# The effect of genetic defects on pregnancy loss in Swedish dairy cattle

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## ABSTRACT

The effect of carrier status of 10 lethal recessive genetic defects on pregnancy maintenance in Swedish dairy cattle was examined. The genetic defects were Ayrshire Haplotype 1, Ayrshire Haplotype 2, BTA12, BTA23, and Brown Swiss Haplotype 2 in Red Dairy Cattle (RDC), and Holstein Haplotype 1, 3, 4, 6, and 7 (HH1–HH7) in Holstein. Effects of carrier status of BTA12 and HH3 on conception rate (CR), interval from first to last service (FLS), and milk production were also examined. Data were obtained for 1,429 herds in the Swedish milk recording system, while information on carrier status of genetic defects was obtained from the Nordic Cattle Genetic Evaluation. In total, data on 158,795 inseminations in 28,432 RDC and 22,018 Holstein females were available. Data permitted separate analyses of BTA12 and HH3, but carrier frequencies of other defects were too low to enable further analysis. Pregnancy loss was defined as failure to maintain pregnancy, where pregnancy status was confirmed with manual and chemical pregnancy diagnosis, insemination, calving, sales and culling data. Odds ratios (OR) and probabilities of pregnancy loss and CR were estimated using generalized linear mixed models, while pregnancy loss, CR, FLS, milk, protein, and fat yields were analyzed using linear mixed models. Pregnancy losses were reported on average within the first month post-AI. At-risk matings were more prone to suffer pregnancy loss in BTA12 (OR = 1.79) and HH3 carriers (OR = 1.77) than not-at-risk matings. At-risk matings also had lower CR (OR = 0.62 and 0.63 for BTA12 and HH3, respectively) than not-at-risk matings. Carrier females of BTA12 had longer FLS and higher milk production than noncarriers. Conception rate and pregnancy maintenance could be improved by avoiding at-risk matings. This finding could help reduce pregnancy loss due to genetic defects in the breeding program for improved fertility.

**Key words:** pregnancy loss, genetic defects, *Bos taurus* autosome 12, Holstein Haplotype 3

## INTRODUCTION

In the past, lethal recessive genetic defects were determined based on clinical cases and inheritance traced through breeding trials. However, this approach fails to identify most genetic defects that cause embryonic or fetal losses, because the phenotype is not clearly observed. Due to the rapid increase in genotyping of dairy cattle, lethal genetic defects can now be identified via tracking haplotypes that show lower than expected homozygotes in living animals in the population, and associated impaired fertility (VanRaden et al., 2011; Fritz et al., 2013). The carrier status of these defects could be used in selection to avoid at-risk matings (i.e., carrier male mated with carrier female) and reduce carrier frequencies (VanRaden et al., 2011; Cole et al., 2016; Bengtsson et al., 2022). The information could also be useful when making culling decisions in the herd (Cole et al., 2016).

Genomic tests are currently available for 10 recessive genetic defects associated with pregnancy loss, which are included in the SNP chip used for genotyping by the Nordic Cattle Genetic Evaluation (**NAV**, http://www.nordicebv.info) of Nordic Red Dairy Cattle (**RDC**, including Swedish Red, Danish Red, and Finnish Ayrshire) and Swedish Holstein (**SH**). The defects evaluated are Ayrshire Haplotype 1 (**AH1**), Ayrshire Haplotype 2 (**AH2**), BTA12, BTA23, and Brown Swiss Haplotype 2 (**BH2**) in RDC, and Holstein Haplotype 1, 3, 4, 6, and 7 (**HH1**–**HH7**) in SH. The most common defect in RDC is BTA12, which according to Kadri et al. (2014) primarily affects pregnancy maintenance during the first 5 mo of gestation. They identified a 660-kb deletion encompassing 4 genes as the causative variant, out of which the ribonuclease H2 subunit B (*RNASEH2B*) gene was suggested as the candidate gene because it is known to cause embryonic lethality when knocked-out in mice. However, it is possible that the other coding genes in the deletion (*GUCY1B2* and *FAM124A*) or *DLEU7* and the 2 noncoding RNA genes

**Table 1.** Number of inseminations in Nordic Red Dairy Cattle (RDC) and Swedish Holstein (SH) for which data were available in this study

| Item | RDC and SH | RDC | SH |
|---|---|---|---|
| Females | 50,450 | 28,432 | 22,018 |
| Inseminations | 158,795 | 97,551 | 61,244 |
| Heifers | 69,776 | 42,301 | 27,475 |
| First parity | 48,944 | 30,444 | 18,500 |
| Second parity | 27,514 | 16,905 | 10,609 |
| Third parity | 12,561 | 7,901 | 4,660 |

(*DLEU7-AS1*; *C13orf42*) are partly responsible for the embryonic lethality as well.

The most frequent defect in the US Holstein population is HH3, with pregnancy loss occurring during the first 60 d post-AI (McClure et al., 2014). The deleterious effect is due to a missense variant of the structural maintenance of chromosomes 2 (*SMC2*) gene, where phenylalanine has been replaced by serine (p.Phe1135Ser) on chromosome 8 (McClure et al., 2014; Häfliger et al., 2022).

Pregnancy loss is currently not directly considered in genetic evaluation in the Nordic countries (NAV, 2023), despite reports of high incidence (Nyman et al., 2018; Ask-Gullstrand et al., 2021). If pregnancy losses due to genetic defects are substantial, carrier status could be used in the breeding program to optimize mating plans and avoid at-risk matings (Bengtsson et al., 2022). Considering pregnancy loss in routine genetic and genomic evaluations of fertility in dairy cattle could genetically improve cow fertility and reduce pregnancy loss in production, while also preventing economic losses arising from extended service period and calving interval, and premature culling due to infertility.

The aims of this study were to estimate the frequency of different genetic defects in Swedish dairy cattle (RDC and SH); to analyze the effect of these genetic defects on conception rate (**CR**) and pregnancy maintenance in RDC and SH; and to assess the effect of carrier status of BTA12 and HH3 on interval from first to last insemination (**FLS**). The starting hypothesis was that at-risk matings result in a decrease in CR and in favorable pregnancy outcomes, and longer FLS in carrier females.

## MATERIALS AND METHODS

Pedigree, calving, insemination, sales, and culling data were extracted for RDC and SH females in 1,429 Swedish dairy herds in the cow database maintained by Växa (Stockholm, Sweden). No ethical approval was needed for this study because data from a database were used and no handling of animals was performed. Data on a total of 1,974,494 insemination events from 2014 to 2021 were available, with up to 7 insemination records per lactation for virgin heifers and cows up to third parity. The insemination data were corrected for double inseminations within the same cycle (within ≤ 6 d), excluding 417 inseminations. A minimum of 5 insemination records was required per contemporary group for inclusion in the final dataset.

Data on carrier status of genetic defects were obtained from the 2020 NAV, which uses the Illumina 50k chip (Illumina Inc.) to analyze for genetic defects and FImpute software to impute genotypes of animals with lower-density chips to 50k. Information about carrier status was first made available in October in 2018 in Sweden, and the genomic tests are currently available for everyone who genotypes their animals. Information on genetic defects was available for 57,536 animals (1,259 males and 56,277 females). Only animals with known carrier status (carrier or noncarrier) for 10 genetic defects (AH1, AH2, BTA12, BTA23, BH2, HH1–HH7) were included in the final dataset, which comprised 158,795 inseminations in 28,432 RDC and 22,018 SH females (Table 1). A total of 402 and 154 at-risk matings for BTA12 and HH3, respectively, were available for analysis. The remaining defects had too low carrier frequencies to enable further analysis (Table 2).

### Trait Definitions

Conception rate was defined in line with the NAV trait definition rules used in genetic evaluation of fertility (Muuttoranta et al., 2019; NAV, 2023). Accordingly, each insemination was assigned a phenotypic value of failure to conceive (0) or successful conception

**Table 2.** Number of inseminations with different carrier status in Red Dairy Cattle (AH1–BH2) and Swedish Holstein (HH1–HH7) in the dataset[1]

| Carrier status[2] | AH1 | AH2 | BTA12 | BTA23 | BH2 | HH1 | HH3 | HH4 | HH6 | HH7 |
|---|---|---|---|---|---|---|---|---|---|---|
| NCM × NCF | 95,586 | 96,769 | 81,344 | 96,357 | 97,341 | 57,779 | 55,605 | 59,525 | 60,942 | 61,150 |
| NCM × CF | 1,581 | 392 | 3,541 | 563 | 186 | 1,722 | 2,872 | 1,541 | 302 | 94 |
| CM × NCF | 381 | 389 | 12,264 | 6,331 | 24 | 1,704 | 2,613 | 171 | 0 | 0 |
| CM × CF | 3 | 1 | 402 | 0 | 0 | 39 | 154 | 7 | 0 | 0 |

[1]AH1 = Ayrshire Haplotype 1; AH2 = Ayrshire Haplotype 2; BH2 = Brown Swiss Haplotype 2; HH1 = Holstein Haplotype 1; HH3 = Holstein Haplotype 3; HH4 = Holstein Haplotype 4; HH6 = Holstein Haplotype 6; HH7 = Holstein Haplotype 7.

[2]NCM = noncarrier male; NCF = noncarrier female; CM = carrier male; CF = carrier female.

(1), which was evaluated based on subsequent inseminations, pregnancy diagnoses (manual and chemical), calving records, data on sales of animals during the service period, and culling data, to assess the pregnancy outcome. Pregnancy status was determined based on manual and chemical pregnancy diagnosis performed in the herds during gestation until expected calving date. Pregnancy outcome was compared with subsequent inseminations, calving, and sales and culling records, to confirm gestation or pregnancy loss. A maximum service period of 163 d (mean + 2SD) was allowed for FLS.

### Statistical Analysis

Generalized linear mixed models [Equation 1] were fitted using SAS 9.4 Proc GLIMMIX (SAS Institute Inc.) to study pregnancy outcome (success or failure) and CR, with a binary distribution and logit link function. The model took the following form:

$$\ln [p/(1 - p)] = \mathbf{X\beta} + \mathbf{Zu}, \qquad [1]$$

where p is probability of pregnancy loss, $\mathbf{X}$ is the design matrix for the fixed effects, $\boldsymbol{\beta}$ is a vector of the effects associated with the columns of $\mathbf{X}$, $\mathbf{Z}$ is the design matrix for the random effect, and $\mathbf{u}$ is the vector of the random effect $\left[\mathbf{u} \sim N\left(0, \sigma_u^2\right)\right]$, where $\sigma_u^2$ is the variance of service bull (RDC) or cow (SH). The model for pregnancy loss and CR in RDC included the fixed effects of type of mating of BTA12 (not-at-risk or at-risk mating), parity, insemination number, and the random effect of service bull. The model for pregnancy loss and CR in SH included the fixed effects of type of mating of HH3, parity, insemination number, and the random effect of female. The models for the 2 breeds differed because of insufficient memory of SAS to handle the effect of female in RDC, due to a larger dataset compared with SH.

Linear mixed models were used to estimate LSM, where model 2 [Equation 2] was used for pregnancy loss and conception rate, and model 3 [Equation 3] was used for FLS, and milk, protein, and fat yield.

$$\mathbf{y} = \mathbf{X\beta} + \mathbf{Z}_h\mathbf{h} + \mathbf{Z}_a\mathbf{a} + \mathbf{Z}_s\mathbf{s} + \mathbf{Z}_p\mathbf{p} + \mathbf{e}, \qquad [2]$$

$$\mathbf{y} = \mathbf{X\beta} + \mathbf{Z}_h\mathbf{h} + \mathbf{Z}_a\mathbf{a} + \mathbf{Z}_p\mathbf{p} + \mathbf{e}, \qquad [3]$$

where $\mathbf{y}$ is a vector of phenotypic observations; $\boldsymbol{\beta}$ is a vector of fixed effects with corresponding incidence matrix $\mathbf{X}$; $\mathbf{h}$ is the random effect of herd by insemination year and season (with 1,429 herds, 8 yr (2014–2021), and 4 seasons (Dec–Feb, Mar–May, Jun–Aug,

Sep–Nov), where $\mathbf{h} \sim N\left(0, \mathbf{I}\sigma_h^2\right)$, with variance $\sigma_h^2$; $\mathbf{s}$ is the random effect of service bull with $\mathbf{s} \sim N\left(0, \mathbf{I}\sigma_s^2\right)$, where $\sigma_s^2$ is the variance of the service bull; $\mathbf{a}$ is the random effect of the female with $\mathbf{a} \sim N\left(0, \mathbf{I}\sigma_a^2\right)$, where $\sigma_a^2$ is the additive genetic variance; $\mathbf{p}$ is the random effect of permanent environment with $\mathbf{p} \sim N\left(0, \mathbf{I}\sigma_p^2\right)$, where $\sigma_p^2$ is the permanent environment variance; $\mathbf{Z}_h$, $\mathbf{Z}_a$, $\mathbf{Z}_s$, and $\mathbf{Z}_p$ are incidence matrices of herd-year-season, service bull, female, and permanent environment, respectively; and $\mathbf{e}$ is a residual vector, where $\mathbf{e} \sim N\left(0, \mathbf{I}\sigma_e^2\right)$, and $\sigma_e^2$ is the residual variance. Model 2 included type of mating (not-at-risk or at-risk mating), parity (0–3), and number of insemination (1–7) as fixed effects, while model 3 included fixed effect of carrier status (noncarrier or carrier), effect of parity, and linear regression of calving interval.

### RESULTS

Carrier frequency of BTA12 and HH3 was 12.8% and 3.1%, respectively, in males, and 15.4% and 4.2%, respectively, in females during 2020 (Table 3). We observed a decrease in carrier frequencies from 32.2% in BTA12 in 2014 to 12.8% in 2020 in sires, but an increase from 0% in 2014 to 15.4% in females in 2020. The increase in carrier frequency in HH3 was less pronounced. Pregnancy losses were reported on average within the first $36 \pm 27.1$ d (mean $\pm$ SD) and $32 \pm 14.7$ d post-AI in BTA12 and HH3 at-risk matings, respectively, with 95% of pregnancy losses occurring before 79 d and 61 d post-AI in BTA12 and HH3 at-risk matings, respectively (Figure 1).

At-risk matings were more prone to result in pregnancy loss in both BTA12 carriers (odds ratio [$\mathbf{OR}$] = 1.79) and HH3 carriers (OR = 1.77) than not-at-risk matings (Table 4). Estimated probabilities of pregnancy loss obtained using generalized linear mixed models were very close to estimated LSM from linear mixed models, especially for HH3. The difference in probability of pregnancy loss between at-risk matings and not-at-risk matings for BTA12 was 13.4% and the difference between LSM from the linear model was 14.1%. For HH3, the corresponding differences were 14.0% and 14.9%, respectively.

Conception rates were considerably lower in BTA12 and HH3 at-risk matings (0.31 and 0.37, respectively) than in not-at-risk matings (0.42 and 0.49, respectively; Table 5).

Carrier females of BTA12 had significantly ($P = 0.0004$) longer FLS than noncarriers, $37 \pm 1.5$ d and $31 \pm 0.3$ d, respectively. However, there was no difference ($P = 0.0779$) in FLS depending on carrier status in SH

**Table 3.** Carrier frequencies in percent of 10 genetic defects in Red Dairy Cattle (AH1–BH2) and Swedish Holstein (HH1–HH7) during the study period 2014 to 2021

| Item[1] | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 |
|---|---|---|---|---|---|---|---|---|
| AH1 | | | | | | | | |
| Males | 2.27 | 1.22 | 0.68 | 0.27 | 0.34 | 0.06 | 0.08 | 0.13 |
| Females | 0.6 | 0.37 | 0.51 | 2.5 | 3.03 | 2.27 | 1.35 | 1.55 |
| AH2 | | | | | | | | |
| Males | 0 | 1.15 | 2.73 | 0.25 | 0.05 | 0.02 | 0 | 0 |
| Females | 0.05 | 0 | 0 | 0.02 | 0.18 | 0.95 | 1.49 | 2.19 |
| BTA12 | | | | | | | | |
| Males | 32.16 | 17.23 | 11.38 | 13.73 | 17.16 | 12.73 | 12.75 | 4.3 |
| Females | 0 | 0.44 | 0.64 | 0.77 | 0.69 | 8.3 | 15.44 | 13.76 |
| BTA23 | | | | | | | | |
| Males | 0.04 | 1.59 | 0.39 | 3.02 | 0.71 | 0 | 0 | 0.04 |
| Females | 0.05 | 0.15 | 0.1 | 0.1 | 0.18 | 1.56 | 1.81 | 1.42 |
| BH2 | | | | | | | | |
| Males | 0.86 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Females | 0.05 | 0.15 | 0 | 0.1 | 0.28 | 0.4 | 0.32 | 0.43 |
| HH1 | | | | | | | | |
| Males | 0 | 3.1 | 1.37 | 2.61 | 7.27 | 2.74 | 1.74 | 0.8 |
| Females | 0 | 0.39 | 3.09 | 3.03 | 2.07 | 2.2 | 3.92 | 3.52 |
| HH3 | | | | | | | | |
| Males | 0 | 0.97 | 0.75 | 5.03 | 2.94 | 3.93 | 3.13 | 5.95 |
| Females | 2.21 | 2.71 | 4.46 | 5.7 | 4.36 | 4.87 | 4.23 | 3.73 |
| HH4 | | | | | | | | |
| Males | 0 | 0 | 3.71 | 0.69 | 0.44 | 0.04 | 0 | 0 |
| Females | 0 | 1.16 | 5.15 | 2.83 | 2.86 | 1.88 | 1.52 | 1.34 |
| HH6 | | | | | | | | |
| Males | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Females | 0 | 0 | 0.07 | 0.17 | 0.9 | 0.68 | 0.45 | 0 |
| HH7 | | | | | | | | |
| Males | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Females | 0 | 0 | 0 | 0.14 | 0.03 | 0 | 0.28 | 0.29 |

[1]AH1 = Ayrshire Haplotype 1; AH2 = Ayrshire Haplotype 2; BH2 = Brown Swiss Haplotype 2; HH1 = Holstein Haplotype 1; HH3 = Holstein Haplotype 3; HH4 = Holstein Haplotype 4; HH6 = Holstein Haplotype 6; HH7 = Holstein Haplotype 7.
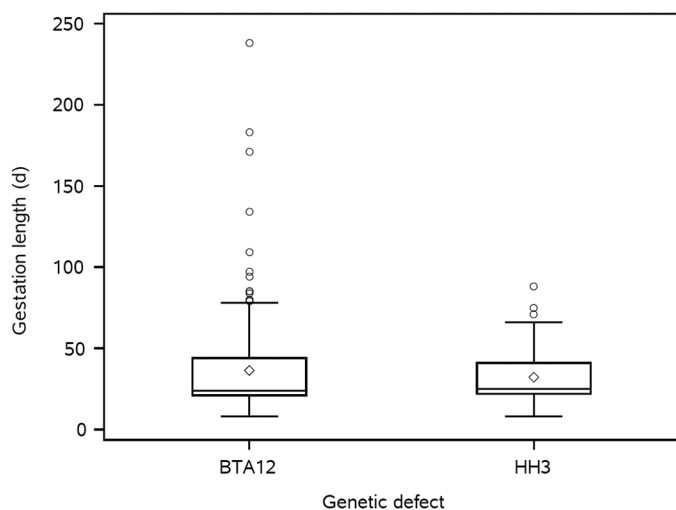


**Figure 1.** Distribution of pregnancy losses occurring within the gestation period in at-risk matings in Red Dairy Cattle females carrying BTA12 and Swedish Holstein females carrying Holstein Haplotype 3 (HH3), where boxes indicate the first to third quartiles, lines are the median, diamonds are the mean, whiskers indicate minimum and maximum values, and dots are outliers.

(39 ± 1.5 d in carriers compared with 37 ± 0.4 d in noncarriers).

There were significant differences in milk production traits depending on carrier status of BTA12, where carriers had on average higher yield (Table 6). However, carrier status of HH3 did not result in any difference in milk yield.

## DISCUSSION

Increasing conception rates and reducing pregnancy losses in dairy cattle is important to increase reproductive performance and production efficiency. This study examined the pattern of pregnancy loss related to BTA12 and HH3 at-risk matings, estimated the effect of type of mating (at-risk or not-at-risk mating) on pregnancy outcome and CR, and evaluated the effect of carrier status of females on FLS and 3 milk production traits in RDC and SH.

For carriers of genetic defect HH3, 95% of pregnancy losses occurred before 61 d post-AI, which is comparable to values reported in previous studies (McClure

**Table 4.** Odds ratios (OR) with 95% CI, probability, and LSM of pregnancy loss in at-risk and not-at-risk matings in Red Dairy Cattle females carrying the BTA12 lethal haplotype and Swedish Holstein females carrying Holstein Haplotype 3 (HH3)

| Item | OR (95% CI) | Probability $\pm$ SE (%) | LSM $\pm$ SE (%) |
|---|---|---|---|
| BTA12 | | | |
| At-risk matings | 1.79 (1.44–2.22) | 69.9 $\pm$ 2.43 | 66.0 $\pm$ 2.76[a] |
| Not-at-risk matings | | 56.5 $\pm$ 0.78 | 51.9 $\pm$ 0.76[b] |
| HH3 | | | |
| At-risk matings | 1.77 (1.25–2.50) | 62.7 $\pm$ 4.23 | 62.1 $\pm$ 4.28[a] |
| Not-at-risk matings | | 48.7 $\pm$ 0.97 | 47.2 $\pm$ 0.99[b] |

[a,b]Values with different superscripts within columns are significantly different ($P \leq 0.05$).

et al., 2014). However, the majority of pregnancy losses in BTA12 at-risk matings occurred much earlier in gestation in the present study (95% by d 79) than in a study by Kadri et al. (2014), where only 20% to 25% of embryonic losses occurred by 35 d post-AI and 79% to 88% of pregnancies failed by 150 d post-AI. This difference was seen despite a delay in recording when pregnancy loss actually occurred in the present study, as pregnancy status was primarily evaluated based on pregnancy diagnosis and subsequent insemination data, rather than on estrus detection in the herd. Although embryonic losses are more frequently observed (Nyman et al., 2018; Ask-Gullstrand et al., 2021), the economic effect of pregnancy loss increases when it occurs later in the gestation period, owing to an extension of the service period and causing a delay to next lactation (Cole et al., 2016). Prolonged calving interval and unproductive drying-off period also increase the risk of premature culling, further affecting herd profitability.

Carrier frequency of BTA12 was 12.8% in males and 15.4% in females in 2020 in the present study, and 12.9% in a study by Wu et al. (2020). However, Kadri et al. (2014), who first reported the BTA12 haplotype, found higher carrier frequencies for RDC (13%, 23%, and 32% in Danish, Swedish, and Finnish Red Cattle, respectively). In 2014, the carrier frequency of BTA12 in males in Sweden was 32.2%, however, it was 0% in females possibly due to lack of genotyping of older cows during this time. Kadri et al. (2014) suggested that while BTA12 is deleterious in homozygotes, it is still maintained at high frequency in the population because it is associated with a positive effect on milk yield and composition in carriers. A positive effect on milk yield was observed in the present study. However, in the long term, the negative effect on fertility could outweigh the increase in production efficiency in the individual herd.

The carrier frequency of BTA12 in males has more than halved in 7 yr. This is probably due to increased genotyping and re-genotyping of older bulls with the newer SNP chip, and information on carrier status becoming available, enabling avoidance of carrier bulls and undesirable at-risk matings. The availability of data on carrier status has probably also facilitated continued use of carrier bulls that have high genetic gain in other desirable traits (Cole et al., 2016; Bengtsson et al., 2022) or have valuable pedigrees, rather than excluding these completely from selection (Bengtsson et al., 2022). Further, while the overall carrier frequency of BTA12 has been declining, Bengtsson et al. (2022) reported large variation in Swedish herds, where some herds completely lacked carriers while others had up to 36% carrier frequency among their females.

Beneficial effects on milk production traits in BTA12 carriers were observed in the present study, however, we observed no significant change in milk production in HH3 carriers. This is in contrast to Cole et al. (2016) who observed lower milk and protein yield in HH3 carrier cows. For HH3, lower haplotype frequencies have also been reported, ranging between 2.9% and 3.1% (Fritz et al., 2013; Cole et al., 2016).

**Table 5.** Odds ratios (OR) with 95% CI, probability, and LSM of conception rate in at-risk and not-at-risk matings in Red Dairy Cattle females carrying the BTA12 lethal haplotype and Swedish Holstein females carrying Holstein Haplotype 3 (HH3)

| Item | OR (95% CI) | Probability $\pm$ SE | LSM $\pm$ SE |
|---|---|---|---|
| BTA12 | | | |
| At-risk matings | 0.62 (0.50–0.78) | 0.31 $\pm$ 0.025 | 0.36 $\pm$ 0.027[a] |
| Not-at-risk matings | | 0.42 $\pm$ 0.008 | 0.47 $\pm$ 0.008[b] |
| HH3 | | | |
| At-risk matings | 0.63 (0.45–0.89) | 0.38 $\pm$ 0.042 | 0.36 $\pm$ 0.042[a] |
| Not-at-risk matings | | 0.49 $\pm$ 0.009 | 0.50 $\pm$ 0.010[b] |

[a,b]Values with different superscripts within columns are significantly different ($P \leq 0.05$).

**Table 6.** Interval between first and last service (FLS), and milk yield (MY, kg), protein yield (PY, kg), and fat yield (FY, kg) in 305-d lactation in Red Dairy Cattle females carrying or not carrying the BTA12 lethal haplotype and Swedish Holstein females carrying or not carrying Holstein Haplotype 3 (HH3)

| Item | FLS $\pm$ SE | MY $\pm$ SE | PY $\pm$ SE | FY $\pm$ SE |
|---|---|---|---|---|
| BTA12 | | | | |
| Carriers | $37 \pm 1.5^a$ | $9,781 \pm 59.8^a$ | $359 \pm 2.1^a$ | $428 \pm 2.6^a$ |
| Noncarriers | $31 \pm 0.3^b$ | $9,634 \pm 15.8^b$ | $353 \pm 0.6^b$ | $421 \pm 0.7^b$ |
| HH3 | | | | |
| Carriers | $39 \pm 1.5$ | $11,081 \pm 67.6$ | $392 \pm 2.2$ | $454 \pm 2.6$ |
| Noncarriers | $37 \pm 0.4$ | $11,091 \pm 22.8$ | $391 \pm 0.8$ | $452 \pm 0.9$ |

[a,b]Values with different superscripts within columns are significantly different ($P \leq 0.05$).

This study defined pregnancy loss due to genetic defects as a potential trait to be included in genetic evaluations, this trait definition is scarce in literature. In line with our results, previous studies have observed a loss of fertility in at-risk matings of both BTA12 and HH3 carrier heifers and cows. Cole et al. (2016) found a decrease in daughter pregnancy rate, heifer CR, and cow CR in HH3 carrier cows compared with noncarriers. Likewise, Fritz et al. (2013) observed a negative effect of HH3 on calving rates in both heifers and cows in matings between carrier bulls and daughters of carrier bulls. Further, significantly lower nonreturn rates have been reported for HH3 and BTA12 at-risk matings in the Nordic dairy cattle population (Wu et al., 2019; Wu et al., 2020), and for HH3 at-risk matings in German Holstein (Segelke et al., 2016). This reduction in fertility in carriers in at-risk matings, despite higher milk yield, results in an economic loss because production efficiency is influenced by a delay of the next lactation owing to the increased number of inseminations necessary for a successful pregnancy, thus increasing the calving interval and the risk of premature culling due to infertility.

## CONCLUSIONS

This study found that pregnancy loss was more likely in at-risk matings between carriers of genetic defects than in not-at-risk matings in both RDC and SH. The majority of pregnancy losses in BTA12 and HH3 at-risk matings were reported to the Swedish cow database within the first 3 mo post-AI. At-risk matings were also associated with a large negative effect on CR. Carrier females of BTA12 (RDC) had longer FLS, but higher milk yield, than noncarriers. Carrier status can therefore be used to avoid at-risk matings and prevent economic losses arising from extended service period and calving interval. These initial results indicate a way to reduce pregnancy loss due to genetic defects in the breeding program for improved fertility in Swedish dairy cattle.

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