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INTEGRATION OF GENOMIC INFORMATION INTO NATIONAL CATTLE AND SHEEP EVALUATIONS – PAST, PRESENT AND FUTURE

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SUMMARY

National (two-step) genomic evaluations for Holstein-Friesian dairy cattle have been available in Ireland since 2009; retrospective analysis reveals minimal bias in prediction and more accurate rankings compared to pedigree index. The size of the training population for dairying (up to 5,105 animals) has increased 5-fold in recent years through sharing of genotypes. One-step multi-breed genomic predictions for beef cattle will become official in autumn 2015 made possible through a genotyped population of over 100,000 individuals. Genotypes of all cattle are from the custom International Dairy and Beef genotype panel developed in Ireland; this panel consists of 18,217 SNPs. Genotyping of 11,400 sheep for the development of genomic predictions has just begun.

GENOMIC EVALUATIONS IN DAIRY

Past. Genomic selection was launched in Ireland in February 2009 for animals that were >87.5% Holstein-Friesian, but no more than 12.5% Friesian; the cost was €50 per animal and was freely available to all (i.e., both national and international farmers, breeders, breeding companies). Analyses revealed poor accuracy of genomic predictions in pure Friesians at the time so an initiative was undertaken to genotype high reliability pure Friesian males; genomic predictions for Friesians were available in 2010. The initial training population consisted of 998 high reliability Holstein-Friesian AI sires. Predictions were (and still are) undertaken based on a two-step approach using custom developed software. Predicted transmitting abilities (PTAs) from domestic genetic evaluations, weighted by their reliability were the dependent variables; later years used MACE evaluations as the dependent variable. The number of animals in the training population increased in the following years through bilateral sharing agreements and in 2015 includes up to 5,105 animals. Sharing was (and continues to be) on the basis that genotypes will not be passed onto third parties, but more importantly that no restrictions are imposed on who can obtain a genomic evaluation. For example, genomic predictions are undertaken by the Irish Cattle Breeding Federation (ICBF) for thousands of animals annually for non-indigenous breeding companies.

Present. Once a bull has >50% reliability for direct calving difficulty (a crucial trait in Ireland) in Ireland, then that bull is available for widespread use. Ireland maintains a national breeding program (i.e., G€N€ IR€LAND) to ensure robust genetic evaluations especially for calving difficulty and monitoring of congenital defects. No financial incentives exist for G€N€ IR€LAND farmers other than reduced semen cost. The most recent daughter-based national genetic evaluation of 182 bulls genomically tested between the years 2009 and 2012 but now with >70% reliability for milk production and reproduction are in Table 1; the correlation with their respective pedigree index predictions and their first genomic predictions in their year of sale are in Table 1.

Genotypes of all cattle are generated using the custom International Dairy and Beef (IDB) genotype panel developed in Ireland. This panel includes 18,217 SNPs which include an extra 5,765 SNPs, additional to the Illumina low-density base content for imputation to higher density (especially in beef). Also included are 1,927 SNPs for imputation to microsatellites for parentage testing as well as four lethal mutations and causal (or tightly linked) SNPs in major genes associated with performance or congenital defects. A total of 2,973 SNPs as part of on-going research projects are also included on the panel.

Table 1. Mean (reliability) daughter-based PTAs from the most recent genetic evaluation as well as past parental average (PA) or genomic-based PTAs; also included is the correlation with the most recent daughter PTA for both PA and genomic PTAs

	Mean			Correlations	
Trait	Daughter	PA	Genomic	PA	Genomic
Milk (kg)	116 (90)	168 (41)	108 (61)	0.71	0.79
Fat (kg)	10.4	11.9	10.2	0.55	0.7
Protein (kg)	7.8	9.6	7.7	0.63	0.75
Fertility (d)	-4.5 (71)	-3.1 (30)	-3.7 (46)	0.6	0.63
Survival (%)	2.01	1.52	1.7	0.41	0.63

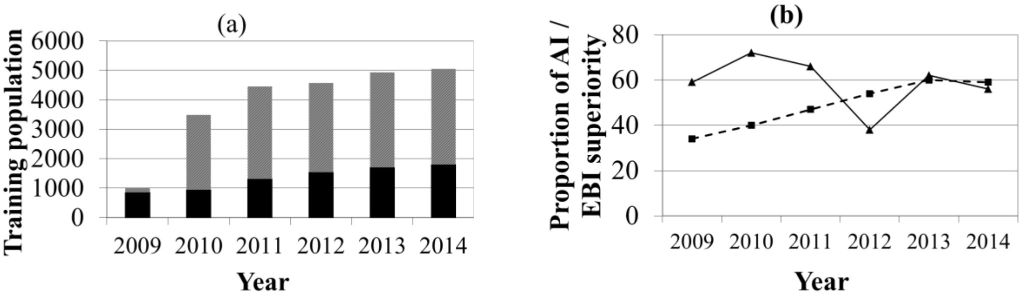

Figure 1. (a) Number of animals in the training population generated within Ireland (Black) or from bilateral sharing (grey) and (b) proportion of semen sales from genomically tested sires (broken line) and genetic superiority (€) of used genomically tested sires relative to used proven bulls (continuous line); standard deviation of national index (EBI) is €72.

Future. Attempts to exchange Jersey genotypes were largely unsuccessful; therefore an initiative began in 2014 to genotype commercial crossbred Jersey cows with the view to developing genomic predictions for Jersey animals in 2015. Farmers paid half the cost of the genotyping; 2,811 genotypes from Jersey crossbred cows now exist with more being genotyped in 2015. Research is currently underway on the potential of undertaking a one-step multi-breed genomic evaluation for dairying with possible implementation in spring 2016. Ireland is part of the 1000 Bull Genomes Project and has imputed all dairy genotypes to full sequence. Genome-wide association studies are underway to attempt to more closely track the causal mutations; once useful information is detected it will be added to updated versions of the IDB. Research is also underway on generating estimates of genetic/genomic merit for difficult to measure traits. One such initiative is the global dry matter initiative (gDMI) where across country genomic predictions for feed intake have been undertaken (de Haas et al., 2015) and SNP effects on each country's scale were generated. Results showed a benefit from sharing of phenotypic and genomic information, especially in populations where the phenotypic information was lacking. Interest in Ireland is intensifying on the potential of precision genomic matings especially as part of the national sire advice algorithms.

GENOMIC EVALUATIONS IN BEEF

Past. The initial analysis in 2013 with 4,233 high density genotypes from multiple beef breeds revealed an insufficient population size to derive meaningful genomic predictions. In some instances a negative correlation existed between genomic predictions and progeny-based predictions when the breed in the validation dataset was not included in the reference dataset. A considerably large dataset of phenotyped and genotyped cattle was necessary to implement an accurate multi-breed genomic selection program. With an expectation of changing parentage testing in cattle from microsatellites to SNPs, breed societies were requested to genotype all male calves using the IDB panel in 2014. Considerable transfer of germplasm exists between dairy and beef herds in Ireland.

Present. Funding from the EU to Irish farmers has, for the last 5 years, been conditional on the recording of sire of the calf born and additional phenotypic information; it is a legal requirement to record the dam. In 2014, farmers were also required to genotype at least 15% of their cow herd; animals were optimally selected from the national database to aid in the derivation of genomic predictions – selection was based on genomic diversity, phenotypic diversity and information content (http://www.icbf.com/wp/wp-content/uploads/2014/05/Selection-of-animals-for-use-in-beef-genomic-selection-program.pdf). Within farm, natural mating sires were prioritised. Following edits, 105,561 genotypes imputed to higher density, were available on AI, pedigree and commercial animals. The reliability of genetic evaluations for a series of linear type traits increased when a one-step genomic evaluation was undertaken (Figure 2). Within breed correlations between the genomic EBVs and progeny based EBVs varied from 0.51 to 0.73. No difference existed in predictive ability between high density or 50,000 SNPs.

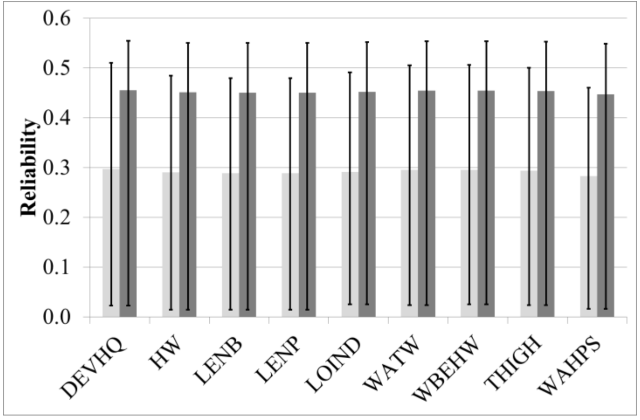

Figure 2. Mean reliability of young bulls based on pedigree index (light bar) and genomic predictions (dark bar) for a selection of type traits; min and max represented as error bars.

Future. Focus is on difficult to measure traits (e.g., feed intake and meat quality); for example it is hoped to genotype and phenotype over 15,000 animals for meat quality in the next 24 months. Because of the short shelf-life of minced-meat, amplicon sequencing with several hundred SNPs for the determination of Angus breed proportion is under investigation to quicken turn-around time for genotyping. The Irish dairy herd is expected to expand by approximately 30%; as reproductive performance improves with selection on the national dairy breeding objective, the scope for mating dairy cows with beef semen is greater. Hence, a breeding program for beef bulls to use on dairy cows has begun.

GENOMIC EVALUATIONS IN SHEEP

Present. Funding to genotype 11,400 sheep exists. In total, 363 highly unrelated sheep from 18 different “breeds” in Ireland have been genotyped on the Illumina high density ovine beadchip. This is to establish breed differentiation and quantify the potential of across breed genomic predictions. Following discussions on whether to genotype commercial crossbred animals with good phenotypes or purebred pedigree animals, it was decided to genotype pedigree animals at the top of the breeding pyramid to, amongst other reasons, maximise the likelihood of genotyping continuing beyond the lifetime of the project. Ear biopsies of all pedigree animals (i.e., rams, ewes and lambs) are currently being collected from participating farms who record information in the national database. Influential parents will be genotyped using the Illumina high density beadchip, less influential parents will be genotyped using the Ovine50 beadchip and the remaining parents will be genotyped using a lower density panel being developed by an international consortium.

Future. A multi-breed genomic evaluation will be attempted. The potential usefulness of an ultra-low density, ultra-low cost genotype panel for parentage assignment (in commercial or progeny test animals) and possible screening for some structural mutations of interest (e.g., scrapie) will also be investigated. Sharing of Texel genotypes with the UK has begun. Suffolk EBVs from both the UK and Ireland have also been exchanged. Table 2 summarises the correlations between EBVs and inferred genetic correlations (following adjustment for accuracy of the respective national EBVs; Calo et al., 1973). The strong correlations that exist between some traits suggest a possible advantage in augmenting the accuracy of genomic evaluations by using the (weighted) UK EBVs as correlated traits in the Irish genomic prediction algorithms. No investment has yet been made in sequencing of sheep in Ireland.

Table 2. Number of animals (n), correlation between EBVs (r_{EBV}) and inferred genetic correlations (r_g) for a series of traits between the UK and Ireland

Trait	n	r_{EBV}	r_g
8-wk weight	222	0.254	0.937
Weight at scanning	222	0.190	0.648
Ewe weight	222	0.012	0.073
Scanned muscle depth	210	0.075	0.258
Scanned muscle fat	210	0.175	0.666
Number of lambs born	215	0.450	0.993

LESSONS LEARNT AND FUTURE PLANS

Not having a national repository for biological samples or DNA bank was a short-sight. Since 2010, two semen samples have to be provided, free-of-charge, to the ICBF for all AI bulls used in Ireland. The decision to develop a custom genotype platform was the correct decision; it did not require considerable effort (approximately 12 weeks to develop although validation of genotypes for some mutations is on-going), or alignment to any one genotyping platform or service provider; it did provide greater flexibility on what variants to include, and the cost per genotype was lower than could be provided by any other service provider with an available custom genotype platform. The list of SNPs included on the international dairy and beef chip is available from the author.

The development of genomic selection in the Irish dairy population cost approximately AUS$0.55 m (including research personnel but excluding the required IT developments for reporting); this was predominantly funded by competitive research grants and bilateral sharing of genotypes. Genomic selection has delivered AUS$23m to the dairy sector since 2009. Genomic selection in sheep (excluding the cost of phenotyping and IT developments) will cost approximately AUS$0.96 m almost exclusively from a competitive research grant. Genomic selection in beef has cost €5.7 m, acquired from competitive research grants (€0.75 m) or EU farmer support mechanisms. Although it does require public investment, retaining public ownership of genomic proofs and the free access to genomic predictions is a considerable advantage. Sharing of genotypes with minimal conditions is also key to success.

Like mobile phones and computers, it appears that the cost of genotyping using arrays is unlikely to reduce considerably in the near future but instead the quantity of SNPs to be included will increase. This will avoid the necessity to impute, improving computing time and accuracy.

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