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CANADIAN NETWORK FOR DAIRY EXCELLENCE

Quantifying Inbreeding Levels and Contemplating Inbreeding in Selection

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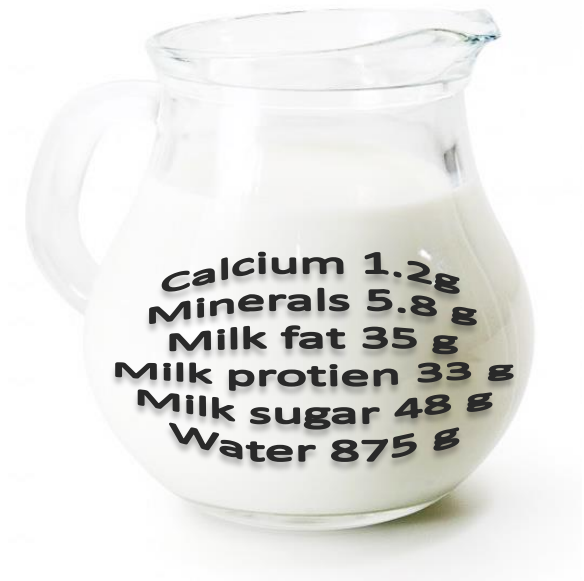
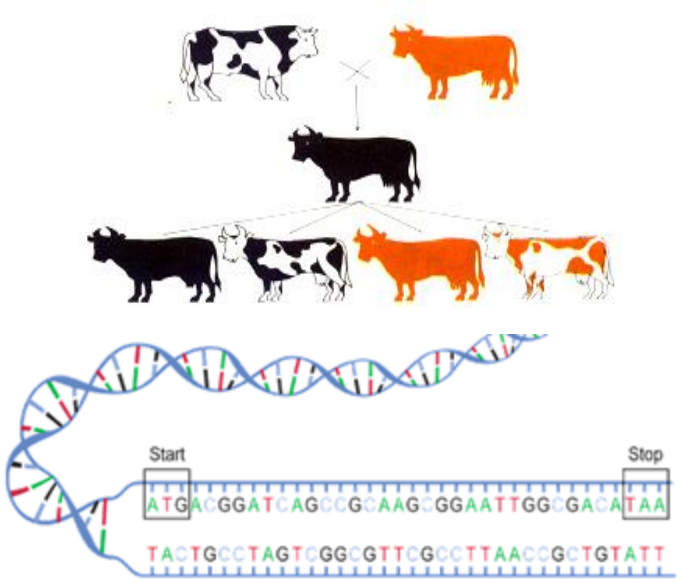
Genetic Selection Today

- Genetic selection in the dairy cattle industry has seen dramatic changes in recent decades
    - Introduction of **genomic selection** in 2009
    - Improved and novel technologies
- Increased popularity and usage of **young GPA bulls**
- Broadening of selection goals and number of traits evaluated
- **Accelerated genetic gains** in most traits under selection
- In the genomics era, we also **need strategies and tools to help control some of the negative consequences** to ensure continued genetic progress

Basics of Genomics

Phenotype = **Genotype** + **Environment**





Phenotype: something (anything!) you can measure or observe

Genotype: the animals genetic information

Environment: how the animal is fed, housed, managed, etc.

Consequences of Genomic Selection

Increased rates of genetic gain

- Increased accuracy of selection for young animals
- Reduced generation interval
- Ability to select for traits recorded in only few animals
- Maintaining herdbook integrity & management/discovery of recessives

Cumulative benefits of genomic selection of **$721 million / year**

Homozygosity (inbreeding) is rising at an increased rate

- Increased occurrence of homozygous recessives (e.g. HCD, JNS, AM)
- More subtle effects of inbreeding:
  - Reduction in phenotypic mean value and selection response
- Potential future implications: **unknown**
- Financial economic losses: **unknown**
  (estimate $US 11 million / year, Cole et al.)

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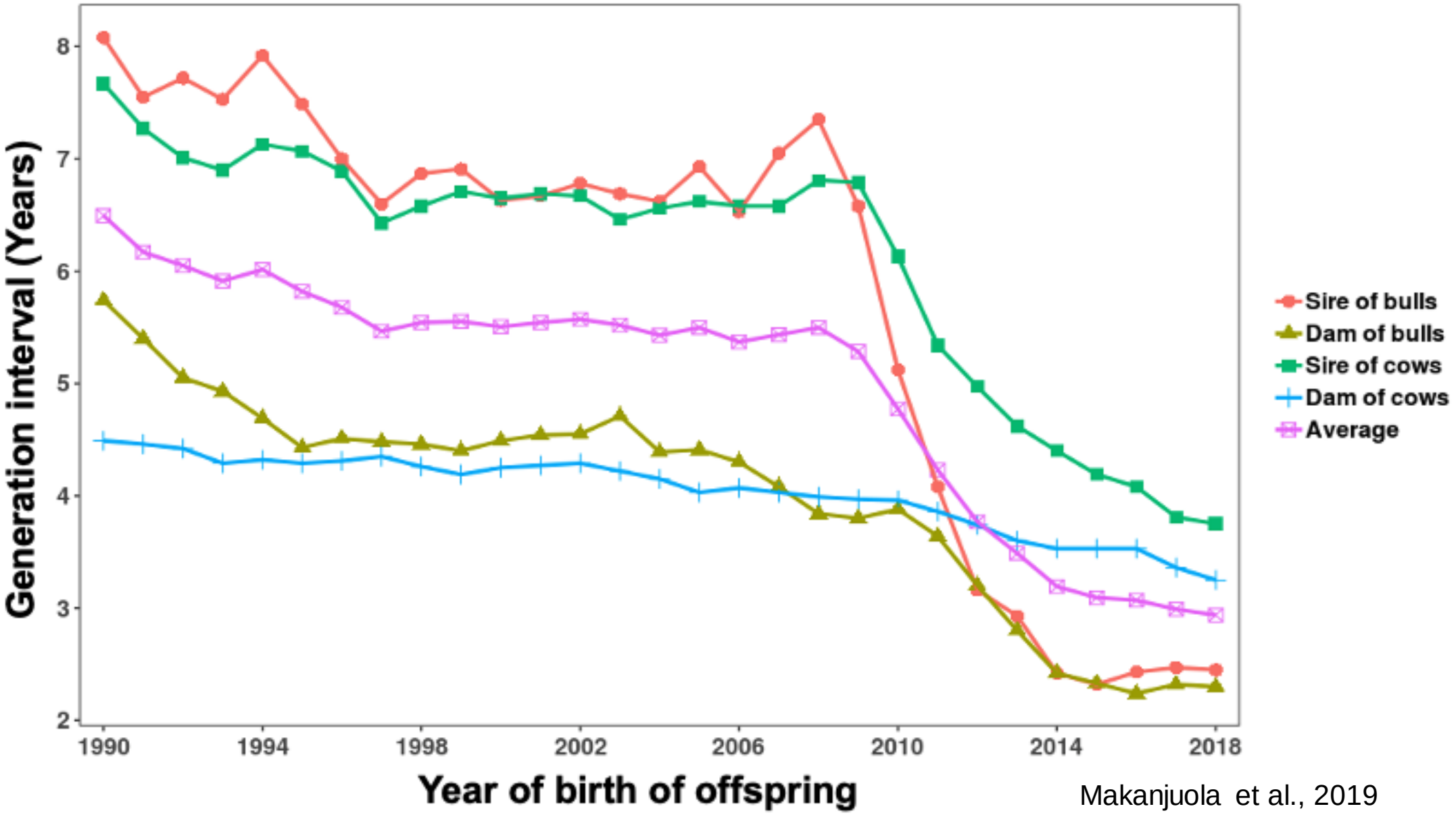
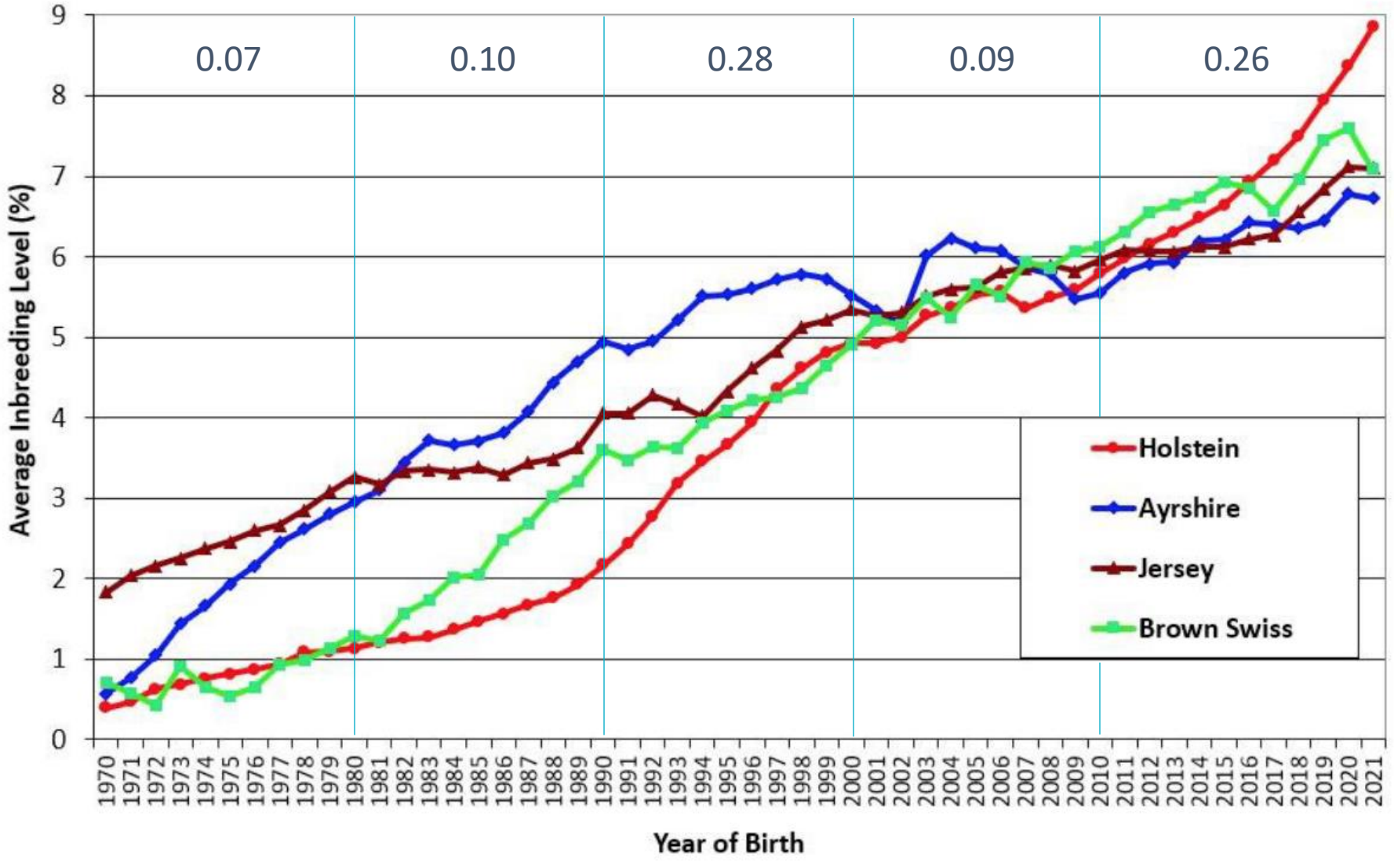
Generation Interval in North American Holsteins



Makanjuola et al., 2019

Inbreeding Trends

The rate of increase and not the absolute value is relevant



For Holstein

Pedigree vs Genomic Inbreeding

The ***coefficient of inbreeding*** (Sewall Wright, 1922) is the probability that two base pairs at a randomly chosen position in the genome (*locus*) are *identical by descent*

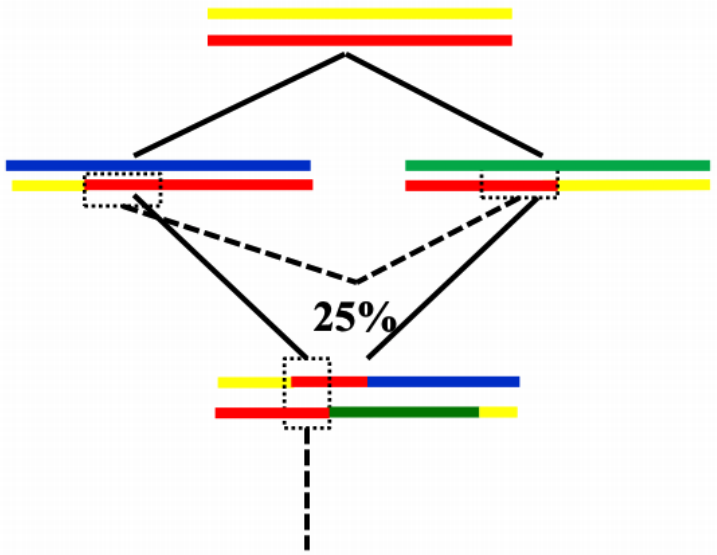
Pedigree Inbreeding

- Classical measure of inbreeding, uses pedigree data and tracing it back to identify common ancestors between the sire and dam
- Formed on averages and are expectations
- Highly dependent upon completeness, depth, and integrity of available pedigree

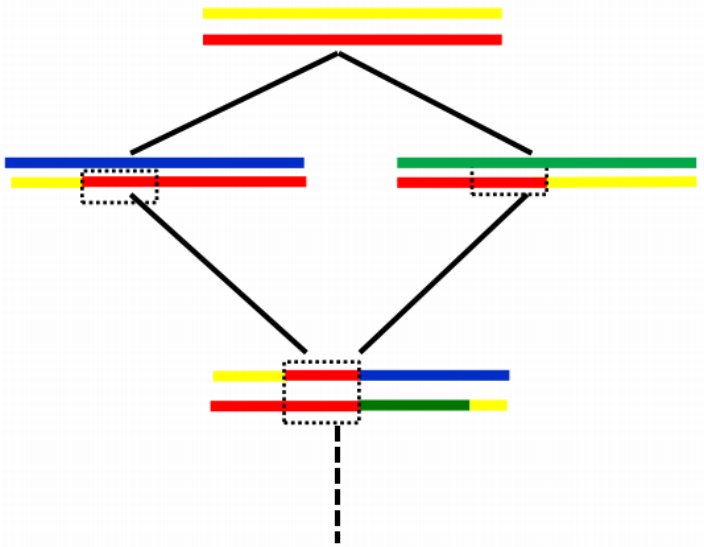
Genomic Inbreeding

- Accounts for Mendelian sampling (chance factor in distributing half the genetic material) between individuals
- Captures realized inbreeding

Pedigree vs Genomic Inbreeding

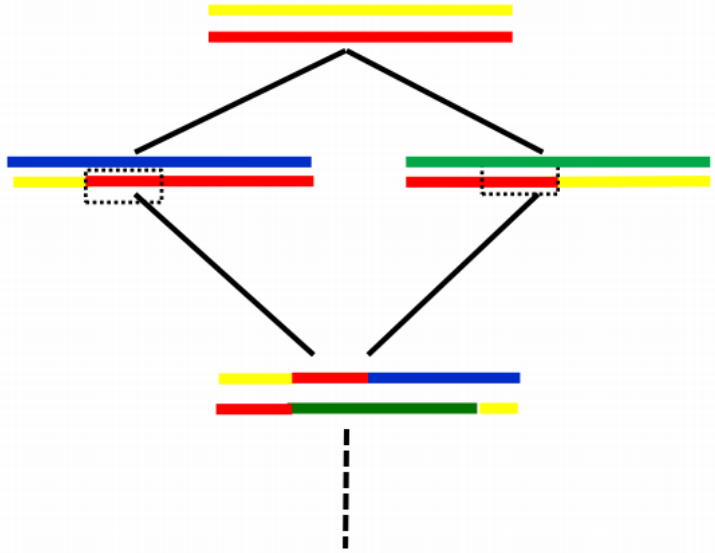


(Expectation) **12.5%**



25%

(Mendelian Sampling)



0%

Perspectives

Industry Perspective

a) I do everything I can to avoid inbreeding at all costs

b) I don't like to see an increase in inbreeding, but there's not much I can do

c) If it ain't broke, don't fix it

Public Perspective

"…the gene pool is about as deep as a pie-plate"


THE WALL STREET JOURNAL.

U.S. | THE NUMBERS

Most Dairy Cows Are Kissing Cousins, and Scientists Are Worried

Selective breeding helps Holsteins produce 94% of the nation's milk, but can also lead to the proliferation of diseases

Academic Perspective

The benefits of intense directional selection currently outweigh the detrimental effects of inbreeding, but there could be a threshold at which lack of genetic diversity causes serious problems

We don't know when/if that would happen

★ Reality

-Inbreeding is unavoidable in intense directional selection programs

-At best, we should **manage and monitor** the **loss** of genetic diversity

Why Care?

- **Short-term consequences**: as populations become smaller and less diverse, relative fitness decreases (i.e., survival and fertility)

- **Long-term consequences**: lower gene diversity means less raw material for adaptations to changing environments, which may affect long-term survival

Current Farmers Priorities

- Average inbreeding levels continue to rise in each breed
- Difficult to find outcross sires of interest with high genetic merit

Realities

- Knowing the inbreeding level of a female and of potential mating sires contributes little to controlling the rate of inbreeding in your herd

- Two important decision points for maintaining genetic diversity in a dairy population:
  - The genetic diversity of young bulls purchased by AI companies
  - The selection of sires when mating a female in your herd

Current Tools and Approaches

- Optimal Contribution Selection - Rarely used in practice
- Top lists dominate conversations / decisions / semen tanks
- “Outcrosses” interesting, but generally unpopular
- Experiments (cross breeding, etc.)

Two important decision points for maintaining genetic diversity in a population:

1. The genetic diversity of young bulls purchased by breeding companies
2. The selection of sires when mating a female in your herd

Lactanet Inbreeding Calculator

- Know the potential inbreeding for specific matings and avoid those above a tolerable level
  - E.g. maintain current inbreeding

	Potential Progeny's Inbreeding and Parent Averages														
POTENTIAL MATES	LPI Code	%INB	LPI	Pro$	MILK	FAT	PROT	%F	%P	SCS	Conf	MS	F&L	DS	RP
PEAK ALTAHOTHAND-ET	GEBV	9.99	3604	3027	1775	93	80	+0.20	+0.16	108	9	7	5	5	7
WESTCOAST ALCOVE	GEBV	10.62	3596	2848	2008	116	85	+0.31	+0.13	101	7	3	6	9	5
FARNEAR DELTA-LAMBDA-ET	GEBV	10.69	3584	2789	1404	74	65	+0.16	+0.14	106	10	7	8	5	6
NO-FLA CAPITAL 45499-ET	GEBV	9.98	3575	2719	1066	73	72	+0.27	+0.29	105	8	8	4	4	2
S-S-I PR RENEGADE-ET	GEBV	9.46	3570	2775	1306	95	74	+0.37	+0.24	103	6	4	5	5	3
PINE-TREE-I PURSUIT	GEBV	10.32	3560	2937	1440	96	71	+0.34	+0.18	103	7	4	8	5	4
OCD BANDARES CABERNET-ET	GEBV	10.48	3550	2919	847	94	62	+0.52	+0.26	105	8	6	6	5	2

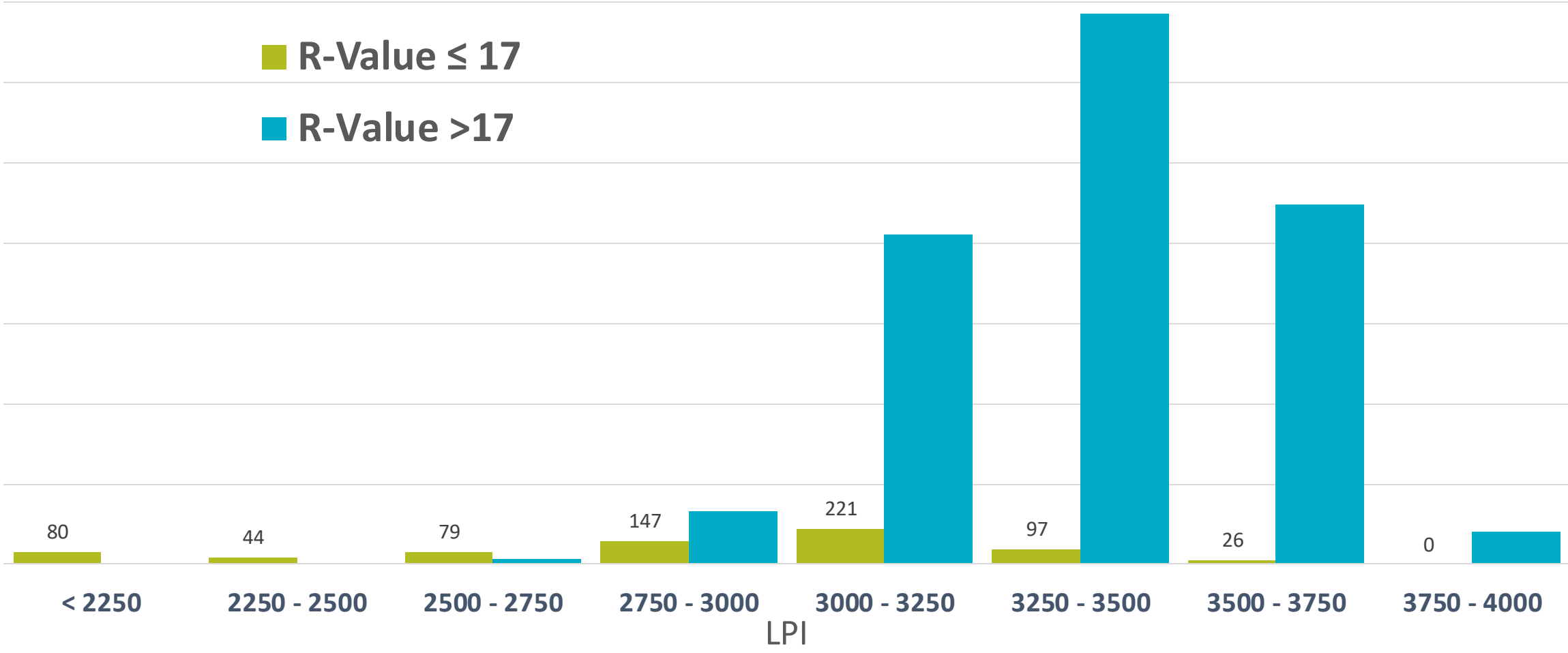
Outcross Bulls

R-value (Relationship-value)

- Represents the percentage of DNA that the bull has in common (i.e. its genetic relationship) with active females of the same breed
- Difficult to find outcross sires of interest with high genetic merit
  - Little advantage for A.I. companies to buy more outcross sires, which normally come with a lower genetic offering
  - Poor demand for their semen

Outcross Bulls

Actively marketed young GPA Holstein bulls



Within-Herd R-values

- Current R-values are on a population level
    - The relationship with animals in a specific herd could be very different
    - A bull may be outcross to one herd but not another
- Need herd specific solutions and tools to make it easier to find diverse bulls
- Help farmers identify sires that will add genetic diversity in their herd

★ Working toward **within herd R-values** to provide lists of **"diversity" bulls** specific to a given herd

Current Plan

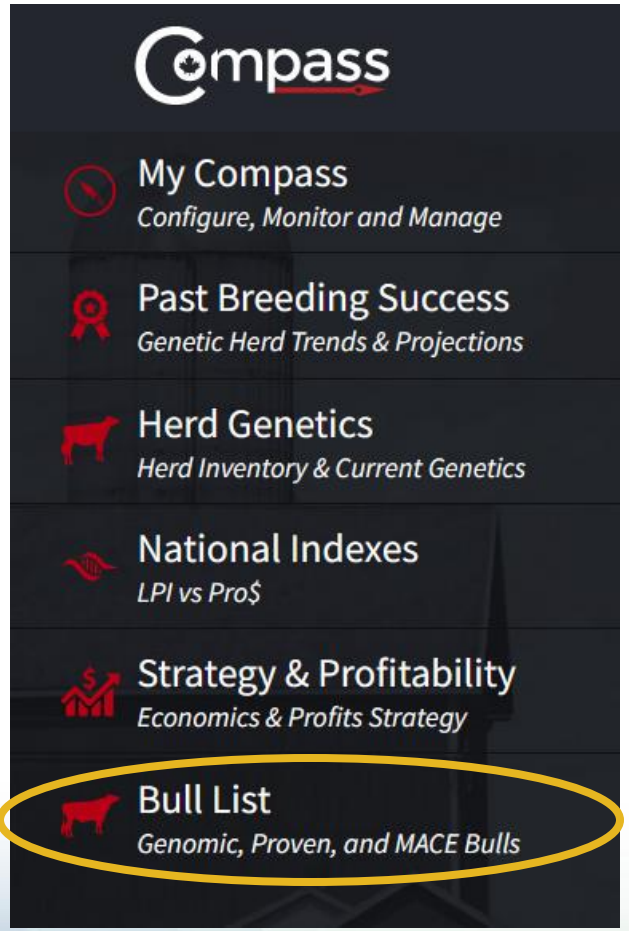
- Compass is a genetics management software tool freely available to all Canadian producers
  - Optimal for herds on milk recording
  - Otherwise, based on Owner Prefix
- Only publicly available tool that is based on the herd's animal inventory

- **Concept**: Expand the tool to provide each user with a list of "Diversity" sires for their herd
- Any bull of interest can then be added to their "My Bulls" list

Compass – Bull List

- List of actively marketed bulls with filtering and sorting capabilities
- Includes Genomic, Proven and MACE bulls
- Maintain a personal list of “My Bulls” you are interested in
- Customize the traits that are displayed

Compass – Bull List



Company

Select Values for Filter

Short Name:

Search by Short name

Free from:

- AH1
- AH2
- AM

Filter for:

Select Values for Filter

Submit

Clear

Semen Code	LPI	Pro$	MILK	FL
200AY01060	3258	2179	1433	3
MELBOURNE 200AY01076	3164	1938	1369	5
SOLICITOR 200AY01090	3128	1692	1023	2
WATERLOO 200AY01073	3108	1691	1132	3
DALTON 200AY01106	3094	1864	1302	9

Source: Allison Fleming, OIS March 2022

Compass – My Bulls

Free from: HCD, HH5, HH6

Filter for: A2 HOMOZYGOUS

Submit Clear

Short Name	Semen Code	LPI	Pro$	MILK	FAT	PROT	MS	FL	HL	MR	HH	DF	BCS
WEEZER	250HO15868	3824	4117	2233	158	96	3	9	106	104	106	102	95
CAPTAIN	551HO04119	3714	3812	1986	140	88	4	4	108	102	113	107	94
ALCOVE	200HO11000	3736	3506	2362	144	93	4	9	103	100	103	101	104
ROLETZ	200HO11905	3479	3185	1334	105	68	6	2	108	106	106	104	106

Source: Allison Fleming, OIS March 2022

Current Plan

- Add a section with “My Bulls” that lists a group of 5-10 “Diversity Candidates”
  - List would change over time
- Sorted by the Compass user’s preferred index of LPI or Pro$
  - Include the same columns as customized by the user
- Allow the user to add any of them to their “My Bulls” list
- The same bulls can be provided to the AI company offering genetic mating services

Second Phase – Breeding Companies

- To-date, there has been little advantage for A.I. companies to buy more outcross sires, which normally come with a lower genetic offering
  - Poor demand for their semen
- Focus continues to be on highest genetic merit
- Still need to develop other tools to help AI companies identify and purchase “Diversity” sires after genotyping new young bull candidates

Genetic Recessives and Abnormalities

- Genomics has aided in the discovery of genetic recessives, but we are also seeing higher occurrences
- Gene testing and management of genetic recessives
    - Avoid carrier bulls and never mate two potential carriers
- Need improved reporting of abnormalities and deaths to discover these as early as possible
    - **Will be working with industry partners to develop an improved method for easy reporting and rapid responses**

Genomic Solutions

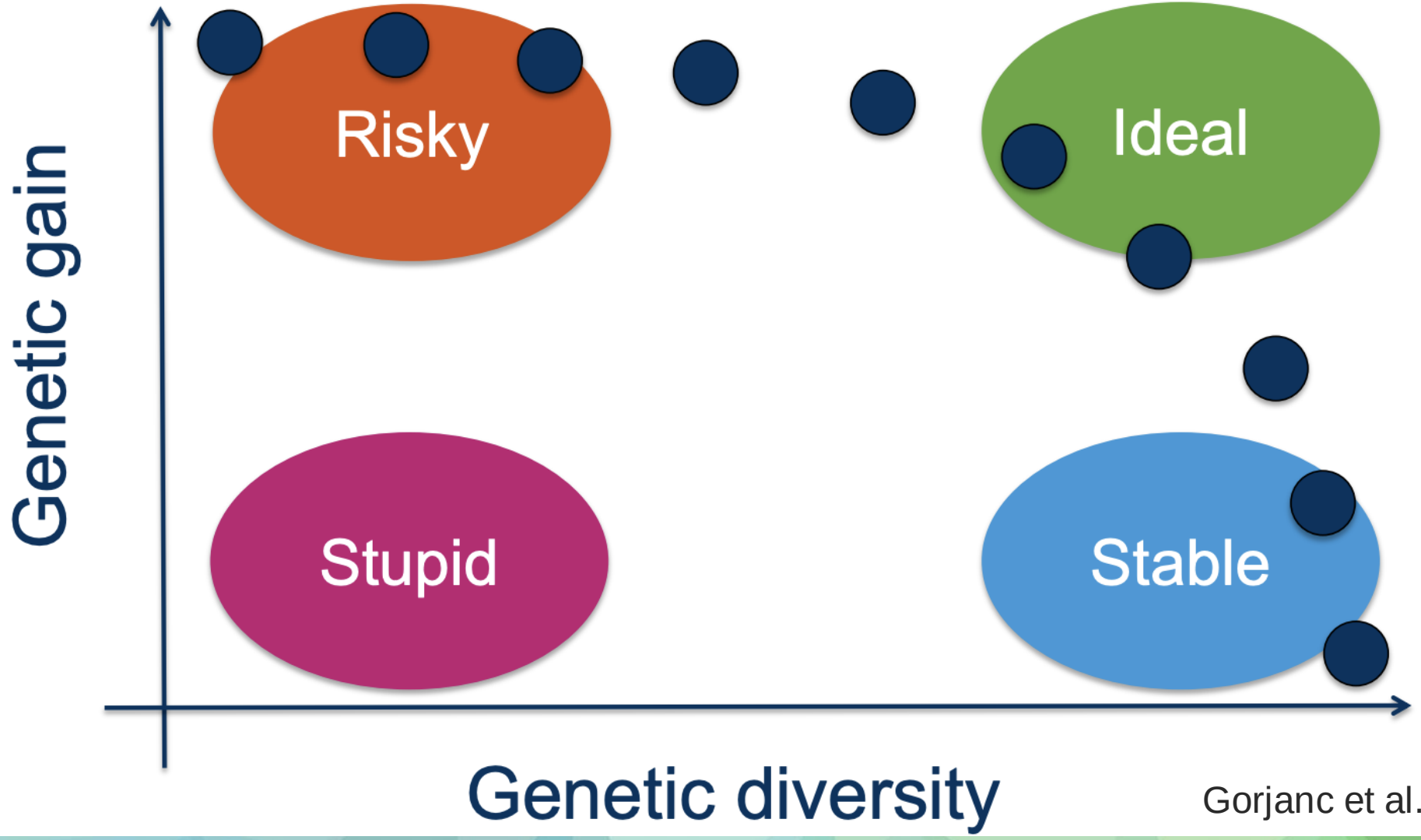
- Move toward looking at **genomic inbreeding or realized** instead of traditional pedigree-based inbreeding
- Future tools should take advantage of genomic information to identify sires to use within a genotyping herd
    - Where both sire and dam are genotyped, genomic relationships can be used **more accurately** than pedigree relationships
- **Not all inbreeding has a negative effect on performance**
    - Sire selection advice can include genomic information for finding complementary genotypes and avoid negative effects of homozygosity

Future Tools

What future services would help Canadian farmers **manage**/maintain genetic diversity?

1. Include genomic information where possible for more accurate measures of relatedness
2. Provide a within-herd tool for producers to see which bulls are LEAST related to their herd
3. Develop other tools to help A.I. companies identify and purchase "Diversity" sires after genotyping new young bull candidates
4. Tool to ease the reporting of genetic abnormalities
5. Continue research using new technologies to further understand (biological, economic) impacts of homozygosity

Breeder's Dilemma



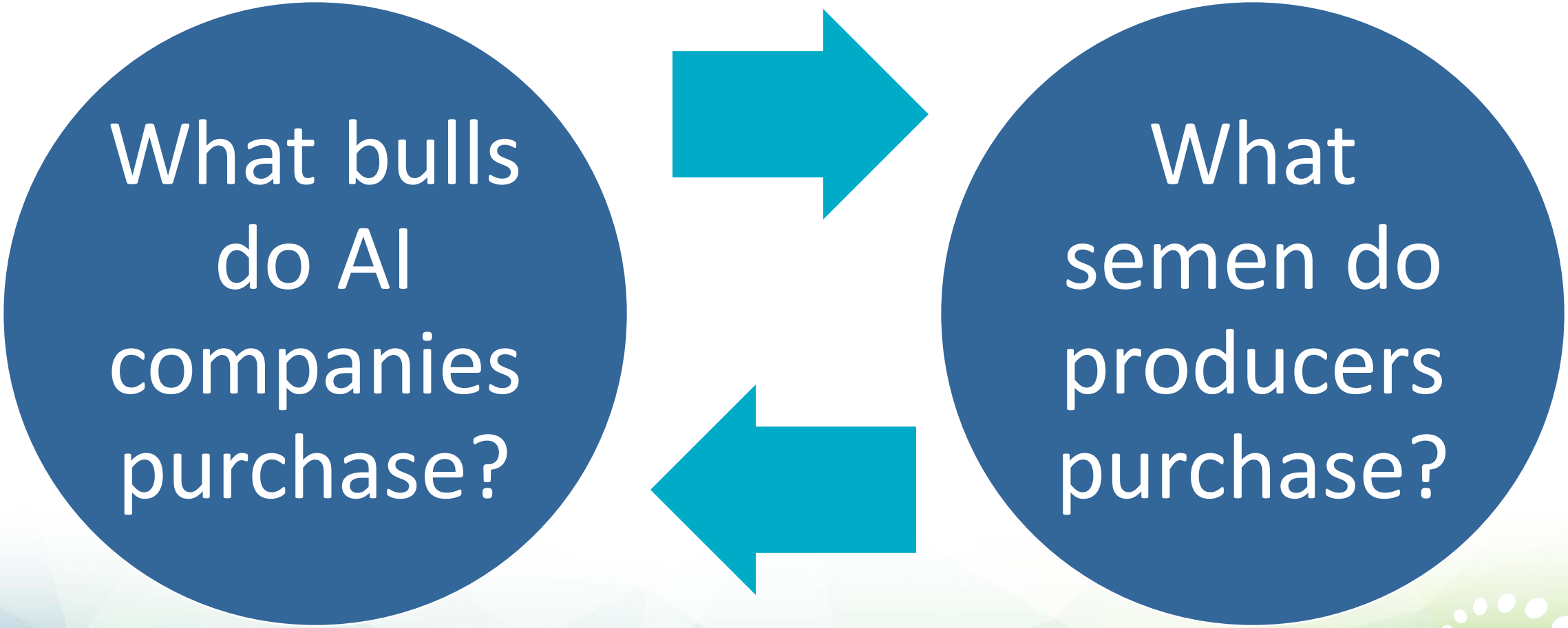
Gorjanc et al.

First Steps

- Inbreeding levels are increasing, and is **unavoidable**
  - Some consequences of inbreeding are still unknown
- Balance genetic gain with increases in inbreeding levels
  - Seek bulls that would be **outcross** to your females
- Do gene testing and manage genetic recessives
- **Genotype females** to also get more information about the current status of inbreeding
- **Continue genomic selection for traits related to health, reproduction, fitness, survival, etc.**

The approach forward involves industry collaboration, but someone needs to make the first move!

Two Critical Decision Points Affecting Diversity of Dairy

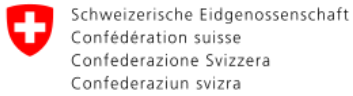


Two Critical Decision Points Affecting Diversity of Dairy

What bulls do AI companies purchase?

What semen do producers purchase?

Acknowledgements



Leveraging Genomics to Achieve Dairy Net-Zero, $16.2M

Recruiting talent for next 4 years

- PhD students
- Post-docs
- Project manager

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EAAP 2023 in Lyon, France, Aug 28-31, 2023