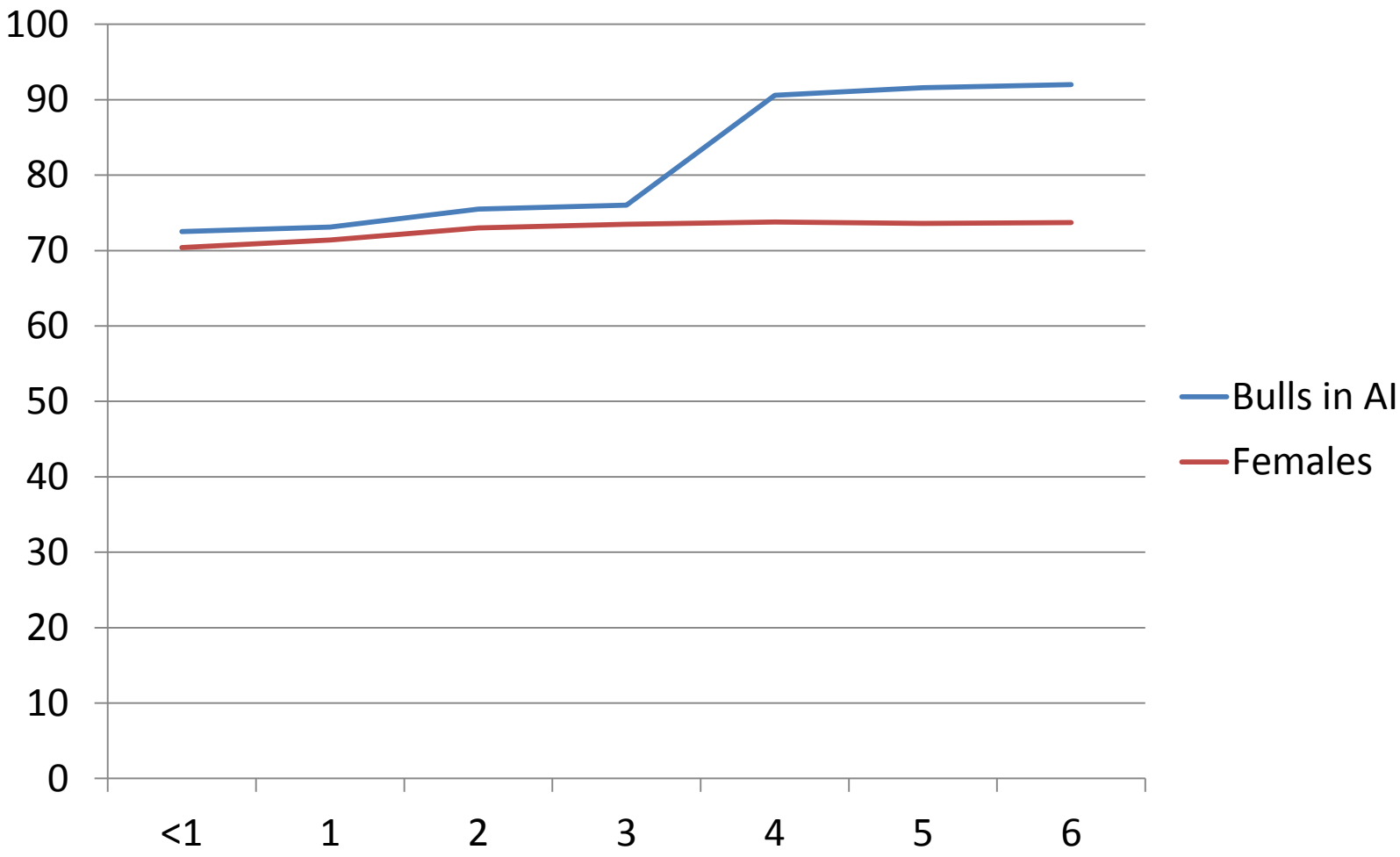
Discussion of BSW results

- Same software used by USA and Intergenomics
- Same data except PA in USA vs. Pedigree Index in IG
  - Bias from dam's PTA and extra weight on PA
  - Yield heritability reduced from 35% to 23% in Dec 2014
- Small test used only 41 bulls with > 50 US daughters
- Full test with all 475 IG bulls gave observed REL much more similar because USA and IG both have only PI for foreign MACE bulls

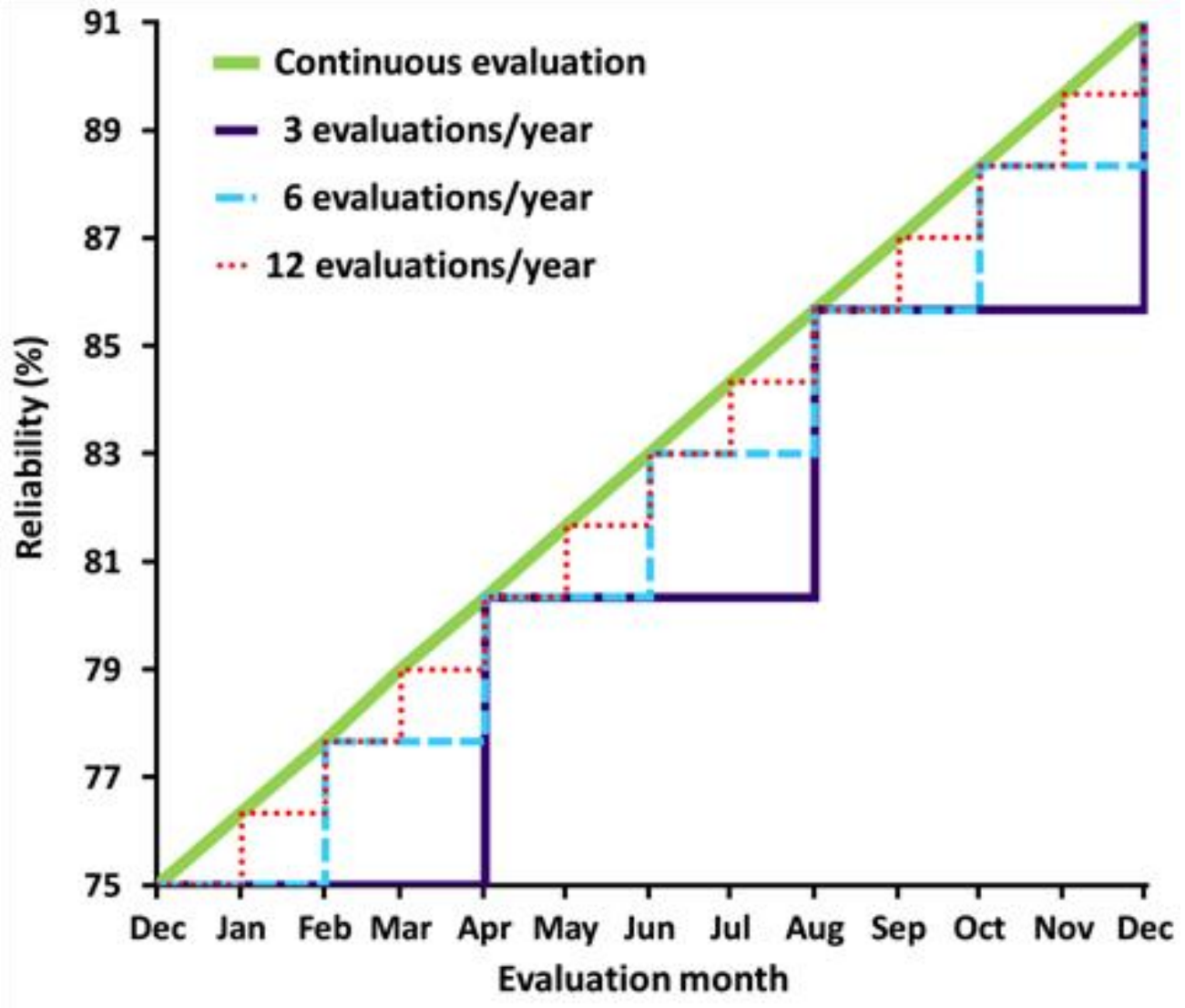
Phenotypic update frequency

- Suppose reliability increases steadily from REL_1 to REL_2 across a year.
- The gain in reliability from n updates per year (REL_n) instead of 1 annual update should average:
- $REL_n = .5 (REL_2 – REL_1) (n - 1) / n$
- Suppose bulls increase from 75% REL_1 to 91% REL_2 when 4 years old (no daughters to many daughters).
- Minimum gain is 0% with an annual update because the bulls would stay at 75% for the whole year.
- Maximum gain is 8% with instant updating. Bulls would average (75 + 91)/2 = 83% during that year.

HOL NM$ average reliability by age



Phenotypic update frequency



Reliability gains by update frequency

Frequency	Updates	Young REL	Marginal Gain	Proven REL	Marginal Gain
Annual	1	73.0		75.0	
6 months	2	73.5	0.5	79.0	4.0
4 months	3	73.7	0.2	80.3	1.3
3 months	4	73.8	0.1	81.0	0.7
2 months	6	73.83	0.03	81.6	0.6
Monthly	12	73.92	0.09	82.3	0.7
Weekly	52	73.98	0.06	82.8	0.5
Daily	365	73.99	0.01	82.97	0.17
Instant	∞	74.0	0.01	83.0	0.03

Assuming that REL begins at 75% and is 91% 1 year later for proven bulls and begins at 73% and is 75% 1 year later for young bulls.

Conclusions

- Exact calculation of genomic reliability is hard, but validation is easy
- Published USA REL averaged 2% too high for HOL, 3% too low for JER, and 1% too low for BSW
- Published Intergenomics REL averaged 4% too low for BSW traits because observed REL were higher
- Updating marker effects more frequently than 3 times per year could improve average REL up to 2.5% for recently proven bulls but < 0.3% for young animals

Acknowledgements

- Interbull Working Group on Genomic Reliability (Zengting Liu, Martin Lidauer, Mario Calus, Vincent Ducrocq, Haifa Benhajali, and Hossein Jorjani)

- Council on Dairy Cattle Breeding and Intergenomics for data

- Suzanne Hubbard for graphs

- USDA-ARS project 1265-31000-101-00, “Improving Genetic Predictions in Dairy Animals Using Phenotypic and Genomic Information”

Validation of genomic reliability and gains from phenotypic updates

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  - Similar to validating EBVs using truncated data
  - Examine published REL for 6 traits and Net Merit
  - Examine 3 breeds (HOL, JER, BSW) on USA scale

Genomic reliability theory

- Selection reduces variance such that Var(EBV) < REL * Var(BV), but not prediction error variances (PEV):
- PEV = Var(EBV – BV) = (1 – REL) Var(BV)
- Variance of EBV differences are proportional to the difference in reliabilities regardless of selection. If EBV_1 and EBV_2 are earlier and later genomic evaluations with reliabilities REL_1 and REL_2, then
- $Var(EBV_2 – EBV_1) = (REL_2 – REL_1)\ Var(BV)$
- If REL_2 is known, high, and accurate, then solve for
- $REL_1 = REL_2 – Var(EBV_2 – EBV_1) / Var(BV)$

Data to validate genomic reliability

- Published genomic evaluations from April 2014
- Published genomic evaluations from April 2017
- SD of difference in genomic PTAs
- REML estimates of true TA SD from Interbull MACE
- Example for Holstein protein validation bulls:
- Average published REL_1 was 0.76, REL_2 was 0.95, SD of change was 8.4, and REML TA SD was 17.5. The observed REL_1 for protein was calculated as
- Observed $REL_1 = 0.95 - (8.4)^2 / (17.5)^2 = 0.72$

Observed vs. published reliability, 2014

Trait	Observed	Published	Diff	Observed	Published	Diff
	Jerseys			Holsteins		
Milk	73	68	+5	72	76	-4
Fat	72	68	+4	74	76	-2
Protein	71	68	+3	72	76	-4
Longevity	47	55	-8	65	70	-5
SCS	64	62	+2	77	73	+4
Preg Rate	63	52	+11	69	68	+1
NetMerit	68	64	+4	68	73	-5
Average	65	62	+3	71	73	-2

Observed vs. published reliability, BSW

Trait	Observed	Published	Diff	Observed	Published	Diff
	Brown Swiss - USA			BSW - Intergenomics		
Milk	62	63	-1	70	68	+2
Fat	64	63	+1	76	68	+8
Protein	57	63	-6	66	68	-2
Longevity	57	55	+2	63	61	+2
SCS	64	59	+6	71	66	+5
Preg Rate	56	51	+5	67	58	+9
Average	60	59	+1	69	65	+4

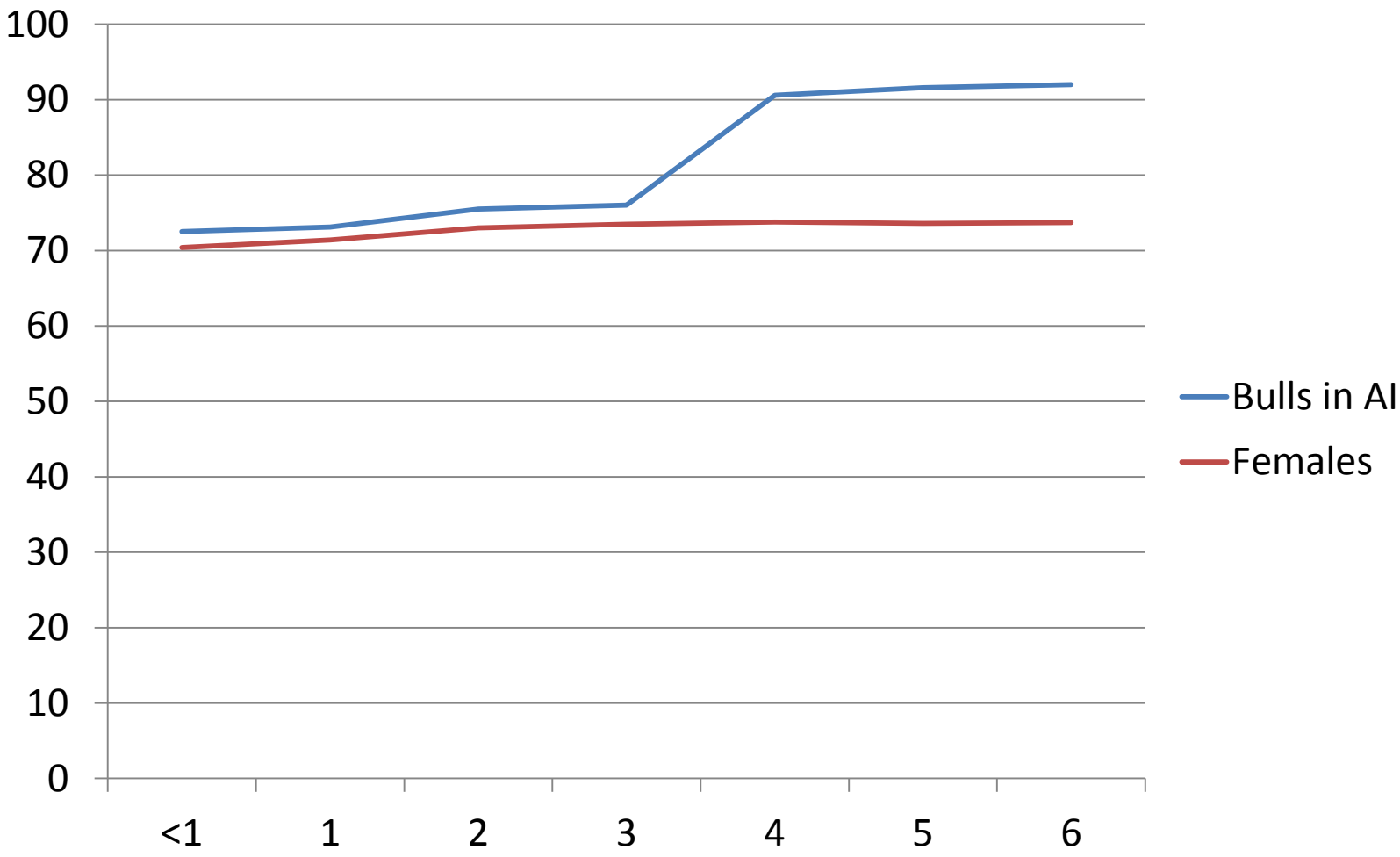
Discussion of BSW results

- Same software used by USA and Intergenomics
- Same data except PA in USA vs. Pedigree Index in IG
  - Bias from dam's PTA and extra weight on PA
  - Yield heritability reduced from 35% to 23% in Dec 2014
- Small test used only 41 bulls with > 50 US daughters
- Full test with all 475 IG bulls gave observed REL much more similar because USA and IG both have only PI for foreign MACE bulls

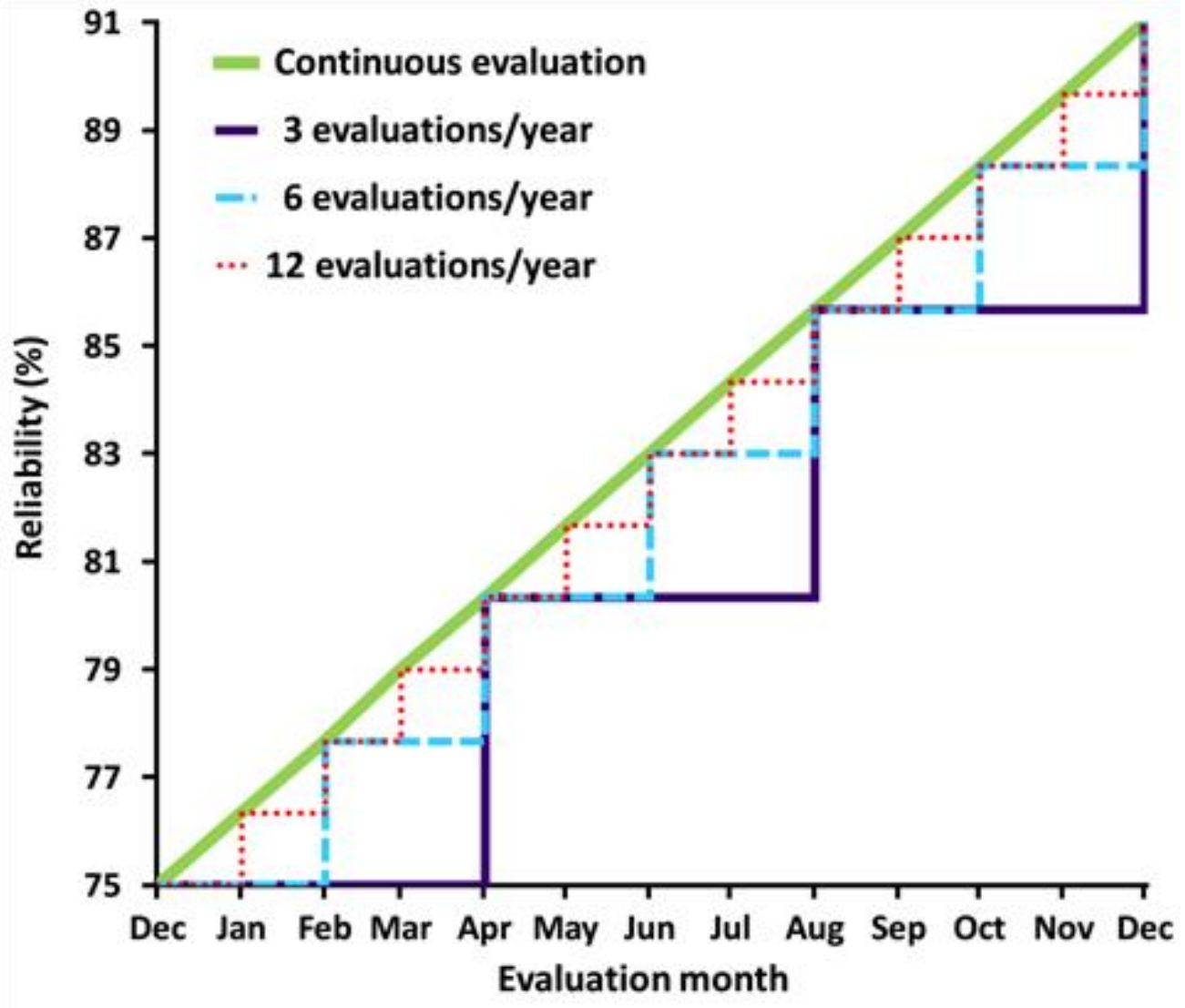
Phenotypic update frequency

- Suppose reliability increases steadily from REL_1 to REL_2 across a year.
- The gain in reliability from n updates per year (REL_n) instead of 1 annual update should average:
- $REL_n = .5 (REL_2 – REL_1) (n - 1) / n$
- Suppose bulls increase from 75% REL_1 to 91% REL_2 when 4 years old (no daughters to many daughters).
- Minimum gain is 0% with an annual update because the bulls would stay at 75% for the whole year.
- Maximum gain is 8% with instant updating. Bulls would average (75 + 91)/2 = 83% during that year.

HOL NM$ average reliability by age



Phenotypic update frequency



Reliability gains by update frequency

Frequency	Updates	Young REL	Marginal Gain	Proven REL	Marginal Gain
Annual	1	73.0		75.0	
6 months	2	73.5	0.5	79.0	4.0
4 months	3	73.7	0.2	80.3	1.3
3 months	4	73.8	0.1	81.0	0.7
2 months	6	73.83	0.03	81.6	0.6
Monthly	12	73.92	0.09	82.3	0.7
Weekly	52	73.98	0.06	82.8	0.5
Daily	365	73.99	0.01	82.97	0.17
Instant	∞	74.0	0.01	83.0	0.03

Assuming that REL begins at 75% and is 91% 1 year later for proven bulls and begins at 73% and is 75% 1 year later for young bulls.

Conclusions

- Exact calculation of genomic reliability is hard, but validation is easy
- Published USA REL averaged 2% too high for HOL, 3% too low for JER, and 1% too low for BSW
- Published Intergenomics REL averaged 4% too low for BSW traits because observed REL were higher
- Updating marker effects more frequently than 3 times per year could improve average REL up to 2.5% for recently proven bulls but < 0.3% for young animals

Acknowledgements

- Interbull Working Group on Genomic Reliability (Zengting Liu, Martin Lidauer, Mario Calus, Vincent Ducrocq, Haifa Benhajali, and Hossein Jorjani)

- Council on Dairy Cattle Breeding and Intergenomics for data

- Suzanne Hubbard for graphs

- USDA-ARS project 1265-31000-101-00, “Improving Genetic Predictions in Dairy Animals Using Phenotypic and Genomic Information”

Genomic reliability algorithm for a single step marker model

Bevin Harris
LIC, New Zealand

Outline

- Brief method outline
- Multi-breed adjustments
- Computational feasibility
- Results for 2 traits and 2 SNP panels
- Conclusions

Method Outline

1. Build SNP marker MME and invert
2. Compute reliability for the genotyped animals and adjust for prediction R^2 : Rel_g
3. Compute reliability from using information source (IS) method:
    1. using only phenotypes of genotyped animals Rel_{ag}
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6. If fitting an polygenic effect in the model weight Rel_t and Rel_a by the proportions of total genetic variance assigned to the marker and polygenic effect

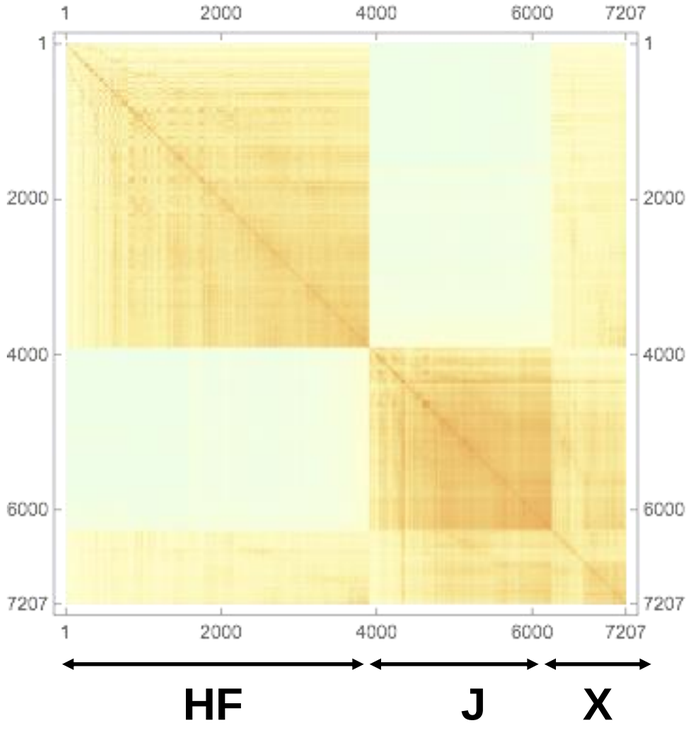
Multiple breeds

- New Zealand
  - Mixture of Holstein Friesian, Jersey and crossbred animals (HFxJ)
  - SNP allele frequencies differ between the Holstein Friesian and Jersey breeds
  - Potentially impact the SNP marker reliability calculations

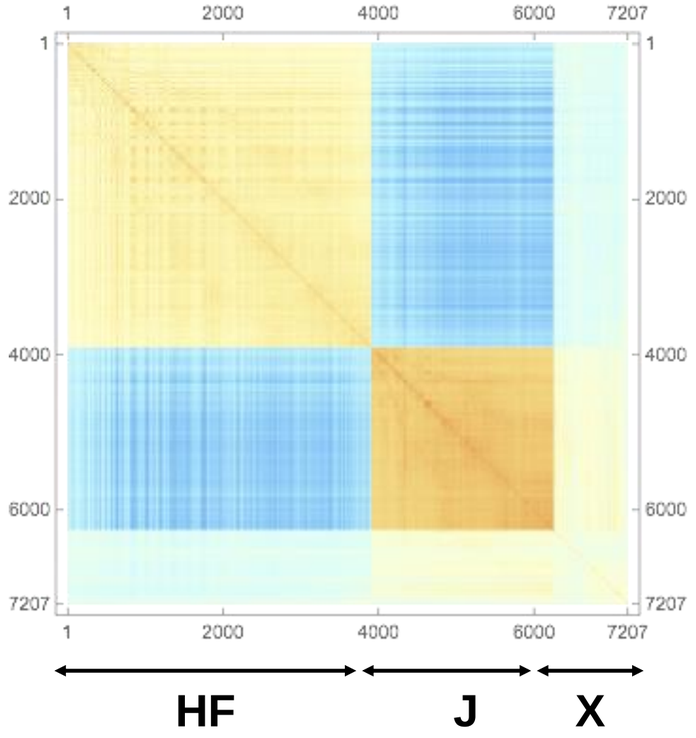
Multiple breeds

- 7207 Sires with 3902 HF, 2356 J and 949 HFxJ
- 50k SNP panel (35k SNP)

A Matrix



G Matrix



Multiple breeds

- Compute $\mathbf{Z}$ as
$(\mathbf{M}_i - 2\hat{p})/\hat{\omega}$ where $\hat{\omega} = \sqrt{2\Sigma\hat{p}(1-\hat{p})}$ and $\hat{p} = \sum_{j=1}^{m} brd_j\bar{p}_j$

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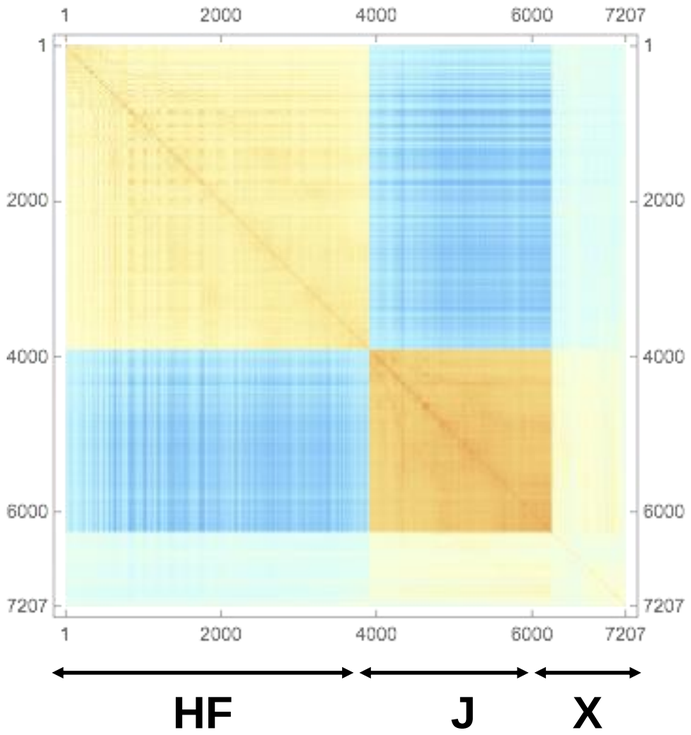
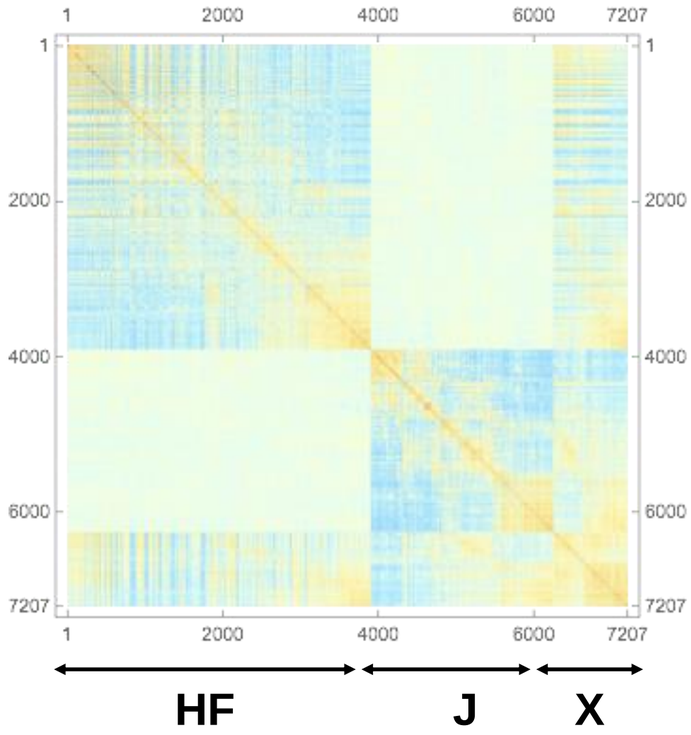


Breed Adjusted G Matrix



Examples

- New Zealand national population 29m animals
  - Dataset 1: 35K SNP on 140K animals
  - Dataset 2: 24K SNP on 70K animals (genotypes up to 2015)
  - 2 Traits
    - Liveweight h^2= 0.35, 1.9m records
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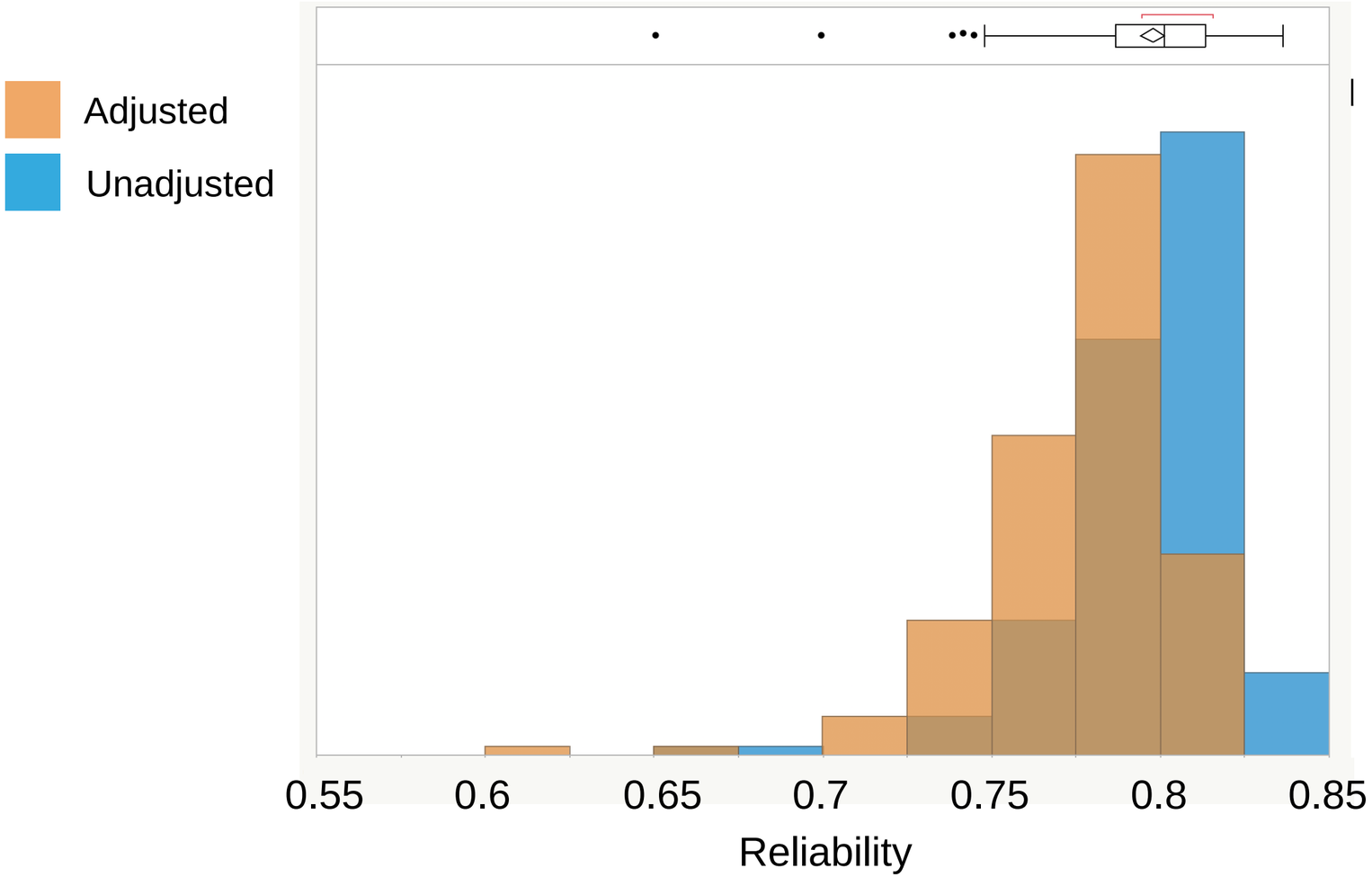
Multiple breeds

- Results of breed adjustments on SNP reliability for live weight
  - Last three sire birth year cohorts with no daughters
  - Similar results observed for fertility

		35k SNP and 140K N	
Young Sires	**A Matrix**	**SNP**	**SNP breed adjusted**
Holstein Friesian	0.34	0.73	0.73
Jersey	0.37	0.80	0.77
HF x J	0.34	0.75	0.75

Multiple breeds

Reliability distributions for Jersey



Computation Time

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Computation Time

24 Cores Simultaneously

- SNP Reliability
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Results Liveweight

		35K SNP 140K N	24k SNP 70K N
Proven Sires	A Matrix	0.85	0.85
	Genomic	0.88	0.87
Young Sires	A Matrix	0.34	0.34
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- Method is computational feasible for our national data set
  - For very large numbers of genotyped animals computing in individual reliabilities $(\mathbf{Z}\mathbf{C}^{22}\mathbf{Z}')_{ii}$ from the marker model inversion may be problematic

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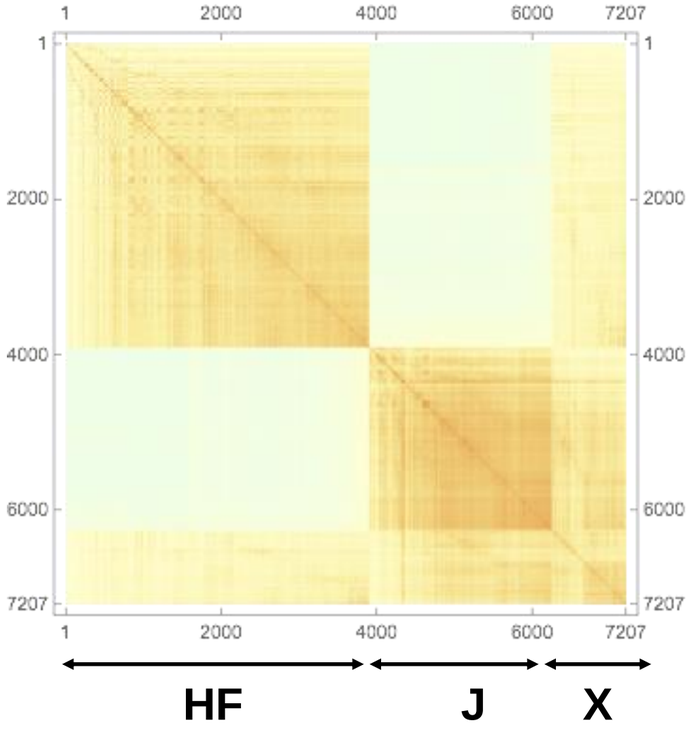

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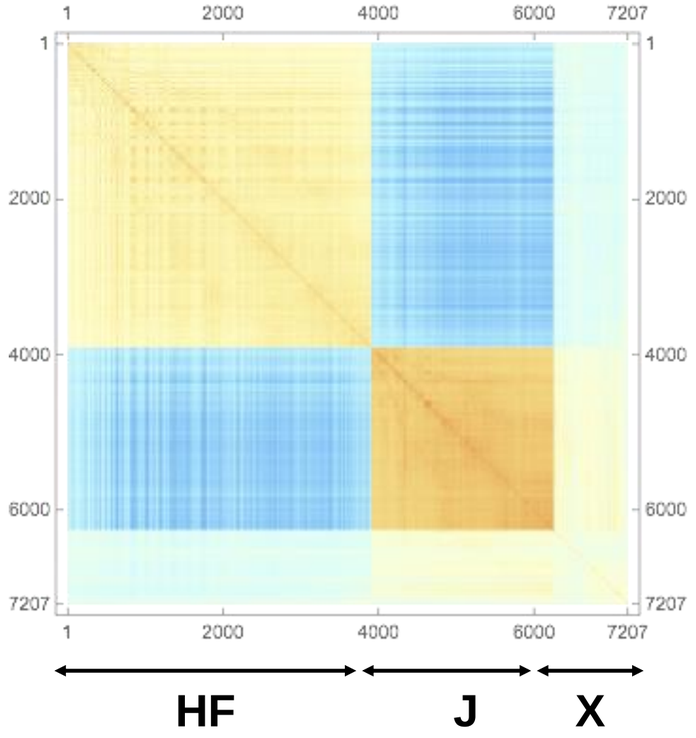

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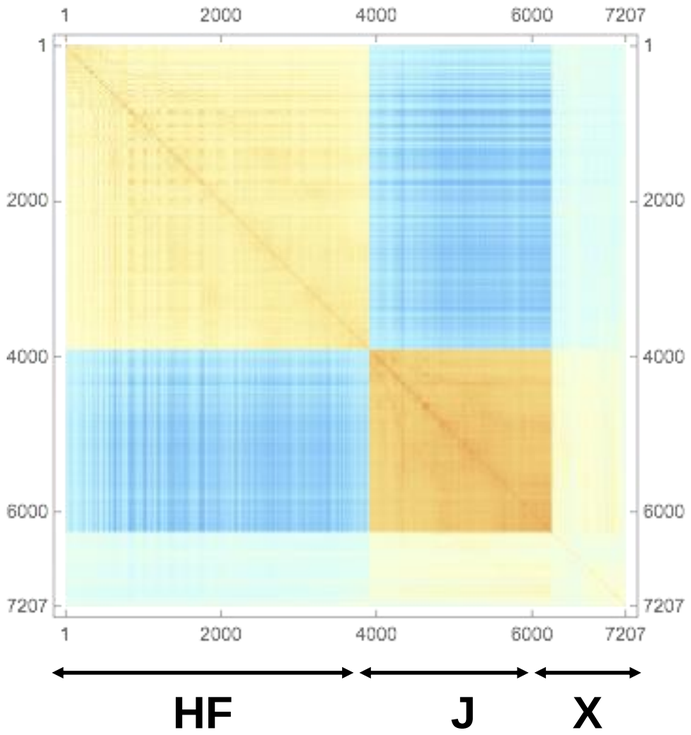

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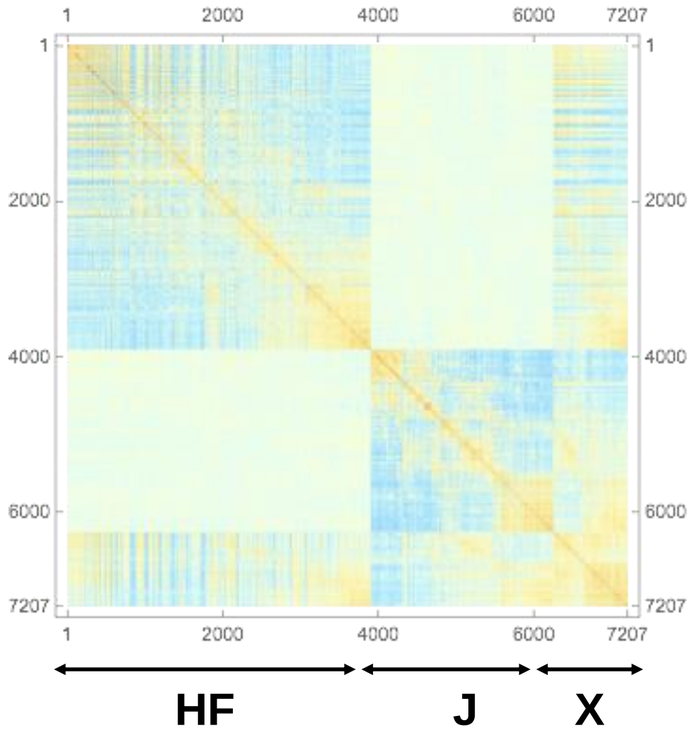

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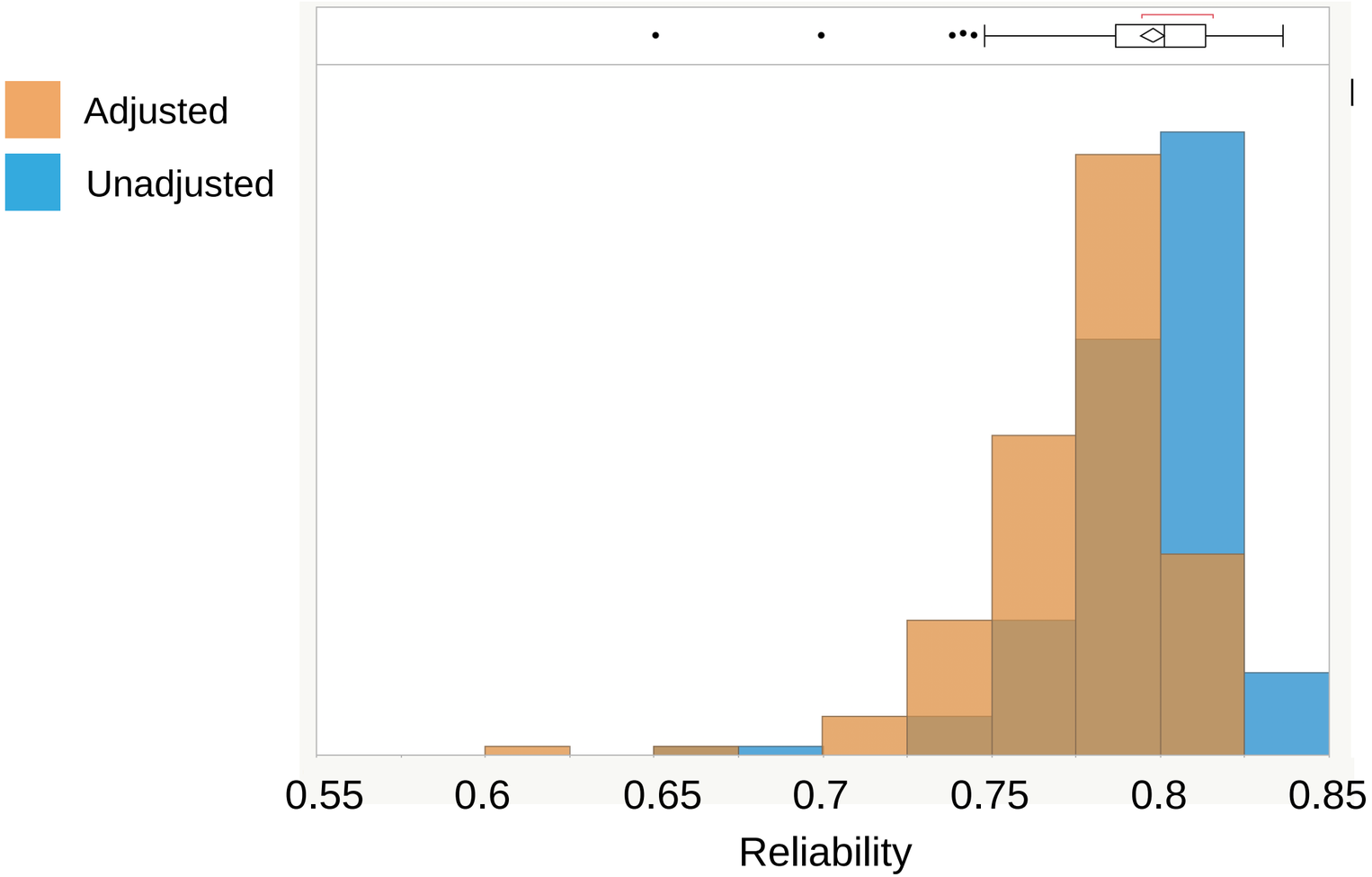

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Integration of foreign estimates of SNP effects into a domestic SNPBLUP

J. Vandenplas, M.P.L. Calus, G. Gorjanc

WAGENINGEN
UNIVERSITY & RESEARCH

100years
1918 — 2018

ROSLIN

Introduction

- Genomic evaluation
  - Aim: more accurate genomic EBVs

- SNP-based evaluations under study/testing

➔Future: exchange of estimates of SNP effects?

➔How to integrate them into SNPBLUP?

Aim

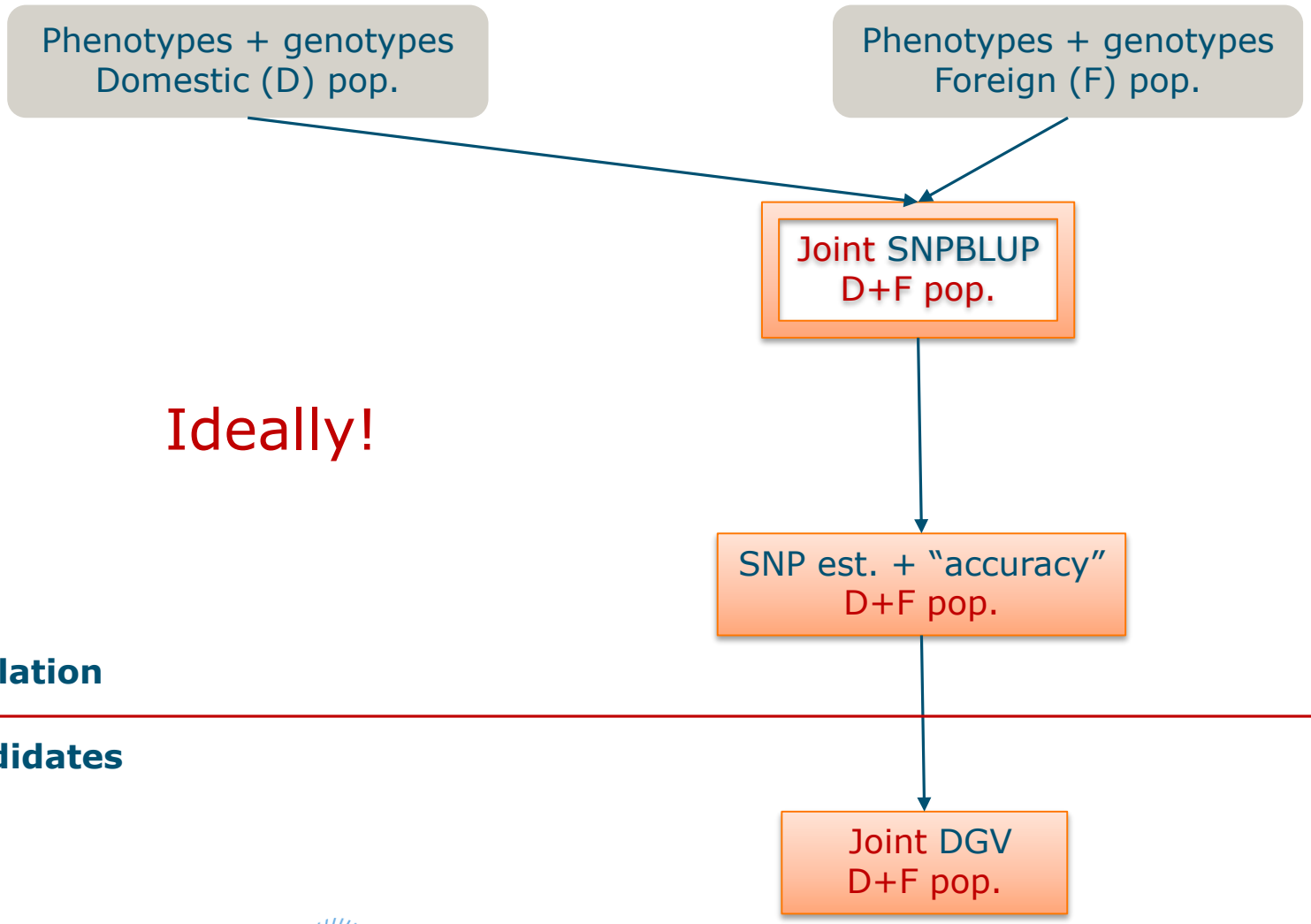
Developing and testing procedures to integrate

estimates of SNP effects and measures of precision

from a foreign SNPBLUP

into a domestic SNPBLUP

Methods – joint SNPBLUP



Methods – joint SNPBLUP

$$\begin{bmatrix} \mathbf{y}_d \\ \mathbf{y}_f \end{bmatrix} = \begin{bmatrix} \mathbf{X}_d & \mathbf{0} \\ \mathbf{0} & \mathbf{X}_f \end{bmatrix} \begin{bmatrix} \boldsymbol{\beta}_d \\ \boldsymbol{\beta}_f \end{bmatrix} + \begin{bmatrix} \mathbf{Z}_d \mathbf{W}_d \\ \mathbf{Z}_f \mathbf{W}_f \end{bmatrix} \boldsymbol{\alpha} + \begin{bmatrix} \mathbf{e}_d \\ \mathbf{e}_f \end{bmatrix}$$

$$\boldsymbol{\alpha} \sim MVN\left(\mathbf{0}, \mathbf{I}\sigma^2_{\alpha_J}\right) \qquad \begin{bmatrix} \mathbf{e}_d \\ \mathbf{e}_f \end{bmatrix} \sim MVN\left(\begin{bmatrix} \mathbf{0} \\ \mathbf{0} \end{bmatrix}, \begin{bmatrix} \mathbf{R}_d & \mathbf{0} \\ \mathbf{0} & \mathbf{R}_f \end{bmatrix} \sigma^2_e\right)$$

$\mathbf{y}_i$ = *vector of phenotypes*

$\boldsymbol{\beta}_i$ = *vector of fixed effects*

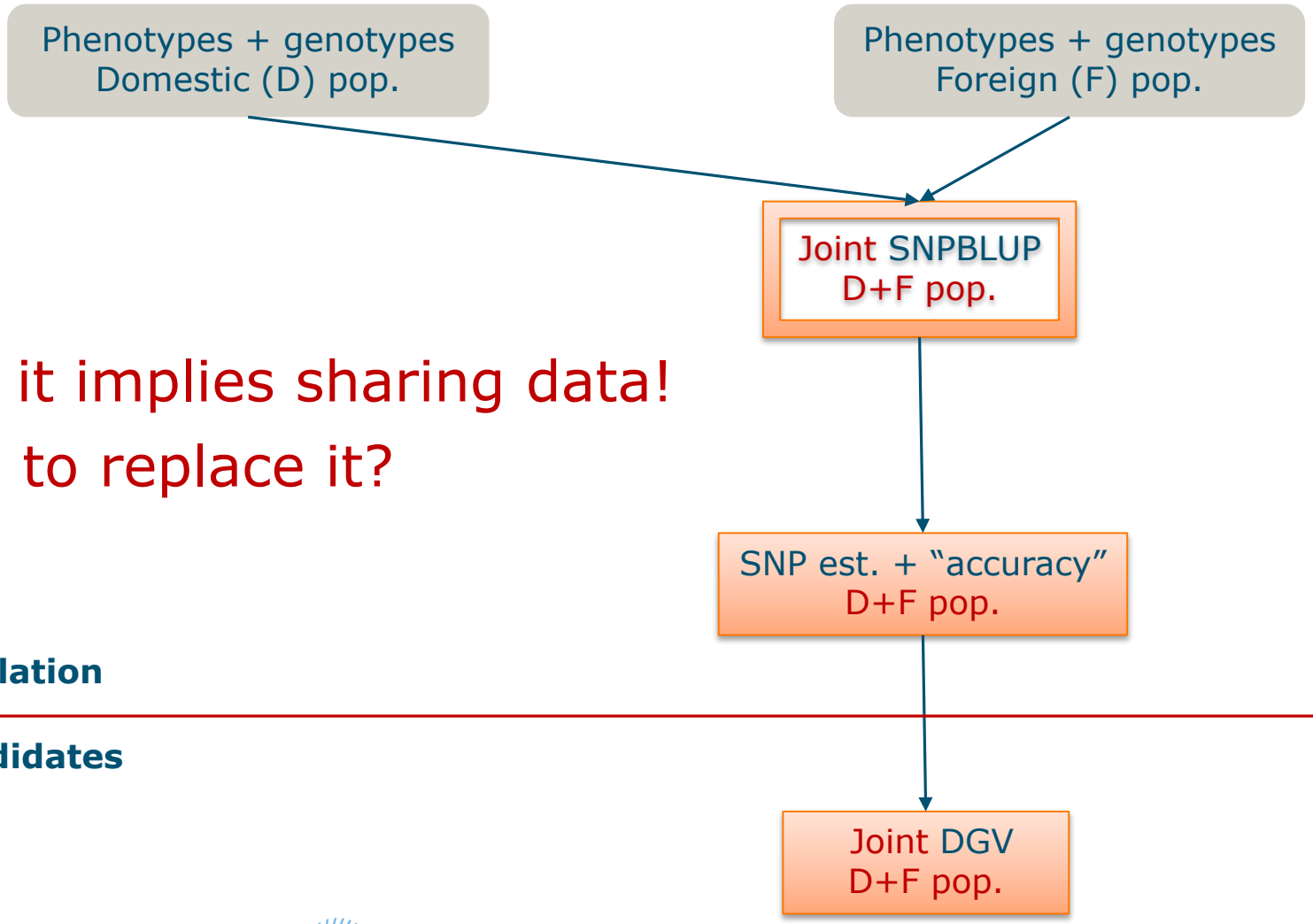
$\boldsymbol{\alpha}_i$ = *vector of SNP effects*

$\mathbf{e}_i$ = *vector of residuals*

$\mathbf{W}_i$ = *matrix of SNP genotypes*

$\mathbf{X}_i$, $\mathbf{Z}_i$ = *incidence matrices*

Methods – joint SNPBLUP



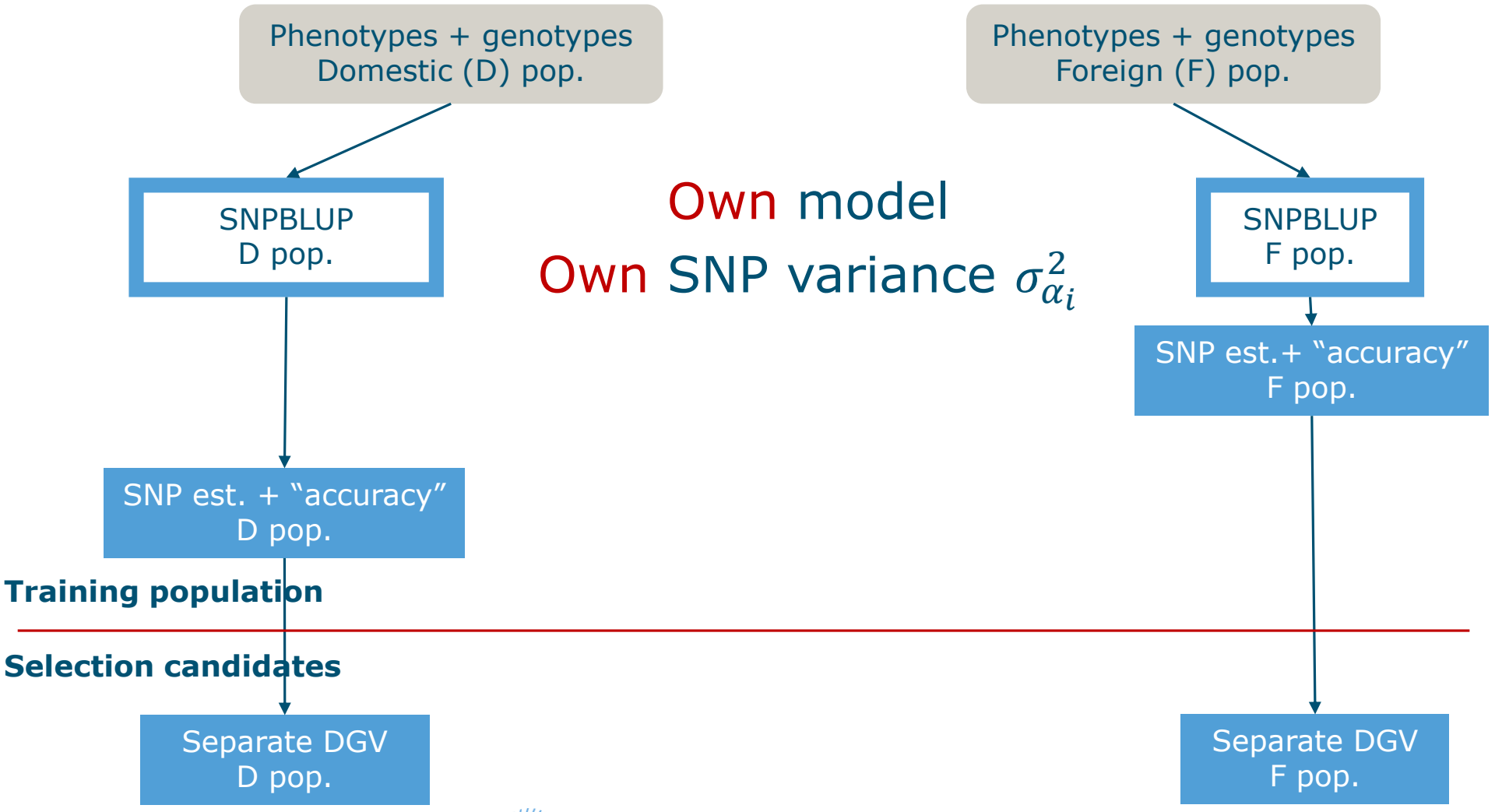
Issue: it implies sharing data!

➔How to replace it?

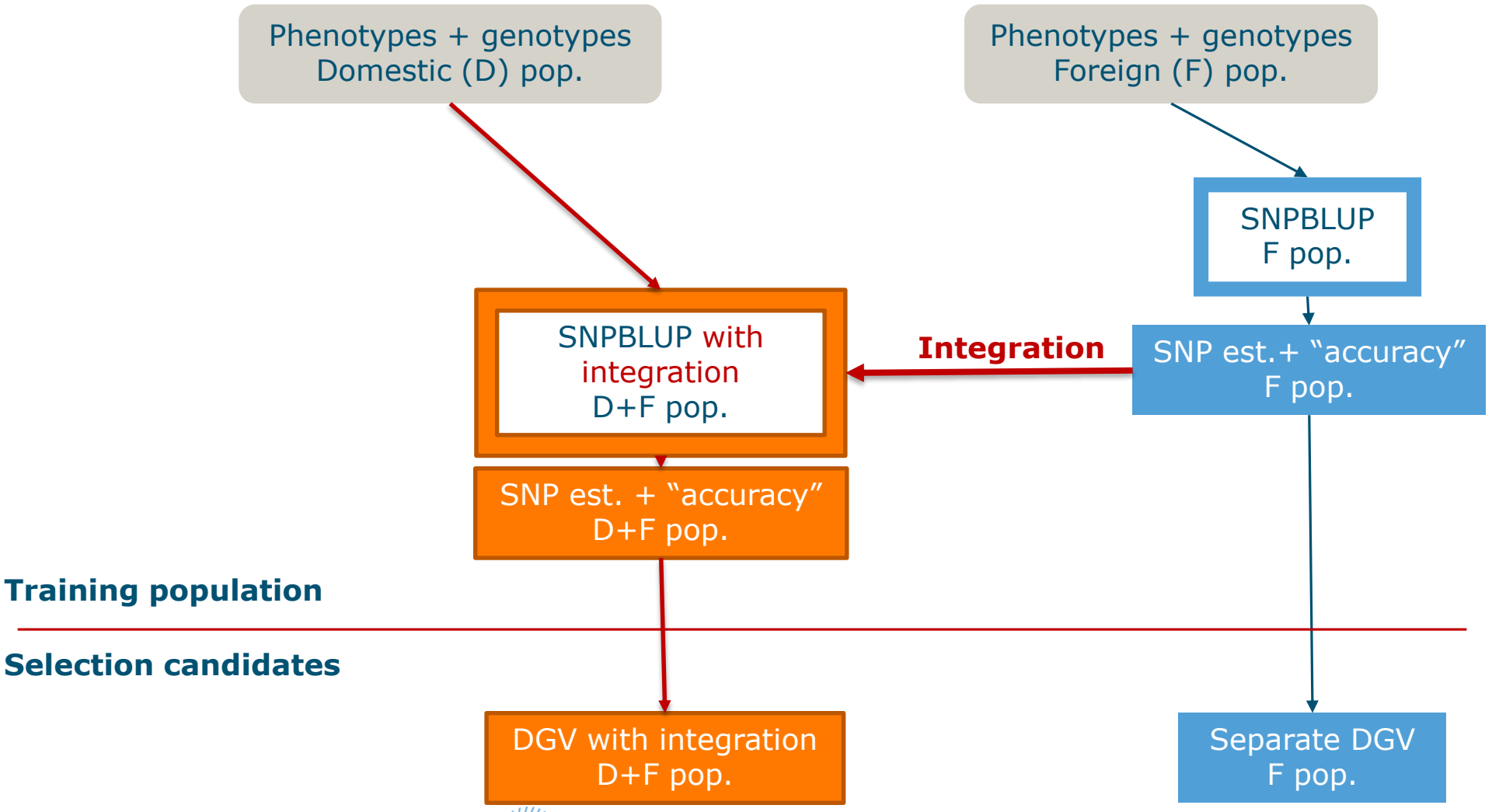
Training population

Selection candidates

Methods – separate SNPBLUP



Methods – SNPBLUP with integration



Methods –SNPBLUP with integration

- Assumptions
  - Same model/variances (σ_e^2 & $\sigma_{\alpha_J}^2$) as joint SNPBLUP
  - Same genotype (scaling) across all SNPBLUP

Methods –SNPBLUP with integration

$$\begin{bmatrix} \mathbf{X}_d'\mathbf{X}_d\,\sigma_e^{-2} & \mathbf{X}_d'\mathbf{Z}_d\,\mathbf{W}_d\,\sigma_e^{-2} \\ \mathbf{W}_d'\mathbf{Z}_d'\mathbf{X}_d\,\sigma_e^{-2} & \mathbf{W}_d'\mathbf{Z}_d'\mathbf{Z}_d\,\mathbf{W}_d\,\sigma_e^{-2} + \underbrace{\left(PEC\left(\widehat{\boldsymbol{\alpha}_f}\right)\right)^{-1} - \mathbf{I}\sigma_{\alpha_f}^{-2}}_{\mathbf{W}_f'\mathbf{Z}_f'\mathbf{M}_f\,\mathbf{Z}_f\,\mathbf{W}_f\,\sigma_e^{-2}} + \mathbf{I}\sigma_{\alpha_J}^{-2} \end{bmatrix} \begin{bmatrix} \widehat{\boldsymbol{\beta}_d} \\ \widehat{\boldsymbol{\alpha}} \end{bmatrix} =$$

$$\begin{bmatrix} \mathbf{X}_d'\mathbf{y}_d\,\sigma_e^{-2} \\ \mathbf{W}_d'\mathbf{Z}_d'\mathbf{y}_d\,\sigma_e^{-2} + \underbrace{\left(PEC\left(\widehat{\boldsymbol{\alpha}_f}\right)\right)^{-1}\widehat{\boldsymbol{\alpha}_f}}_{\mathbf{W}_f'\mathbf{Z}_f'\mathbf{M}_f\,\mathbf{y}_f\,\sigma_e^{-2}} \end{bmatrix}$$

Least-squares part of the foreign SNPBLUP

RHS of the foreign SNPBLUP

➔Several ways to approximate $\left(PEC\left(\widehat{\boldsymbol{\alpha}_f}\right)\right)^{-1}$

Methods – approximations of $\left(PEC(\widehat{\boldsymbol{\alpha}_f})\right)^{-1}$

1) No approximation *(reference)*: $\left(PEC(\widehat{\boldsymbol{\alpha}_f})\right)^{-1}$

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3) $\left(PEC(\widehat{\boldsymbol{\alpha}_f})\right)^{-1} \approx \left(PEV(\widehat{\boldsymbol{\alpha}_f})\right)^{-1}$

4) $\left(PEC(\widehat{\boldsymbol{\alpha}_f})\right)^{-1} \approx \left(\boldsymbol{\Lambda}_f \left(f(\mathbf{LD}_f, \mathbf{p})\right) \boldsymbol{\Lambda}_f \sigma_e^{-2} + \mathbf{I}\sigma_{\alpha_f}^{-2}\right)$

p : allele frequencies in the training set

$\mathbf{LD}_f$ computed from foreign selection candidates

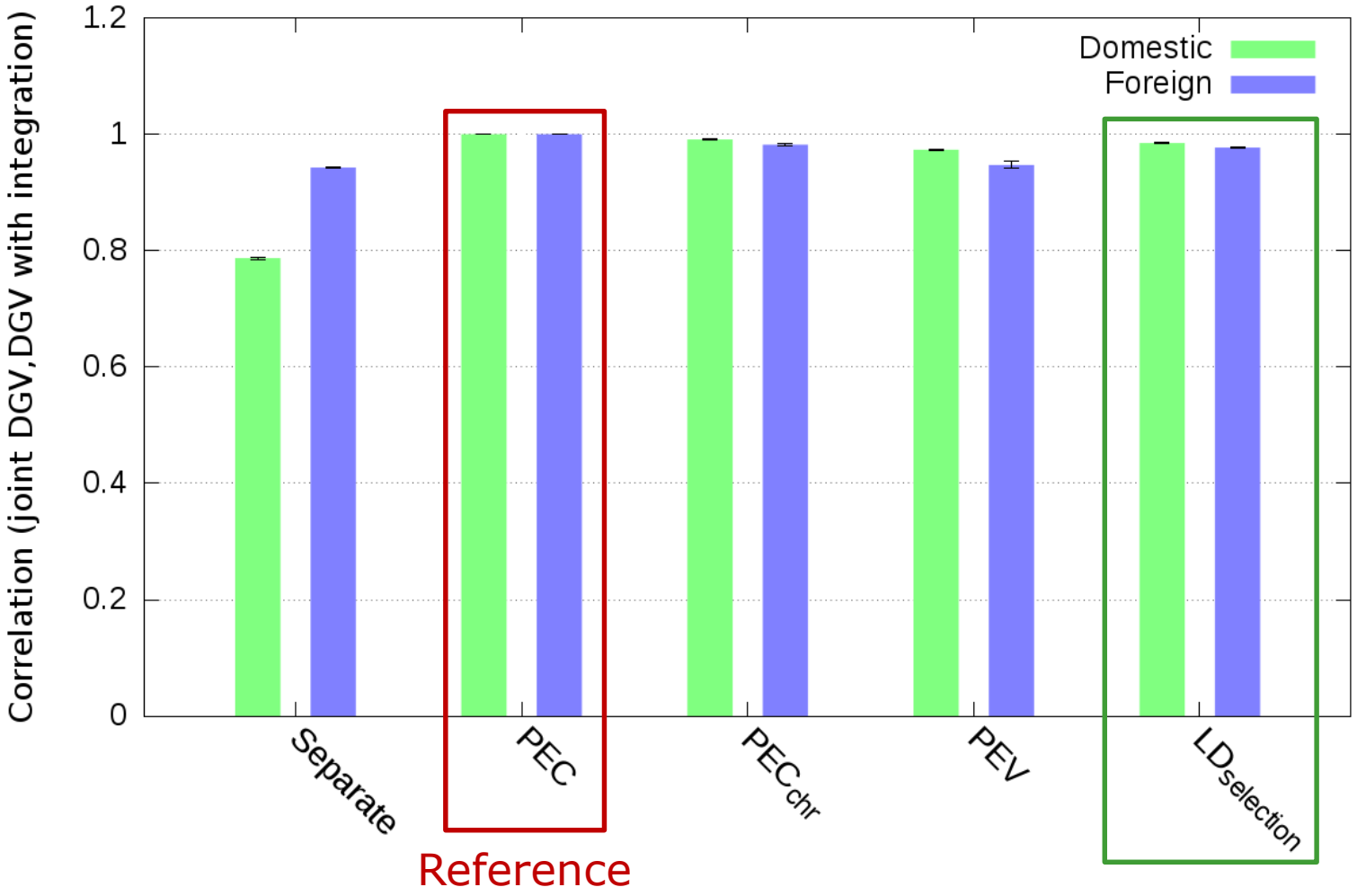
$\boldsymbol{\Lambda}_f$: effective number of records per SNP

- Estimated from $PEV(\widehat{\boldsymbol{\alpha}_f^*})$, $\mathbf{LD}_f$, and **p**

Simulation

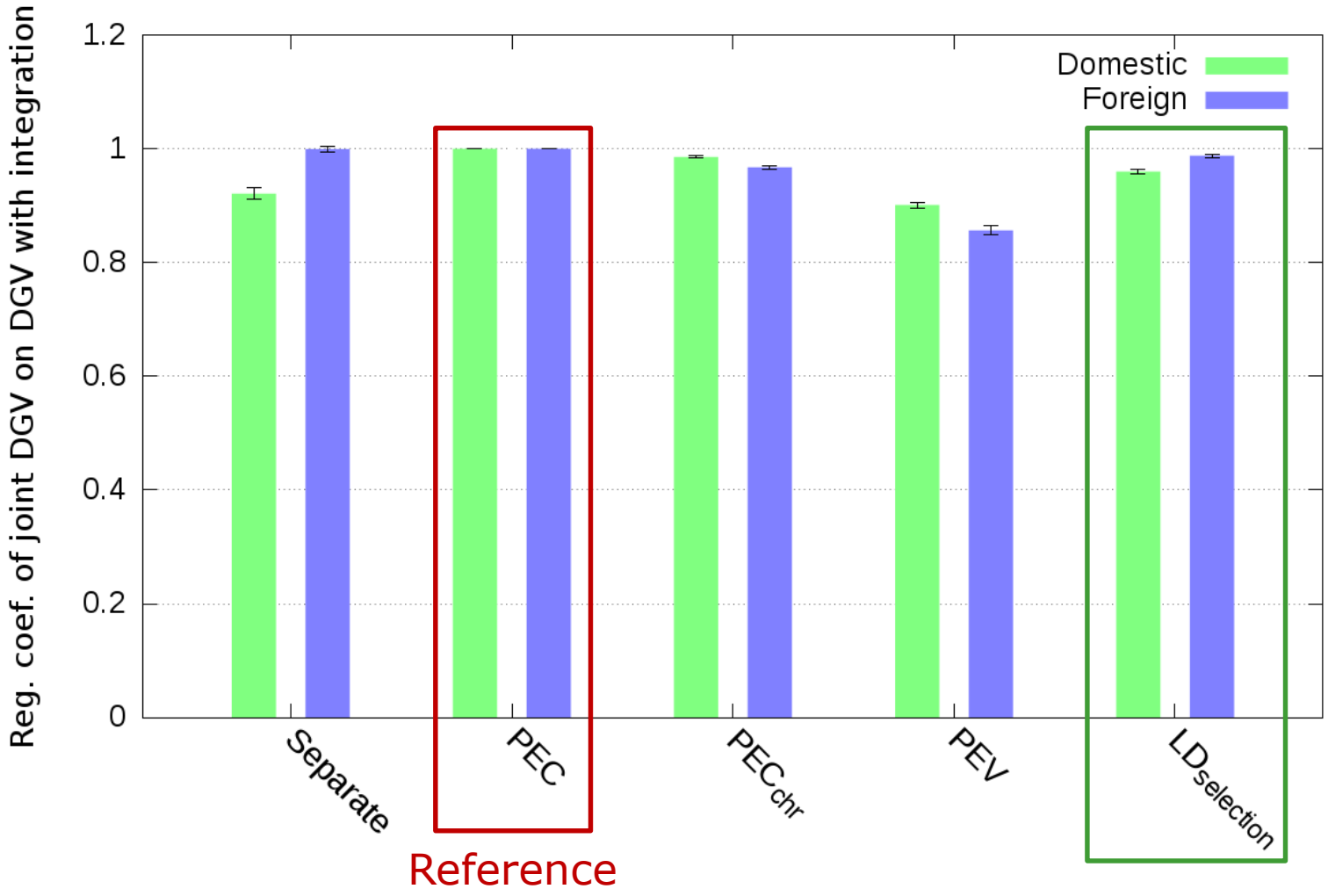
- 2 Holstein-like populations
  - 1 trait (h^2 = 0.30 - 60K SNPs)
- Training populations
  - 5,000 animals / population
  - Randomly sampled from gen. 1 to 6
  - Domestic: own performance records
  - Foreign: pseudo-records (~DYD, DRP) + weights
- Selection candidates
  - 10,000 animals from gen. 7 / population

Results – correlations



- Accurate integration
  - Even with only PEV and LD information

Results – bias



Almost no bias, except for PEV

Conclusions

- Accurate integration of estimates of SNP effects
  - Without exchanging genotypes/phenotypes
- Procedure similar to integration of foreign EBVs

  ➔Similar assumptions/issues/solutions
- Easy extensions
  - Multiple populations, multiple traits, ...
  - Special case: SNP-MACE

Thank you!

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