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Estimating Myostatin gene effect on milk performance traits using estimated gene content for a large number of non-genotyped cows

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Context

- Situations
  - where estimation of single gene effects for quantitative traits is important
- Different scenarios
  - ↗ genetic gain:
    - By selecting animals with desirable gene variants
  - To avoid overemphasis on single gene variants

Context

- Difficult to obtain reliable estimates
  - Not all (few) genotyped animals
  - Genotyping more → Expensive
  - Genotyping all → Impossible
- Other solution: estimating missing genotypes
  - Different methods (*e.g.*, Van Arendonk *et al.*, 1981)
  - Estimating gene content (number of alleles) (Gengler *et al.*, 2007)

Context

- Deletion in Myostatin gene: ‘mh’ allele
  - Responsible for double-muscling in all cattle breeds (Bellinge *et al.*, 2005)
  - Present in Dual-Purpose Belgian Blue (DP-BBB)
  - Influence on milk performance traits?
    - But, not well known → few genotyped animals
    - However, important in DP-BBB & used as selection tool

➔Estimation of ‘mh’ allele effect on milk production traits

Materials & Methods

- Data structure & genotypes
  - – Data used for the official routine genetic evaluation for Walloon Region of Belgium
  - – 13,992,889 test-day records for 1st, 2nd & 3rd lactation
    - 799,778 cows
    - Breeds:
      - ➢ Holstein, Belgian Blue Breed (BBB), Others Red-White breeds
    - Mixed herds and crossbreds
  - – Heterogeneous breed composition

➔Additional issue for genotype estimation

Materials & Methods

- Data structure & genotypes
  - Pedigree file: 1,429,939 animals
  - 1,416 genotyped DP-BBB animals (→ 1,183 cows)
    - Few genotyped animals

➢ Can other genotypes be assumed?

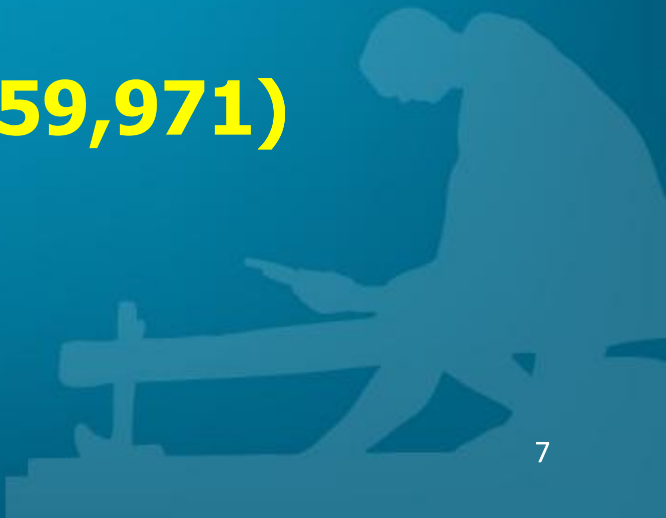
Materials & Methods

- Addition «assumed» known genotypes
  - – BBB animals (sires) from the meat type
    - Used for AI
    - Born after 1985

  ➔ **Assumed to be mh/mh (n=830)**

  - – Purebred non-BBB animals

  ➔ **Assumed to be +/+ (n=659,971)**



Materials & Methods

- Gene content estimation
  - For other animals (n=767,722)
    - Estimation of gene content (Gengler *et al.*, 2007)
  - For the founders
    - 10 genetic groups
      - According to breed
      - By distinguishing:
        - BBB & non-BBB animals
        - Herd-book type of animal (meat & DP)
        - Year of birth

Results & Discussion

- Estimated gene content of non-genotyped animals
  - Development of Myostatin gene content over time

Group of animals	Estimated average gene content[1]	Number of individuals
Non-BBB	**0.002**	**924,325**
BBB-M 1971 to 1980	**0.532**	**10,694**
BBB-M 1981 to 1990	**1.352**	**37,479**
BBB-M 1991 to 2000	**1.817**	**74,761**
BBB-M > 2000	**1.931**	**42,504**
DP-BBB 1971 to 1980	**0.798**	**358**
DP-BBB 1981 to 1990	**1.186**	**4,034**
DP-BBB 1991 to 2000	**1.176**	**4,687**
DP-BBB > 2000	**1.239**	**2,347**

BBB = Belgian Blue Breed; M = meat type; DP = dual-purpose type.

[1] Values between 0 (+/+) and 2 (mh/mh) represent the gene content for ‘mh’ allele

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Results & Discussion

- Estimated gene content of non-genotyped animals
  - Hypothesis
    - Necessity to use genetic groups and to include animals with assumed genotypes to obtain valid estimations of gene content
  - To test this hypothesis
    - Estimation without these genetic groups & assumptions
      - Estimated mean gene content of 1.349
    - Unrealistic results because:
      - Extreme founder allele frequency obtained only from genotyped BBB animals
      - Weak or non-existing (different breeds) links between genotyped and non-genotyped animals

Results & Discussion

- Estimated gene content of non-genotyped animals
  - More realistic results
  - Show potential for gene content estimation with:
    - Use of genetic groups
    - Use of assumptions
      - » when few genotyped animals in a large heterogeneous population under selection
  - However, its accuracy depends mainly on:
    - ↗ with increasing number of genotyped relatives
    - ↗ when closer relationships between genotyped and non-genotyped animals

Materials & Methods

- Statistical model to estimate ‘mh’ effect
  – Based on routine genetic evaluation model for milk production traits (Auvray & Gengler, 2002; Croquet *et al*., 2006)
    - Multi-lactation, multi-trait random regression model
    - (Co)variance components

    \+ Fixed regression on observed or estimated gene content

  – Standard errors for regression coefficients
    - Mixed model conjugate gradient normal equations (Harville, 1979; Croquet *et al*., 2006)

Results & Discussion

- Allele substitution effects of the ‘mh’ allele
  - ✓ On milk, fat and protein yield (kg/305 days) through all lactations & for each lactation (n= 13,992,889)

Lactation										
	Mean	**1**			**2**			**3**		
Trait	**Effect**	**Effect**	**s.e.**	***t*-value**	**Effect**	**s.e.**	***t*-value**	**Effect**	**s.e.**	***t*-value**
Milk	**-76.06**	**-70.80**	**8.30**	**8.53*****	**-72.88**	**10.07**	**7.24*****	**-84.52**	**12.14**	**6.92*****
Fat	**-3.62**	**-3.02**	**0.35**	**8.62*****	**-3.76**	**0.44**	**8.55*****	**-4.09**	**0.53**	**7.71*****
Protein	**-2.84**	**-2.57**	**0.25**	**10.28*****	**-2.84**	**0.32**	**8.88*****	**-3.10**	**0.38**	**8.71*****

- ✓ 1 copy of the ‘mh’ allele
  - ▪ Very high significant decrease in milk, fat and protein yields

Results & Discussion

- Additive effects
- The power to detect a candidate gene effect depends
    - on the magnitude of the effect that was estimated
    - on the standard error of this estimation
- In this study, estimated ‘mh’ allele effects were large enough to be significant
    - Although standard errors ↗ with increasing lactation number
        - Because less records in higher lactation number
- However,
    - Potentially biased allele effect estimation as effects lower than in other studies (Buske *et al.*, 2010)
        - Selection of animals for genotyping randomly?
        - Inclusion of a large number of animals with estimated genotypes?

Conclusion

- To estimate more accurately gene content of large heterogeneous population
  - Inclusion of additional assumptions
    - As information about genetic groups
      (here based on breeds, phenotypic selection and year of birth)
  - Groups expressing differences in expected founders allele frequencies
- Estimation of the ‘mh’ allele effect possible

Thank you for your attention

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