High Immune Response Genomic Evaluations for Angus Cattle

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55th Annual BIF Research Symposium and Convention

July 5, 2023

Improvement of Beef Cattle Health

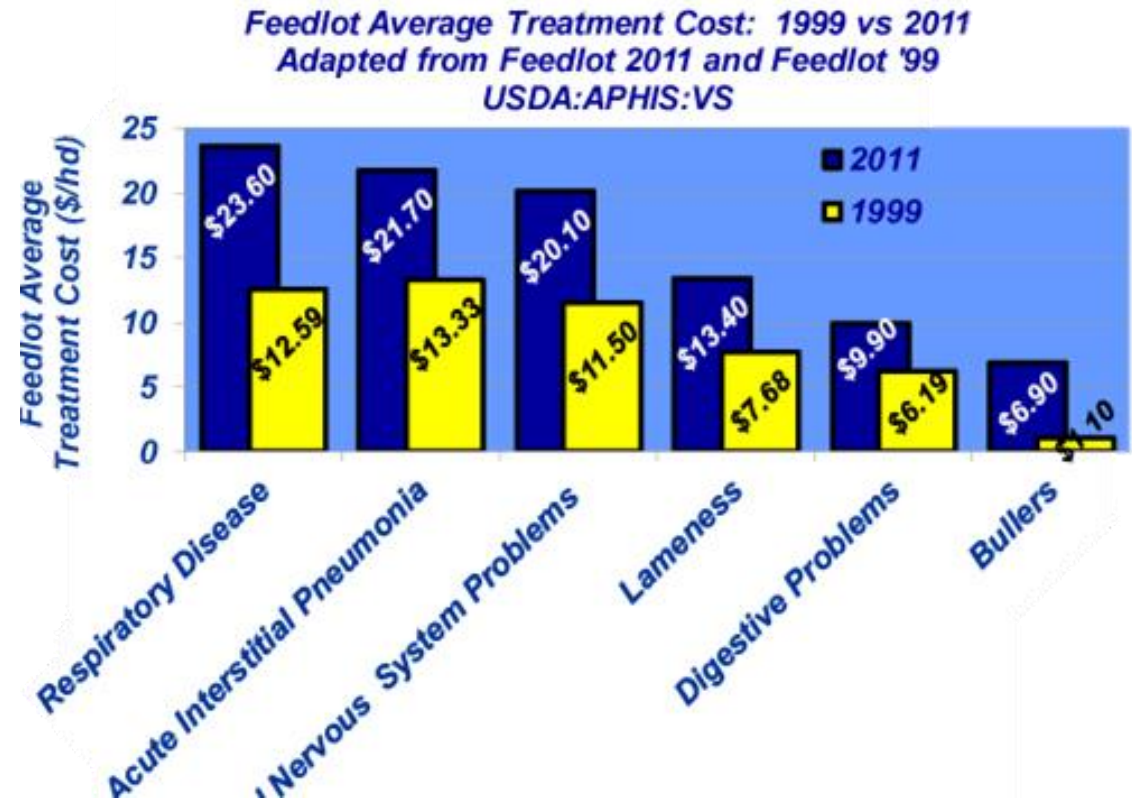|				
Lower disease severity and occurrence	Reduced treatment costs	Reduced production loss	Improved response to commercial vaccines	Better conception rates
Better colostrum and milk quality	Increased food quality and safety	Improved fertility	Less mastitis	Improved average daily gain
Less incidence of calf loss	Less incidence of lameness	Less requirement for treatment	Less use of antimicrobials	Less resistance developed
	Increased animal health and welfare	Increased consumer trust	Validate in commercial setting	

Economics of Improved Health

- Disease management, treatment, and loss ~7% production cost

- Production losses

- Consumer confidence in beef

  - Consumer perception = driver for change

  - Use of antibiotics

- Disease outbreaks

  - Impact on profitability of individual operations

  - Industry if market access is closed
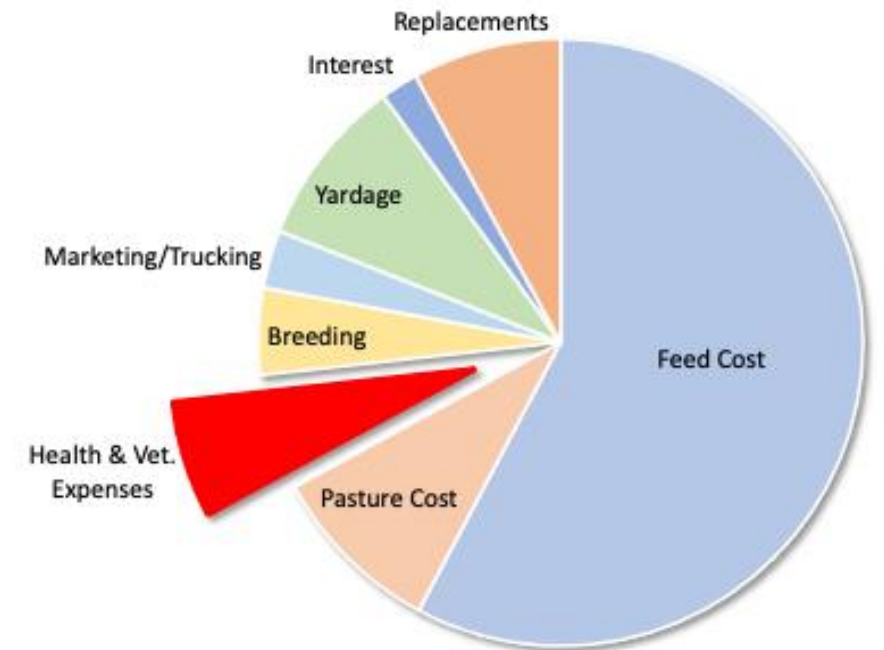
Average Expenses for a Cow-Calf Beef Operation (OMAFRA, 2020)

Bovine Respiratory Disease (BRD)

- Any disease of the upper or lower respiratory tracts

- Can be caused by bacterial or viral pathogens acting simultaneously in various combinations

- Estimated that BRD causes up to 80% of disease and up to 70% of deaths in some feedlots and costs several billion dollars to the industry in prevention, control, and treatment (Beef Cattle Research Council, 2019).

Feedlot Average Treatment Cost: 1999 vs 2011
Adapted from Feedlot 2011 and Feedlot '99
USDA:APHIS:VS

Feedlot Average Treatment Cost ($/hd)

■ 2011
□ 1999

Category	2011	1999
Respiratory Disease	$23.60	$12.59
Acute Interstitial Pneumonia	$21.70	$13.33
Nervous System Problems	$20.10	$11.50
Lameness	$13.40	$7.68
Digestive Problems	$9.90	$6.19
Bullers	$6.90	$1.10

Breeding For Healthier Cattle

- Breeding for cattle that have better ability to resist disease could significantly reduce costs associated with disease while helping to reduce the use of antibiotics

- Immune response traits have not yet been incorporated into breeding programs for beef cattle in North America
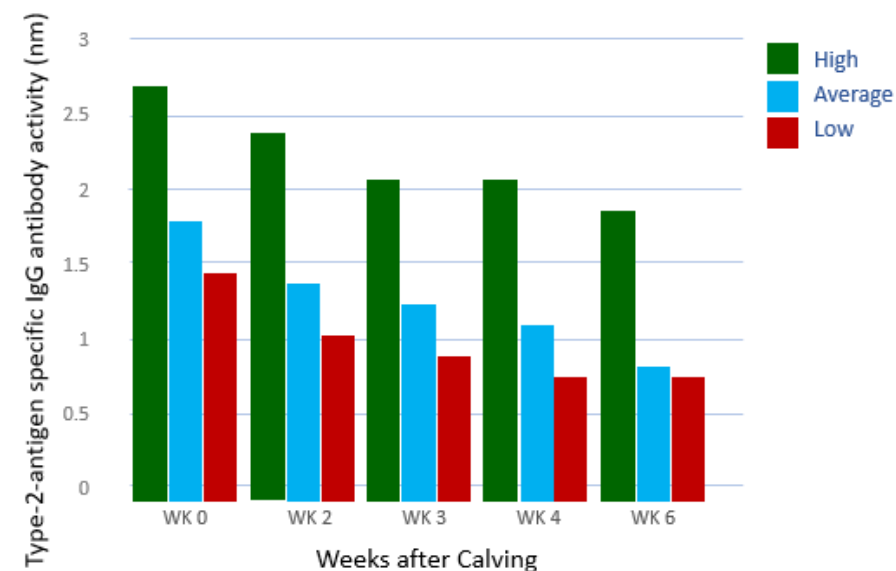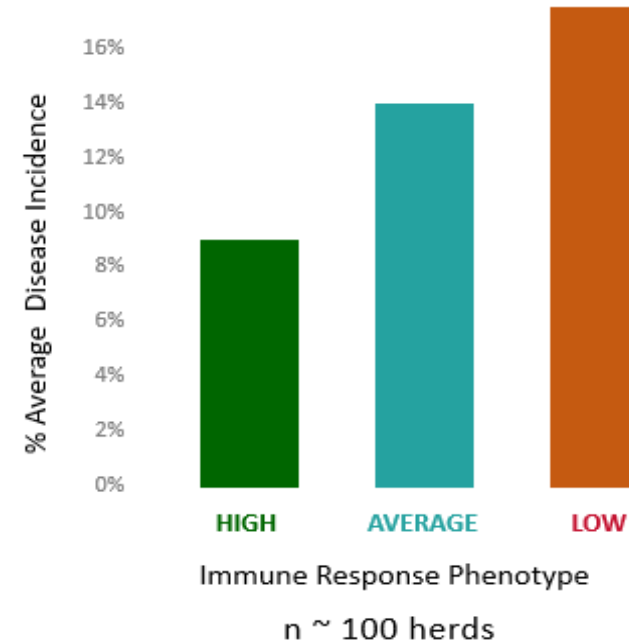
Challenges:

- Inconsistency and difficulty in disease diagnosis and recording

- Selection to fight one disease may be counter-productive to other diseases

- Difficult to improve genetically - low heritability of single diseases
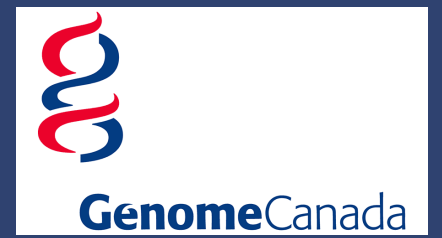
High Immune Response (HIR™) Technology

- Identifies animals with superior heritable immunity

- Directly evaluates antibody-mediated (AMIR) (bacteria, fungi, parasites) and cell-mediated (CMIR) (intracellular viruses and bacteria) immune response

- Allows for the calculation of an estimated breeding value for total immune response

- **Immunity+™**: Implemented for dairy cattle by Semex in 2012

- H² in Dairy ~0.37 for AMIR and 0.16 for CMIR

HIR™ in Dairy

- Reduced disease by almost 50%

- Increased milk production

- Better quality milk and colostrum

- Less mastitis infection

- Requirement for antibiotics

- Increased conception rates

- Better response to commercial vaccine

Mallard et al., 1998; Wagter et al., 2000; Thompson-Crispi et al., 2012, 2013; Aleri et al 2015; Cartwright, 2017; Larmer & Mallard, 2017

Translating High Immune Response Testing For Angus Cattle

Overall Project Goals

- Provide a better understanding of the genetic background of immune response traits for beef cattle

- Determine the feasibility of including immune response traits into genetic evaluations for Angus cattle

HIR™ Immunophenotyping Protocol

Day 0:

- Blood collection
- IM immunization with 1.0 mL of a preparation of type-1 and type-2 test antigens

Day 14:

- Blood collection
- Baseline skinfold thickness measurements
- ID immunizations:
  - 0.1 mL of PBS in the left tail fold (control site)
  - 0.1 mg of the type-1 test antigen in 0.1 mL PBS in the right tail fold (test site)
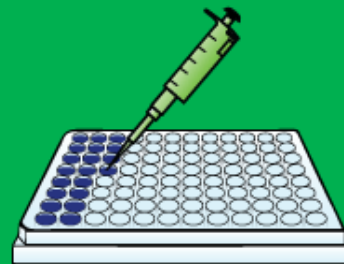
Day 15:

- 24-hour skinfold thickness measurements

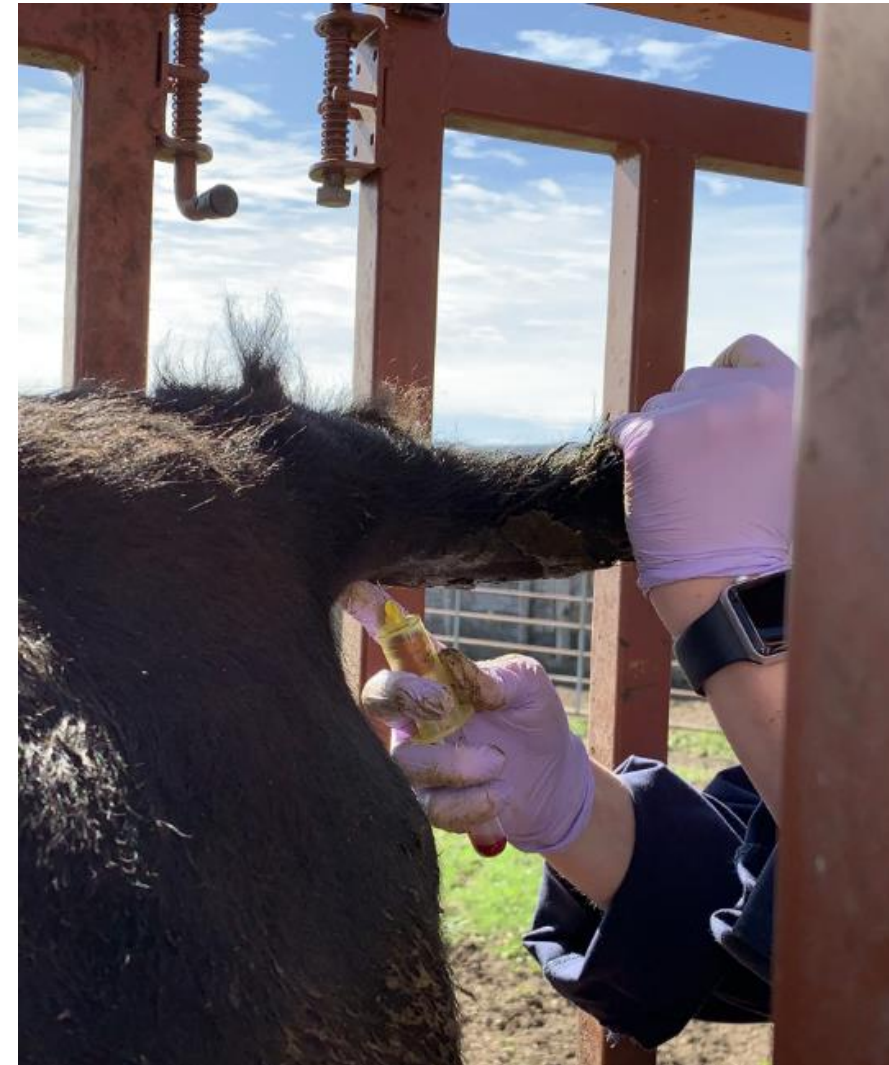**AMIR measured by ELISA on serum pre- and post-immunization with test antigen**

CMIR measured by skinfold thickness pre- and post-immunization with test antigen

Preliminary Results

Cattle were immunized to induce AMIR and CMIR using HIR™ technology

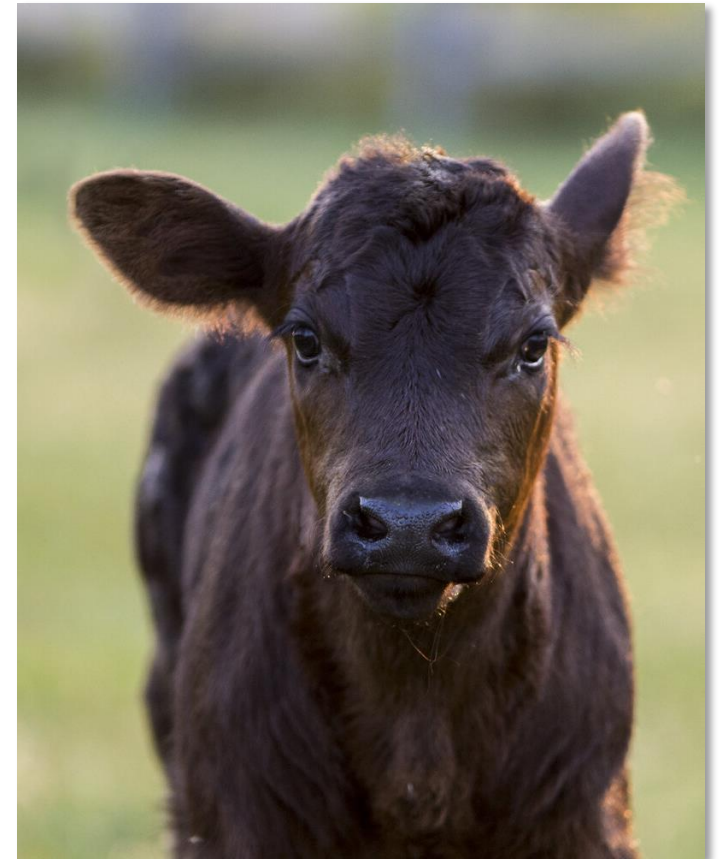|	
Total Tested	4,359
Canada	3,619
U.S.	740

Genetic Parameters

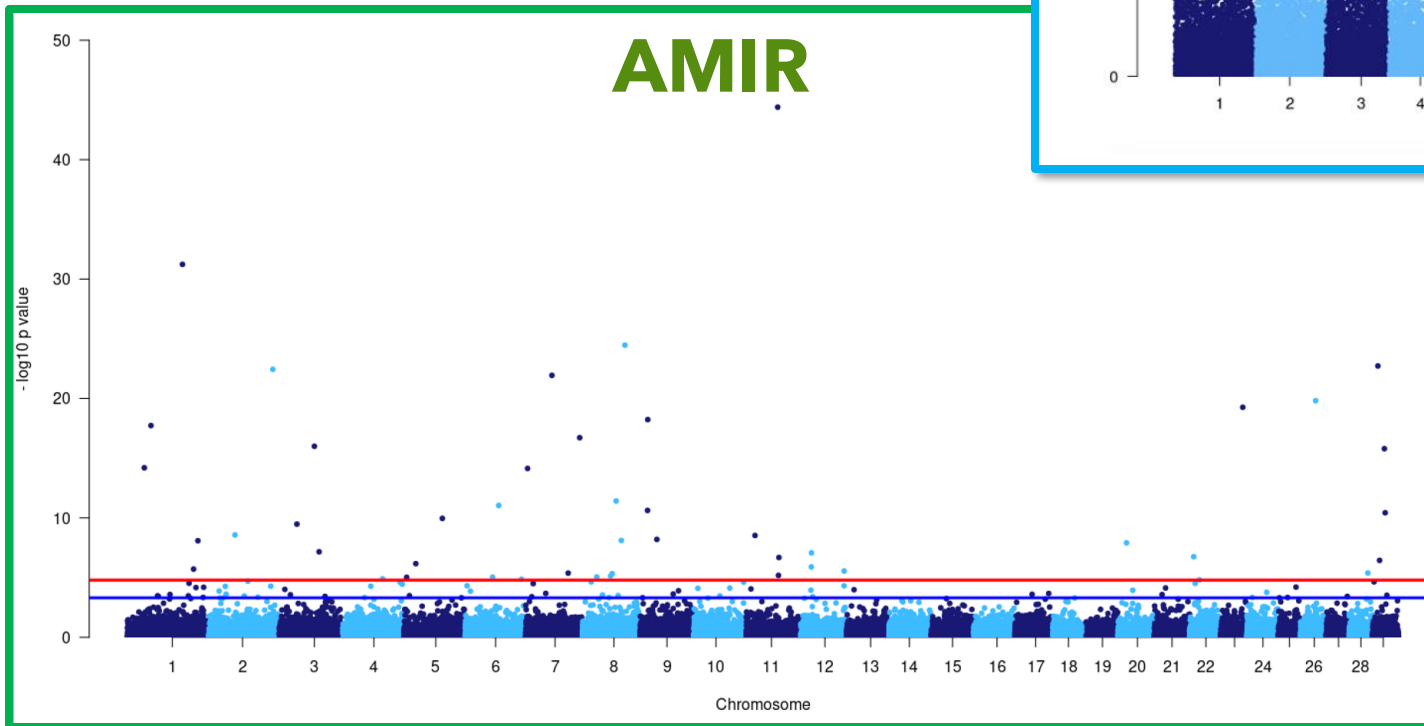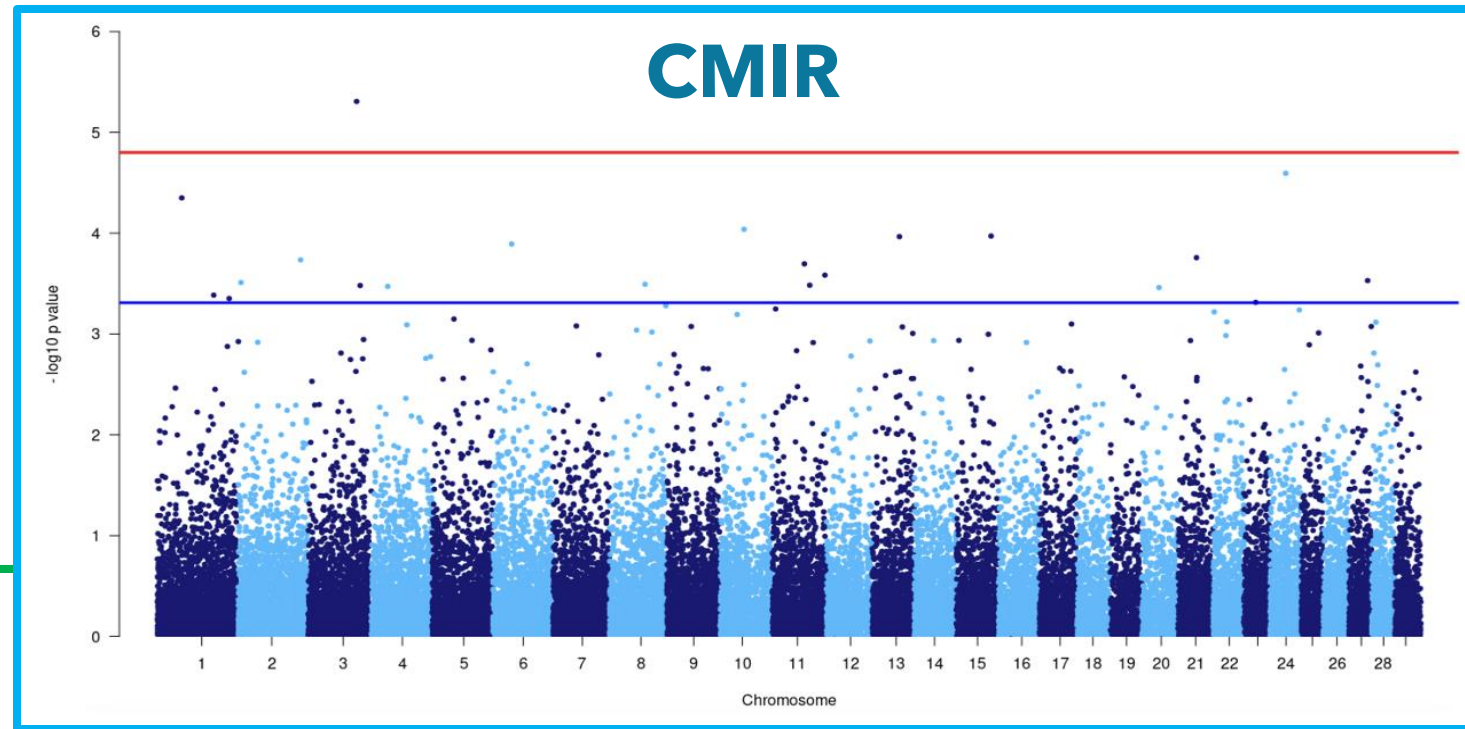Genomic heritability (diagonal), genetic correlations (above diagonal) and phenotypic correlations (below diagonal)

Dataset	Trait	AMIR	CMIR
All (N = 3,832)	AMIR	**0.25** ± 0.03	0.03 ± 0.11
	CMIR	0.04 ± 0.02	**0.12** ± 0.02

No significant Pearson correlations between EPDs for routinely evaluated traits and AMIR or CMIR
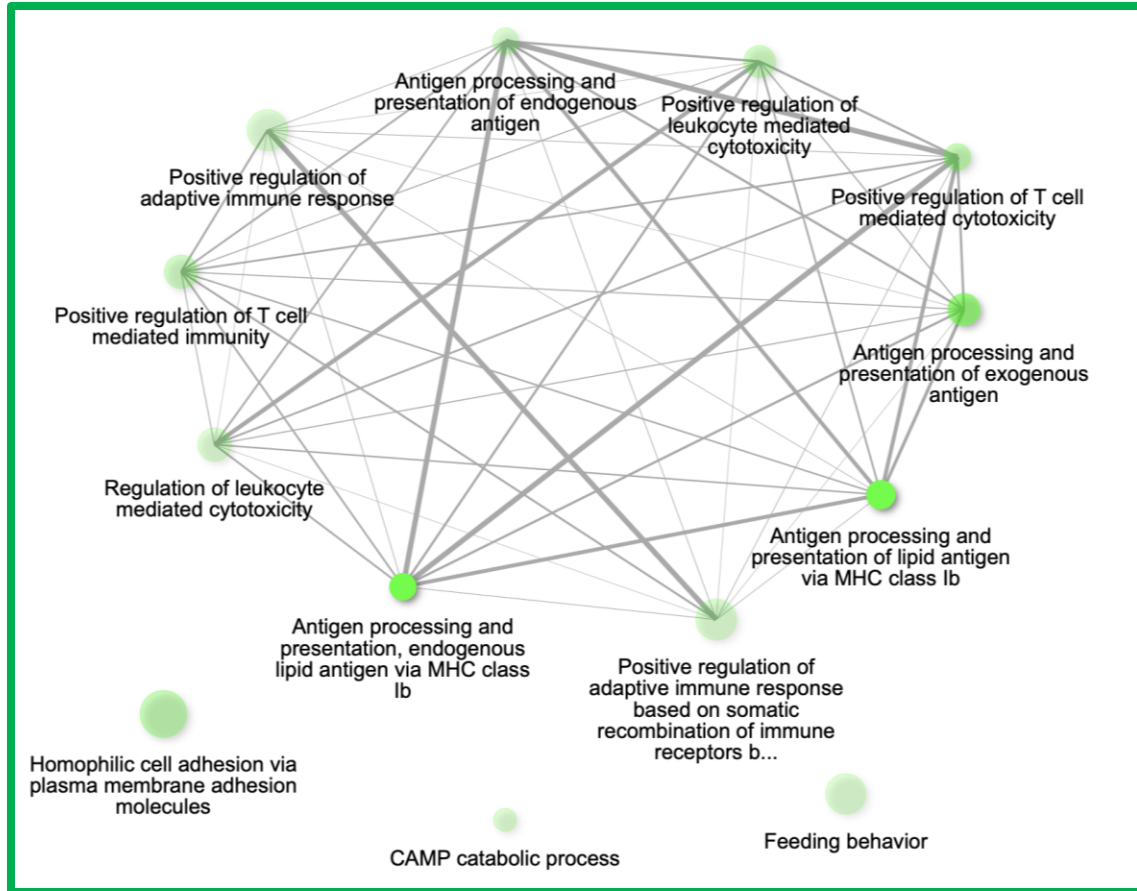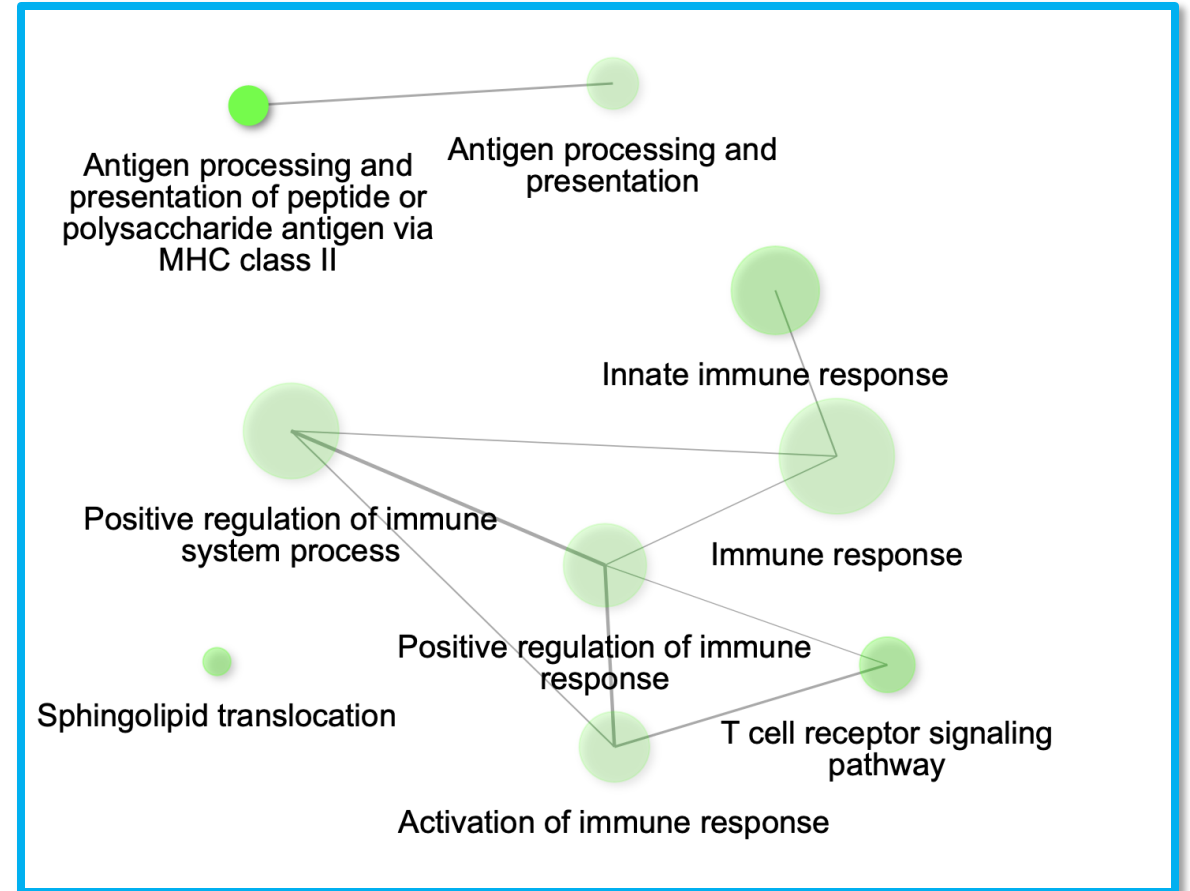
Manhattan Plots

Biological Processes

AMIR

Antigen processing and presentation of endogenous antigen

Positive regulation of leukocyte mediated cytotoxicity

Positive regulation of adaptive immune response

Positive regulation of T cell mediated cytotoxicity

Positive regulation of T cell mediated immunity

Antigen processing and presentation of exogenous antigen

Regulation of leukocyte mediated cytotoxicity

Antigen processing and presentation of lipid antigen via MHC class Ib

Antigen processing and presentation, endogenous lipid antigen via MHC class Ib

Positive regulation of adaptive immune response based on somatic recombination of immune receptors b...

Homophilic cell adhesion via plasma membrane adhesion molecules

cAMP catabolic process

Feeding behavior

CMIR

Antigen processing and presentation of peptide or polysaccharide antigen via MHC class II

Antigen processing and presentation

Innate immune response

Positive regulation of immune system process

Immune response

Positive regulation of immune response

Sphingolipid translocation

Activation of immune response

T cell receptor signaling pathway

Conclusions

- Cattle were immunophenotyped across regions in Canada and the United States, and **significant phenotypic variation** was observed
  - Likely suggests sufficient genetic variation for possible genetic selection
  - Age, sex, region, and maximum THI on the day of testing were found to significantly affect phenotypes and should be accounted for when evaluating immunophenotypes

- Immune response traits measured using the HIR™ technology are heritable
  - **Moderate heritability of AMIR and CMIR** suggests that breeding beef cattle for improved immunity to minimize the impact of disease and improve overall health is feasible

- **AMIR and CMIR are genetically and phenotypically uncorrelated**
  - Selection for both traits simultaneously is suggested as a breeding strategy to maintain a balanced immune system capable of successfully responding to a diverse set of pathogens

Conclusions (cont.)

- EPDs calculated for AMIR and CMIR had **no significant correlations with routinely evaluated traits**

  - Indicates that these traits can be safely selected for without negative impacts on genetic gain for other traits, particularly production and carcass traits

- Insights into the genetic architecture underpinning immune response and disease resistance in Angus cattle were found

  - Several significant SNP markers and biological pathways were associated with AMIR and CMIR

- Implementation of genomic selection will be beneficial to improving immune response traits, given their **polygenic nature**

Next Steps

- Calculation of research EPDs

- Calculation of genetic correlations between immune response EPDs and EPDs for other measured traits

- Validation

  - Determine associations between immune response EPDs and feedlot health and disease records or lung lesion scores

- Continue collecting phenotypes to expand training dataset

Fertility Update: North American Angus Evaluation

Curating whole-herd data is important

- **American Angus Association**
  - **Voluntary inventory reporting**
    - **Fall and Spring Enrollment**
    - **2014**
    - **97,094**

- **Canadian Angus Association**
  - **Voluntary Performance Program**
  - **Mandatory Whole-herd reporting**
  - **1993, 80% cows**

This started out at University of Guelph

Using Random Regression Models to Genetically Evaluate Functional Longevity Traits in North American Angus Cattle

Hinayah R Oliveira [1] [2], Luiz F Brito [2], Stephen P Miller [3], Flavio S Schenkel [1]

Affiliations + expand

PMID: 33339420   PMCID: PMC7766511   DOI: 10.3390/ani10122410

Abstract

This study aimed to propose novel longevity indicators by comparing genetic parameters for traditional (TL; i.e., the cow's lifespan after the first calving) and functional (FL; i.e., how long the cow stayed in the herd while also calving; assuming no missing (FLa) or missing (FLb) records for unknown calving) longevity, considering different culling reasons (natural death, structural problems, disease, fertility, performance, and miscellaneous). Longevity definitions were evaluated from 2 to 15 years of age, using single- and multiple-trait Bayesian random regression models (RRM). The RRM fitting heterogenous residual variance and fourth order Legendre polynomials were considered as the optimal models for the majority of longevity indicators. The average heritability estimates over ages for FLb (from 0.08 to 0.25) were always higher than those for FLa (from 0.07 to 0.19), and higher or equal to the ones estimated for TL (from 0.07 to 0.23), considering the different culling reasons. The

Dr. Hinayah Rojas de Oliveria - Lactanet

The data – Early research on the trait

- Cows born after 1990

- Must have calved before 30 months of age with a minimum age of first calving at 19 months

- Maximum culling age was 20 years (more on this)

- 527,283 records from USA & 77,260 records Canada

Classified culling codes into 7 different classes

Table 1. Description of the different groups of culling reason in North American Angus cattle.

Group	Class	N	N_{Total}
Natural Death	Died due to non-apparent reasons	55,232	150,229
	Culled due to age	94,997	
Structural Problems	Eye problem	499	24,804
	Body structure	13,101	
	Teat and udder conformation	5845	
	Rectal prolapse	73	
	Vaginal prolapse	103	
	Feet conformation	5183	
Disease	Illness or disease	4994	4994
Fertility	Fertility	124,696	154,419
	Missed calving opportunity	29,723	
Performance	Productivity or progeny performance	53,837	62,005
	Temperament	8168	
Miscellaneous	Culled as miscellaneous	44,563	208,092
	Sold as commercial	163,529	
All Reasons	All	604,543	604,543

Fertility #1 reason cows are leaving the herd

Data outside inventory reporting being investigated

Heritability of "Longevity" was estimated for every class

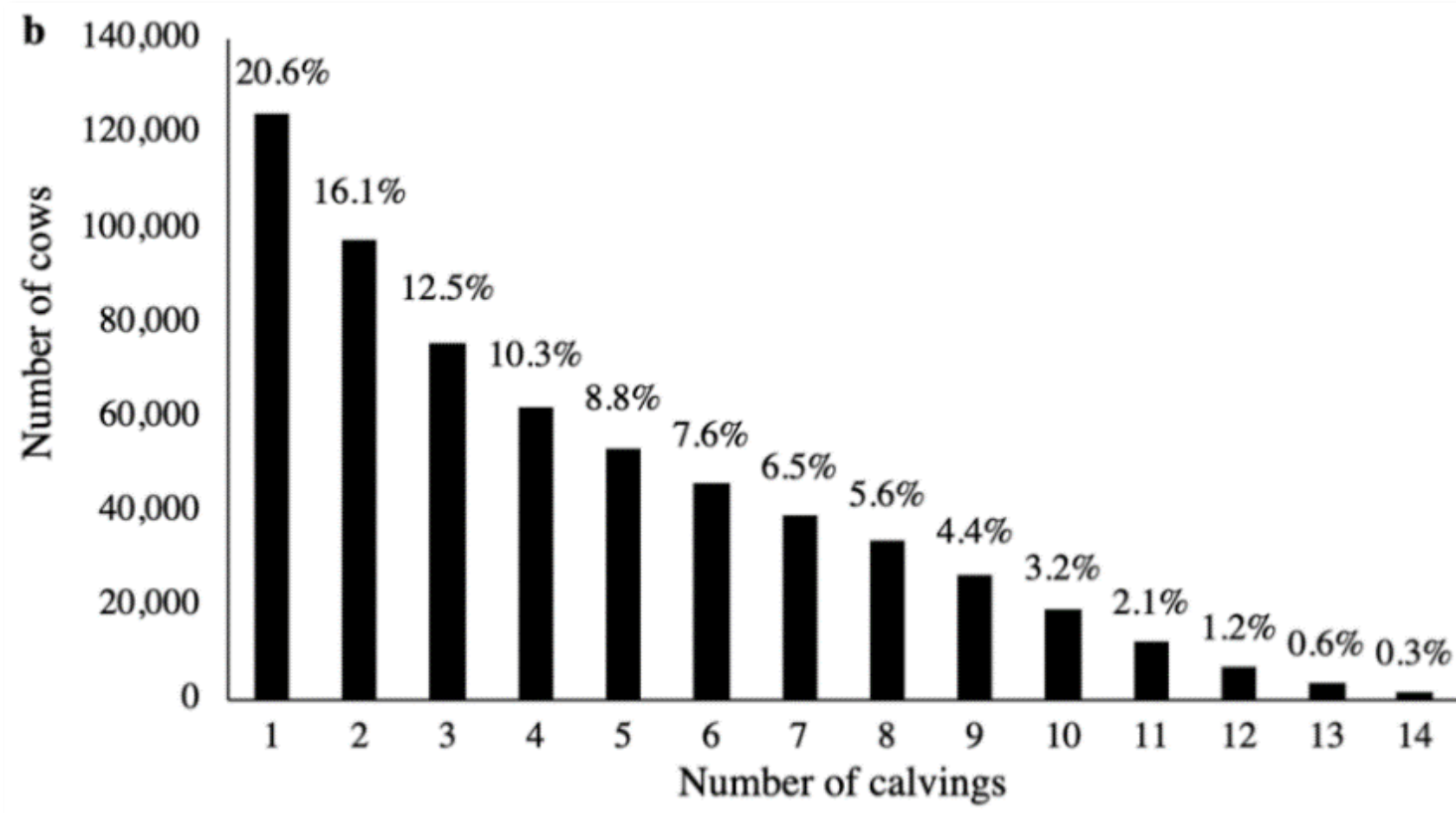| Culling Reason	All	3-12 Years
Natural Death	0.15 ± 0.02	0.17 ± 0.02
Structural problems	0.17 ± 0.03	0.21 ± 0.02
Disease	0.19 ± 0.04	0.23 ± 0.02
Fertility	0.07 ± 0.05	0.09 ± 0.01
Performance	0.08 ± 0.06	0.10 ± 0.01
Miscellaneous	0.07 ± 0.07	0.09 ± 0.01
All	**0.09 ± 0.08**	**0.09 ± 0.01**

Predicting a trait for each individual culling code is not feasible for deployment or easily implemented for production practices. A combined approach has been taken forward.

Number of cows by culling age for cumulative culling codes
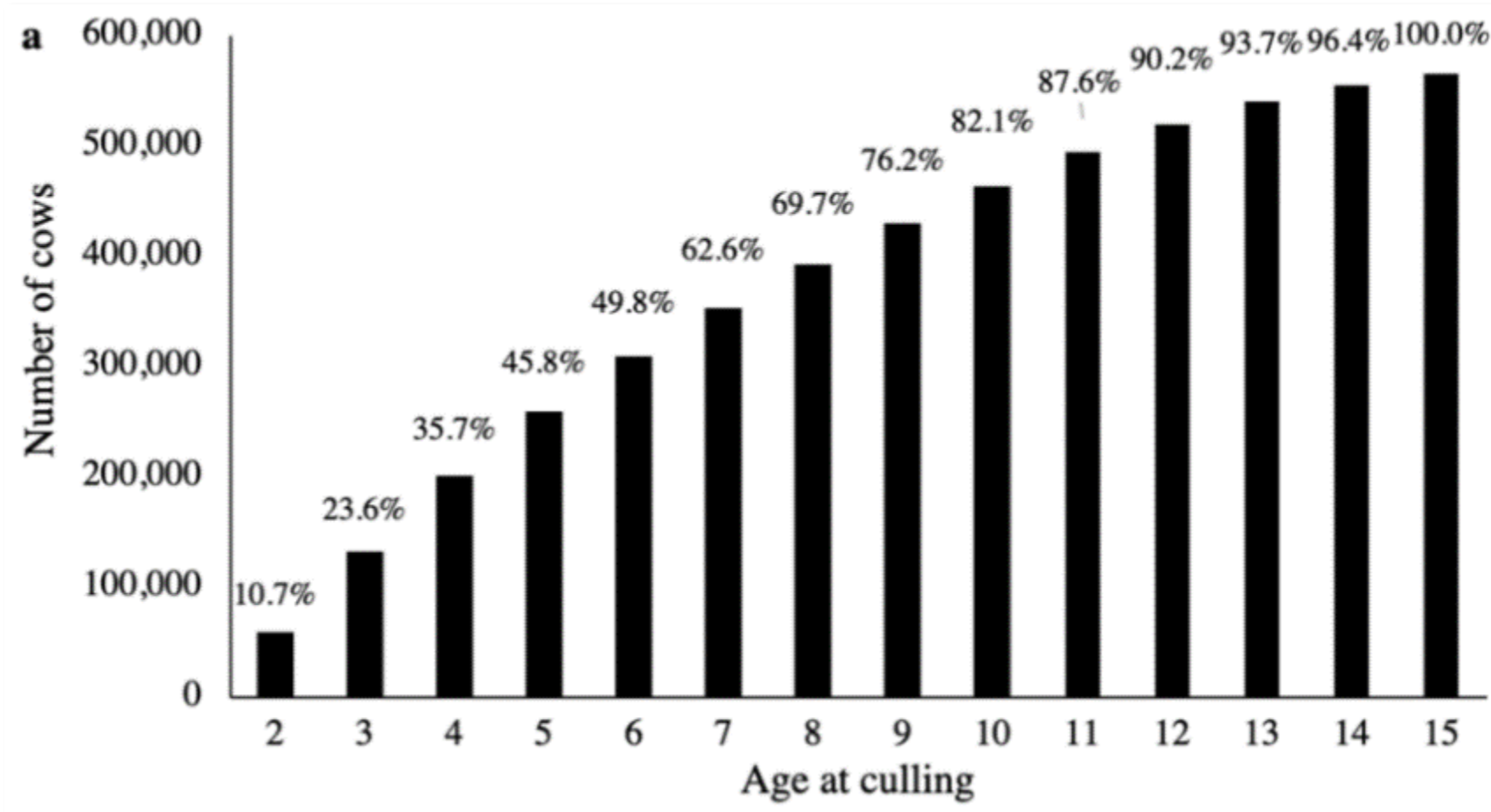
Age at culling equal to 15 included cows culled from 15 to 20 years-old.

Number of cows by number of calvings reported to the database.

Age at culling equal to 15 included cows culled from 15 to 20 years-old.

Defining the trait

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Functional longevity with missing records also had the highest combined heritability estimates
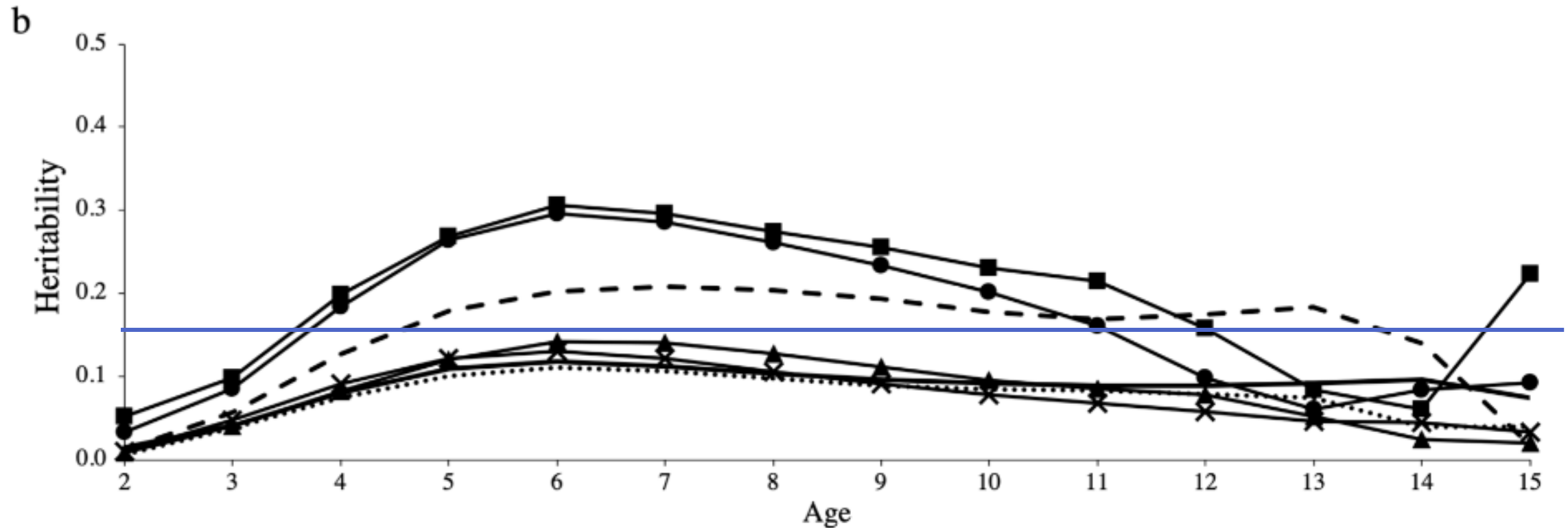
Final assumptions utilized for the daughters

Functional longevity with missing records.

Data: Calving and culling records reported; counting the number of calves

Prediction: number of calves a sire's daughters are predicted to produce in her lifetime.

It's not about the individual cow

- Genetic improvement for this trait isn't about the individual female.
  - Some Angus females will be in the herd and calve every year but may not have the BEST longevity EPD.
  - It is about the aggregate information provided by a sire's daughters.

Roll out to the industry in a research format

- Research EPDs (Fall 2023)
  - A.I. Sires with an obtained amount of accuracy
  - Individual cowherds that are enrolled on the AHIR Inventory Reporting System at AAA and enrolled in the Canadian Angus Association Performance Program
- American Angus Association: Work to fit this trait inside of the Maternal Weaned Calf Value ($M) subsequently $C
- Canadian Angus Association: Work to fit this trait inside of the Canadian Balanced Index