Selecting For Fertility Traits in Dairy Cows: Waste of Effort or Light at the End of the Tunnel?

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Take Home Messages

- The advent of artificial insemination has markedly improved the production potential of dairy cows in all systems of production and transformed the dairy industry in many countries.
- Unfortunately, breeding objectives focused solely on milk production for many years. This resulted in a major decline in genetic merit for fertility traits.
- Poor genetic merit for fertility traits is associated with multiple defects across a range of organs and tissues that are antagonistic to achieving satisfactory fertility performance.
- The principal defects include excessive mobilization of body condition score, unfavourable metabolic status, delayed resumption of cyclicity, increased incidence of endometritis, dysfunctional estrous expression, and inadequate luteal phase progesterone concentrations.
- On a positive note, it is possible to identify sires that combine good milk production traits with good fertility traits. Sire genetic merit for daughter fertility traits is improving rapidly in the dairy breeds, including the Holstein.
- With advances in animal breeding, especially genomic technologies to identify superior sires, genetic merit for fertility traits can be improved much more quickly than they initially declined.

Introduction

Dairy cow fertility can be defined as ‘the ability of the animal to conceive and maintain pregnancy if served at the appropriate time in relation to ovulation’

(Darwash et al., 1997). Reproductive performance of high yielding dairy cows underwent a major decline during the last 50 years of the 20^{th} century (1950 to 2000). A steady increase in both genetic potential for milk production and phenotypic milk output was observed over the same time frame.

The decline in fertility is not apparent, or at least not as marked, in heifers. For many years, this was suggested to indicate that there was no underlying genetic influence on dairy cattle fertility. This ignored the fact that the physiological environment of the dairy cow abruptly undergoes a fundamental change following initiation of lactation. It is now generally accepted that the hormonal and metabolic adaptations necessary for the initiation and maintenance of lactation are antagonistic to optimal reproductive performance in modern dairy cows. While intensive research has been carried out in the area of reproductive physiology, the precise underlying physiological mechanisms responsible for the decline in fertility still remain poorly understood. It is, however, widely accepted that breeding values for fertility traits underwent a major decline while breeding objectives were focused solely on milk production, and metabolic stressors associated with the initiation and maintenance of lactation perturb the finely tuned biological processes necessary for pregnancy establishment.

▪ Selecting for Improved Fertility

The initial selection indices in most countries focused primarily on milk production traits. In addition to selection for cows that produced more milk, greater angularity or sharpness was also considered favourable (i.e., cows also *looked* like they produced more milk). Body condition score (BCS) is a key driver of cow health and fertility. Favourable BCS, however, is the opposite of favourable angularity. It is likely that selecting for angularity directly contributed to the decline in phenotypic fertility and increased the incidence of metabolic disorders. Genetic correlations between BCS and pregnant 63 days after the start of breeding season ranged from 0.29 to 0.42 (Berry et al., 2003), and hence selecting for greater BCS has been identified as a strategy to improve health and fertility.

Scandinavian Example

For many decades, fertility and health traits have been incorporated into the breeding index of the Scandinavian breeds. While fertility globally declined between 1985 and 2005, non-return rates, culling rates due to infertility and calving interval remained relatively constant in the Norwegian Red breed (Refsdal, 2007). The incidence of veterinary treatments for reproductive disorders in 503,683 first-lactation daughters of 1,058 Norwegian Red sires was 3.1% for silent heats, 0.9% for metritis, 0.5% for cystic ovaries, and 1.5% for retained placenta (Heringstad, 2010). The low incidence of fertility disorders and maintenance of high phenotypic fertility performance provide support for the objective of selecting for improved fertility.

▪ Strategies In Other Countries

In Ireland, the Irish national breeding program introduced a multi-trait selection index called the Economic Breeding Index (EBI) in 2001. As the name 'Economic Breeding Index' suggests, the EBI is designed to identify genetically superior animals for profitability (Veerkamp et al., 2002). Since its introduction, the EBI has evolved to include 6 sub-indexes (relative emphasis in parenthesis): milk production (33%), fertility/survival (35%), calving performance (10%), beef carcass (9%), maintenance (6%) and health (3%) (http://www.icbf.com). The fertility sub-index is comprised of 2 traits; calving interval (24%) and survival (11%).

In the U.S., productive life was incorporated into the index in 1994 and daughter pregnancy rate was added in 2003 (Cole et al., 2009). Currently, these two traits account for 33% of the Net Merit index (22% and 11%, respectively). This halted roughly 40 years of a continuous decline in sire and dam breeding values for fertility (Weigel, 2006). The decline in phenotypic fertility performance was similarly halted and has started to improve (Norman et al., 2009).

In the U.S., productive life was incorporated into the index in 1994 and daughter pregnancy rate was added in 2003 (Cole et al., 2009). Until December 2014, these two traits accounted for 33% of the Net Merit index (22% and 11%, respectively). The December 2014 revision incorporated heifer conception rate and cow conception rate. The emphasis on productive life, daughter pregnancy rate, heifer conception rate and cow conception rate in the current net merit index is 19%, 7%, 1.5% and 1.7%, respectively (VanRaden and Cole, 2014). Selecting for improved fertility has halted roughly 40 years of a continuous decline in sire and dam breeding values for fertility (Weigel, 2006). It has also been reported that the decline in phenotypic fertility performance has similarly been halted and started to improve (Norman et al., 2009).

In Canada, the Lifetime Profit Index currently includes 3 sub-indexes (relative emphasis for Holstein breed in parenthesis): production (51%), durability (34%) and health and fertility (15%). The specific traits linked to survival and reproduction are herd life (6.8% emphasis) and daughter fertility (10.1% emphasis), resulting in a total emphasis on fertility traits of 16.9% (Canadian Dairy Network, 2014).

▪ Breed Variation and Improvement Over Time

The distributions of sire predicted transmitting ability (PTA) for calving interval and survival for the main dairy breeds are illustrated in Figure 1. On average, the Holstein breed is genetically inferior to the other breeds for both calving interval and survival. It is apparent, however, that the greatest variation for both traits also exists within the Holstein breed (i.e., the flattest distribution). This means that Holstein sires with good fertility exist, and that these lines can be quickly dispersed. The distributions of Holstein sire PTA for both fertility traits based on year of birth are illustrated in Figure 2. The PTA for both fertility traits was poorest prior to the introduction of the EBI in 2001. Successive generations now provide superior genetics for fertility traits compared to the last (Butler, 2013).

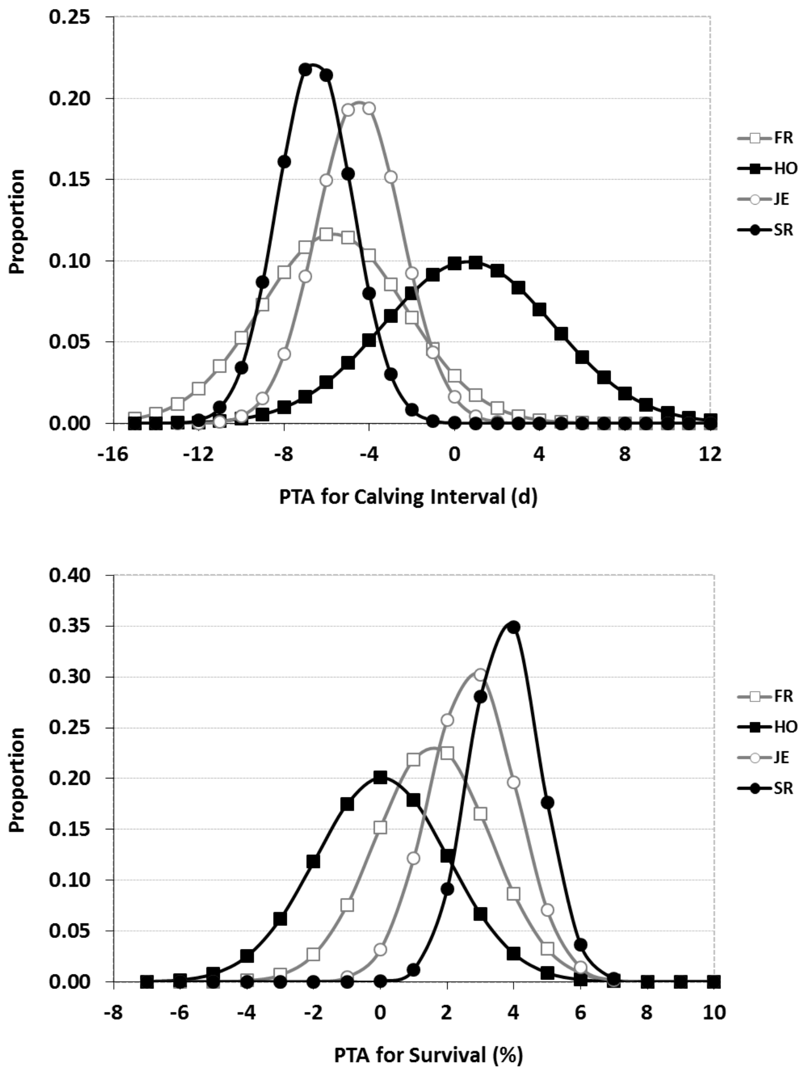

Figure 1. Probability density functions illustrating PTA for Calving Interval (top) and Survival (bottom) for the main dairy breeds. FR = Friesian (n = 224); HO = Holstein (n = 1882); JE = Jersey (n = 41); SR = Scandinavian Reds (Swedish and Norwegian Red breeds; n = 21). The dataset was filtered to retain only sires with ≥60% reliability for fertility traits. Data source: http://www.icbf.com/services/evaluations/dairy.php file downloaded Jun 22nd 2013. Reprinted with permission from Butler (2013) © CSIRO Publishing.

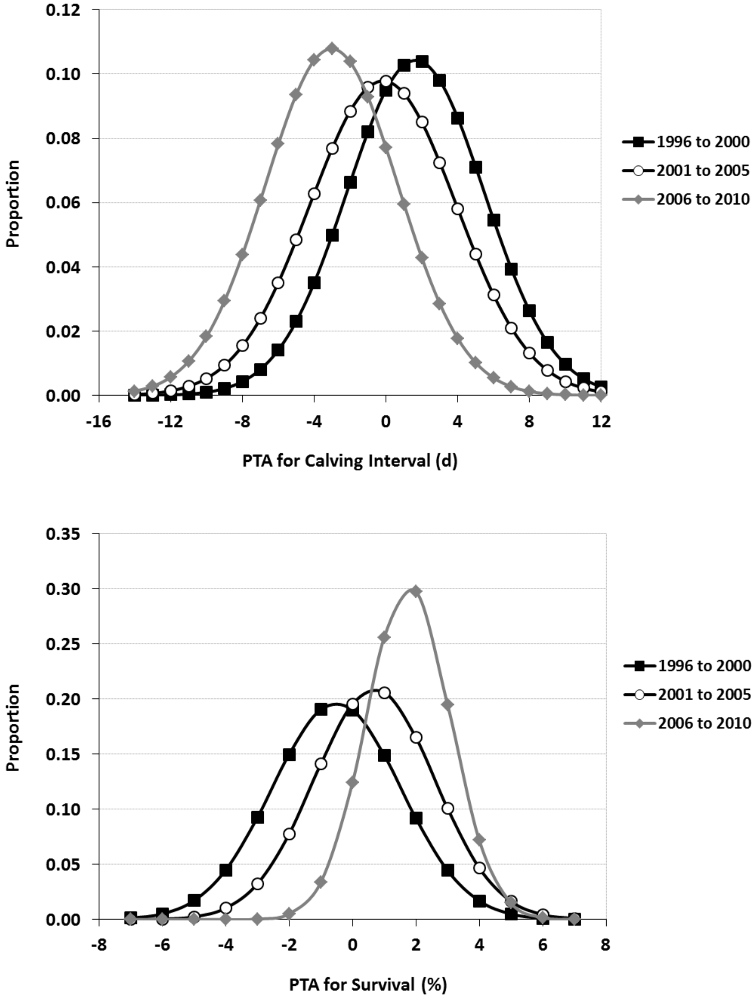

Figure 2. Probability density functions illustrating PTA for Calving Interval (top) and Survival (bottom) for dairy bulls based on birth date. The number of AI bulls born from 1996 to 2000, 2001 to 2005, and 2006 to 2010 was 450, 361, and 162, respectively. The dataset was filtered to retain only sires with ≥60% reliability for fertility traits. Data source: http://www.icbf.com/services/evaluations/dairy.php file downloaded Jun 22nd 2013. Reprinted with permission from Butler (2013) © CSIRO Publishing.

It is well established that PTA for calving interval is positively correlated with PTA for milk (Figure 3, top panel). This means that, on average, selecting a sire that has high PTA for milk will mean selecting a sire that has a long PTA for calving interval. Of course, this is undesirable, and the real challenge is to identify sires with good genetic merit for both fertility traits and milk production traits. A scatterplot of sire milk and fertility EBI sub-indexes is illustrated in Figure 3 (bottom panel). Arbitrary divisions at > €50 for the milk sub-index and > €100 for the fertility sub-index were inserted to identify superior sires. Of the 814 bulls that were born between 1996 and 2000 (i.e., before introduction of the EBI), 236 bulls had a milk sub-index > €50 (~29%), 89 bulls had a fertility sub-index > €100 (~11%), and 16 bulls had both a milk sub-index > €50 and a fertility sub-index >€100 (~2%). Of the 55 bulls born in 2011 (i.e., 10 years after introduction of the EBI), 45 bulls had a milk sub-index > €50 (~82%), 48 bulls had a fertility sub-index > €100 (~87%), and 39 bulls had both a milk sub-index > €50 and a fertility sub-index > €100 (~71%). This highlights the plasticity of animal genetics when sire selection is based on a particular breeding objective, and also that herd owners are acutely interested in selecting for improved fertility.

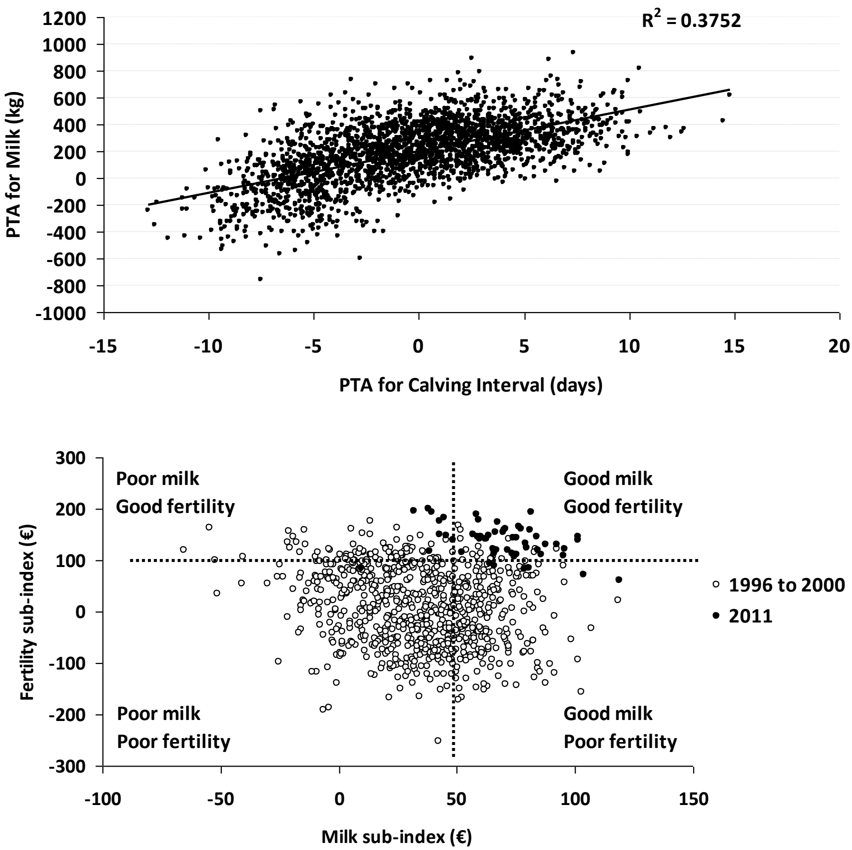

Figure 3. Breeding for better milk and fertility. Top: Scatterplot of the relationship between PTA for milk kg and calving interval. The general relationship is positive, so increasing genetic merit for milk yield reduces genetic merit for calving interval. The bulls of interest are those that combine good milk and calving interval traits. Bottom: Scatterplot of the EBI milk and fertility sub-indices for dairy bulls born between 1996 and 2000 (open circles) or in 2011 (closed circles). Data source: http://www.icbf.com/services/evaluations/dairy.php file downloaded Jun 22nd 2013. Reprinted with permission from Butler (2013) © CSIRO Publishing.

Fert+ and Fert- Cows

It is desirable to disentangle the effects of high merit for milk yield and poor merit for fertility traits. Cows with high genetic merit for milk production generally have poorer fertility than cows with average genetic merit for milk production. However, it is unlikely that high phenotypic milk production *per se* is directly responsible for poor fertility. Indeed, a number of studies have indicated similar or even superior fertility in high yielding cows compared to lower yielding herd mates. As a result, it is difficult to identify specific mechanisms under genetic control responsible for poor fertility using animal models that differ in phenotypic milk production potential in addition to a wide range of associated phenotypes (milk composition, body weight, feed intake capacity, etc.).

To address this issue, a lactating cow model with similar genetic merit for milk production, but either good (Fert+) or poor (Fert-) genetic merit for fertility traits was recently developed and validated at Teagasc Moorepark. A schematic outline of how the animals were assembled is outlined in Figure 4, and reported in detail by Cummins et al. (2012b). These animals have similar proportions of Holstein genetics, and similar body weight, milk yield and milk composition. Fertility performance, however, is markedly poorer in the Fert- cows compared to the Fert+ cows. The research conducted to date with this animal model has clearly demonstrated that the causes of reduced fertility in the Fert- cows are multifactorial.

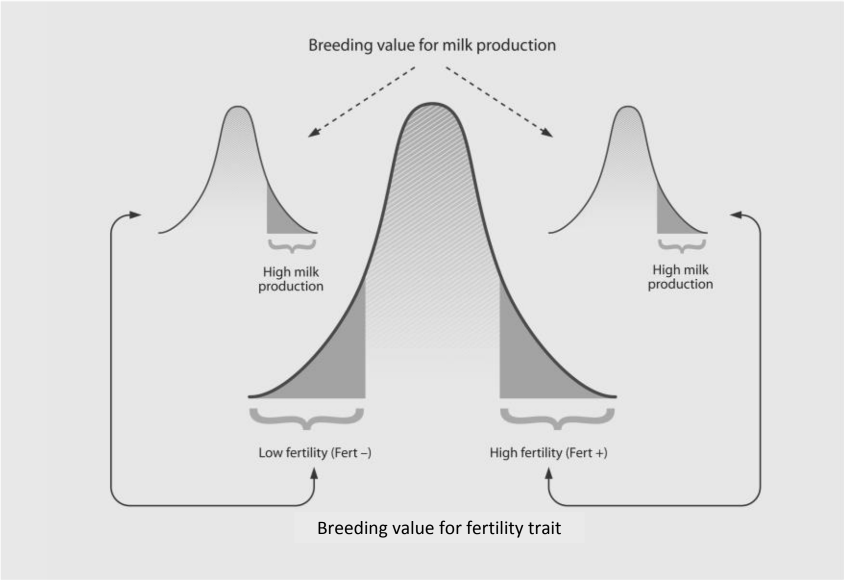

Figure 4. Schematic outline of the derivation of the animal model. Pregnant heifers with good (Fert+) or poor (Fert-) breeding values for fertility traits were identified within the national herd database. Within these two extremes, animals with similar breeding values for high milk production were identified and purchased. Reprinted with permission from Butler (2013) © CSIRO Publishing.

Metabolic Status and BCS

There is a large body of evidence linking postpartum BCS loss and BCS at the time of breeding with improved phenotypic fertility performance. Compared with Fert- cows, Fert+ cows maintain a greater threshold BCS throughout the gestation-lactation cycle and mobilize less BCS after calving (Cummins et al., 2012b; Moore et al., 2014a). Insulin-like growth factor 1 (IGF1) is a metabolic hormone that is correlated with bioenergetic status, and is well established as having a positive association with reproductive outcomes. Fert+ cows have greater circulating concentrations of IGF1 throughout lactation (Cummins et al., 2012b; Moore et al., 2014a).

In addition to greater IGF1, Fert+ cows have greater circulating insulin and glucose concentrations during the immediate postpartum period. Elevated glucose in the immediate peripartum period has been linked to likelihood of early ovulation (Butler et al., 2006) and likelihood of conception at breeding (Garverick et al., 2013). Consistent with their superior metabolic status, Fert+ cows maintained greater BCS during lactation and had reduced BCS loss after calving compared with Fert- cows. Maintenance of greater BCS in Fert+

cows during early lactation is facilitated by greater DMI (Moore et al., 2014a). Hence, we can conclude that cows with high genetic merit for fertility are more likely to ingest sufficient feed to meet nutrient requirements in early lactation, which results in improved metabolic status and less BCS loss.

Postpartum Resumption of Cyclicity

The postpartum interval to first ovulation is under genetic control, and has previously been shown to be heritable. By 6 weeks post-calving, 86% of Fert+ cows had resumed normal estrous cyclicity. At the same stage, however, only 20% of Fert- cows had resumed normal estrous cyclicity (Moore et al., 2014a). We can conclude that prolonged postpartum anestrous contributes to the inferior fertility performance of the Fert- cows.

Uterine Health

The reproductive tract of all cows becomes exposed to microbial pathogens while the cervix remains open after delivery of the calf and fetal membranes. The development of uterine disease is associated with reduced subsequent fertility (Sheldon et al., 2009). We examined uterine health in Fert+ and Fert- cows by assessing vaginal mucus scores weekly after calving and also by examining uterine cytology at 3 and 6 weeks postpartum (Moore et al., 2014a). Both the vaginal mucus scores and uterine cytology results indicated greater incidence of endometritis in the Fert- cows. A striking contrast between the rates of uterine recovery based on cytology exams is illustrated in Figure 5. Despite similar management and housing, Fert+ cows had a more rapid recovery in uterine health compared with Fert- cows. This likely indicates that the Fert+ cows were capable of mounting a stronger and/or timelier immune response following exposure to microbial pathogens. It is likely that better metabolic status during the earlier postpartum period in the Fert+ cows is linked to the reduced incidence of uterine disease.

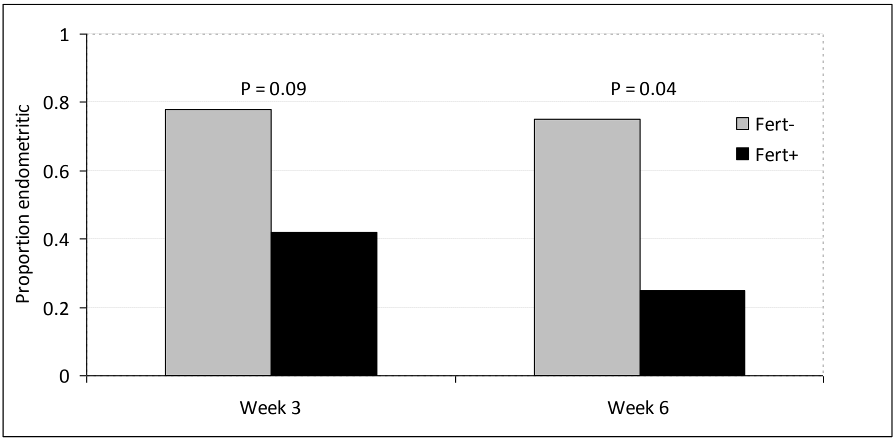

Figure 5. Incidence of endometritis in Fert+ and Fert- cows at week 3 and 6 postpartum based on polymorphonuclear neutrophil (PMN) count in uterine cytology samples. Samples with >18% and >10% PMN were diagnosed as endometritic at week 3 and 6, respectively. Reprinted with permission from Butler (2013) © CSIRO Publishing.

The Estrous Cycle

The estrous cycle was 4.1 days longer in Fert- cows compared with Fert+ cows (25.1 vs. 21.0 days; Cummins et al., 2012a). After ovulation, a corpus luteum forms on the ovary, and this structure produces a hormone called progesterone (P4). Progesterone has been termed 'the hormone of pregnancy' because of its vital role in pregnancy establishment. Circulating progesterone concentrations were similar during the first 5 days of the estrous cycle, but from day 5 to day 13, circulating P4 concentrations were 34% greater in Fert+ cows. The difference in circulating P4 was associated with a 16% larger corpus luteum in Fert+ cows. Progesterone influences oocyte competence, uterine receptivity to the developing embryo, maternal recognition of pregnancy and likelihood of pregnancy establishment. Inherent differences in circulating P4 concentrations likely represent a key phenotype responsible for fertility differences in these two strains (Cummins et al., 2012a; Moore et al., 2014b).

Table 1. Summary of the principal physiological differences identified to date between Fert+ and Fert- cows.

Early postpartum (parturition to wk 7)	At Breeding (wk 8 to 16 postpartum)
Greater DMI	Stronger oestrous expression
Greater BCS	Fewer silent heats
Earlier resumption of cyclicity	Less ovulation failure after oestrus
Superior uterine health	Greater luteal phase circulating progesterone
More favourable metabolic status (glucose, insulin, IGF-I)	More favourable uterine environment
	More favourable metabolic status (IGF-I)

Estrous Behaviour

Another major area of reproductive loss identified was the incidence of silent heats (defined as an ovulation event that was not preceded by estrous behaviour) and the incidence of cows failing to ovulate after expressing estrus (Cummins et al., 2012a). Cows were synchronized and estrous behaviour (measured using automated activity meters and electronic mount detectors) and the timing of ovulation (measured using transrectal ultrasound) were recorded at the synchronized estrus and at the subsequent spontaneous estrus. The main findings are summarized in Table 2. There was a significant difference in the incidence of silent heats. In a dairy farm operation, these cows do not get inseminated at the appropriate time, and at least 3 weeks is added onto the calving interval. A greater proportion of Fert- cows also displayed signs of estrus, but subsequently failed to ovulate. In a dairy farm operation, these cows do get inseminated, but fertilization cannot occur, again adding at least 3 weeks to the calving interval. Of the estrus events recorded, 36% fell into the combined categories of silent heats and heats without ovulation in Fert- cows, whereas only 2% fell into the combined categories in Fert+ cows. Clearly, this is an area of substantial reproductive loss and a cause of major frustration on dairy farms.

Table 2. Summary of estrus-related differences between Fert+ and Fert- cows.

	Fert+	Fert-	P-value
Silent estrus	2%	22%	0.02
Estrus without ovulation	0%	14%	0.04
Duration of estrus (hr)	7.53	5.86	0.08
Peak estrus activity*	168	119	0.01

*Measurement taken from activity collars

■ Conclusions

The main phenotypes that are different between cows with good and poor genetic merit for fertility traits are summarized in Table 2. These are all economically important phenotypes. It is readily apparent that Fert+ cows are inherently more fertile and easier to manage compared with Fert- animals, but achieve similar levels of milk output. It is essential that herd owners recognize the importance of selecting for improved genetic merit for fertility traits. Continued aggressive selection for increased milk output will increase the incidence of the undesirable phenotypes identified in the Fert- cows, increasing the requirement for interventions and involuntary culling due to fertility failure, ultimately eroding farm profit. After many decades of declining fertility, genetic merit for fertility and phenotypic reproductive performance are now on the opposite trajectory. The emphasis placed on fertility traits within the breeding index used in each country will affect the rate of genetic gain for fertility traits and recovery of phenotypic fertility performance.

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