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Complete List of Authors:	Granleese, Tom; University of New England, Animal Science Clark, Samuel A; University of New England, Animal Science Van der Werf, Julius
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Genotyping strategies of selection candidates in livestock breeding programs

T. Granleese[1,2*], S.A. Clark[1,2], J.H.J. van der Werf[1,2]

[1]Sheep Cooperative Research Centre, Armidale, Australia 2351

[2] School of Environmental & Rural Science, University of New England, Armidale, Australia 2351

* corresponding author: Phone: +61 2 6773 2569; Email: tgranle2@une.edu.au

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Abstract

Benefits of genomic selection in livestock breeding operations are well known particularly where traits are sex-limited, hard to measure, have a low heritability and/or measured later in life. Sheep and beef breeders have a higher cost:benefit ratio for genomic selection compared to dairy. Therefore strategies for genotyping selection candidates should be explored to maximise the economic benefit of genomic selection. We investigated via simulation the optimal proportion of male selection candidates to be genotyped via truncation selection using a selection index that contained an easy and early in life measurement (such as post-weaning weight) as well as a hard to measure trait (such as intra-muscular fat). We also evaluated the optimal proportion of female selection candidates to be genotyped in breeding programs using natural mating and/or artificial insemination (NatAI), multiple ovulation and embryo transfer (MOET) or juvenile *in vitro* fertilisation and embryo transfer (JIVET). For NatAI and MOET breeding programs females were selected to have progeny by 2 years of age, while one month old females were required for JIVET. Genomic testing the top 20% of male selection candidates achieved 80% of the maximum additional benefit from genomic selection when selection of male candidates prior to genomic testing had an accuracy of 0.36, while 54% needed to be tested to get the same benefit when the prior selection accuracy was 0.11. To achieve 80% of the maximum additional benefit in female selection required 66%, 47% and 56% of female selection candidates to be genotyped in NatAI, MOET and JIVET breeding programs, respectively. While JIVET and MOET breeding programs achieved the highest annual genetic gain, genotyping male selection candidates provides the most economical way to increase rates of genetic gain facilitated by genomic testing.

Introduction

The use of genotyping arrays with many genetic markers has become common place in animal breeding. Meuwissen *et al.* (2001) showed that the resulting genotypes can be used to estimate breeding values and several studies have demonstrated the theoretical and realised benefits of genomic selection (GS) in breeding programs. Schaeffer (2006) demonstrated that benefits in dairy breeding programs could be significant given the sex-limited expression of most traits and long generation intervals. GS was quickly implemented in dairy and made most dairy bull screenings by progeny testing a concept of the past (Pryce *et al.* 2012). The cost of genomic testing is considerably less than that of progeny testing and AI companies can afford to genotype many bull selection candidates with less thought for cost (Boichard and Ducrocq 2015). However genotyping dairy cows usually comes at the cost of the breeders (Pryce and Daetwyler 2012). In sheep and beef, the benefits are considerably less compared to dairy and the cost of investment in phenotyping and genotyping selection candidates are usually absorbed by the individual breeders (Amer *et al.* 2007). Therefore, the cost of genotyping all animals in a breeding program can be a significant economic consideration in the uptake of GS in the sheep and beef cattle industry.

Van der Werf *et al.* (2014) and Horton *et al.* (2015) assessed cost effectiveness of strategies to genotype selection candidates in sheep. Both studies found that genotyping 20% of male selection candidates can return up to 80% of the potential additional benefit achieved if all males were genotyped), assuming young rams were selected for genotyping based on some prior knowledge about their genetic merit. Van der Werf *et al.* (2014) also discussed that in the case of a lower correlation between prior knowledge and breeding objective, e.g. in indexes for multiple traits with unfavourable correlations between them, more candidates would need to be

genomically tested to achieve the same proportion of additional benefit. Breeding objectives increasingly contain traits that are hard-to-measure, e.g. net feed intake, fertility and eating quality (Swan *et al.* 2015), and genotyping strategies should be investigated in the light of such objectives. When deciding on the proportion of animals to be genotyped, the amount of information that is known about selection candidates prior to genotyping is important, and this will depend on the age at selection. For example, screening candidates for genomic testing can be based on a pre-measurement genomic test where animals are screened on breeding values which have no performance records. Alternatively, post-measurement genomic testing can be based on breeding values that include measurements from some traits in the breeding objective.

Studies by Van Eenennaam *et al.* (2011) and Horton *et al.* (2015) demonstrated the value of increased genetic gain, facilitated by genomic selection of males and females. Others have demonstrated the strong synergies with genomic selection and female reproductive technologies (Pryce *et al.* 2010; Granleese *et al.* 2015). However, these studies assume all selection candidates are genotyped. Investigation into optimisation of genotyping strategies for female selection candidates when using reproductive technologies is warranted.

This paper aims to investigate genotyping strategies for pre-measurement and post-measurement selection of male selection candidates using a multi-trait index with a hard to measure trait to compare benefits from various proportions selected. This paper also investigates genotyping strategies for female selection candidates in breeding programs implementing natural mating or multiple ovulation and embryo transfer (MOET) or juvenile *in vitro* embryo production and transfer (JIVET).

Methods

Simulation

Stochastic simulation was used to model closed breeding schemes with 500 progeny born per year. For each scenario we generated a base population of unrelated animals, and subsequently established a 15-year breeding program with overlapping generations. The genetic values for the base individuals were simulated using the formula:

$$a_{ij} = L_i' \cdot z_{1j}$$

where a_{ij} is the breeding value for trait i for animal j and L_i is the ith row of a lower tridiagonal matrix resulting from a Cholesky decomposition of the genetic (co)variance matrix for n traits and z_1 is an n x 1 vector with independent standard normal random deviates referring to animal j. Phenotypes for base animals were calculated using $p_{ij} = a_{ij} + e_{ij}$ where e_{ij} was simulated as:

$$e_{ij} = C_i' \cdot z_{2j}$$

where z_{2j} is another vector with independent random variables drawn from a standard normal distribution z~ N(0,1) and C_i' is the ith row from the Cholesky decomposition of the environmental (co)variance matrix.

The true breeding values for the subsequent generations were obtained using the following equation: $a_{ij} = ((a_{sij} + a_{dij})/2) + MS_{ij}$ where a_{si} and a_{di} are the breeding values for trait i of animal j's sire and dam, respectively. MS_{ij} is the Mendelian sampling effect for trait i and individual j simulated as $MS_{ij} = \sqrt{(.5(1-\bar{F}))} \cdot L_i' \cdot z_3$ where $\bar{F}$ is the average inbreeding

coefficient of an individual's parents. The number of breeding females required in each breeding program is defined in Table 1.

The breeding objective was defined with two traits with equal value per unit of genetic standard deviation. One trait was measured early-in-life on all candidates while the second trait was not measured on any selection candidates (Table 1), but there was assumed sufficient data for a genomic prediction. Both traits had a heritability of 0.4 and a negative genetic correlation between them of -0.1.We did not model genomic relationships and information due to genotyping was included as a pseudo phenotype for genotyped animals for the genomic trait. These pseudo phenotypes were deterministically simulated for each animal as genomic breeding values for each trait following the method of Dekkers (2007). The genomic breeding value for each trait was assumed to have a heritability of 0.999 and a correlation r_i to the actual breeding value of trait i, where r_i is the assumed accuracy of the genomic breeding value (0.5 for both traits). The assumed correlation between GBV trait 1 and GBV trait 2 was calculated as per Dekkers (2007).

Estimating Breeding Values

Each year in the simulation program, EBVs were estimated using multiple trait Best Linear Unbiased Prediction (BLUP) using the ASREML 3.0 program (Gilmour *et al.* 2009). A 4-trait model was used. The model assumed was:

$$y = 1\mu + Za + e$$

where y is a vector of phenotypes with animals ordered within trait, 1 is a vector of ones, μ is the mean of the base population , Z is a design matrix allocating records to breeding values, a is a vector of breeding values with $V(a) = \mathrm{G} \otimes \mathrm{A}$ where G is an n x n genetic covariance matrix for

the 4 traits in the analysis, with A the numerator relationship matrix and $\otimes$ denotes the Kronecker product matrix operation, and e is a vector of residuals. Information from all previous generations were used in the estimation of EBVs.

Multi-trait index values were calculated for each individual animal as

$$\sum_{i=1}^{n} v_i \hat{a}_i$$

where v_i is the economic value of trait i and $\hat{a}_i$ is the estimated breeding value. The economic values for the third and fourth "genomic traits" were zero.

Genomic testing scenarios

In all testing scenarios potential genomic testing candidates were sorted based on index breeding values. Table 1 summarizes the scenarios indicating whether either males or females were genotyped, and whether a phenotype was available prior to sorting candidates for genotyping. Male and female genotyping strategies were evaluated separately as total gain is a simple sum of the gain achieved in the male and female selection pathways. The percentage of animals selected for genotyping ranged from zero percent (control) to 100 percent (maximum benefit) in all testing scenarios.

Genomic testing of males

Two breeding programs were simulated testing male genotyping strategies. In the first breeding program male candidates to be genomically tested were sorted based on an EBV that did not include an own phenotypic measurement on Trait 1 (GT-M) while in the second breeding program Trait 1 phenotypic information on the candidates were included in the EBVs (GTP-M). No female selection candidates were genotyped in these two scenarios, and no female

reproductive technologies were used. At the end, ten sires selected out of 10 current sires and 250 male selection candidates that became available each year for selection.

Genomic testing females in breeding programs

Three breeding programs scenarios were compared where female reproductive technologies were used and females were selected for genomic testing and subsequently for breeding. In these scenarios, males were not genotyped. Females had their first progeny at two years of age for natural mating (GTP-F) or MOET (GTP-MOET) breeding programs. They also had a phenotypic measurement of Trait 1 in their EBVs prior to sorting candidates to genomically test. In the JIVET breeding program (GT-JIVET), females did not have Trait 1 measured as their first progeny were born by the time they were one year of age. Numbers of dams in each breeding program can be observed in Table 1 with MOET and JIVET matings following similar methods to Granleese *et al.* (2015). At the end, five hundred dams (or 125 or 63 in the case of MOET or JIVET) were selected out of 500 current dams and 250 female selection candidates that became available each year (Table 1).

Results

Overall rates of genetic gain vs proportion genomic tested in the two different breeding programs of males are shown in Figures 1 and 2. Rates of genetic gain vs proportion genomically tested are then compared between the three female breeding programs (Figures 1 and 3). Both male and female breeding programs are then compared with each other demonstrating the different gains and efficiencies between each breeding program (Figures 1-3). Finally individual trait responses to breeding program GTP-M are analysed as proportion of male selection candidates are genomic tested (Figure 4).

Genotyping strategies in male selection candidates

The maximum benefit of genotyping all male selection candidates was 42% extra gain compared to no male selection candidates genotyped for both of the GT-M and GTP-M programs (Figure 1). However, significantly fewer male selection candidates needed to be tested in GTP-M compared to GT-M to obtain the same additional benefits of genomic testing in male selection candidates (Figure 2). The accuracy of index of potential candidates prior to genomic testing was on average 0.11 and 0.30 for the GT-M and GTP-M scenarios, respectively (Table 2).

Genotyping strategies in female selection candidates in different breeding programs

The maximum benefit of genomic selection in breeding programs GTP-F, GTP-MOET and GT-JIVET was 16%, 33% and 68% additional genetic gain, respectively (Figure 1), which occurred if all females would be genotyped. When all female selection candidates were tested, genetic gain was 21% and 57% higher in GT-JIVET breeding programs than GTP-MOET and GTP-F breeding programs, respectively. GTP-MOET breeding programs (where 125 females are selected per year) required the lowest proportion of females to be genotyped to provide 80% of the benefit of genomic testing with 47% of candidates tested (Figure 3). This is compared to 65% in natural mating (GTP-F) programs who used post-measurement genomic testing with 500 females selected per year (Figure 3). Despite only needing 64 females selected per year (half to MOET) in JIVET breeding programs, the GT-JIVET required 56% of selection candidates needing genomic testing to provide 80% of the maximum benefit of genomic selection (Figure 3). While JIVET breeding programs significantly out-perform MOET and natural mating programs when 100% of selection candidates are genotyped, MOET breeding programs have higher annual genetic gain until more than 22% of selection candidates are genotyped in each breeding program (Figure 1).

Comparison of genotyping male and female selection candidates

When none of the selection candidates were genomically tested there was no difference in rates of genetic gain between any of the natural mating breeding programs (GT-M, GTP-M and GTP-F) (Figure 1). However, GTP-MOET and GT-JIVET achieved 18% and 14% higher rates of annual genetic gain compared to the natural breeding programs without genomic testing, respectively (Figure 1). When all selection candidates were genomically tested, GTP-MOET and GT-JIVET resulted in 13% and 32% higher rates of annual genetic gain compared to GTP-M (Figure 1). This demonstrates that MOET breeding programs in this study lost some of its advantage using genomic testing, whereas JIVET breeding programs increased its advantage as genomic testing increased. When all selection candidates are genomically tested in GTP-M and GTP-F, GTP-M resulted in genetic gain 24% higher (Figure 1) hence male selection benefits relatively more from genomic testing than female selection. The difference between proportion genotyped and proportion of benefit received is not as big when comparing GT-JIVET vs GTP-MOET (Figure 3) to GT-M vs GTP-M (Figure 2) due to 8 and 4 progeny born per dam for JIVET and MOET, respectively. Despite lower selection accuracies in JIVET the selection intensity is double for dam when comparing JIVET to MOET.

Rates of gain of individual traits vs number candidates genomically tested

Relative rates of gain in the two simulated traits changed as more selection candidates were genomically tested. With no genomic testing gains in the measured trait were highest, while the unmeasured trait were lowest (Figure 4). The negative gains in the unmeasured trait are attributed to no phenotype being available on selection candidates on the traits and a slightly negative and unfavourable genetic correlation (-0.1) between the two traits. As the proportion of selection candidates that are genomically tested increases, the annual rate of gain decreases for

the measured trait by 10% when comparing no males genomically tested vs all males genomically tested (Figure 4). However, the unmeasured moves from -.027 to 0.094 standard deviation gains annually when none and all males are genomically tested, respectively (Figure 4). These gains in the unmeasured trait and decrease in the unmeasured trait is caused by more information known on the unmeasured trait and the antagonistic relationship between the two traits.

Discussion

Genomic testing male selection candidates is the most cost effective method to increase rates of genetic gain when comparing the benefits to genomic testing females and/or using reproductive technologies. A higher proportion of the potential extra gain can be extracted from genomic testing a small proportion of male selection candidates, which is also due to the high selection intensity of the males, i.e. few males are ultimately selected, so the chance for the lower ranked males at stage 1 (before genotyping) to be selected at stage 2 (after genotyping) is low. Breeding programs using female reproductive technologies and/or genomic testing significantly increases annual rates of genetic gain. However, compared to male selection a larger proportion of females is still needed for breeding in either program. Moreover, a larger proportion of females needs to be genotyped to achieve most of the genotyping benefits. The optimal proportion to be genotyped depends strongly on the EBV accuracy before making decisions on who to genotype, i.e. whether some initial phenotypic information of selection candidates can be incorporated into breeding value estimation. Using some phenotypic information on the candidates provides a more accurate method of choosing selection candidates to genotype, compared to selecting candidates based on mid-parent breeding values alone. This discussion will explore these major points and look at the cost/benefit of such breeding program investments.

Van der Werf *et al.* (2014) deterministically simulated genomic testing with a similar selection index with a higher unfavourable correlation between measured and unmeasured traits, but lower genomic prediction accuracies of 0.3. They discuss that testing 20% of the youngest top male selection candidates were genotyped each year returned most of the maximum benefit of genomic testing. This proportion is determined by the accuracy of index and accuracy of added information on the selection candidates needing testing. Horton *et al.* (2015) also found that testing 20% male selection candidates is most profitable method of genotyping selection candidates where benefits are captured in lower tiers from the nucleus. Our stochastic simulation study confirmed these earlier results that were based on deterministic prediction. We found that lower efficiencies were observed in breeding programs with lower initial accuracy of EBVs when sorting out who to genomically test (GT-M) or with testing females due to lower selection intensities of females (GTP-F, GTP-MOET and GT-JIVET).

The importance of initial measurements when generating breeding values before making genotyping decisions on selection candidates has been demonstrated in our study. The GT-M program had no access to phenotypic measurement on selection candidates prior to screening for genomic testing resulting in less efficient sorting of potential genomic testing candidates due to lower index accuracies compared the GTP-M program. Table 2 displays the initial accuracies of selection candidates and the breeding program. Note that not only the accuracy, but also the information used impacts on selection decisions. When no phenotypic measurements on the selection candidates are included in the EBV calculations the ranking of candidates largely relies on family information leading to increased co-selection of relatives.

Despite the female selection candidates eligible for genomic testing having phenotypic measurements prior to sorting (GTP-F) and the same EBV accuracy as GTP-M males, the

maximum benefit of genomically testing females was 63% less than genomic testing of males (GT-M or GTP-M). Furthermore, 100% of female selection candidates need to be genotyped annually in the GTP-F scenario to receive the same additional benefit of genomic testing compared to testing 5% of male selection candidates in the GTP-M testing scenario (Figure 1). This is a fair comparison as zero genotyping in either scenario results in the same rates of genetic gain (Figure 1). In beef and sheep enterprises where profit-margins are comparatively low compared to dairy breeding programs, there would be little incentive in genotyping females selection candidates with the current cost of genotyping ($25 AU per test) due to the relatively small increase in genetic gain (Figures 1, 3 and 4). More female selection candidates are needed to be genotyped in natural breeding programs due to a low fecundity rates. Because the benefits are low, due to low selection intensity of females in natural or AI breeding programs. In this study we also evaluated breeding scenarios where both male and female selection candidates were genomically tested. We observed that the genetic gain and the additional benefits were additive and therefore strategies for males and females selection can be evaluated separately.

Traits that are "hard to measure" (HTM) have usually low EBV accuracy and are therefore difficult to improve, even if they have a significant weightings in the breeding objective. Typically selection candidates will then be ranked predominantly on traits with more information and higher accuracy. The problem becomes exacerbated when there is an unfavourable genetic correlation between traits. In absence of genomic selection there maybe a negative genetic gain in the hard to measure trait (Figure 4) despite a considerable economic weighting. However as information on HTM traits increases (e.g. via genomic testing) we can observe rates of gain to change considerably among breeding objective traits, as demonstrated in Figure 4. This was also illustrated by van der Werf *et al.* (2014) and discussed in further detail by Dekkers and van der

Werf (2014). The conditions under which trait changes are sensitive to accuracy increases are outlined by Van der Werf *et al.* (2018), with a greater sensitivity if the value of a standard deviation of the EBV is more similar. When hard to measure traits that rely on genomic information are more important in the breeding objective, a larger proportion is required to be genotyped as effectively the accuracy of predicting the breeding objective before genotyping is lower for such a case.

Breeding objectives in most species and breeds now have combinations of easy to measure and hard to measure traits (Meuwissen *et al.* 2016). With the advent of genomic selection and advances in measuring technology this study demonstrates the importance of increasing accuracy for hard-to-measure traits in breeding objectives. Not only does increasing information on traits increase rates of gain in unmeasured traits, but the increased accuracy is also mainly attributed to information about the within family variation allowing more within family selection which can decrease the rates of inbreeding (Caballero *et al.* 1996).

We can observe the effect of genomic testing on rates of inbreeding in the breeding program scenarios in Figure 5. Figure 5 shows that increasing the number of selection candidates genomically tested decreases rates of inbreeding. We observed inbreeding rates to decrease by 28%-30% when males were genomically tested (Figure 5). The decrease in inbreeding was 11% and 13% for MOET and JIVET programs (Figure 5). When using female reproductive technologies inbreeding rates increased significantly in this study. Without genomic selection, inbreeding rates in MOET and JIVET programs were up by 147% and 360%, respectively, when compared with natural mating breeding programs (Figure 5). This corresponds to previous studies investigating the benefits of reproductive technologies (Smith 1986, Brash *et al.* 1996, Pryce *et al.* 2010). Granleese *et al.* (2015) evaluated optimal contribution selection (Wray and

Goddard, 1994; Meuwissen, 1997) to maximise genetic gain under restricted inbreeding and found that the highest rate of genetic gain could almost be achieved with sustainable rates of inbreeding at 1% increase per generation. If optimal contribution were used, the optimal number of selection candidates to genomic test may alter due to potential constraints made on future co-ancestry.

Similar to Granleese *et al.* (2015), this study demonstrated the synergies that exist between genomic selection and reproductive technologies in multi-trait selection indexes. Using genomic selection in female selection candidates is common in dairy nucleus breeding programs. Genomic testing is used less in beef and is rare in sheep breeding programs. In this study we observed that using genomic testing can help increase rates of genetic gain when using reproductive technologies and costs can be kept limited when applying both genotyping and reproductive technologies to optimal proportions of females, as demonstrated by Granleese *et al*, 2015. It is usually not a practical or financially viable option to apply MOET and/or JIVET to the entire cohort of breeding females. The optimum number or candidates to genomic test will depend on initial EBV index accuracy. Despite our simulation giving JIVET females a higher selection intensity with an average of 8 progeny born per donor and MOET 4 progeny born, we can observe that MOET requires a lower optimal proportion to be genomic tested due to higher EBV index accuracies. It is generally not possible to record traits prior to generating EBVs with JIVET breeding programs given the selection candidates would need to have their DNA sampled at birth as oocyte collection happens at 4-12 weeks of age in sheep and cattle.

To consider the cost-effectiveness of genomic testing or reproductive technologies we can assume some costs to each breeding program, e.g. $20 per natural progeny, $100 per MOET or JIVET progeny, and $25 per genomic test, and determine cost required to achieve a genetic

change of one standard deviation of the breeding objective in a 500 progeny breeding nucleus. Figure 6 shows that the costs of breeding programs using reproductive technologies (GTP-MOET and GT-JIVET) with genomic testing of females to increase the genetic merit by 1 genetic standard deviation is almost 4 times higher than the cost of programs that do not use reproductive technologies (GTP-F). This increased cost is caused mostly by cost of reproductive technologies rather than the cost of genomic testing. When comparing MOET and JIVET breeding programs, the cost of generating genetic gain becomes more efficient for JIVET when more than 20% of selection candidates are tested (Figure 1). When looking at natural mating breeding programs (GT-M, GTP-M and GTP-F), we can observe in Figure 7 that there are optimal amounts of male selection candidates to genomic test in each breeding program when measuring dollars spent to increase the genetic merit by one standard deviation. If female genomic testing in artificial insemination/natural mating (GTP-F) is used as linkage between Figures 6 and 7 we can observe that although breeding programs with reproductive technologies are effective in driving extra rates of genetic gain, genomic testing males is a cheaper method of increasing rates of genetic gain. However, bulk amounts of MOET and/or JIVET may not be practical or affordable at nucleus level, but could be considered to contribute to some part of a nucleus breeding program. Granleese *et al.* (2018) demonstrated that optimal contribution selection can consider the cost of respective reproductive technologies in the objective function when selecting female candidates. Commercial mating programs like Matesel (Kinghorn 2011) can help optimise matings when using different combinations of reproductive technologies with natural mating and/or artificial insemination.

Conclusion

Genotyping proportions of selection candidates can return similar benefits of genomic selection of genotyping all selection candidates. Genomic testing male selection candidates is a more cost-effective way to increase rates of genetic gain rather than investing in female reproductive technologies with genomic testing. Increasing rates of genetic gain using reproductive technologies should only be considered when used in conjunction with genomic testing both male and female selection candidates.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

TG performed the simulation, analyses and drafted the manuscript. TG, SAC and JHJW conceived and designed the experiment. All authors have read and approved the final manuscript.

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References

Amer, P.R., Nieuwhof, G.J., Pollott, G.E., Roughsedge, T., Conington, J., Simm, G. (2007) Industry benefits from recent genetic progress in sheep and beef populations. *Animal* **1**(10), 1414-1426.

Boichard, D., Ducrocq, V., Fritz, S. (2015) Sustainable dairy cattle selection in the genomic era. *Journal of Animal Breeding and Genetics* **132**(2), 135-143.

Caballero, A., Santiago, E., Toro, M.A. (1996) Systems of mating to reduce inbreeding in selected populations. *Animal Science* **62**(3), 431-442.

Goddard, M. (2009) Genomic selection: prediction of accuracy and maximisation of long term response. *Genetica* **136**(2), 245-257.

Dekkers, J.C.M. (2007) Prediction of response to marker-assisted and genomic selection using selection index theory. *Journal of Animal Breeding and Genetics* **124**, 331-341.

Dekkers, J.C.M., van der Werf, J.H.J. (2014) Breeding goals and phenotyping programs for multi-trait improvement in the genomics era. In *'World Congress on Genetics Applied to Livestock Production*', 2014, Vancouver, Canada, p. 352.

Gilmour, A.R., Gogel, B.J., Cullis, B.R., Welham, S.J., Thompson, R. (2009) ASReml User Guide Release 3.0 VSN International Ltd, Hemel Hempstead, HP11ES, UK

Granleese, T., Clark, S.A., Swan, A.A., van der Werf, J.H.J. (2015) Increased genetic gains in sheep, beef and dairy breeding programs from using female reproductive technologies combined with optimal contribution selection and genomic breeding values. *Genetics Selection Evolution* **47**(1), 1.

Granleese, T., Clark, S.A., Kinghorn, B.P., van der Werf, J.H.J. (2018) Optimising female allocation to reproductive technologies considering merit, inbreeding and cost in nucleus breeding programs with genomic selection. *Journal of Animal Breeding and Genetics,* submitted.

Horton, B.J., Banks, R.G., van der Werf, J.H.J. (2015) Industry benefits from using genomic information in two- and three-tier sheep breeding systems. *Animal Production Science* **55**(4), 437-446.

Kinghorn, B.P. (2011) An algorithm for efficient constrained mate selection. *Genetics Selection Evolution* **43**(4).

Meuwissen, T.H.E. (1997) Maximizing the response of selection with a predefined rate of inbreeding. *Journal of Animal Science* **75**(4), 934-40.

Meuwissen, T.H.E., Hayes, B.J., Goddard, M.E. (2001) Prediction of total genetic value using genome-wide dense marker maps. *Genetics* **157**(4), 1819-1829.

Meuwissen, T.H.E., Hayes, B.J., Goddard, M.E. (2016) Genomic selection: A paradigm shift in animal breeding. *Animal Frontiers* **6**(1), 6-14.

Pryce, J.E., Goddard, M.E., Raadsma, H.W., Hayes, B.J. (2010) Deterministic models of breeding scheme designs that incorporate genomic selection. *Journal of Dairy Science* **93**(11), 5455-5466.

Pryce, J.E., Daetwyler, H.D. (2012) Designing dairy cattle breeding schemes under genomic selection: a review of international research. *Animal Production Science* **52**(3), 107-114.

Schaeffer, L.R. (2006) Strategy for applying genome-wide selection in dairy cattle. *Journal of Animal Breeding and Genetics* **123**(4), 218-223.

Swan, A.A., Pleasants, T., Pethick, D. (2015) Breeding to improve meat eating quality in Terminal sire sheep breeds. *Proceedings of Association for the Advancement of Animal Breeding and Genetics, 28th– 30th September* **21**, 29-32.

van der Werf, J.H.J., Banks, R.G., Clark, S.A., Lee, S.J., Daetwyler, H.D., Hayes, B.J., Swan, A.A. (2014) Genomic Selection in Sheep Breeding Programs. In *'World Congress on Genetics Applied to Livestock Production*', 2014, Vancouver, Canada, p. 352.

van der Werf, J.H.J., Banks, R.G., Dekkers, J.C.M. (2018) Optimizing multiple trait selection. In *'World Congress on Genetics Applied to Livestock Production'*, 2018, Auckland, New Zealand.

Van Eenennaam, A.L., van der Werf, J.H.J., Goddard, M.E. (2011) The value of using DNA markers for beef bull selection in the seedstock sector. *Journal of animal science* **89**(2), 307-320.

Figures

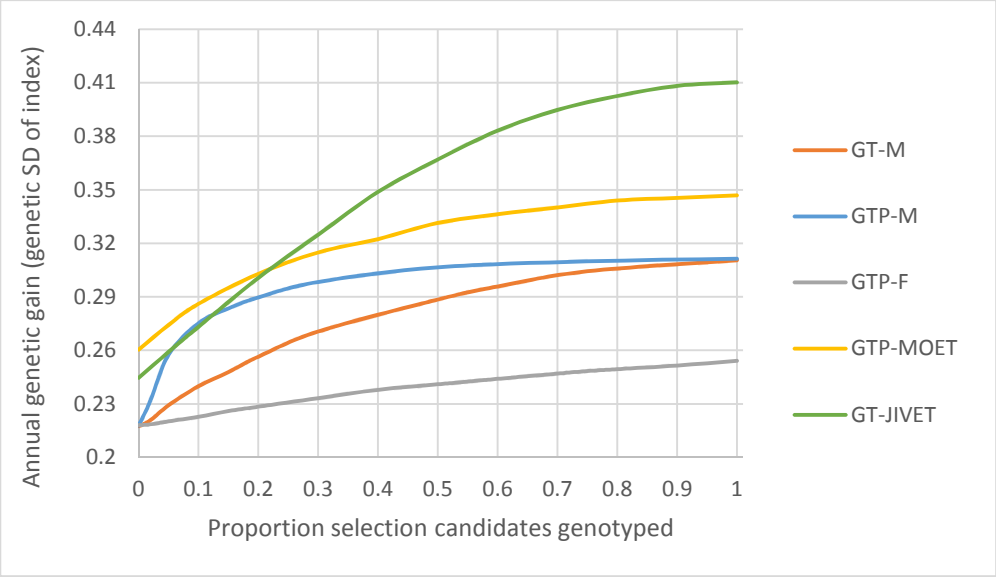

Figure 1: Annual genetic gain measured in genetic standard deviations in each scenario where increasing proportions of selection candidates are tested. SEM of all breeding programs are <0.007 genetic standard deviations

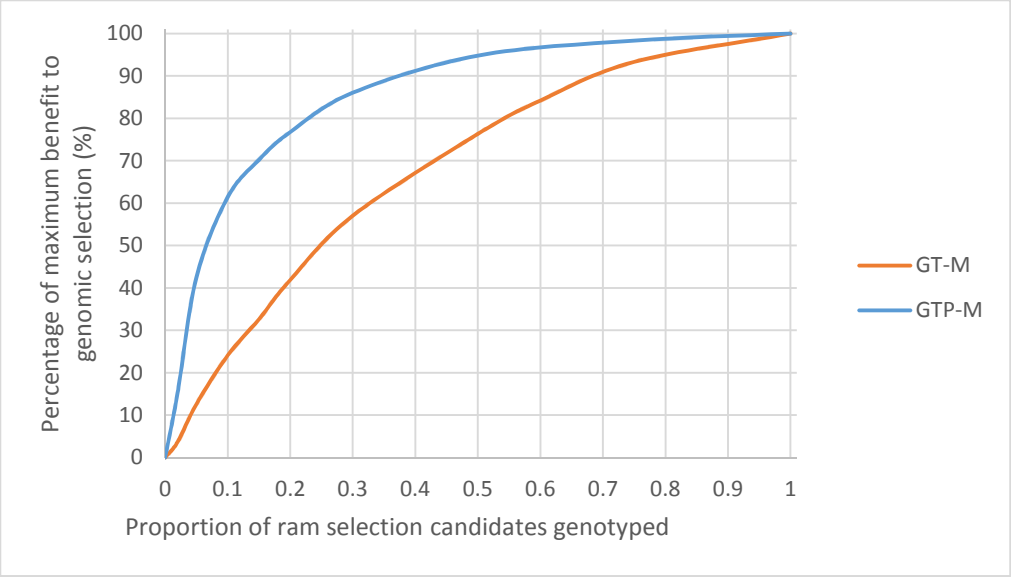

Figure 2: Proportions of the maximum benefit of genetic gain from genotyping male selection candidates. Note that 100% of genotyped selection candidates gives 100% of the benefit

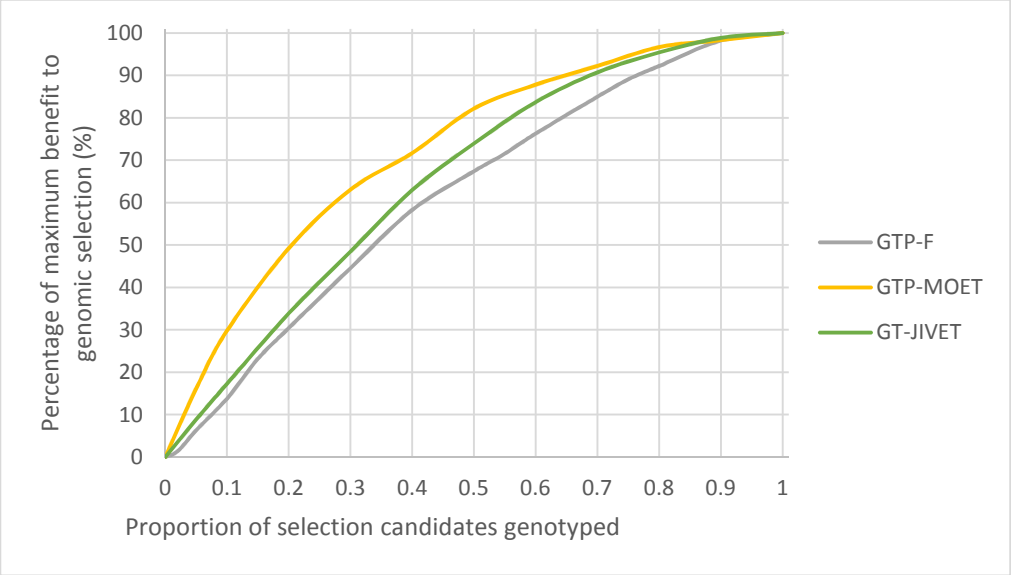

Figure 3: Proportions of the maximum benefit of genetic gain from genotyping female selection candidates. Note that 100% of genotyped selection candidates gives 100% of the benefit

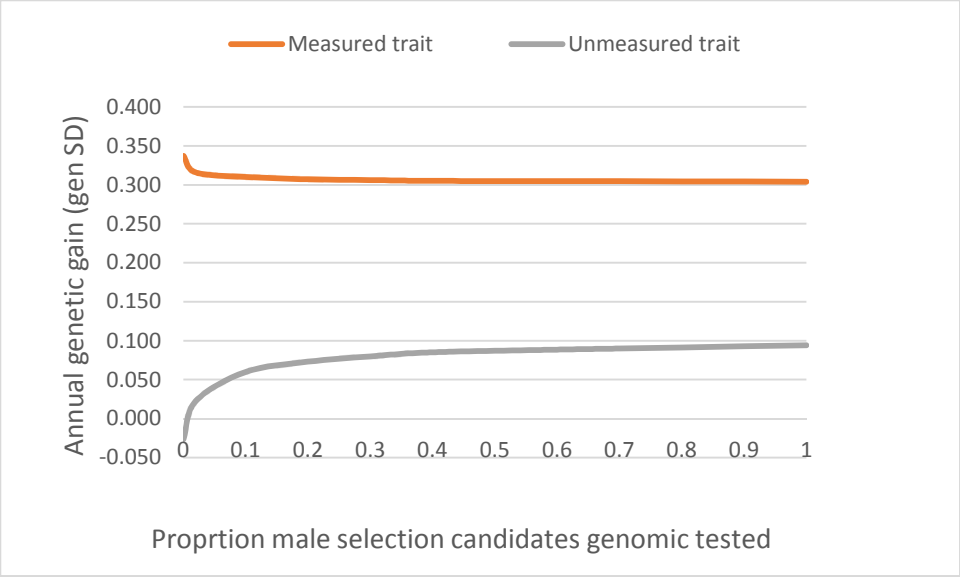

Figure 4: Annual genetic gain for the two individual traits (early measured and unmeasured trait) in response to number of male selection candidates genomic tested in post-measurement genomic selection (GTP-M)

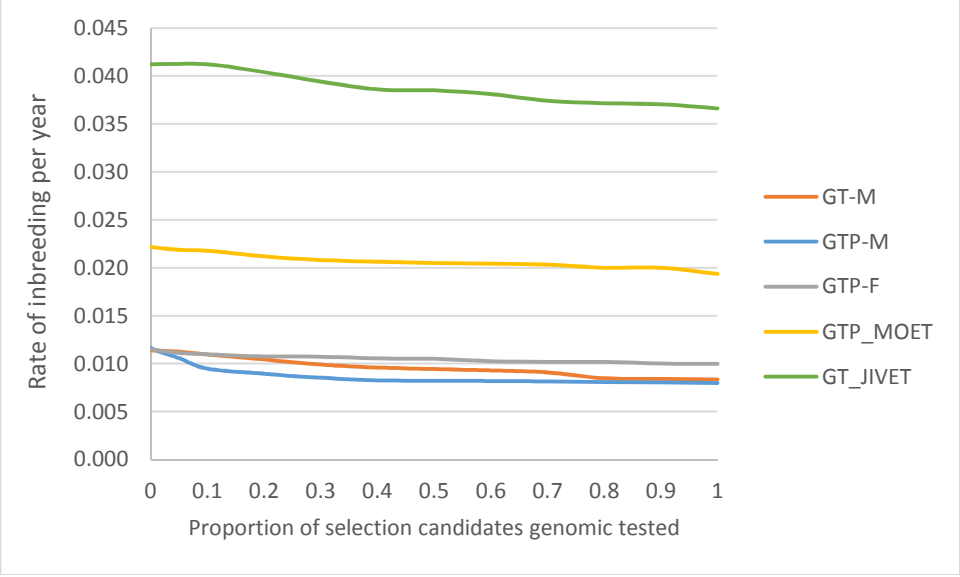

Figure 5: Annual increases of inbreeding of breeding programs vs proportions of selection candidates genotyped

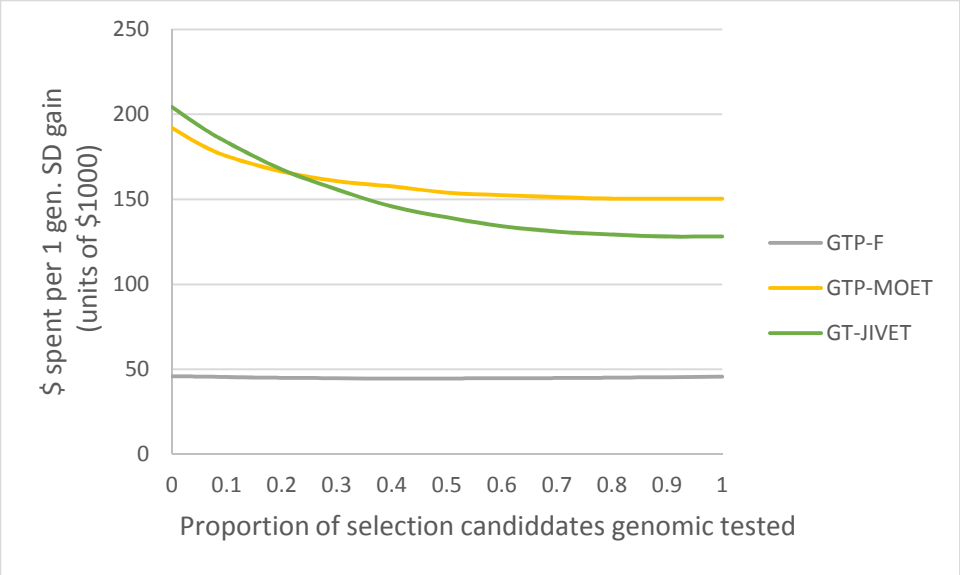

Figure 6: Estimated costs of female breeding programs vs proportions of selection candidates genotyped

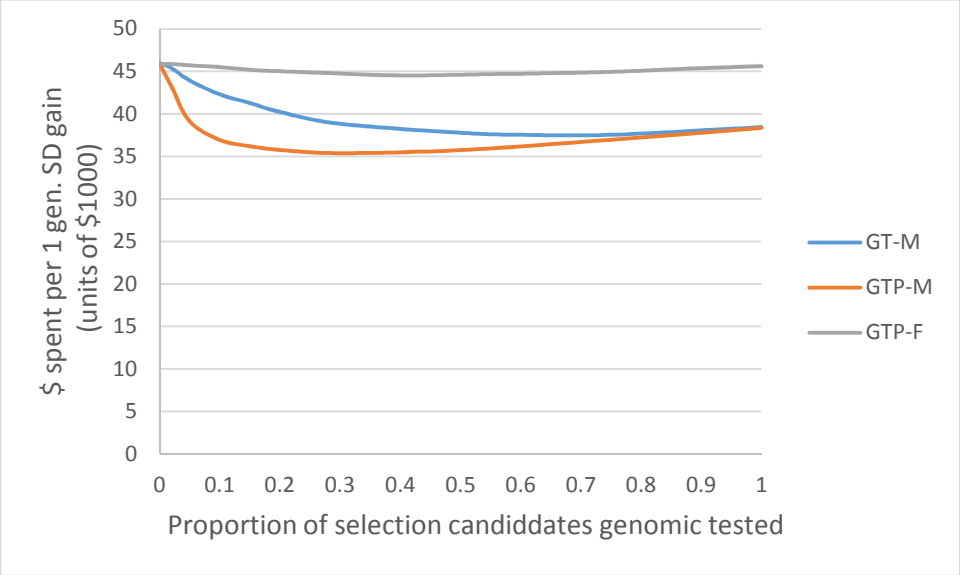

Figure 7: Estimated costs of natural or artificial insemination breeding programs vs proportions of selection candidates genotyped

Tables

Table 1: Overview and names of breeding programs which include whether males or females were genomic tested pre or post-measurement of trait 1, how many dams were selected and how many dams sires were mated to in each breeding program

Scenario	Males	Females	Nr dams	Average nr	Average nr	Trait 1

	genotyped	genotyped	mated per year	progeny per dam	of dams each sire mated to~	measured prior to GT*
GT-M	✓	-	500	1	50	-
GTP-M	✓	-	500	1	50	✓
GTP-F	-	✓	500	1	50	✓
GTP-MOET	-	✓	125	4	12.5	✓
GT-JIVET	-	✓	63	8	6.3	-

^ Genomic testing (GT) males before Trait 1 phenotypes are known (GT-M), Genomic testing males post-measurement of trait 1(GTP-M), Genomic testing females post-measurement of trait 1 (GTP-F), Genomic testing females post-measurement of trait 1 –all progeny born via MOET (GTP-MOET), Genomic testing females pre-measurement of trait 1 – all progeny born via JIVET (GT-JIVET)

~10 sires per year were mated

*Trait 1 measured in both sexes; Trait 2 not measured in any part of breeding program for either sex

Table 2: Breeding value accuracies for first-time selection candidates which includes or does not include genomic information

	Genomic information	EBV Accuracies Trait 1	Trait 2	Index
No measurement*	no	0.31	0.01	0.23
No measurement *	yes	0.56	0.42	0.45
Trait 1 measured	no	0.57	0.06	0.35
Trait 1 measured	yes	0.71	0.51	0.54

*Assumed all parents have phenotypes of trait 1 measured