Increased genetic gains in sheep breeding programs from using female reproductive technologies combined with genomic selection.

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ABSTRACT: Reproductive technologies such as MOET and JIVET can boost rates of genetic gain but they can also increase rates of inbreeding. We used optimal contribution selection to explore these potential benefits while managing inbreeding and we evaluated the synergies that exists between genomic selection (GS) and reproductive technologies. When selecting for a trait that can be measured early in life and on both sexes, GS combined with MOET and JIVET gave 46% more gain. When selecting on a late measured trait, use of MOET was not beneficial without GS. However, breeding programs combining GS with MOET or MOET + JIVET had increased genetic gain of 39% and 83%, respectively, while the inbreeding was limited to a 10% increase over 20 years. This provides evidence that reproductive technologies and genomic selection can be useful tools for nucleus breeders.
Keywords: MOET; JIVET; Genomic selection; Optimal contribution selection

Introduction

Reproductive technologies are used by breeders to accelerate genetic gain in breeding programs. These technologies allow higher selection intensity in males and females (multiple ovulation and embryo transfer – MOET; juvenile in vitro fertilization and embryo transfer – JIVET) and the latter also allows breeding from a younger age.

There are some limitations to using female reproductive technologies, especially when applying them to very young breeding animals. Selection of young females for MOET or JIVET has to be based on lowly accurate estimated breeding values (EBVs) and EBVs among sibs are highly correlated due to the high emphasis on common family information. However, in conjunction with marker assisted selection (Meuwissen and Goddard (1996)), MOET and JIVET could become more viable as EBVs become more accurate at a younger age and are less correlated among relatives. Therefore, increased rates of genetic gain can be achieved while keeping inbreeding at a sustainable level.

Previous studies have explored the benefits of using reproductive technologies with Horton (1996) simulating a 3% increase in genetic gain with a comparatively high inbreeding rate of 8% increase per year in a closed Merino flock implementing artificial insemination (AI). Brash et al. (1996) showed that in a closed nucleus Merino stud MOET can increase rates of genetic gain by 22% per year. However, these additional gains also resulted in a 50% increase in inbreeding rate. Pryce et al. (2010) used a deterministic model for a dairy breeding program to show

210% more genetic gain when using JIVET and genomic selection compared to a proven sire AI program, but with an increase of inbreeding rate by 165%.

Clearly, such benefits of reproductive technologies are unrealistic, as the associated increase in rates of inbreeding are not sustainable. Optimal contribution selection methods focus on balancing long-term genetic merit and genetic diversity among animals selected to become parents (Wray and Goddard (1994)) where controlling the latter is equivalent to controlling the rate of inbreeding (Meuwissen (1997)). Nielsen et al. (2010) demonstrated the benefits of optimal contribution selection using both BLUP and genomically enhanced EBVs (GEBVs) in aquaculture breeding programs with 80% higher genetic gain while maintaining inbreeding levels at sustainable levels. Clark et al. (2013) found up to 16% increase in selection differential at the same level of co-ancestry among bulls when selecting on GEBVs versus traditional BLUP selection.

This paper aims to explore the potential benefit of MOET and JIVET in sheep breeding programs while managing inbreeding and comparing with and without genomic selection. We compare selection for early and late measureable traits and various levels of inbreeding restrictions. We use optimal contribution selection and optimally allocate matings to using either AI or natural breeding (AI/N), MOET or JIVET.

Materials and Methods

Simulation. We used stochastic simulation to model a closed nucleus breeding program generating 250 progeny per year. For each scenario we generated a base population of unrelated animals, and subsequently established a breeding program with overlapping generations. Phenotypes for a single trait were simulated with a heritability of 0.3. We simulated a trait that could be measured within the first year (before sexual maturity) and compared that scenario with a scenario where a trait could only be measured after two years. Each year, EBVs were estimated using Best Linear Unbiased Prediction (BLUP). Each breeding program was run for 20 years and replicated 75 times.

Optimal Contribution Selection. Optimal contribution selection was used to maximise genetic gain while maintaining genetic diversity. Using Wray and Goddard's (1994) formula, genetic merit (M) was balanced with co-ancestry (C), where, M= x'b, b is a vector of EBVs and x is

a vector of genetic contributions. Inbreeding rates were managed by penalizing the average co-ancestry among selected animals; $C=\lambda x'Ax$, where A is an (n x n) relationship matrix among candidates and λ is the penalty to restrict inbreeding. Price and Storn's (1997) evolutionary algorithm was used to find optimal solutions for M + C. Various values of λ were used to explore a 'frontier' of optimal selection outcomes which resulted in different levels of inbreeding and genetic gain.

Breeding Programs. In this study, three breeding programs were compared: 1) AI/N mating only, 2) AI/N + MOET and 3) AI/N + MOET + JIVET. In each breeding program AI could be used and therefore, depending on the inbreeding restriction, a single male could be assigned to all dams (200+). Females however were mated once to a male if they were assigned AI/N or MOET matings. Juvenile females were assigned three matings (due to oocyte numbers recovered and individual oocyte mating ability in IVF process) if they were selected to JIVET. Males were eligible for mating once they were seven months old. Ewes in AI/N or MOET programs were also only eligible once they were seven months old. Ewes in the JIVET program were eligible within their first month of age. If any individuals did not get selected in a breeding program, they were culled after 2 years. However, in the JIVET program, if a ewe was not selected as a lamb it was again eligible for selection at 7 and 18 months of age which is the same as AI/N and MOET programs. Any animal over five years old was culled. A mortality rate of 10% was applied each year. The probability of producing a certain number of live progeny for AI/N, MOET and JIVET is summarized in Table 1.

Table 1: Probability of producing a certain number of live progeny per female per mating for the various reproductive methods

Prog	AI/N[^a]	AI/N[b]	MOET[b]	JIVET[c]
0	0.40	0.10	0.10	0.25
1	0.58	0.70	0.05	0.05
2	0.02	0.20	0.05	0.18
3			0.15	0.18
4			0.25	0.10
5			0.15	0.10
6			0.13	0.07
7			0.07	0.04
8			0.05	0.03
Ave	0.62	1.1	4.02	8.37*

[^]Chance of ewe at 7 months age having a lamb
[a] Bunter and Brown (2013)
[b] Gibbons and Marcella (2011)
[c] Armstrong et al. (1997)
*predicted average of total progeny of 3 JIVET matings

Genomic Selection. Each of the six breeding program x trait combinations were using GEBVs instead of EBVs. Genomic information was simulated by generating three "pseudo progeny" at birth for selection candidates, therefore giving them a modest increased EBV accuracy at a younger age.

Results and Discussion

In all breeding programs, the highest genetic gain coincided with the highest level of inbreeding (Figure 1-2). This is achieved when applying no penalty on inbreeding. When selecting for an early measured trait there is little difference between AI/N + MOET and AI/N + MOET + JIVET breeding programs without genomic selection if inbreeding is restricted below 20% (Figure 1). The absence of benefit using JIVET is likely caused by inaccurate selection and a high correlation among EBVs of full siblings for JIVET as they only receive a parent average breeding value. With genomic selection an increase of 46% genetic gain is observed in AI/N + MOET + JIVET (GS) at 10% inbreeding after 20 years compared to the same scenario without genomic selection (Figure 1). There is little benefit to using genomic section with AI/N and/or MOET when a phenotype is measured and EBV calculated before the earliest possible selection (Figure 1).
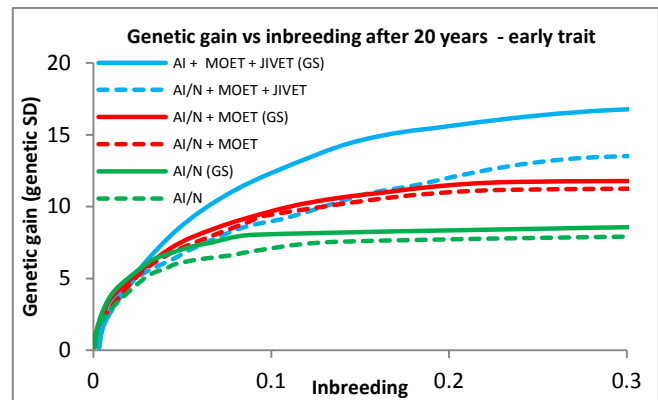

Figure 1: Genetic gain and inbreeding after 20 years in early measured trait using reproductive technologies and genomic selection
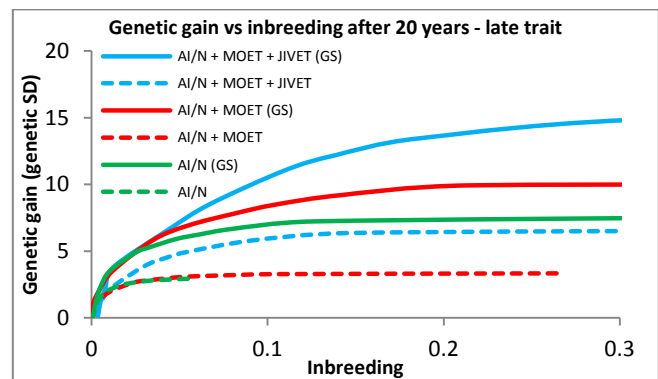

Figure 2: Genetic gain and inbreeding after 20 years in late measured trait using reproductive technologies and genomic selection

By contrast, when selecting for a late measured trait there is no difference in genetic gain between breeding programs AI/N and AI/N + MOET in the absence of genomic selection (Figure 2). This is likely due to the accuracy of EBVs being too low at the time of first selection. The AI/N + MOET + JIVET program shows a 147% increase in genetic gain over AI/N + MOET programs, both without genomic selection, which should be mainly attributed to a decreased generation interval. With the addition of GS to each breeding program for the late measured trait, large additional genetic gains were achieved, with 178%, 239% and 79% for AI/N (GS) AI/N + MOET (GS) AI/N + MOET + JIVET (GS), respectively, at 10% inbreeding after 20 years (Figure 2) compared to the same breeding program without GS. At this level of inbreeding we can also see that AI/N + MOET + JIVET (GS) is 27% higher than AI/N + MOET (GS). The large gains are attributed to increased accuracy of EBVs at selection and lower correlation between EBVs of superior siblings. We mimicked genomic selection with by giving young animals 3 progeny records. Similar to a genomic test, this source of information increases accuracy by explaining some of the within family variation due to Mendelian sampling (Clark et al. (2013))

Results in this study showed that when selecting for a late measureable trait a 22% higher annual genetic gain at 10% inbreeding after 20 years can be achieved when using MOET and JIVET combined with genomic selection when compared to AI/N. Pryce et al. (2010) found a 210% higher genetic gain comparing JIVET programs to traditional progeny test when selecting for a sex-limited trait. The large difference is mainly due to the different rate of inbreeding that was allowed. We used optimal contribution selection rather than truncation selection and we maintained rates of inbreeding at a more sustainable level.

This study optimally allocated females to enter a reproductive technology. Table 2 demonstrates how reproductive technologies are allocated in the different programs when inbreeding is restricted to 0.5% increase per year. In AI/N + MOET – late trait, a large proportion of ewes are assigned MOET with no genetic benefit (Figure 2). Apparently, the allocation of females to MOET did not increase genetic gain. The high MOET allocation was possible because the cost of implementing such technologies was not taken into account was possible because the cost of implementing such technologies was not taken into account. We observed a shift in proportion (larger) of JIVET assigned when GS is used in JIVET breeding programs at the expense of MOET (Table 2). This is expected due to the higher accuracy of the EBVs calculated for juvenile ewes.

Table 2: Proportion of ewes assigned to mating type in each breeding program with inbreeding restricted to 10% after 20 years

	AI/N	MOET	JIVET	TOTAL[*]
Early Trait				
1	0.33	0.25	0.42	94.45
2	0.53	0.40	0.07	95.34
3	0.52	0.48		117.58
4	0.50	0.50		116.13
Late Trait				
1	0.51	0.19	0.30	98.23
2	0.63	0.29	0.08	109.62
3	0.49	0.51		114.37
4	0.48	0.52		118.11

1 = AI/N + MOET + JIVET (GS) 2 = AI/N + MOET + JIVET 3 = AI/N + MOET (GS) 4 = AI/N + MOET
* All total ewe numbers SEM <1.2

Conclusion

Reproductive technologies combined with genomic selection can substantially   enhance rates of genetic gain without compromising inbreeding. In the absence of genomic selection, application of MOET or JIVET does not result in much additional genetic gain if inbreeding is restricted to 0.5% per year. Genomic selection gives an increase in rates of genetic gain but only when applying JIVET, in the case of an early measured trait, and in all cases when selecting for a late measured trait.

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