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Mating allocations in Holstein combining genomic information and linear programming optimization at the herd level

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ABSTRACT

In this study, we explored mating allocation in Holstein using genomic information for 24,333 Holstein females born in Denmark, Finland, and Sweden. We used 2 data sets of bulls: the top 50 genotyped bulls and the top 25 polled genotyped bulls on the Nordic total merit scale. We used linear programming to optimize economic scores within each herd, considering genetic level, genetic relationship, semen cost, the economic impact of genetic defects, polledness, and β-casein. We found that it was possible to reduce genetic relationships and eliminate expression of genetic defects with minimal effect on the genetic level in total merit index. Compared with maximizing only Nordic total merit index, the relative frequency of polled offspring increased from 13.5 to 22.5%, and that of offspring homozygous for β-casein (A2A2) from 66.7 to 75.0% in one generation, without any substantial negative impact on other comparison criteria. Using only semen from polled bulls, which might become necessary if dehorning is banned, considerably reduced the genetic level. We also found that animals carrying the polled allele were less likely to be homozygous for β-casein (A2A2) and more likely to be carriers of the genetic defect HH1. Hence, adding economic value to a monogenic trait in the economic score used for mating allocation sometimes negatively affected another monogenetic trait. We recommend that the comparison criteria used in this study be monitored in a modern genomic mating program.

Key words: mating allocation, polledness, Nordic total merit, β-casein (A2A2)

INTRODUCTION

Historically, mating programs at the herd level aim to maximize genetic value while minimizing expected inbreeding using pedigree information (Weigel and Lin, 2000). Genotyping provides breeders with new insights at the single nucleotide level that can be used in mating programs. For instance, SNP markers offer the possibility to calculate genomic relationships between potential parents. Genomic estimates of relationships are expected to be more accurate than when using pedigree information, because they do not rely on pedigree completeness or correctness. Genomic relationships can also differentiate between animals with the same pedigree that inherit partly different genetic variants from their parents (VanRaden, 2008; de Cara et al., 2013). In addition, SNP markers provide information about certain known monogenic traits such as defects, as well as some desired traits.

Holstein is the most common cattle breed in Denmark, Finland, and Sweden (**DFS**), with approximately 600,000 milk-recorded cows. Genotyping of females has attracted great interest in DFS in the past decade, and today approximately 25% of all females born are genotyped. However, current (2022) mating programs in the Nordic countries still use pedigree relationship information and ban at-risk matings for recessive genetic defects. The SNP array (Borchersen, 2019) currently used for genotyping in DFS includes 7 Holstein recessive genetic defects, polledness, and β-CN status. Minimizing the risk of obtaining offspring homozygous for recessive genetic defects has an economic value for farmers (Pryce et al., 2012) and is also important for animal health and welfare (EFFAB, 2020).

Other types of monogenic traits, such as horn status, also influence animal welfare. For decades, dehorning of cattle has been common practice. Dehorning is performed for several reasons, including reduced risk of injury to other cattle and improved safety for animal keepers. However, dehorning has been shown to cause behavioral, neuroendocrine, and physiological changes, indicating it to be a stressful and painful experience (Stock et al., 2013). Since 2022, organic farms in the European Union have to seek a permit if they want to dehorn their cattle (EU Commission Regulation No

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889/2008; EU, 2008). The cost of dehorning in DFS is estimated to be between €2.7 and €7.3 per head, considering veterinary costs, gas/electricity, and extra labor (Sørensen et al., 2018). However, this estimate does not consider the current situation, in which dehorning is strictly regulated in organic herds in the European Union.

Another example of a monogenic trait of economic importance is β-casein variant. Animals that are homozygotic for the A2 allele produce so-called A2 milk, which is often marketed as a healthier option than regular cow milk, although the human health benefits of consuming A2 milk are still being debated (Summer et al., 2020). Despite this lack of confirmed benefits, some countries are seeking to increase consumption of A2 milk and some dairies pay extra for A2 milk (Bisutti et al., 2022).

The new genetic insights and possibilities available require new methods that combine relevant information based on their economic value when setting up mating plans. Several studies have created economic scoring systems to rank each potential mating (Carthy et al., 2019; Bérodier et al., 2021; Bengtsson et al., 2022). The economic score often includes genetic level, expected inbreeding, the probability of conceiving an offspring homozygous for a genetic defect, and semen price (Bérodier et al., 2021; Bengtsson et al., 2022). The economic score is flexible and can be adjusted to match economic conditions on a specific farm, such as a price premium for A2 milk or polled animals. Using linear programming to maximize every herd's mean economic score, subject to necessary constraints, is a fast and effective method (Carthy et al., 2019; Bérodier et al., 2021). Linear programming has also been shown to outperform other mating methods, such as sequential mate allocation (Sun et al., 2013; Carthy et al., 2019; Bérodier et al., 2021).

Our objective in this study was to investigate the ability of different approaches for mating allocation in DFS Holstein, considering polledness, β-CN, and several recessive genetic defects. We also optimized the mating allocations on total merit index while limiting parent relationships. We investigated all mating allocations at the herd level with real data and used linear programming to optimize different economic scores within each herd.

MATERIALS AND METHODS

Breeding values, pedigree data, SNP data, and data on monogenic traits were obtained from the Nordic Cattle Genetic Evaluation (**NAV**) database (NAV, 2019). No ethical approval was needed for this study because no animal procedures were performed.

Genotype Data

Single nucleotide polymorphism information was available for all genotyped Holstein animals born between 2011 and 2020 in Denmark, Finland, and Sweden. The NAV database uses the Illumina 50k chip (Illumina Inc.) as standard for genomic prediction, and all lower-density chips are imputed by NAV to that format using FImpute (Sargolzaei et al., 2014). The EuroG MD beadchip (Borchersen, 2019) has been used since late 2018. In total, genotypes for 261,198 animals (225,298 females and 35,900 males) were available.

Total Merit

We used Nordic Total Merit (**NTM**) values from the NAV breeding evaluation performed in May 2020, which are expressed in standardized units with a mean of 0 and genetic standard deviation of 10. At the time of data extraction, NTM was composed of 15 sub-indices, covering yield index, longevity, growth, youngstock survival, udder health, udder, feet and legs, frame, hoof health, milkability, daughter fertility, general health, temperament, calving direct, and calving maternal (NAV, 2019).

Data Selection

Females. We selected 289 herds that had genotyped more than 40 Holstein females born in 2019. In total, 24,333 Holstein females were available for mating allocations. The EuroG MD beadchip (Borchersen, 2019), used since late 2018, includes information about all monogenic traits considered in this study (Table 1).

Bulls. We used 2 data sets of bulls, Bull50 and Bull25Polled (Table 2). The main bull data set (Bull50) included the top 50 genotyped bulls on the NTM scale, available from the Nordic breeding cooperative VikingGenetics. The data set Bull25Polled included the top 25 genotyped polled bulls on the NTM scale, also available from VikingGenetics, comprising 21 heterozygous polled (**Pp**) bulls and 4 homozygous polled bulls (**PP**). Bulls in both data sets were born between January 2017 and August 2019. At VikingGenetics, the program EVA (Berg et al., 2006) is used for optimum contribution selection to select breeding animals using pedigree relationships (Hanna Driscoll, product manager Holstein, VikingGenetics; personal communication, January 19, 2022).

Relationship Measures

Pedigree Relationships. Two pedigree relationships were calculated. The first relationship coefficient

Table 1. Description of monogenic traits considered in this study, code used in the Online Mendelian Inheritance in Animals (OMIA) database, and the effect in conceptus or offspring, available with a genomic test in Holstein

Monogenic trait	OMIA code	Description
Holstein Haplotype 1 (HH1)	000001-9913	Early abortion of homozygous conceptus[1]
Holstein Haplotype 3 (HH3)	001824-9913	Early abortion of homozygous conceptus[2]
Holstein Haplotype 4 (HH4)	001826-9913	Early abortion of homozygous conceptus[3]
Holstein Haplotype 6 (HH6)	002194-9913	Early abortion of homozygous conceptus[3]
Holstein Haplotype 7 (HH7)	001830-9913	Early abortion of homozygous conceptus[3]
Bovine leukocyte adhesion deficiency (BLAD)	000595-9913	Extreme susceptibility to infection and early mortality in homozygous offspring[4]
Progressive retinal degeneration (RP1)	000866-9913	Progressive blindness in homozygous offspring[5]
Polledness	000483-9913	Absence of horns in offspring carrying at least one copy of the polled allele (Celtic and Friesian allele considered)[6]
β-CN	002033-9913	A cow produces so-called A2 milk if she has 2 copies of the A2 allele[7]

[1] Adams et al. (2016).

[2] Daetwyler et al. (2014).

[3] Fritz et al. (2013).

[4] Schuster et al. (1992).

[5] Bradley et al. (1982).

[6] Medugorac et al. (2012).

[7] Gallinat et al. (2013).

traced the pedigree 3 generations back from the parents of the potential mating ($\mathbf{a_{3Gen}}$), reflecting the current Nordic mating programs. The second pedigree relationship coefficient was based on all available pedigree information ($\mathbf{a_{AllGen}}$).

For most cases, the pedigree for genotyped animals had already been corrected for mismatches by NAV. We found 143 genotyped animals with missing or mismatching parents, which were excluded from further analyses. The discrete generation equivalent (Woolliams and Mäntysaari, 1995) for the mated animals was 16.0, and the equivalent for complete generations (Maignel et al., 1996) was 12.7. The 5-generation pedigree completeness for mated animals was 99.4%.

Genomic Relationships. Three genomic relationship coefficients were used, one SNP-by-SNP genomic relationship and 2 based on shared genomic segments. The SNP-by-SNP genomic relationship coefficient ($\mathbf{g_{SNP}}$) was calculated according to VanRaden (2008), using the software SNP1101 (Sargolzaei, 2014), as follows:

$$g_{SNP_{ij}} = \frac{\sum_m \left(x_{im} - 2p_m\right) \times \left(x_{jm} - 2p_m\right)}{2\sum_m p_m \ (1 - p_m)},$$

where x_{im} and x_{jm} are the genotype scores of animal i and animal j at marker m, coded as 0 = homozygote, 1 = heterozygote, and 2 = alternative homozygote; and p_m is the frequency of the alternative allele of marker m in the founder population. Because we did not know the founder population frequency, the allele frequency

Table 2. Descriptive statistics on the Holstein females and bulls selected for mating allocations

		Data set	
Trait	Females 289 herds	Bull50	Bull25Polled
Number of animals	24,333	50	25
Average Nordic Total Merit (NTM)	12.10	33.93	27.17
Carriers of defect HH1 (%)	3.45	2.00	16.00
Carriers of defect HH3 (%)	3.62	4.00	0.00
Carriers of defect HH4 (%)	1.31	0.00	0.00
Carriers of defect HH6 (%)	0.30	0.00	0.00
Carriers of defect HH7 (%)	0.29	0.00	0.00
Carriers of defect BLAD (%)	0.27	0.00	0.00
Carriers of defect RP1 (%)	0.63	0.00	0.00
Heterozygous polled (Pp) (%)	3.74	14.00	84.00
Homozygous polled (PP) (%)	0.10	0.00	16.00
Heterozygous β-casein (A1A2) (%)	37.11	30.00	44.00
Homozygous β-casein (A2A2) (%)	57.12	66.00	48.00

of all genotyped Holstein was used. Using observed allele frequency instead of founder population frequency is an approximation often used for genomic evaluation (Wang et al., 2014).

The 2 genomic relationship coefficients based on shared genomic segments ($\mathbf{g_{SEG}}$) were calculated following de Cara et al. (2013):

$$g_{SEG_{ij}} = \frac{\sum_k \sum_{ai=1}^{2} \sum_{bj=1}^{2} \left[L_{SEGk}\left(a_i b_j\right)\right]}{2L_{AUTO}},$$

where L_{SEGk} is the length (in bp) of the kth shared segment measured over homolog a of animal i and homolog b of animal j, and L_{AUTO} is the total length of the autosomes covered by the SNP (in bp).

The 2 segment-based genomic relationship coefficients were based on different minimum lengths of segments: 1 cM ($\mathbf{g_{SEG1}}$) and 4 cM ($\mathbf{g_{SEG4}}$), assuming 1 cM = 1,000,000 bp (Gautier et al., 2007). These segment lengths were chosen to represent short and long segments, similarly to other studies (Zhang et al., 2015; Martikainen et al., 2017; Forutan et al., 2018; Makanjuola et al., 2020). Phasing of genotypes was performed in Beagle 4.1 with default settings (Browning and Browning, 2007), and segments of minimum chosen length were extracted in RefineIBD with the default setting except for the logarithm of odds (**LOD**) score (base 10 log of the likelihood ratio), where we used LOD = 0.1 (Browning and Browning, 2013). The LOD score is used to prune out shared segments that are not common in the population. Hence, default LOD = 3.0 in RefineIBD was considered too high for our purposes, as reported in a recent study (Olsen et al., 2020).

Mate Allocation

Mate allocation was programmed in R version 3.6.3 (https://www.r-project.org/), using the "Lp_solve" package (Berkelaar, 2020). A mating linear programming problem has several integer properties. However, linear programming can be used instead of integer programming because the coefficient matrix has a structure that guarantees integer solutions if the right hand side of the equation are integers (Jansen and Wilton, 1985). Lp_solve is a mixed integer linear programming solver, and hence is suitable for the mating linear programming problem. A mating R script was provided by Bérodier et al. (2021) and modified to allow it to handle favorable monogenic traits. The R script set up constraints considered in linear programming optimization. We used the following constraints: 1 mating per female and a threshold percentage for the maximum number of females per bull and herd, for which we evaluated 2 levels, 5% and 10%, similarly to Bérodier et al. (2021). The threshold for the number of females per bull and herd was in line with current recommendations in DFS.

Economic Score

For each potential mating between female i and bull j, we calculated an economic score:

$$Score_{ij} = \left(\frac{NTM_i + NTM_j}{2} + \lambda \text{F}_{ij} + p\left(\text{BetaC}\right) \times \ \text{v}_{BetaC}\right) \times \text{prob}\left(\text{Fem}\right) - \sum_{r=1}^{\text{n}_r} p\left(\text{aa}\right)_r \times \ \text{v}_r + p\left(\text{P}\right) \times \text{v}_{\text{P}} - \text{semen cost},$$

where NTM_i and NTM_j are the values in euros (€) of the Nordic Total Merit units for female i and bull j, λ is the economic consequence of a 1% increase in inbreeding, F_{ij} is the pedigree- or genome-based co-ancestry (relationship/2), p(BetaC) is the probability of a homozygous offspring for β-CN (A2A2), v_{BetaC} is the value of a homozygous offspring for β-CN (A2A2), $\text{prob}\left(\text{Fem}\right)$ is the probability of producing a female conceptus, n_r is the number of recessive genetic defects considered, $p(\text{aa})_r$ is the probability of expression of genetic defect r, v_r is the economic cost associated with recessive genetic defect r, p(P) is the probability of a polled offspring, v_{P} is the value of a polled offspring, and semen cost is the average amount (€) spent on semen for a pregnancy.

An index unit of NTM is worth €25.4 over the lifetime of a Holstein female in DFS (Fikse and Kargo, 2020). We considered sexed semen with 0.9 probability of producing a female conceptus (Burnell, 2019). The economic consequence of a 1% increase in inbreeding was set to €25.4. The Swedish mating program "Genvägen" uses a penalty of 1 NTM unit per 1% increase in inbreeding, which would correspond to €25.4 (Lina Baudin, expert in breeding routines, Växa Sverige; personal communication, March 5, 2021). This is in line with other studies citing US$25 (about €25; Cole, 2015) and US$24 (Smith et al., 1998).

We assumed the cost of an early abortion (HH1, HH3, HH4, HH6, HH7; Table 1) to be €80, based on the resulting longer calving interval (€30–€40/month) and the cost of extra insemination(s) (€30; Oskarsson and Engelbrekts, 2015; Sørensen et al., 2018). Bulls carrying BLAD and RP1 are not allowed in the breeding program at VikingGenetics, so we did not estimate any cost for them. We tested different economic val-

Table 3. Description of the mating scenarios considered[1]

Scenario	Economic score includes				
	NTM	Relationship	Genetic defect value	Polled value (€)	β-casein value (€)
MaxNTM	Yes	No	No	0	0
3Gen	Yes	a_{3Gen}	Yes	0	0
AllGen	Yes	a_{AllGen}	Yes	0	0
GSNP	Yes	g_{SNP}	Yes	0	0
GSEG1	Yes	g_{SEG1}	Yes	0	0
GSEG4	Yes	g_{SEG4}	Yes	0	0
GSNPPolled10	Yes	g_{SNP}	Yes	10	0
GSNPPolled50	Yes	g_{SNP}	Yes	50	0
GSNPPolled100	Yes	g_{SNP}	Yes	100	0
GSNPBetaC10	Yes	g_{SNP}	Yes	0	10
GSNPBetaC50	Yes	g_{SNP}	Yes	0	50
GSNPBetaC100	Yes	g_{SNP}	Yes	0	100
GSNPPolledBetaC10	Yes	g_{SNP}	Yes	10	10
GSNPPolledBetaC50	Yes	g_{SNP}	Yes	50	50
GSNPPolledBetaC100	Yes	g_{SNP}	Yes	100	100
Random	All possible combinations of females and bulls				

[1] MaxNTM = mating scenario where mates were selected based on maximizing an economic score including Nordic Total Merit (NTM), sexed semen, and semen cost; 3Gen = mating scenario where mates were selected based on maximizing an economic score including NTM, sexed semen, semen cost, a pedigree relationship including 3 generations of ancestors (a_{3Gen}), and a penalty for genetic defects; AllGen = mating scenario where mates were selected based on maximizing an economic score including NTM, sexed semen, semen cost, a pedigree relationship including all available ancestors (a_{AllGen}), and a penalty for genetic defects; GSNP = mating scenario where mates were selected based on maximizing an economic score including NTM, sexed semen, semen cost, a genomic relationship calculated according to VanRaden (2008) (g_{SNP}), and a penalty for genetic defects; GSEG1 = mating scenario where mates were selected based on maximizing an economic score including NTM, sexed semen, semen cost, a genomic relationship based on shared genomic segment calculated according to de Cara et al. (2013) with a minimum genomic segment length of 1 cM (g_{SEG1}), and a penalty for genetic defects; GSEG4 = mating scenario where mates were selected based on maximizing an economic score including NTM, sexed semen, semen cost, and a genomic relationship based on shared genomic segment calculated according to de Cara et al. (2013) with a minimum genomic segment length of 4 cM (g_{SEG4}), and a penalty for genetic defects; Polled €0, €10, €50, €100 = economic value of a polled offspring, added to the economic score GSNP; BetaC €0, €10, €50, €100 = economic value of an offspring homozygous for β-CN (A2A2), added to the economic score GSNP; Polled BetaC €0, €10, €50, €100 = economic value of a polled offspring and offspring homozygous for β-CN (A2A2), added to the economic score GSNP.

ues (€0, €10, €50, and €100) for polledness and β-CN (A2A2).

We used the prices for sexed semen set by VikingGenetics in 2021. The semen price depends on the bull's NTM and polledness status. A dose of semen from a horned bull with NTM >35, 33 to 34, 30 to 32, and <30 costs €26, €23, €20, and €17, respectively. Semen of polled bulls (homozygous or heterozygous for the polled allele) costs €3 more than semen of horned bulls with the same NTM (Hanna Driscoll, product manager Holstein, VikingGenetics; personal communication, January 19, 2022). Detailed information about the mating scenarios can be found in Table 3. Sexed semen and semen cost were considered in all scenarios. The objective in linear programming was always to maximize the economic score.

Mating Allocation

The suggested planned matings were compared by (1) average NTM; (2) average genetic relationships (a_{3Gen}, a_{AllGen}, g_{SNP}, g_{SEG1}, g_{SEG4}); (3) at-risk matings, as a percentage of matings of 2 carriers of the same recessive genetic defects (the most common defects, HH1 and HH3); (4) average cost of semen for a pregnancy, calculated in the same way as in the economic score; (5) total number of bulls used; (6) number of bulls used to the maximum number of doses allowed on the threshold (5 and 10%) of females per bull and herd; and (7) predicted carrier frequency of HH1 and HH3 in the next generation (%), calculated from the proportion of matings with a carrier (assuming a 50% probability of the defect allele being inherited from a carrier parent); (8) predicted percentage of polled offspring; and (9) predicted percentage of offspring homozygous for β-CN (A2A2) in the next generation.

Statistical Analysis

We used SAS software version 9.4 (SAS Institute Inc.) and R version 3.6.3 (https://www.r-project.org/) for statistical analysis. A chi-squared test was conducted

Table 4. Descriptive statistics on relationships (mean, SD, minimum and maximum values) between all possible combinations of 24,333 females and 50 bulls

Relationship coefficient[1]	Mean	SD	Minimum	Maximum
a_{3Gen}	0.015	0.031	0	0.545
a_{AllGen}	0.132	0.031	0.035	0.647
g_{SNP}	0.010	0.040	−0.106	0.576
g_{SEG1}	0.269	0.042	0.089	0.853
g_{SEG4}	0.181	0.041	0.039	0.763

[1] Coefficients: a_{3Gen} = pedigree relationships using 3 generations of ancestors, a_{AllGen} = pedigree relationships using all available pedigree information, g_{SNP} = genomic relationship calculated according to VanRaden (2008), g_{SEG1} (g_{SEG4}) = genomic segment-based relationship according to de Cara et al. (2013) with a minimum segment length of 1 (4) cM.

Table 5. Correlation between the different relationship coefficients for all possible combinations of 24,333 females and 50 bulls[1]

	Relationship				
Relationship	a_{3Gen}	a_{AllGen}	g_{SNP}	g_{SEG1}	g_{SEG4}
a_{3Gen}	1	0.95	0.75	0.69	0.70
a_{AllGen}		1	0.76	0.75	0.76
g_{SNP}			1	0.88	0.87
g_{SEG1}				1	0.97

[1] Coefficients: a_{3Gen} = pedigree relationships using 3 generations of ancestors, a_{AllGen} = pedigree relationships using all available pedigree information, g_{SNP} = genomic relationship calculated according to VanRaden (2008), g_{SEG1} (g_{SEG4}) = genomic segment-based relationship according to de Cara et al. (2013) with a minimum segment length of 1 (4) cM.

in SAS to test association between polledness genotype and HH1, HH3, or β-CN genotype.

RESULTS

The presented mating results are between the 24,333 females selected for matings and data set Bull50, unless otherwise specified.

Genetic Relationship Coefficients

For all possible combinations of females and males, the mean value of the relationship coefficient ranged from 0.010 to 0.269, and the standard deviation ranged from 0.031 to 0.042 (Table 4). For all correlations between different genetic relationship coefficients, the value of correlation coefficient was ≥0.69. The strongest correlation was between g_{SEG1} and g_{SEG4} ($r = 0.97$). Further, all correlations between a_{AllGen} and genomic relationships were of similar strength (0.75–0.76), whereas those between a_{3Gen} and the genomic relationships showed a wider range (0.69–0.75; Table 5). The coefficients of regression from genomic relationship coefficients on a_{AllGen} were all close to 1. They were highest for g_{SEG1} and g_{SEG4}, and somewhat lower for a_{3Gen} and g_{SNP} (Figure 1).

Mate Allocation

Using Bull50. In scenario MaxNTM, the NTM level improved compared with scenario Random (Table 6), but the genetic relationship did not decrease. Including the cost of the known recessive genetic defects when optimizing mating strategies avoided at-risk matings (mating of 2 animals carrying the same recessive genetic defect). In 3Gen, Allgen, GSNP, GSEG1, and GSEG4, all genetic relationships were decreased compared with Random and MaxNTM. Including pedigree relationships in the economic score decreased genomic relationships compared with Random and MaxNTM, but they were further decreased when using a genomic relationship.

The number of bulls used in the scenarios considering genomic relationships was generally higher (49 to 50) than in the scenarios considering pedigree relationships (32 to 36) and the difference was even larger when allowing 10% females per bull. Furthermore, fewer bulls were used for the maximum number of permitted inseminations considering genomic relationships compared with scenarios considering pedigree relationships with the same constraints. We observed a lower percentage of polled offspring when more bulls were used; for example, 15.7% in scenario 3Gen compared with 7.5% in GSEG4.

Including an extra economic value for the polledness trait in the economic score used for mating allocations increased the expected percentage of polled offspring in the next generation (Table 7). For example, when using a constraint of 5% females per bull and herd, the expected percentage of polled offspring increased from 9.7% in GSNP to 17.0% in GSNPPolled€100. In general, the other mating parameters were minimally affected when adding economic value to the polledness trait, with the same constraints. However, when using a constraint of 10% females per bull, we observed a decline in the expected percentage of β-CN (A2A2) offspring: 66.4% in GSNPPolled€0 and 62.2% in GSNPPolled€100.

Including an economic value for β-CN (A2A2) in the economic score used for mating allocations increased the expected percentage of offspring homozygous for β-CN (A2A2), with a minor effect on the average NTM level and genetic relationships (Table 8). The highest percentage of offspring homozygous for β-CN (A2A2) was observed in Beta-C€100 (75.0%) with a constraint of 10% females per herd and bull. We observed a decline in the expected percentage of polled offspring

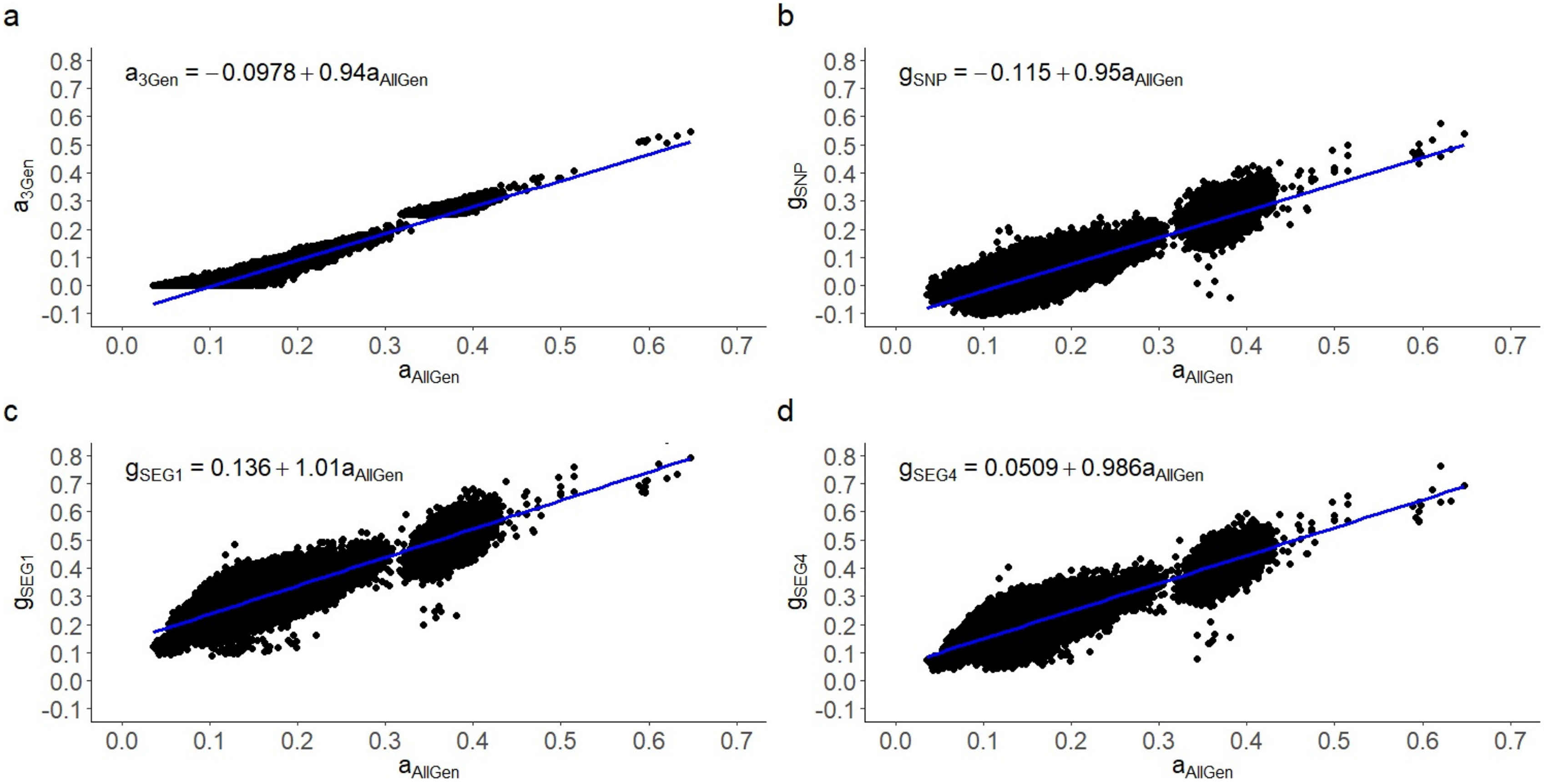

Figure 1. Relationship coefficients estimated from (a) pedigree data with 3 generations of ancestors (a_{3Gen}), (b) SNP data (g_{SNP}; VanRaden, 2008), (c) shared genomic segments with a minimum segment length of 1 cM (g_{SEG1}), and (d) shared genomic segments with a minimum length of 4 cM (g_{SEG4}; de Cara et al., 2013), all plotted against relationship coefficients estimated from pedigree data using all available ancestors (a_{AllGen}). The relationships shown are for all possible combinations of 24,333 Holstein females and 50 bulls.

Table 6. Results of 13 mating scenarios, including 24,333 Holstein females; available bulls were 50 Holstein bulls marketed by VikingGenetics (Bull50)

		5% females/bull scenarios[2]						10% females/bull scenarios[2]					
Comparison criterion[1]	Random	Max NTM	3Gen	AllGen	GSNP	GSEG1	GSEG4	Max NTM	3Gen	AllGen	GSNP	GSEG1	GSEG4
Average Nordic Total Merit (NTM)	23.0	24.3	24.3	24.3	24.2	24.2	24.2	25.4	25.4	25.3	25.2	25.1	25.1
Average a_{3Gen} between parents	0.026	0.028	0.010	0.012	0.018	0.017	0.017	0.026	0.012	0.014	0.018	0.018	0.018
Average a_{AllGen} between parents	0.132	0.132	0.115	0.113	0.121	0.120	0.120	0.129	0.116	0.114	0.121	0.120	0.120
Average g_{SNP} between parents	0.010	0.011	−0.006	−0.009	−0.040	−0.035	−0.033	0.011	−0.003	−0.004	−0.034	−0.030	−0.028
Average g_{SEG1} between parents	0.269	0.268	0.253	0.250	0.226	0.218	0.221	0.268	0.256	0.254	0.231	0.223	0.226
Average g_{SEG4} between parents	0.181	0.180	0.165	0.162	0.141	0.135	0.133	0.180	0.169	0.166	0.146	0.139	0.137
At-risk matings (%)	0.20	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Average cost of semen for a pregnancy (€)	44.4	48.8	48.8	48.6	48.4	48.1	48.2	50.7	50.9	50.4	50.2	49.5	49.6
Number of bulls used	NA[3]	30	32	36	50	50	49	13	16	17	46	39	36
Number of bulls used to a maximum	NA	20	16	16	8	7	10	10	8	7	2	3	4
Predicted HH1 carrier frequency in the next generation (%)	2.7	1.7	1.7	1.7	1.8	1.8	1.8	1.7	1.7	1.7	1.7	1.7	1.7
Predicted HH3 carrier frequency in the next generation (%)	3.8	4.1	4.1	4.1	3.9	4.3	4.2	1.8	2.4	3.2	2.6	3.1	3.1
Percentage of polled offspring	8.8	10.6	10.7	9.5	9.7	8.2	8.4	13.5	15.7	11.8	11.7	7.6	7.5
Percentage of homozygous A2A2 offspring	61.2	61.8	60.6	61.1	61.0	62.5	62.1	66.7	64.1	65.3	66.4	67.1	67.2

[1] Average NTM level, 5 different genetic relationships, at-risk matings: percentage of matings with 2 carriers of the same recessive genetic defect HH1, HH3, the average cost of semen for a pregnancy, the number of bulls used, the number of bulls used to a maximum number of doses based on the 5% and 10% constraint of females per bull and herd, predicted genetic defect HH1 and HH3 carrier frequency in the next generation, predicted percentage of polled offspring in the next generation, and predicted percentage of offspring homozygous for β-CN (A2A2) in the next generation.

[2] Maximum percentage of females per bull and herd set to 5% or 10%. MaxNTM = mating scenario where mates were selected based on maximizing an economic score including NTM, sexed semen, and semen cost; 3Gen = mating scenario where mates were selected based on maximizing an economic score including NTM, sexed semen, semen cost, a pedigree relationship including 3 generations of ancestors (a_{3Gen}), and a penalty for genetic defects; AllGen = mating scenario where mates were selected based on maximizing an economic score including NTM, sexed semen, semen cost, a pedigree relationship including all available ancestors (a_{AllGen}), and a penalty for genetic defects; GSNP = mating scenario where mates were selected based on maximizing an economic score including NTM, sexed semen, semen cost, a genomic relationship calculated according to VanRaden (2008) (g_{SNP}), and a penalty for genetic defects; GSEG1 = mating scenario where mates were selected based on maximizing an economic score including NTM, sexed semen, semen cost, a genomic relationship based on shared genomic segment calculated according to de Cara et al. (2013) with a minimum genomic segment length of 1 cM (g_{SEG1}), and a penalty for genetic defects; GSEG4 = mating scenario where mates were selected based on maximizing an economic score including NTM, sexed semen, semen cost, and a genomic relationship based on shared genomic segment calculated according to de Cara et al. (2013) with a minimum genomic segment length of 4 cM (g_{SEG4}), and a penalty for genetic defects.

[3] NA = not applicable.

Table 7. Results of 9 mating scenarios investigating extra economic value for the polledness trait, including 24,333 Holstein females; available bulls were 50 Holstein bulls marketed by VikingGenetics (Bull50)

		5% females/bull scenarios[2]				10% females/bull scenarios[2]			
		GSNP				GSNP			
Comparison criterion[1]	Random	Polled €0	Polled €10	Polled €50	Polled €100	Polled €0	Polled €10	Polled €50	Polled €100
Average Nordic Total Merit (NTM)	23.0	24.2	24.2	24.2	24.1	25.2	25.2	25.2	25.0
Average a_{AllGen} between parents	0.132	0.121	0.121	0.121	0.122	0.121	0.121	0.121	0.122
Average g_{SNP} between parents	0.010	−0.040	−0.040	−0.040	−0.039	−0.034	−0.034	−0.034	−0.034
At-risk matings (%)	0.2	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Average cost of semen for a pregnancy (€)	44.4	48.4	48.5	48.7	48.7	50.2	50.3	50.7	50.8
Number of bulls used	NA	50	50	49	49	46	46	45	41
Number of bulls used to a maximum	NA	8	8	7	7	2	2	3	3
Predicted HH1 carrier frequency in the next generation (%)	2.7	1.8	1.8	2.3	3.8	1.7	1.7	1.8	2.4
Predicted HH3 carrier frequency in the next generation (%)	3.8	3.9	3.8	3.7	3.4	2.6	2.5	2.4	2.2
Percentage of polled offspring	8.8	9.7	10.3	13.2	17.0	11.7	12.6	16.4	22.5
Percentage of homozygous A2A2 offspring	61.2	61.0	60.9	60.8	60.8	66.4	65.9	64.0	62.2

[1] Average NTM level, 2 different genetic relationships, at-risk matings: percentage of matings with 2 carriers of the same recessive genetic defect HH1, HH3, the average cost of semen for a pregnancy, the number of bulls used, the number of bulls used to a maximum number of doses based on the 5% and 10% constraint of females per bull and herd, predicted genetic defect HH1 and HH3 carrier frequency in the next generation, predicted percentage of polled offspring in the next generation, and predicted percentage of offspring homozygous for β-CN (A2A2) in the next generation. a_{AllGen} = a pedigree relationship including all available ancestors.

[2] Maximum percentage of females per bull and herd set to 5% or 10%. GSNP = mating scenario where mates were selected based on maximizing an economic score including NTM, sexed semen, semen cost, a genomic relationship calculated according to VanRaden (2008) (g_{SNP}), and penalty for genetic defects. Polled €0, €10, €50, €100 = economic value of a polled offspring, added to the economic score GSNP.

Table 8. Results of 9 mating scenarios investigating extra economic value for β-CN (A2A2), including 24,333 Holstein females; available bulls were 50 Holstein bulls marketed by VikingGenetics (Bull50)

		5% females/bull scenarios[2]				10% females/bull scenarios[2]			
		GSNP				GSNP			
Comparison criterion[1]	Random	BetaC €0	BetaC €10	BetaC €50	BetaC €100	BetaC €0	BetaC €10	BetaC €50	BetaC €100
Average Nordic Total Merit (NTM)	23.0	24.2	24.2	24.2	24.1	25.2	25.2	25.2	25.1
Average a_{AllGen} between parents	0.132	0.121	0.121	0.121	0.122	0.121	0.121	0.121	0.121
Average g_{SNP} between parents	0.010	−0.040	−0.040	−0.040	−0.039	−0.034	−0.034	−0.034	−0.033
At-risk matings (%)	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Average cost of semen for a pregnancy (€)	44.4	48.4	48.4	48.2	47.7	50.2	50.2	49.9	49.7
Number of bulls used	NA	50	50	48	48	46	45	46	46
Number of bulls used to a maximum	NA	8	8	6	6	2	2	3	2
Predicted HH1 carrier frequency in the next generation (%)	2.7	1.8	1.8	1.8	1.9	1.7	1.7	1.7	1.8
Predicted HH3 carrier frequency in the next generation (%)	3.8	3.9	3.5	2.4	2.3	2.6	2.3	1.9	1.9
Percentage of polled offspring	8.8	9.7	9.5	8.8	7.9	11.7	11.2	9.3	8.0
Percentage of homozygous A2A2 offspring	61.2	61.0	62.9	69.2	72.9	66.4	68.2	72.8	75.0

[1] Average NTM level, 2 different genetic relationships, at-risk matings: percentage of matings with 2 carriers of the same recessive genetic defect HH1, HH3, the average cost of semen for a pregnancy, the number of bulls used, the number of bulls used to a maximum number of doses based on the 5% and 10% constraint of females per bull and herd, predicted genetic defect HH1 and HH3 carrier frequency in the next generation, predicted percentage of polled offspring in the next generation, and predicted percentage of offspring homozygous for β-CN (A2A2) in the next generation. a_{AllGen} = a pedigree relationship including all available ancestors.

[2] Maximum percentage of females per bull and herd set to 5% or 10%. GSNP = mating scenario where mates were selected based on maximizing an economic score including NTM, sexed semen, semen cost, a genomic relationship calculated according to VanRaden (2008) (g_{SNP}), and a penalty for genetic defects. BetaC €0, €10, €50, €100 = economic value of an offspring homozygous for β-CN (A2A2), added to the economic score GSNP.

when adding economic value to β-CN (A2A2) in the economic score.

Adding economic value to both the polledness trait and β-CN (A2A2) in the economic score used for mating allocations increased the expected number of polled offspring and offspring homozygous for β-CN (A2A2) compared with GSNPPolled€0 (Table 9). Using both constraints of 5% and 10% females per herd and bull, a simultaneous increase in the 2 traits occurred as the economic value increased.

Using BullPolled25. When 25 polled bulls (21 Pp bulls, 4 PP bulls) were available for mating allocations, it was possible to further increase the expected percentage of polled offspring (Table 10). For example, when using BullPolled25 and a constraint of 5% females per herd and bull, the expected percentage of polled offspring was 60.1% in GSNPPolled100€, compared with 17.0% using Bull50. Considering the same example, the average NTM level was 20.2 using BullPolled25 compared with 24.1 using Bull50. The average genetic relationships using BullPolled25 were slightly higher than those using Bull50 with the same constraints and economic scores. The expected percentage of offspring homozygous for β-CN (A2A2) was lower and the predicted HH1 carrier frequency was higher, for BullPolled25 compared with Bull50.

Association Between Monogenic Traits

Among the 24,333 mated females, polled females (Pp and PP) were less likely to be homozygous for β-CN (A2A2) (or A2A2 females were less likely to carry the polled allele; Figure 2). For example, 58% of the horned females but only 44% of the heterozygous polled (Pp) females were homozygous for β-CN (A2A2). The chi-squared test showed a significant unfavorable association between polled and β-CN genotype ($P < 0.0001$) in the data. Polled females were also more likely to be HH1 carriers (or HH1 carriers were more likely to be polled). For example, 23% of the heterozygous polled females were carriers of HH1, whereas only 3% of the horned animals were carriers (Figure 3). The chi-squared test showed a significant unfavorable association between polledness and HH1 genotype ($P < 0.0001$) in the study data. We observed no association between polledness and HH3 genotype (results not shown).

DISCUSSION

We explored mating allocations in Holstein dairy cattle, taking into account genomic information. The results showed that it was possible to reduce genetic relationships and eliminate expression of genetic defects with minimal effect on the genetic level, as we found previously in a study on Red Dairy Cattle (Bengtsson et al., 2022). The results also showed that it was possible to increase the percentage of polled offspring substantially in one generation when competitive bulls were available, without any significant negative effect on other comparison criteria. It was also possible to increase the number of homozygous β-CN (A2A2) offspring without any negative effect on other comparison criteria. Using only semen from polled bulls, which might be necessary if dehorning is banned, had a substantial impact at the genetic level. We also found that animals in this study carrying the polled allele were less likely to be homozygous for β-CN (A2A2) and more likely to be carriers of the genetic defect HH1. Hence, adding economic value to a monogenic trait in the economic score used for mating allocations sometimes negatively affected another monogenetic trait. Therefore, it may be necessary to monitor comparison criteria, as used in this study, in a modern genomic mating program.

Breeding for the Polledness Trait

Polled calves can easily be achieved by mating all females to homozygous (PP) bulls. However, no homozygous polled bulls were available in Bull50. Other authors have highlighted the absence of competitive homozygous polled bulls (Spurlock et al., 2014; Mueller et al., 2019). The reason for the difference in genetic level is not clear. Other authors have hypothesized that it could be due to lack of selection emphasis on production traits of polled bulls. Alternatively, it could be due to pleiotropic effects of chromosomal segments, or genes linked to the polled locus could contribute to a poorer genetic level for production traits (Spurlock et al., 2014). At the population level, it has been shown to take somewhere between 10 and 25 generations to get most bulls homozygous polled, from a starting allele frequency of 0.03 (Scheper et al., 2016), which is between the polled allele frequency of the mated females and bulls in this study. The large difference in number of generations required depends on many factors, including available tools such as level of genotyping and the goal of genetic gain and inbreeding. Hence, 100% homozygous (PP) bulls cannot be expected in the DFS Holstein population in the near future.

In this study, the economic value for the polledness trait had to be higher than €50 before we observed a fundamental change in the expected number of polled offspring (Table 7). We observed a lower percentage of polled offspring when more bulls were used; for example, 15.7% in 3Gen compared with 7.5% in GSEG4. This was because heterozygous polled bulls were more commonly ranked in the top half of the Bull50 data set than in the bottom half. The high ranking of hetero-

Table 9. Results of 9 mating scenarios investigating extra economic value for the polledness trait and β-CN (A2A2), including 24,333 Holstein females; available bulls were 50 Holstein bulls marketed by VikingGenetics (Bull50)

		5% females/bull scenarios[2]				10% females/bull scenarios[2]			
		GSNP				GSNP			
Comparison criterion[1]	Random	Polled BetaC €0	Polled BetaC €10	Polled BetaC €50	Polled BetaC €100	Polled BetaC €0	Polled BetaC €10	Polled BetaC €50	Polled BetaC €100
Average Nordic Total Merit (NTM)	23.0	24.2	24.2	24.2	24.1	25.2	25.2	25.2	25.1
Average a_{AllGen} between parents	0.132	0.121	0.121	0.122	0.122	0.121	0.121	0.121	0.122
Average g_{SNP} between parents	0.010	−0.040	−0.04	−0.039	−0.038	−0.034	−0.034	−0.033	−0.032
At-risk matings (%)	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Average cost of semen for a pregnancy (€)	44.4	48.4	48.5	48.6	48.5	50.2	50.3	50.5	50.4
Number of bulls used	NA	50	50	48	48	46	45	44	41
Number of bulls used to a maximum	NA	8	8	7	7	2	2	2	2
Predicted HH1 carrier frequency in the next generation (%)	2.7	1.8	1.8	2.7	4.0	1.7	1.7	1.9	3.0
Predicted HH3 carrier frequency in the next generation (%)	3.8	3.9	3.5	2.2	2.0	2.6	2.3	1.9	1.8
Percentage of polled offspring	8.8	9.7	10.2	13.1	15.4	11.7	12.2	14.1	18.5
Percentage of homozygous A2A2 offspring	61.2	61.0	62.8	68.5	71.1	66.4	67.7	70.4	71.8

[1] Average NTM level, 2 different genetic relationships, at-risk matings: percentage of matings with 2 carriers of the same recessive genetic defect HH1, HH3, the average cost of semen for a pregnancy, the number of bulls used, the number of bulls used to a maximum number of doses based on the 5% and 10% constraint of females per bull and herd, predicted genetic defect HH1 and HH3 carrier frequency in the next generation, predicted percentage of polled offspring in the next generation, and predicted percentage of offspring homozygous for β-CN (A2A2) in the next generation. a_{AllGen} = a pedigree relationship including all available ancestors.

[2] Maximum percentage of females per bull and herd set to 5% or 10%. GSNP = mating scenario where mates were selected based on maximizing an economic score including NTM, sexed semen, semen cost, a genomic relationship calculated according to VanRaden (2008) (g_{SNP}), and a penalty for genetic defects. Polled BetaC €0, €10, €50, €100 = economic value of a polled offspring and offspring homozygous for β-CN (A2A2), added to the economic score GSNP.

Table 10. Results of 9 mating scenarios investigating extra economic value for the polledness trait, including 24,333 Holstein females; available bulls were 25 polled Holstein bulls marketed by VikingGenetics (BullPolled25)

		5% females/bull scenarios[2]				10% females/bull scenarios[2]			
		GSNP				GSNP			
Comparison criterion[1]	Random	Polled €0	Polled €10	Polled €50	Polled €100	Polled €0	Polled €10	Polled €50	Polled €100
Average Nordic Total Merit (NTM)	19.6	20.2	20.2	20.2	20.2	22.4	22.4	22.4	22.3
Average a_{AllGen} between parents	0.129	0.121	0.121	0.121	0.121	0.125	0.125	0.125	0.125
Average g_{SNP} between parents	0.010	−0.034	−0.034	−0.034	−0.034	−0.028	−0.028	−0.027	−0.027
At-risk matings (%)	0.5	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Average cost of semen for a pregnancy (€)	41.42	41.91	41.91	41.91	41.91	46.10	46.10	46.10	46.10
Number of bulls used	NA	25	25	25	25	20	20	19	19
Number of bulls used to a maximum	NA	16	17	17	17	7	6	6	5
Predicted HH1 carrier frequency in the next generation (%)	10.0	10.2	10.1	10.1	10.1	8.0	7.9	7.5	8.0
Predicted HH3 carrier frequency in the next generation (%)	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8
Percentage of polled offspring	59.0	59.5	59.7	60.0	60.1	53.6	54.3	57.3	60.9
Percentage of homozygous A2A2 offspring	53.0	54.3	54.3	54.3	54.3	57.7	57.7	57.9	56.0

[1] Average NTM level, 2 different genetic relationships, percentage of matings with 2 carriers of the same genetic defect (HH1, HH3), the average cost of semen for a pregnancy, the number of bulls used, the number of bulls used to a maximum number of doses based on the 5% and 10% constraint of females per bull and herd, predicted genetic defect HH1 and HH3 carrier frequency in the next generation, predicted percentage of polled offspring in the next generation, and predicted percentage of offspring homozygous for β-CN (A2A2) in the next generation. a_{AllGen} = a pedigree relationship including all available ancestors.

[2] Maximum percentage of females per bull and herd set to 5% or 10%. GSNP = mating scenario where mates were selected based on maximizing an economic score including NTM, sexed semen, semen cost, a genomic relationship calculated according to VanRaden (2008) (g_{SNP}), and a penalty for genetic defects. Polled €0, €10, €50, €100 = economic value of a polled offspring, added to the economic score GSNP.

zygous polled bulls on the NTM scale was surprising compared with the findings of Spurlock et al. (2014) and Mueller et al. (2019), where polled bulls were not competitive on net merit. We believe that the high ranking of heterozygous polled bulls is mainly a coincidence. However, it sets the Nordic Holstein in a good position to spread the polled allele without compromising on genetic level. When using BullPolled25, the frequency of polled offspring further increased to 60.9% in GSNP-polled€100, using a constraint of 10% females per herd and bull. However, the NTM level was lower using BullPolled25 compared with using Bull50. We also observed a negative effect on the number of offspring homozygous for β-CN (A2A2) and more carriers of the genetic defect HH1 in the next generation. Hence, the benefit of having more polled animals should be weighed carefully against the negative effect that this might have on other comparison criteria.

Some of the homozygous polled bulls in BullPolled25 were not used to their maximum allowed usage, mainly because their genetic level was too low (Table 10). For example, using a constraint of 10% females per herd and bull, the number of polled offspring did not increase compared with using the 5% females per herd bull constraint, even if the homozygous polled bulls were allowed to be used more. Hence, the highest economic value for polledness (€100) considered in this study was not enough for the homozygous polled bulls to be used to their maximum allowed usage.

Using BullPolled25, the predicted number of carriers of the genetic defect HH1 increased substantially in the next generation compared with the number of HH1 carriers among the mated females (Table 10). Hence, as we observed for the mated females (Figure 3), the top polled bulls on the NTM scale seemed more likely to be HH1 carriers. We believe it is unlikely that only polled bulls would be used for the whole Nordic Holstein population; thus, the increase in the number of HH1 carriers would be smaller in practice. Breeding companies could also limit the usage of polled carriers of HH1, for example, by stopping selling polled carriers of HH1 after fewer doses than usual. Despite the higher percentage of bulls carrying HH1, at-risk mating could be avoided. We argue that these scenarios show the importance of monitoring genetic defects at the population level because, even if at-risk matings were avoided, there could be a risk of genetic defects increasing in frequency.

Breeding for the β-Casein Trait

It was possible to increase the percentage of offspring homozygous for β-CN (A2A2) with a minor effect on the average NTM level and genetic relationships (Table 8). The A2 allele has been associated with a positive effect on milk yield traits (Freyer et al., 1999). Olenski et al. (2010) found a positive effect on milk and protein yield, but a negative effect on fat percentage. Our results confirm that the A2A2 bulls were at a competitive NTM level. The highest expected percentage of offspring homozygous for β-CN (A2A2) was observed in Beta-C€100 (75.0%), achieved with 10% females per herd and bull constraint, compared with 61.2% in the Random, β-CN, and Polledness scenarios. This difference was because homozygous animals are required to achieve the desired milk type for β-CN, whereas only one polled allele is needed to achieve the preferred phenotype for polledness. Hence, achieving 100% desired milk type for β-CN in one generation by only using β-CN (A2A2) bulls is impossible if the A1 allele is still segregating, as in the Nordic Holstein female population.

Breeding for Both Polledness and β-Casein

The expected number of polled offspring declined when adding value to β-CN (A2A2) in the economic score. Hence, bulls that were A2A2 were less likely to carry the polled allele (or polled bulls were less likely to be A2A2). This was also the case for the mated females (Figure 2). To our knowledge, no other study has investigated this. However, when giving both polledness and β-CN an economic value in the economic score, it was possible to increase the number of polled offspring and offspring homozygous for β-CN (A2A2) simultaneously, with little effect on NTM (Table 9).

Other Mating Studies

A few recent studies have used linear programming for genomic mating allocation (Carthy et al., 2019; Bérodier et al., 2021; Bengtsson et al., 2022). Carthy et al. (2019) only included genetic level and a genetic relationship in their economic score, whereas Bérodier et al. (2021) and Bengtsson et al. (2022) used an economic score similar to our scenarios 3Gen, Allgen, GSNP, GSEG1, and GSEG4. Bérodier et al. (2021) found that linear programming was better than random and sequential mating in reducing the number of recessive genetic defects expressed. However, they could not completely avoid the expression of recessive genetic defects due to restrictions in the matings. For example, only 8 bulls could be mated to heifers due to restrictions for calving ease. Bengtsson et al. (2022) found that at-risk mating could be avoided if the economic value for recessive genetic defects were included in the economic

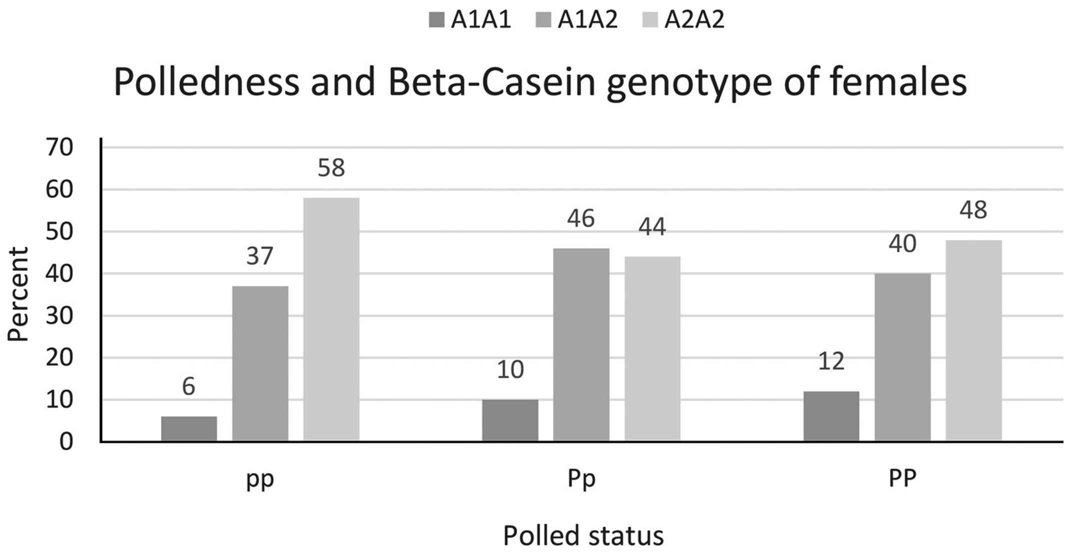

Figure 2. Polledness (pp = horned, Pp = heterozygous polled, PP = homozygous polled) and β-CN genotype (A1A1, A1A2, and A2A2) among the 24,333 mated Holstein females. A cow homozygous for the A2 allele produces so-called A2 milk.

score, which is similar to our findings in 3Gen, Allgen, GSNP, GSEG1, and GSEG4 scenarios (Table 6). There were also higher genetic defect carrier frequencies, up to 14% among females and available bulls, in Bengtsson et al. (2022). Hence, we argue that linear programming can help avoid the expression of genetic defects unless possible matings are restricted (only a few noncarrier bulls are available and a carrier female has to be mated with a carrier bull).

Genetic Relationships

We found correlations between pedigree relationship and genomic relationship estimates of ≥0.69 for a_{3Gen} and ≥0.75 for a_{AllGen}, which were within the range reported in other studies (0.57–0.88; VanRaden et al., 2011; Pryce et al., 2012; Carthy et al., 2019; Bengtsson et al., 2022). Pedigree depth is important for a strong correlation between pedigree and genomic relationships

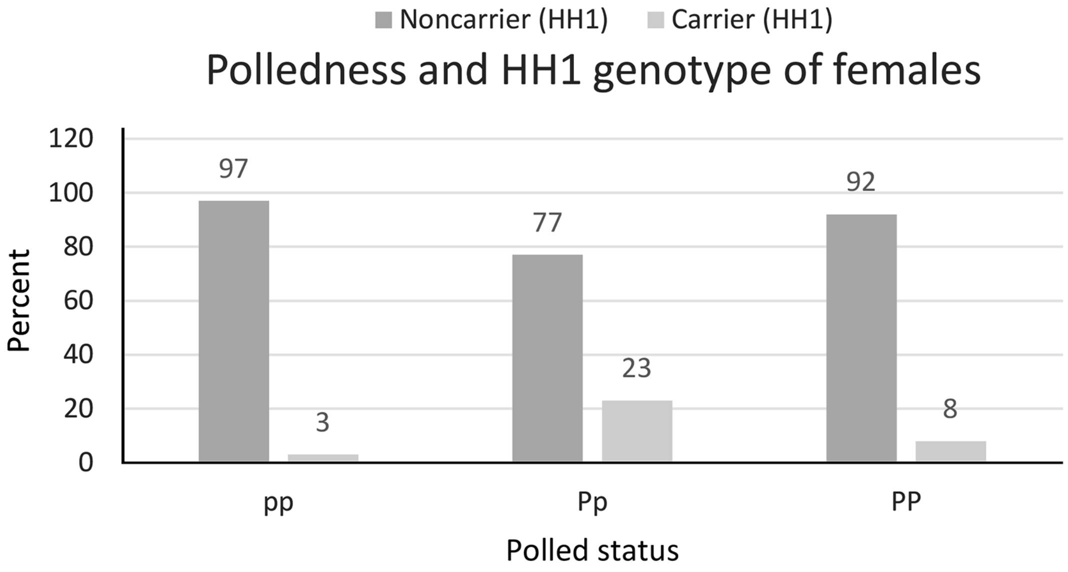

Figure 3. Polledness (pp = horned, Pp = heterozygous polled, PP = homozygous polled) and carrier status for the HH1 genotype among the 24,333 mated Holstein females. A conceptus homozygous for the HH1 allele results in an early abortion.

(Pryce et al., 2012). This was evident in our study, where we found stronger correlations between a_{AllGen} and genomic relationship than between a_{3Gen} and genomic relationship. In our previous study in Red Dairy Cattle (Bengtsson et al., 2022), we found stronger correlations (≥0.83) between pedigree and genomic relationship estimates than were found for Holstein in this study. Pedigree depth was similar to that in Bengtsson et al. (2022), so the difference is most likely linked to some other factor(s). One possibility is that the pedigree correctness is greater in Red Dairy Cattle than in Holstein due to the less common exchange of bulls and their pedigrees worldwide for Red Dairy Cattle, where most animals are kept within the Nordic countries.

There are several arguments for using genomic estimates of relationship and inbreeding instead of pedigree. First, they do not rely on pedigree data, which can be incorrect or have limited depth (Carthy et al., 2019; Makanjuola et al., 2020). Our data were corrected for possible mismatches by the Nordic Cattle Genetic Evaluation, and hence we did not explore the benefit that genomic information brings in the form of assigning the right parents to an animal. Approximately 5% of genotyped animals in Sweden have at least one parent incorrectly assigned (Lina Baudin, expert in breeding routines, Växa Sverige; personal communication, March 5, 2021). Second, even if the pedigree data are correct and complete, genomic relationships are still more accurate because they consider the fact that the genome is transmitted in chromosomes and not as infinite unlinked loci (Hill and Weir, 2011). Third, the assumption of 50% probability of an allele being selected is not true in a population under selection (Forutan et al., 2018). Hence, we argue that genomic estimates should be prioritized in a modern mating program.

In general, genomic relationships were good at keeping each other low when included in an economic score used for mating allocations, and the largest benefit would be to implement one of these instead of pedigree relationships. Using a segment-based relationship, we aimed to reduce the number of runs of homozygosity (**ROH**) in the potential offspring. In a meta-analysis on the effects of inbreeding in livestock, Doekes et al. (2021) showed that genomic measures were a better indicator of inbreeding depression than pedigree measures, but found no differences between SNP-based measures and ROH. However, those authors highlighted the limited number of studies investigating ROH and inbreeding depression and scale and arbitrary definitions of ROH. In principle, ROH are enriched for deleterious alleles that mainly cause inbreeding depression (Charlesworth and Willis, 2009). Long ROH reflect new inbreeding and are expected to contain more deleterious alleles than short ROH, due to purging and recombination through the generations (Stoffel et al., 2021). Pryce et al. (2014) found that long regions (>3 Mb) were associated with inbreeding depression for milk yield in Holstein and Jersey cattle. However, Zhang et al. (2015) found that enrichment of deleterious variants was significantly higher in short (<0.1 to 3 Mb) than in long (>3 Mb) regions in the Holstein, Red Dairy Cattle, and Jersey. Hence, the optimal segment length for use in segment-based relationships remains to be determined. However, we showed that g_{SEG1} and g_{SEG4} kept each other low when included in an economic score, so the difference is most likely marginal for the outcome of the mating allocations.

The number of bulls used in the scenarios considering genomic relationships was, in general, higher than in the scenarios considering pedigree relationships (Table 6). We believe that the primary explanation for this is that genomic relationships can capture variations not detected by the pedigree, which makes some of the lower ranked bulls on the NTM scale being used more.

Economic Assumptions

The cost of dehorning in DFS is estimated to range between €2.7 and €7.3 per animal, considering veterinary costs, gas/electricity, and extra labor (Sørensen et al., 2018). Thompson et al. (2017) estimated the cost of dehorning in the United States to be between $6 and $25 per head. However, such calculations do not consider the current situation, where dehorning is strictly regulated in organic herds in the European Union. If dehorning is completely banned, farmers may be more or less forced to breed polled animals. Consequently, it is difficult to place an economic value on the polledness trait. We tackled that problem by testing a large range of economic values of the polledness trait. In addition, we used only polled bulls in BullPolled25, to represent a situation where farmers are forced to breed polled animals.

In some countries, demand for and the price of A2 milk have increased (Bisutti et al., 2022). For a farmer aiming to produce A2 milk, a female not carrying 2 copies of the A2 allele might be substantially less valuable than a female that does. The exact value for A2 milk is difficult to quantify, and most likely varies between farms. In DFS, the demand for A2 milk is still limited, to our knowledge. Hence, we believe it is uncommon for farmers in DFS to breed to increase the percentage of A2A2 offspring, and even more uncommon to breed for β-CN and more polled animals simultaneously. However, our results for β-CN and polledness illustrate the interactions that can occur when breeding for 2 favorable monogenic traits. It is also likely that new monogenic traits (e.g., κ-casein) will be added to the

SNP array (Chessa et al., 2020) or unknown monogenic traits may be discovered. The methods used in this study could also be adopted by other breeds or livestock species where other monogenic traits may be of economic importance.

The defects we considered in mating allocations all cause early abortions. Our value of €80 for an early abortion was in line with Segelke et al. (2016), who estimated a cost of €70, and Bérodier et al. (2021), who estimated a cost of €75. There are differences between countries in the cost of an insemination (Sørensen et al., 2018). The economic score could be made more farm-specific by adjusting the calculation to match the conditions on a specific farm.

We used a penalty of €25.4 per 1% increase in inbreeding, which is in line with the US$25 (about €20) used by Cole (2015) and US$24 used by Smith et al. (1998). Pryce et al. (2012) used a range up to AU$20 (about €13), whereas Bengtsson et al. (2022) tested €10 to €40 and found that mating results were not sensitive in that range. Hence, even if the cost for inbreeding in Nordic Holstein is still unknown, €25.4 appears to be a reasonable estimate.

Implementation Opportunities

We decided to use linear programming in this study because it has been shown to outperform other mating methods such as sequential solving (Sun et al., 2013; Carthy et al., 2019). When data on genetic relationships, NTM, and monogenic traits were available, linear programming using a regular laptop maximized the economic score within seconds for the herds studied. Hence, the method is suitable for implementation in mating software that farmers or advisors can use. Genotype phasing and extracting the genomic segments was the most time-consuming calculation, and required a more powerful computer. Further, estimating allele frequencies and genotype phasing require information from more than one farm. Therefore, we suggest that this be done at a central level, like today's breeding value estimation, and that genetic relationships could then be made available for downloading to the mating program. In this study, g_{SNP} was the fastest genomic relationship to calculate and it was relatively good at keeping the segment-based relationships low, making it an efficient implementation alternative. However, computation time aside, a segment-based relationship should be considered, because it is most likely better in prediction of inbreeding depression.

In this study, we optimized matings with a within-herd focus and only looked one generation ahead. Future studies should address how this type of mating allocation would affect a population over several generations. Matings optimal at the herd level are not necessarily optimal for the population. Hence, the mating allocation suggested in this study should not be seen as a replacement for optimum contribution selection for breeding organizations.

Breeders of other livestock species could also adopt the mating scenarios presented here, but they would need to be adopted to each specific situation. Further, including genomic relationships and information about genetic defects, as in this study, requires genotypes from both females and males. An economic score could also be developed for crossbred animals where the focus is to maximize heterosis instead of minimizing parent relationships. In this study, we did not consider ungenotyped animals. An option for ungenotyped animals could be to impute their genotype, as done by Carthy et al. (2019) using the method described by Gengler et al. (2007). Sun et al. (2013) suggested use of the **H** matrix in single-step genomic evaluation. However, farmers who do not genotype their females might have to avoid using carrier bulls to completely avoid at-risk mating for known genetic defects.

CONCLUSIONS

We explored mating allocations at the herd level with real data and found that it was possible to reduce genetic relationships and eliminate expression of genetic defects with minimal effect on the genetic level for NTM. It was also possible to increase the percentage of polled and β-CN homozygous (A2A2) offspring substantially in one generation when competitive bulls were available, without any significant negative effect on other mating criteria. Compared with maximizing only NTM index, the frequency of polled offspring increased from 13.5 to 22.5%, and that of offspring homozygous for β-CN (A2A2) from 66.7 to 75.0%, in one generation, without any substantial negative effect on other comparison criteria. Using only semen from polled bulls, which might be necessary if dehorning is banned, considerably affected the genetic level. We also found that animals in the data set carrying the polled allele were less likely to be homozygous for β-CN (A2A2) and more likely to be carriers of the genetic defect HH1. Based on this, we recommend monitoring of the comparison criteria used in this study in a modern genomic mating program.

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