Turbo på fremgang i NTM gennem bedre nøgletal på populationsniveau

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Abstract

The purpose of this study was to improve the economy for the Nordic dairy farmer through better breeding schemes. The introduction of genomic selection has led to changes in dairy cattle breeding schemes. The design of breeding schemes has large effects on the genetic gain and the rate of inbreeding in the populations. Therefore it is important to routinely evaluate and ensure that the most optimal breeding schemes are used and thus the best bulls become fathers to the next generation of Nordic dairy cows. The first part of this study reviewed the current literature in genomic cattle breeding schemes. In the second part an optimal genomic breeding scheme was described and discussed with regard to the current literature.

A farmer economy efficient breeding scheme is hard to describe in actual numbers due to fluctuating conditions in the literature. Instead this breeding scheme tried to highlight important aspects and focus areas from where a planned breeding scheme could be developed. It is clear that genomic selection has enhanced dairy cattle breeding schemes. The greatest benefit in form of genetic gain is the possibility for more accurate breeding values for young animals which makes it possible to reduce the generation interval. The more accurate breeding values for young animals have also enhanced reproductive technologies. It is also clear that phenotypes are more important in the genomic era, especially when more and more females are included in the reference population. The current recording strategies should therefore be evaluated for improvements. If the price for genotyping continues to fall it would be a huge benefit genomic breeding schemes. Further, there are still more to explore within the genomic field. Some important topics that were highlighted in this study were renewal and composition of the reference population and how to best optimize the use of genomic information in control of inbreeding and selection.

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Introduction

Breeding schemes need a well-designed structure to maximize long term genetic gain. It has been proposed that the design of breeding schemes has been overlooked since the start of the genomic era. In practice genomic information has mainly been used to rank animals, hence there might be undiscovered advantages of genomic information and improvement opportunities in dairy cattle breeding schemes.

The theory of genomic selection was introduced by Meuwissen et al. (2001) and has been the base in dairy cattle breeding schemes over the past decade. The long-term genetic gain depends on the accuracies of breeding values, the selection intensity, generation intervals and the inbreeding. With genomic selection more accurate breeding values can be predicted for young animals and thereby the generation interval can be shortened substantially compared to a progeny testing scheme. At the same time genetic diversity has to be maintained to achieve long-term genetic gain and inbreeding and genetic disorders have to be monitored and handled.

In 2002 the Nordic Cattle Genetic Evaluation was established. Kolmodin et al. (2003) estimated genotype-by-environment interactions (G×E) and found only small differences within and across the Nordic countries. This means that most of the genes have the same effect in all the Nordic countries. This resulted in increased collaborations between the Nordic countries. The Nordic cooperation enables a higher genetic gain as a result of a larger population and higher selection intensity. It also makes it easier for the farmers to compare bulls and cows from the different Nordic countries (Kargo et al., 2014).

The purpose of this study was to improve the economy for the Nordic dairy farmer through better breeding schemes. The introduction of genomic selection has led to changes in dairy cattle breeding schemes. The design of breeding schemes has large effects on the genetic gain and the rate of inbreeding in the populations. Therefore it is important to routinely evaluate and ensure that the most optimal breeding schemes are used and thus the best bulls become fathers to the next generation of Nordic dairy cows.

The first part of this study reviewed the current literature in genomic cattle breeding schemes. In the second part an optimal genomic breeding scheme was described and discussed with regard to the current literature.

Section 1: Literature review

Genomic information in breeding schemes

Pre-screen genomic breeding schemes

During the early years of the genomic era, genomic information was mainly used to pre-screen bull calves and thereby only partially replace progeny testing. De Roos et al. (2011) showed an increase in genetic gain by 30% when they compared a pre-screen breeding scheme with GEBV reliabilities of 100% to a conventional progeny testing scheme. However, de Roos et al. (2011) suggested that it was more realistic that the reliabilities of the GEBV were 40% which increased genetic gain by 12% compared to a conventional progeny testing scheme. Further, Pryce et al. (2010) compared a pre-screen breeding scheme with GEBV reliabilities of 60% to a conventional progeny testing scheme and found that the former increased genetic gain by 16%.

Hybrid genomic breeding schemes

As genomic information extended its position in dairy cattle breeding, hybrid genomic breeding schemes became more popular. Thomasen et al. (2014a) evaluated a hybrid genomic breeding scheme which used both progeny tested bulls (PB) and young bulls (YB) and compared it with a conventional progeny testing scheme without genomic information. The simulated population was constructed to reflect a small dairy cattle population, in the presented study the Danish Jersey cattle population. There were 68,000 cows registered in the population and yearly 1,500 bull dams were screened to produce 500 genotyped bull. Further, 60 YB of the 500 genotyped bulls were selected to be progeny tested. The breeding goal consisted of two unfavorably correlated traits, a production trait with heritability of 0.30 and a functional trait with a heritability of 0.04. The main evaluation criterion was annual monetary genetic gain (AMGG) and discounted profit was used to evaluate the economic results. Four parameters varied: 1) the increase in reliability of genomic prediction due to genomic information, 2) the proportion of bull dam sires that were young bulls, 3) the number of genotyped bulls, and 4) the proportion of cow sires that were young bulls. The results showed that the hybrid genomic breeding scheme gave a higher AMGG and was economically superior to a conventional progeny testing scheme. If low reliabilities of genomic prediction were considered, the highest AMGG was achieved through a use of both YB and PB as bull sires.

Juvenile genomic breeding schemes

Further, juvenile genomic breeding schemes (juvenile schemes) become more common. In juvenile schemes young bulls replace progeny testing almost completely. Studies have indicated an increase in genetic gain varying from +28% to + 108% in juvenile schemes compared to conventional progeny testing schemes. The gain differs depending on three parameters. Firstly, the selection intensity which in this case is the number of genotyped bulls versus the number of selected sires. The highest selection intensities were achieved when as few bulls as possible were selected in a population with many genotyped bulls. Secondly, the generation interval which mainly depends on the ages of parents for selected animals. Thirdly, the accuracy of GEBV which depends on the reference population size and how genetically similar the reference population is to the main population (Köning och Swalve, 2009; Pryce et al., 2010; Winkelman and Spelman, 2010, Buch

2011, Lillehammer et al., 2011; de Roos et al., 2011; McHugh et al., 2011). Thomasen et al. (2014a) compared a juvenile scheme with a hybrid genomic breeding scheme and found that the juvenile scheme became more genetically superior when the increase in reliability due to genomic information was over 5 percentage points compared to the hybrid genomic breeding scheme.

Phenotypes

Genomic information has made phenotypes more central in breeding schemes (Henryon et al., 2014). With females in the reference population it may be economically sound to measure novel traits that would be too expensive to measure in a progeny testing breeding scheme and to introduce them in the total merit index. These novel traits do not have to be measured on all cows in the population because large daughter groups for each bull are no longer needed. Thus, it is possible to set up information herds for more detailed recording of for example fertility and udder health. However, this means that reference populations for phenotypes that are hard and expensive to measure, will be smaller than reference populations for phenotypes that are easy to measure (Egger-Danner et al., 2015). Additional data recording must provide direct benefits to the producer to motivate the extra effort required. Recordings also have to benefit beyond genetic improvement in breeding programs. To fulfill those criteria electronic systems that make data easy to capture is a key in long-term breeding schemes (Egger-Danner et al., 2015).

Resources

The value of genotypes increases when matched to more traits (VanRaden et al., 2014). The number of phenotypes that are possible to collect is limited by the available resources. Often there are not resources to phenotype all animals for all traits in a total-merit index. Some traits also require more resources and are harder to measure in a larger scale with well-defined phenotypes. There are also decreased margins when more animals are phenotyped (Hayes et al., 2009). The challenge in dairy cattle breeding is to balance selection for production and at least maintaining udder health, fertility and resistance to metabolic diseases.

Indicator traits

Axelsson et al. (2015) studied the most effective recording strategy regarding annual monetary genetic gain (AMGG) and breakeven price for the recoding of indicator traits. The breeding goal consisted of milk production, a functional trait and an environmental impact trait, with economic values of €83, €82 and €83 respectively. Two scenarios were investigated where the first included only breeding goal traits and no indicator traits. The second scenario investigated all three breeding goal traits and also an indicator trait for environmental impact. The indicator traits were recorded on large, medium or small scale. The large scale included longevity as stayability after first lactation and stature measured in first lactation. Medium scale included live weight and greenhouse gases measured in the breath of the cow during milking. Small scale included residual feed intake and total enteric methane measured in respiration chambers. The results showed that including stayability as indicator trait resulted in 11% higher genetic gain in environmental impact compared to no indicator traits. The breakeven price for recording stayability was €8 per record. Measurement of greenhouse gases during milking resulted in the highest genetic gain, 23% higher compared to no indicator traits. The breakeven price for measuring greenhouse gases during milking was €29 per

record in the reference population. The results from the respiration chamber showed the lowest genetic progress with an indicator trait (Axelsson et al., 2015).

New traits

Yao et al. (2015) proposed that SNP genotypes and health data can be used to predict future phenotypes. Feed efficiency was studied through measurement of residual feed intake (RFI). The RFI was calculated as the difference between the actual intake and the expected feed intake. The study used SNP genotypes and health history for prediction of future dry matter intake (DMI), live body weight, RFI and milk yield. Accuracies were measured as correlations between predicted values and phenotypes. The accuracies without health history for RFI were 8.76% using random forests algorithm and 20.45% using support vector machine algorithm. There was no effect of adding health data on the accuracy for RFI (Yao et al., 2015). Adding health history improved accuracies slightly for the other traits.

Pryce et al. (2014) validated two published studies of genomic prediction of RFI and DMI. The number of lactating cows used was 78 and an accuracy of 0.27 for RFI was achieved when the reference population consisted of 843 Australian and 939 New Zealand heifers. An average accuracy of 0.72 was achieved when a multicountry model was used, which included cows in lactation from two countries; 958 cows from the Netherlands and United Kingdom and also 843 growing Australia heifers (Pryce et al., 2014).

Genotyping strategies

Family structure and the design of the reference population may influence the accuracy of genomic predictions (Pszczola et al., 2012). Pszczola et al. (2012) estimated the effect of different relationship of evaluated animals within the reference population on the reliability of direct genomic breeding values (DGV). The reference population consisted of highly, moderately, lowly related animals, the selection was done through selection of paternal half-sib families of decreasing size. In addition a complete random reference population was evaluated. The randomly chosen animals had the lowest relationship within the reference population. The results showed the randomly chosen reference population achieved the highest reliability. For a trait with a heritability of 0.3 the reliability was 0.53 in the highly related reference population compared to 0.61 in the randomly selected reference population. In addition, the reliabilities increase as the relationship between the selection candidates and the animals in the reference population increases. Also the reliabilities decrease as the number of generations between the selection candidates and the animals in the reference population increases (Pszczola et al., 2012).

Plieschke et al. (2016) evaluated systematic genotyping of cows in a try to improve genomic breeding values. The reference set consisted of only genotyped bulls at start and was thereafter extended with a fixed number of first-crop daughters of each sire in a regular and balanced system of genotyping. The results showed that even with a relative low number of genotyped daughters per sire it led to improvements in the reliability of the predicted breeding values. In the most extended design with 200 genotyped daughters per sire, reliabilities of 80% or more were achieved for traits

with moderate to high heritability. In this case SNP effects were estimated from a reference population of 420,000 cows and 4200 daughters (Plieschke et al., 2016).

Genotyping for reference population

Jiménez-Montero et al. (2012) evaluated different female-selective genotyping strategies for improving predictive accuracy of genomic breeding values in small dairy cattle populations. The study simulated a population of 996 progeny-tested sires and 40,000 dams. The results showed that strategies that genotyped females from the top of the yield deviations and breeding values rankings gave the most biased prediction. However, genotyping animals from both the top and bottom rankings resulted in increased reliability in small reference populations (Jiménez-Montero et al., 2012).

Boligon et al. (2012) used stochastic simulation to evaluate the quality of breeding values with different selective genotyping strategies. The reference population and the generation were fixed at 2500 animals each. Five genotyping strategies were used to find 500 animals in each generation for the reference population: 1) random selected animals, 2) top animals with the largest yield deviation values, 3) bottom animals with the lowest yield deviation values, 4) extreme animals which consisted of the animals with the 250 largest and the 250 lowest yield deviation values, 5) less genetically related animals. Overall the extreme genotyping strategy gave the best predictive ability of breeding values. The authors concluded that the extreme animals were the most informative when training genomic selection models (Boligon et al., 2012).

Chip density and imputation

The density of SNP markers affects the accuracy of GEBV (Meuwissen, 2009, Habier et al., 2009). In theory, a higher density should lead to a higher accuracy but it also leads to an increased cost for genotyping (Peipei, et al 2013). Some countries have genotyped bulls with a 777,000-markers high density chip (777K; high-density, HD), with the purpose of increasing the accuracy (Su et al., 2012). In addition, low density chips with 6,900-markers and 2,900-markers (BovineLD and Bovine3K) have been developed, those should be more suitable for a large scale and have a lower genotype cost (Boichard et al., 2012).

When several chips are used in genomic selection it is important to make use of all available marker data by imputation of missing genotypes. Imputation is also useful to increase the call rate of genotyped animals when the same chip is used (Peipei, et al 2013). Imputing from 3K to 54K gave lower imputation accuracies than imputing from 54K to 777K, 93.5 to 97.1% compared to 97.1 to 99.3% (Peipei, et al 2013).

Reference population

The first steps when predicting GEBV are to divide the genome into small segments and thereafter estimate the marker effects in a reference population where animals are both genotyped and phenotyped. This further means that the next generation can be genotyped for the markers and thereafter the sum of the effects determine their predicted GEBV (Meuwissen et al., 2001). The accuracy of genomic predictions depends on the number of phenotypic records that the marker effects were estimated on. The required size of the reference population also depends of the

heritability; with a higher heritability a lower amount of phenotypic records is required (Meuwissen et al., 2001). Lund et al. (2010) evaluated the increased reliability archived when combining Holstein reference populations. The four organizations were UNCEIA (France), DHV-VIT (Germany), CRV (The Netherland, Flanders) and VikingGenetics (Denmark, Sweden, Finland). Each country contributed with 4,000 genotyped bulls. The average increase in reliability for all traits was 11%-units with a combine reference population. Further, the increase in reliability between traits and countries ranged from 2%-units to 19%-units (Lund et al., 2010).

Females in the reference population

During the early years of genomic selection mainly bulls were genotyped, but when the costs decreased genotyping of heifers became more interesting. For the dairy producer, higher accuracy when selecting replacement animals and better mating plans are some of the main arguments for genotyping heifers (Pryce & Hayes 2012). It has also been shown that expanding the reference population with cows were an efficient way to increase reliability of GEBV (Thomasen et al., 2014b). Koivula et al. (2014) studied the effect of including 5,593, 3,111 or 0 genotyped Nordic Red Dairy cows in the reference population on the gain in accuracy of the genomic predictions. In all evaluations 4,188 genotyped bulls were used. The extra gain in accuracy from cows in the reference population varied from 0.8% to 2.6%-units (Koivula et al., 2014). Wiggans et al. (2011) included 3,559 Holstein females and 388 Jersey females in the reference population. The results showed extra gains in reliabilities of 3.5%-units for Holstein and 0.9%-units for Jersey. Further, Pryce et al. (2012b) demonstrated an increase of 8%-units reliabilities when 10,000 cows were added to a reference population of 3,000 bulls.

Thomasen et al. (2014b) evaluated the effect of including cows in the reference population for a small dairy cattle population. Three scenarios in a period of 15 years were investigated regarding maintaining and updating the reference population. The first scenario included the number of progeny tested bulls which was tested at four levels; 15, 40, 60 100. In the second scenario, 2,000 first lactation cows each year were randomly selected and genotyped. In the third scenario, an additional of 2,000 first lactation cows were selected and genotyped of the first two years. The study evaluated a juvenile breeding scheme and a Hybrid breeding scheme. The breeding goal consisted of a production trait with a heritability of 0.3 and a functional trait with a heritability of 0.04. The study used a stochastic approach as model to the different strategies and the evaluation criteria were AMGG, rate of inbreeding, reliability of genomic predictions and variance of response. The results showed that including cows in the reference population increased AMGG and decreased inbreeding compared to updating the reference population with 60 progeny tested bulls annually. The additional 2,000 cows during the two first years provided extra AMGG. The juvenile breeding scheme outperformed the hybrid breeding scheme regarding AMGG due to the shorter generation intervals. The variance of response which reflected the risk was in general higher using genomic bulls in juvenile schemes compared to using progeny tested bulls, due to the lower reliabilities. The study concluded that genotyping cows are a fast way to increase reliabilities of genomic predictions in small dairy cattle populations (Thomasen et al., 2014b).

Female genomic information

Hugh et al. (2011) investigated the complete effect of genomic female information in juvenile schemes. The study used a stimulation program and the population consisted of 100 males and 100 females and a Fisher-Wright population model was used. The study showed that including females in genomic breeding programs could triple the genetic gain compared with a conventional progeny testing scheme. The main reasons for the extra genetic gain were increased accuracies and shorter generation intervals. The generation interval of males could be decreased by 3.8 years without any reasonable change in inbreeding. In addition the accuracy of the selected males was increased by 73% in the final 3 years in the genomic breeding scheme compared to a traditional BLUB breeding scheme (Hugh et al., 2011).

Genotyping for management

One other use of genotyped heifers is to find the best heifers for replacement on herd level (Pryce & Hayes 2012). The study assumed a herd of 100 cows where the heifers available for selection varied from 20 to 50. The replacement rate varied from 15% to 30%. Three different costs of genotyping were assumed; 5 Australian dollar (AU$5), AU$50 or AU$100. Comparison of genomic selection with parental average (PA) information or no PA information was made. Genotyping heifers became profitable when the price of genotyping was AU$50 with no PA information and at AU$5 when PA information was included. The largest benefit was achieved with a high number of candidates for a few replacement spots. However, their comparison of costs and benefits of genotyping heifers did not take marketing into account. It might be profitable to market heifers or embryos from heifers with breeding values at birth with up to 60% reliability. Other advantages of genotyping heifers may be more optimal mating plans and keeping recessive alleles under control (Pryce & Hayes 2012).

Hjortø et al., (2015) investigated if genotyping females could help to reduce genetic lag on herd level. Genomic test results of females were used in combination with sexed semen or a high management level, which result in a reproductive surplus in the herd. The use of sexed semen was also combined with beef semen to produce crossbred slaughter animals. The study used 2 stochastic simulation programs, the first (SimHerd) estimated economic effects of different strategies and also the distribution of the dams of heifers calves. The second simulation program (ADAM) estimated genetic merit in different scenarios. The annual net return per slot was calculated as the sum of operational return and value of genetic lag minus the cost for genomic test divided by the total number of slots. The results showed that the use of genomic tests for decision making could reduce genetic lag by as much as 0.14 genetic standard deviation units of the breeding goal. In addition, if genomic test were used in combination with strategies for increasing and using a reproducing surplus the genetic lag decreased up 0.30 genetic standard deviation units. However, the current price (€50) for a LD chip genotyping in the Nordic countries was too high to bring any extra profitability (Hjortø et al., 2015).

Reproductive technologies

MOET and OPU

Nicholas & Smith (1983) present that multiple ovulation together with embryo transfer (MOET) could increase genetic improvement by 30% in a dairy cattle breeding scheme. MOET reduces the number of required bulls dams which consequently increases the selection intensity and the genetic gain (Pedersen et al., 2011). Further, ovum pick-up (OPU) combined with in vitro fertilization is another reproductive technology used in dairy cattle (Rick et al., 1996). OPU was first used on problem cows that did not respond to superovulation, but later on it has also been applied on pregnant cows and heifers, including prepubertal heifers (Galli et al., 2014)

There are several studies suggesting that the highest selection intensity in the female pathway is achieved through nucleus breeding schemes. (Pedersen et al., 2009; Pryce et al., 2010). Thomasen et al. (2016) studied how genomic selection interacts with the use of reproductive technologies. The reproductive technologies used were MOET and OPU and their effect on AMGG was monitored. Three factors were taking in consideration: 1) 0 or 2000 genotyped heifers per year, 2) 0 or 50 donors selected at 14 months of age which produced 10 offspring and 3) 2 reliabilities of genomic prediction. In addition, Thomasen et al., (2016) investigated how well different reproductive technologies interacts with the reliability of genomic predictions. A stochastic simulation was used and the number of donor was 25, 50, 100, or 200 and the number of born calves per donor was 10 or 20. Further, the age of donors was 2 or 14 months and the number of sires was 25, 50, 100 and 200. The cost of a born calf was €500 Euro, €1000 euro or €1500. The results showed that reproductive technologies combined with genomic selection have the potential to improve AMGG in dairy cattle breeding. Higher reliabilities of genomic predictions resulted in less inbreeding. A more widespread donor program with more born calves per donor resulted in higher inbreeding. Although, when more sires were used the inbreeding was reduced without markedly lower AMGG. Younger donors resulted in higher AMGG because there was no major loss in selection accuracy when genomic information was available and the generation interval was shorter when donors were 2 months compared to 14 months (Thomasen et al., 2016).

Bouquet et al. (2015) simulated an open MOET nucleus in a juvenile scheme. The study evaluated the number of used bulls, flushed heifers and flushings per heifers. In addition the genotyping capacity allocated to young females was analyzed. The results showed that a MOET program increased genetic gain without increased inbreeding if the nucleus was large enough and the number of used bulls was large enough. The results also showed that increasing the nucleus size could not compensate the loss in genetic gain from closing the nucleus. Increasing the number of flushings per heifer resulted in higher genetic gain and inbreeding than if the number of flushed heifers was higher. Thus, more flushings per heifer was economically superior to more flushed heifers if inbreeding was kept on a healthy level. Regarding the genotyping capacity, the number of genotyped females was increased from 800 to 1800 and 3600 to quantify its impact on genetic gain. Increasing the number of genotyped animals above 800 females had little impact on genetic gain (Bouquet et al., 2015).

Sexed semen

Pedersen et al. (2011) studied sexed semen and MOET and their effect on selection intensity on cow dams. The population consisted of 20,000 cows and each year 2,000 females were selected for genotyping. The bull dams consisting of the 2,000 females were divided into two groups; top bull dams and remaining bull dams. The number of bull dams in the different groups varied depending on the amount of sexed semen usage. The largest genetic benefit from using sexed semen was achieved when X-semen was used in both a nucleus population and production population. However, when MOET was used there was no effect of using sexed semen on genetic gain. The optimal use of MOET depended on the accepted rate of inbreeding. With an accepted inbreeding of 1% the maximum genetic gain was achieved with 100% MOET combined with conventional semen on the top bull dams. The top bull dams group in the maximum genetic gain case consisted of 400 females (Pedersen et al., 2011).

Inbreeding

Inbreeding has been shown to lower the mean phenotyping performance in the inbred animal and also increase the homozygosity levels in the whole population. In general traits associated with survival and fitness like reproduction and health are more susceptible (Miglior et al., 1995). Before the genomic era an increase in genetic gain has been associated with increased inbreeding. However, with genomic information the Mendelian sampling can be better predicted and full sibs can have different breeding values before phenotypic performance is available. The opportunity to select within families could result in less inbreeding (de Roos et al., 2011; Hayes et al., 2009a; Daetwyler et al., 2007).

Lillehammer et al. (2011) estimated that a juvenile scheme led to less inbreeding and higher genetic gain compared to a conventional progeny testing scheme. In general genomic relationships will obtain more information than pedigree-based relationships, due to the use of genetic markers. (Pryce et al., 2012b).

Lethal recessive defects may often be assumed when a homozygote is missing in a population (VanRaden et al., 2011). The access to genomic information from genotyped animals makes it possible to find and keep track of recessive genetic disorders. Several research groups have screened the genomic evaluation genotype pool and found recessive fertility haplotypes (HH1-HH5) in the Holstein breed. In homozygote form the haplotypes (HH1-HH5) can cause embryonic losses and thereby lead to decrease in fertility (VanRaden et al., 2011; Sahana et al., 2013; Cooper et al., 2013; Fritz et al., 2013).

Mating design for control of inbreeding

Mating design structure is an important part of dairy cattle breeding to increase long term genetic gain (Caballero et al., 1996; Sonesson and Meuwissen, 2000). However, it has been suggested that mating designs have received less attention since the introduction of genomic (Henryon et al., 2014). Improved mating plans can improve long-term genetic gain by better family structure. Genomic information might have the possibility to separate genetic contribution more effectively than pedigree information (Henryon et al., 2014).

Liu et al. (2016) studied in a simulation study mating designed regarding inbreeding and genetic gain. The study compared two mating strategies with pedigree and genetic information. The two mating strategies were minimum co-ancestry (MC) and minimizing the covariance between ancestral genetic contribution (MCAC). The result showed that MC and MCAC with genomic information could without reducing genetic gain reduce inbreeding by 6% to 22% compared to MC and MCAC with pedigree information (Liu et al., 2016).

Selection

Optimum-contribution selection (OCS) has been the choice for many conventional breeding schemes (Woolliams, 2007). The theory is that OCS maximizes long-term genetic gains by maximizing the weighted-genetic merit of selected parent and at the same time constraining the relationship between the parents (Wray and Goddard, 1994). Genomic information can contribute more information to OSC. It may trace inheritance of chromosomal segments and estimate more accurately relationships between animals. In practice this means that OCS could help to select candidates carrying favorable but different chromosomal segments from ancestral animals (Henryon et al., 2014).

Control of lethal alleles

Pryce et al. (2012b) investigated 3 strategies for controlling estimated progeny inbreeding in dairy cattle mating plans. The strategies used pedigree inbreeding coefficients, genomic relationships or shared runs of homozygosity. The parameters were genetic gain, progeny inbreeding and the decrease of homozygosity of recessive alleles. Real pedigree genotypes with 43,115 SNP and LD genotypes with 3,123 SNP markers and GEBV from Holstein cattle were used. The study was replicated 50 times and herds consisted of 300 cows and 20 sires were available for mating. Each of the 300 cows were matched to the 1 of 20 sires, with the focus of maximize the genetic gain minus penalty for estimated progeny inbreeding. In addition, the sires could not be mated to more than 10% of the cows. The result showed that the strategies using a genomic relationship matrix (GRM) were more effective in reducing average estimated progeny inbreeding. The GRM strategies also resulted in fewer homozygous SNP. The results from the 43,115 SNP and the LD 3,123 SNP gave similar results. A 1% reduction of inbreeding valued as $5 per cow could be made with little compromise in the overall breeding objective (Pryce et al., 2012b). Cole et al. (2015) modified Pryce et al. (2012b) by also taking economic effects into account. The modified version showed similar effects in reducing estimated inbreeding and lethal alleles. However, the modified version outperformed regarding low-frequencies alleles with small economic effects (Cole et al., 2015).

Egger-Danner et al. (2014) studied genetic defects in Austrian Fleckvieh and what effect erasing lethal alleles carriers from the breeding programs would have on the genetic gain and discounted profit. The allele frequency varied from 0.5% to 7% and the study included 6 genetic disorders. When all bulls were erased from both herdbook cows and mating plans the losses summed up to 7% AMGG and 9% discounted profit.

Section 2: Optimal breeding scheme

General

The following optimal breeding scheme is described and discussed with regard to the literature review (Section 1). It is mainly based on the newest literature in the genomic selection research field. However, it also contains prediction and assumption of the future and should therefore be seen with regard to that. This breeding scheme strived to be optimal from a farmer economy perspective. A breeding scheme can also be optimal from other perspectives that this optimal breeding scheme does not fully covers.

In a breeding scheme there might be external factors like laws and legislations that might affect the optimal breeding scheme but are hard to control. For example a law could help to increase or reduce accuracy of a registered phenotype if controlled by other instance outside breeding schemes. Those kinds of external factors are hard to control in an optimal breeding scheme, but have to be continuously evaluated.

To describe the optimal breeding scheme seven assumptions were made:

- Focus on the Nordic farmers economy
- Maintain three breeds – Holstein, Jersey, Nordic Red (Danish Red, Finnish Ayrshire, Swedish Red)
- Use of genomic selection
- Maximize long term genetic gain with a time horizon over 10 years
- Broad breeding goal (production, health, reproduction, conformation, functional traits)
- More and more females in the reference population
- Mainly use of young bulls as long as these are superior

Phenotypes

The Nordic countries are known for their Broad breeding goal (production, health, reproduction, conformation, functional traits). The heritability of the different traits varies a lot, from a relatively high heritability trait like milk yield to a lower heritability trait like fertility. Milk yield which is relative easy to measure in today's modern farms whereas fertility is more complex to measure even with the most modern techniques. With female genomic information there is no longer the need for large daughter groups for each bull to achieve accurate breeding values. In the Nordic countries this is an opportunity for the smaller breeds where a few number bulls are progeny tested each year. It also pays off to make phenotypes as accurate as possible, because the phenotype of a genotyped animal is more informative than of an ungenotyped. Therefore, it has been argued that genomic information has made phenotypes more central in breeding schemes (Henryon et al., 2014).

The factors affecting the value of a phenotype are the economic value of the trait or the correlated traits, the number of phenotypic records already available for the trait and the heritability. Therefore, the value of phenotype in establishing a genomic selection breeding program must be

evaluated under the particular conditions of the breeding program and its economic breeding objectives (Egger-Danneret al., 2014). Phenotypes also have a value as an important tool to monitor phenotypic trends and thereby evaluate your breeding scheme. This might be even more important in the genomic era as more decisions are made on genomic information.

It is clear, as of 2016 that the Nordic countries are moving towards more and more females in the reference population. This will, as argued require more accurate and well-defined phenotypes. Therefore, it is important with the motivation of farmers and other stakeholders involved in documentation and recording to ensure good data quality. Electronic systems, used in daily management on farm-level will have a major role in reducing bias and getting cheap phenotypes (Egger-Danner et al., 2015). In a biological perspective, an optimal breeding scheme has as many cheap, accurate and well-defined phenotypes as possible. However, if you include costs for phenotypes in the calculation there is an optimal way where the last added phenotype cost more than is its worth in terms of extra genetic gain. Today, most of the phenotypes are free which tends to shift the focus towards accuracies and definitions of phenotypes.

The literature is quite limited regarding current traits and how to choose herds with the best phenotypes. Instead, a lot of focus has been on new traits, some present examples as of 2016 were feed efficiency and greenhouse gases (Pryce et al., 2014; Yao et al., 2015; Axelsson et al., 2015). There are extra values of genotypes when they are matched to more traits. If the heritability of the novel trait is low, a larger reference population is needed. This may favor closely correlated indicator traits that can be measured in larger scale to a lower price (Axelsson et al., 2015). The challenge with three Nordic breeds is then to measure all traits for all breeds. There might also be new measurement of current traits that come closer to the actual trait and are less impacted by man and management. This may increase the heritability and thereby lead to a higher genetic gain. Therefore, it is important to keep track of new technologies and recording methods in an optimal breeding scheme.

Genotyping strategies

The most value out of genotypes is acquired when they are used for several purposes (VanRaden et al., 2014). *Figure 1* shows different purposes of genotypes that the literature suggests. In a breeding scheme perspective it would easiest if all animals were genotyped. However, with the current prices for genotyping there are split opinions if it is profitable or not to genotype all females for management purposes alone (Pryce & Hayes 2012a; Hjortø et al., 2015). Therefore, it is not sure that genotyping all animals is the most economical optimal breeding scheme in a farmer perspective. Instead, to get the most value out of a genotype it is probably necessary with collaborations between farmers and breeding companies, this will split the cost on several stakeholders. There might also be different animals of interest. For example, genotypes for further breeding might not be the right genotypes for the reference population (Plieschke et al., 2016; Pszczola et al., 2012; Pryce & Hayes 2012). This could make it more difficult for farmers and breeding companies to spit the cost fairly.

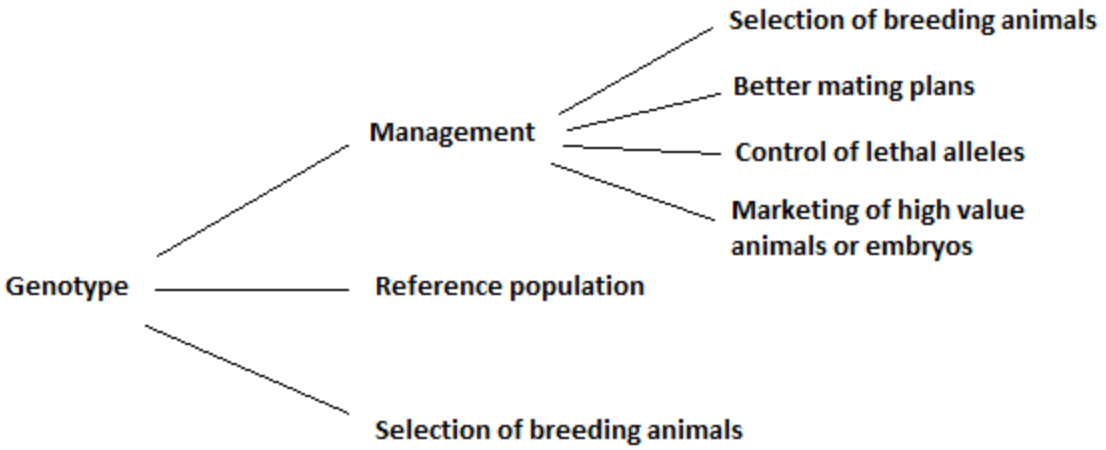

Figure 1. Different purposes of genotyping. Sources: (Pryce & Hayes 2012; Boligon et al., 2012; Pszczola et al., 2012; Koivula et al., 2014; Wiggans et al., 2011).

It is hard to know how the future will look regarding the availability of genotypes. The price for genotyping has decreased and if the genotyping price continues to fall, genotypes might be more accessible for breeding schemes. The best thing from an optimal breeding scheme perspective then might be to improve phenotype recording strategies and thereby increase the accuracies of breeding values. However, as of 2016, the genotype situation requires attention to achieve as optimal breeding scheme as possible. In a situation where genotypes are limited, it is also important to make sure as far as possible that the animals with the most accurate and well-defined phenotypes are genotyped. Further, genotyping should be were the most traits are recorded and thereby is each genotype utilized to its maximum.

Reference population

The required size of the reference population depends of the heritability; with a higher heritability a lower amount of animals are required to reach certain accuracy (Meuwissen et al., 2001). With a broad breeding goal like in the Nordic countries the heritability of the different traits varies a lot and thereby the optimal size of reference population varies depending on trait. However, there are also other optimizations, for example the family structure in the reference population may influence the accuracy of genomic selection (Pszczola et al., 2012). This will affect what animals you want to include in the reference population. Reliabilities increase when the average relationship within the reference population decreases. In practice this means that you want to minimize relationship within the reference population. Further, the reliabilities increased as the relationship between the selection candidates and the animals in the reference population increases.

Moreover, two tailed selection (top and bottom ranked) on parental average or yield deviation have been shown to give the highest accuracies (Jiménez-Montero et al., 2012). This means that you

want genomic information from the most informative animals and thereby the reference population represents the total genetic variation. If you become more and more selective among genotypes and phenotypes, the renewal and composition of the reference population will be important objectives for research.

Combining reference populations with genotyped bulls through cooperation between countries has been shown to be an effective way to increase the reliability (Lund et al., 2010). However, those animals have to be representative and phenotypes have to be well-defined and accurately recorded. Further, it is not sure that the breeding goals include the same traits. For small breeds like the Jersey and the Nordic Red it might also be hard to find cooperation partners due to their less widespreadness compared to Holstein.

Reproductive technologies

Genomic information with the possibility for more accurate breeding values for young animals has enhanced reproductive technologies. The uses of reproductive technologies in form of OPU and MOET have been showed to be an effective way to increase AMGG. What limits the usage of OPU and MOET in a long-term genetic gain perspective is the control of inbreeding. In smaller dairy cattle populations, the profitability of implementing RT as a part of the breeding scheme relies on the possibilities of obtaining a high reliability of genomic prediction and of producing progeny from reproductive technologies at a lower level of cost. If the reliabilities of genomic selection were higher the inbreeding level was lower (Thomasen et al., 2016). More sires could also be used to reduce inbreeding without markedly lower AMGG (Thomasen et al., 2016; Pedersen et al., 2011). The younger donors the higher AMGG, due to the availability of genomic selection no major increase in inbreeding was observed (Thomasen et al., 2016).

In theory there are no known limits for OPU and MOET in terms of AMGG as long as inbreeding is controlled. However, there might be practical, logistic or ethical aspects that the theory does not cover. Practical and logistic factors might be easier to control if the breeding structure is more nucleuses based. There are also several studies suggesting that the highest selection intensity in the female pathway is achieved through nucleus breeding schemes. (Pedersen et al., 2009; Pryce et al., 2010). Further, Bouquet et al. (2015) showed that MOET increased genetic gain without increasing inbreeding if the nucleus and the number of bulls used were large enough. More flushings per heifer was economically superior to more flushed heifers if inbreeding was kept on a healthy level (Bouquet et al., 2015). The biggest challenges with reproductive technologies for the three Nordic breeds are probably also practical or logistic. Animals are spread over several countries and in a relatively large area with a quite open breeding structure. There might also be restriction in how you are allowed to move animals across countries. To make sure the right semen is used on the best females at the right time this will therefore require a lot of planning and logistics.

When using reproductive technologies it is important to be aware of the ethical aspects. For example using MOET, multiple ovulations is brought about by hormone injection. The usage of hormones in food production has been a debated and questioned the last decades. With today's social media, information can spread rapidly and it is important to be able to argue for your

decisions. Therefore, in an optimal breeding scheme it should be preferable with action plans for those kinds of situations.

Selection

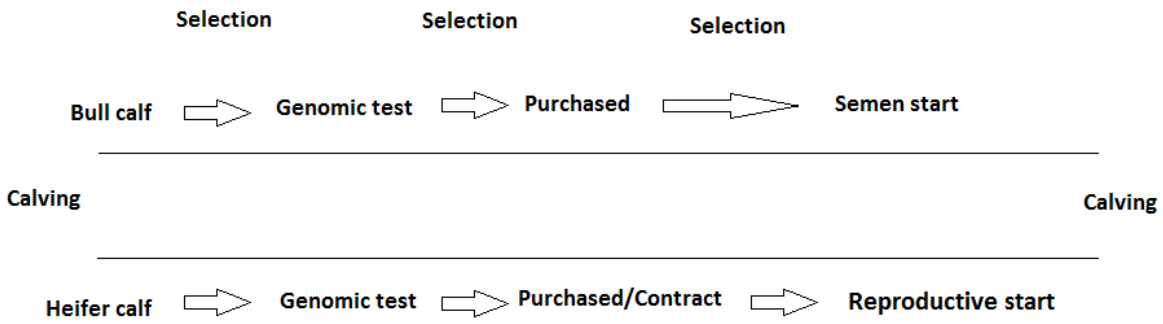

Figure 2. Selection steps for breeding animals. The selection can be divided into different steps. From what calves to genotype to reproductive start and further also a new calving.

In each selection step in *figure 2* there will be a selection decision. The selection could be divided into two phases. The first phase defines how many to select in each step and the second define what animals to choose to maximize long-term genetic gain. The first step in the first phase is to define the number of genotypings. An increasing amount of genotypings (males+females) the optimal proportion off these to spend on females is increased. The value of genotyping females also increase when MOET and OPU are used (Sørensen & Sørensen, 2009). However, females could also be genotyped for different purposes than further breeding (*figure 1*). Regarding the number of genotyped bulls, the farmer has no direct interest in genotyping bull calves, instead this cost will fall on the breeding organizations. In a breeding scheme, where both dams and sires are genotyped it should be possible for a breeding organization with some quite accurate pre-screening. The cost for genotyping bulls could possibly be even more reduced if the breeding scheme is more nucleuses based and thereby you can surround the animals you want to genotype.

The second step in the first phase is to decide how many to buy. In the female case, contracts for MOET or mating suggestions on farm could be solutions. Thereafter, the next step is to choose animals for reproductive animals. There might be changes in breeding values due to new information. Some animals will fall off due to reduced replicability or diseases. Further, there will be a culling decision. However, the most important part is in the start of the reproductive period, where the best animals should be mated which will reduce generation interval as far as possible.

In the second phase the most optimal is to use optimum-contribution selection (OCS), which maximizes the genetic merit of a cohort of animals while constraining the average relationship of the current generation (Henryon et al., 2014). The benefit of OCS, besides reducing the risks of inbreeding, genetic drift, and changes in gene frequencies, is that it can maximize long-term genetic gain. The software program “Eva” (Evolutionary Algorithm) is one example of a program that can help to control of inbreeding and adequate balancing of selection and inbreeding in populations.

The program has been developed at DJF (Faculty of Agricultural Sciences) at Aarhus University, Denmark. From an optimal breeding scheme view, those kind programs will help a lot to optimize and balance selection of breeding animals. The challenge with OCS and genomic information is to define measurements that constrain losses of genetic variation and relationship between parents (Henryon et al., 2014).

Mating

Mating design structure is an important part of dairy cattle breeding schemes to increase long term genetic gain (Caballero et al., 1996; Sonesson and Meuwissen, 2000). In an optimal breeding scheme mating design optimize family structures. Liu et al. (2016) showed that MC and MCAC with genomic information could without reducing genetic gain reduce inbreeding by 6% to 22% compared to MC and MCAC with pedigree information (Liu et al., 2016). However, it requires that both animals are genotyped. MC and MCAC might also be hard to execute from a farmer perspective, especially with genomic information. Therefore, it should be preferable if the breeding companies control as much as possible of the mating structure.

Logistics and optimization

With genomic information and the possibility for more accurate breeding values for young animals there are potentials for better decision making from a very young age or animals that are not even born. This makes it possible for optimizations before an animal is used for breeding. For example, feed optimization could help a bull to start producing semen earlier or a heifer could be mature for MOET earlier. It is also possible to make sure that the right animals are at the right place at the right time. Those factors could for example help to reduce the generation interval and thereby increase genetic gain. However, those factors are rarely captured by the literature but could have considerable effect on an optimal breeding scheme.

There might be need for closer collaborations between breeding companies and farmers. With the need of more accurate phenotypes and genotyping collaboration, the partnerships between farmers and breeding organizations have to be strengthened. This situation is new and will require increased knowledge in the whole community about genomic selection and its effect on the breeding schemes. Further, the breeding scheme should also be regularly evaluated and adjusted when phenotypic trends gets available. It does not matter how theoretical optimal the breeding scheme if the breeding scheme does not add extra value for the farmers.

Inbreeding

In an optimal breeding scheme a healthy level of inbreeding is kept which allows for long-term genetic gain. According to FAO, an inbreeding level below 1% per generation is recommended in order to avoid undesirable effects of inbreeding (FAO, 2007). Inbreeding lowers the mean phenotyping performance in the inbred animal and also increases the homozygosity level in the population. Traditional BLUP-selection uses pedigree information to construct relationship matrices and to constrain the progeny inbreeding. The development of molecular genetics has enabled genotyping of animals and using genomic relationships in the selection process. Pryce et al. (2012b) showed that the strategies using a genomic relationship matrix (GRM) were more effective in

reducing average progeny inbreeding. A 1% reduction in progeny inbreeding (valued at around $5 per cow) could be made with very little compromise in the overall breeding objective (Pryce et al., 2012b). Also, Lillehammer et al. (2011) suggested that a breeding scheme with genomic information led to less inbreeding compared to a conventional breeding scheme.

There are no arguments to adventure the long-term the genetic gain by intensively use of individual bulls. One major key to achieve as little inbreeding as possible is accurate breeding values. To succeed with accurate breeding values in the genomic era the design of reference population is again the important discussion topic. Genomic information may also help to control inbreeding through trace inheritance of chromosomal segments and estimate more accurately relationships between animals. This would help to select candidates carrying favorable but different chromosomal segments from ancestral animals (Henryon et al., 2014). The literature gives no clear suggestion how this is done in the best way. It is however clear that there are more to explore regarding within inbreeding and how to maximize long-term genetic gain in the genomic era. The best thing from an optimal breeding scheme should then be to continuously evaluate new research and thereafter implement it.

Control of lethal alleles

The access to genomic information has also led to detection of recessive genetic disorders. With shorter generation intervals the changes of different alleles frequencies also goes much faster. Therefore, it is important in an optimal breeding scheme with a strategy to control them. Depending of the frequency and economic value of the unwanted recessive allele and each one of them has to be handled differently. Instead of working for full elimination of all harmful alleles, it might be more optimal if animals used for breeding are tested for their breed's most common lethal recessives and by publishing the data, at-risk mating can be avoided.

Areas for more research

The theory of genomic selection was introduced by Meuwissen et al. (2001) and has been an important part in dairy cattle breeding schemes over the past decade. However, there are still more to explore within the genomic field. One example is how to ensure quality assurance of phenotypes. This is extra important in a genomic breeding scheme because the phenotype of a genotyped animal is more informative than of an ungenotyped. Further, the renewal and composition of the reference population should be areas for more research. Until now there has been a focus to get as many animals as possible in the reference population. However, in the future when more animals are genotyped there will be the possibility to be more selective. Jiménez-Montero et al. (2012) and Pszczola et al. (2012) showed the importance of the right genotyping strategies to find the right animals for the reference population. In addition, there are more to explore within genomic information and the control of inbreeding and selection. The literature gives no clear suggestion how to best use genomic information in the control of inbreeding.

Conclusions

This breeding scheme strived to be optimal from a farmer economy perspective. A farmer economy efficient breeding scheme is hard to describe in actual numbers due to fluctuating conditions in the

literature. Instead this breeding scheme tried to highlight important aspects and focus areas from where a planned breeding scheme could be developed. It is clear that genomic selection has enhanced dairy cattle breeding schemes. The greatest benefit in form of genetic gain is the possibility for more accurate breeding values for young animals which makes it possible to reduce the generation interval. The more accurate breeding values for young animals have also enhanced reproductive technologies. It is also clear that phenotypes are more important in the genomic era, especially when more and more females are included in the reference population. The current recording strategies should therefore be evaluated for improvements. If the price for genotyping continues to fall it would be a huge benefit genomic breeding schemes. Further, there are still more to explore within the genomic field. Some important topics that were highlighted in this study were renewal and composition of the reference population and how to best optimize the use of genomic information in control of inbreeding and selection.

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