**The importance of developmental programming in the dairy industry**

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**Highlights**

* Prenatal programming impacts dairy heifer growth, fertility, milk yield, and longevity.
* A mismatch between pre- and postnatal life may be detrimental for future outcomes.
* Selecting heifers based on dam age and birth month may improve longevity.

**ABSTRACT**

The concept of developmental programming suggests that environmental influences during pre- and early postnatal life that can have long-term effects on future health and performance. In dairy cattle, maternal body growth, age, parity and milk yield, as well as environmental factors during gestation, have the potential to create a suboptimal environment for the developing fetus. As a result, the calf’s phenotype may undergo adaptations. Moreover, developmental programming can have long-term effects on subsequent birth weight, immunity and metabolism, as well as on postnatal growth, body composition, fertility, milk yield and even longevity of dairy cows. This review provides an overview of the impact of developmental programming on later health and performance in dairy cows.

**Keywords**

DOHaD; Developmental programming; Dairy cattle; Postnatal health and performance

1. **Introduction**

The Developmental Origins of Health and Disease (DOHaD) hypothesis, refers to the hypothesis that environmental influences during critical periods of early development can have a profound and lasting impact on an individual's health and disease risk throughout postnatal life. This hypothesis emerged from epidemiological observations and research that linked early-life insults, particularly during fetal development and infancy, to the occurrence of chronic diseases in adulthood (Barker, 1990; Hales and Barker, 1992; Barker, 2004; De Boo and Harding, 2006). Entringer et al. (2018) described maternal biophysical, clinical, psychological and behavioural states programming health and disease risk. Physiological outcomes are decided by the exact nature, the timing, and the duration of the insult (Bertram and Hanson, 2001). Yet, another hypothesis is that a “mismatch” between the intrauterine and (early) postnatal environment may be the detrimental programming driver (Singhal and Lucas, 2004). In humans, many findings on developmental programming originate from studies on the health effects of early life exposure to famine. The relatively short-lived Dutch famine, from November 1944 to May 1945, may be considered a “natural experiment” that provided the unique possibility to study the long-term effects of environmental adverse intrauterine conditions on adult morbidity and eventual mortality (van Abeelen et al., 2012). During the height of that famine, caloric consumption dropped from 1800 to 400-800 kcal/day, only to bounce back to 2000 kcal/day post-famine (Roseboom et al., 2006), which can be seen as a “mismatch” between the pre- and postnatal environment. Fetal exposure to famine during any stage of gestation was associated with glucose intolerance later in life. More coronary heart disease, stress responsiveness and obesity were seen in adults prenatally exposed during early gestation (Roseboom et al., 2006). The findings of Roseboom et al. (2006) show that maternal undernutrition during gestation has important effects on health in later life, although the effects depend on its timing during gestation. In contrast, the siege of Leningrad between 1941-1944 lasted considerably longer, in a population that was malnourished before, as well as after the siege. In this study, no effects of intrauterine malnutrition on blood pressure, glucose intolerance, or lipid concentrations in adult life were found (Stanner et al., 1997). A possible explanation of these contradictory findings is that the children in Leningrad suffered malnutrition after birth as well, thus not catching up by accelerated weight gain (Hales and Barker, 2001). In other words, there was a “match” between the pre- and postnatal environment. In livestock, Wu et al. (2006) reviewed the consequences of impaired intrauterine growth and development, and found that compromised fetal growth leads to reduced neonatal survival, permanent stunting of postnatal growth, poor body composition, and impaired long-term health and performance. Well-known influences on the prenatal environment in dairy cattle are maternal age and parity, maternal nutrition, milk yield and energy status, as well as season and ambient temperature (Van Eetvelde and Opsomer, 2017; Wathes, 2022). In this review, we provide a broad overview of the consequences of developmental programming on later health and performance in dairy cattle.

1. **Consequences of developmental programming on dairy cow performance**
	1. Birth weight

In Holstein-Friesian calves, birth weights are quite variable with a reported range of 24-55 kg, and are found to have a significant positive correlation with weight around weaning and first service (Bazeley et al., 2016). Monitoring heifer weights at birth and during the rearing period enables farmers to improve heifer growth rates and so impact both the efficiency of heifer rearing and, potentially, the productivity and performance of the adult herd (Bazeley et al., 2016).

A suboptimal intrauterine environment during critical periods of development may lead to changes in tissue structure and function, with potential long-term consequences on the offspring's physiology and disease susceptibility (Abuelo, 2020). As calf birth weight can act as an indicator of intrauterine growth (Ouellet et al., 2021), it is regularly measured in studies examining the impact of fetal programming. Velazquez et al. (2023) reviewed the preimplantation phase and its role on postnatal health and performance. The preimplantation phase represents a developmental window where developmental programming may occur in response to the embryonic environment *in vivo* or *in vitro* (Velazquez et al., 2023). Assisted reproductive techniques (ART) like multiple ovulation and embryo transfer (MOET) and *in vitro* embryo production (IVEP) resulted in calves with an increased birth weight compared to calves born following artificial insemination (AI) (Siqueira et al., 2017; Baruselli et al., 2022; Crowe et al., 2023), due to ART-induced epigenetic changes and altered gene expression leading to errors in the developmental program of the embryo (Rivera, 2020). Holstein Friesian calves produced via somatic cell nuclear transfer or cloning, had a significantly higher birth weight than calves born after IVEP or AI (Chavatte-Palmer et al., 2002). Both Crowe et al. (2023) and Lafontaine et al. (2023a) found that calves originating from IVEP and MOET displayed longer gestations than calves conceived by AI, which might explain the higher birth weight. Conversely, Siqueira et al. (2017) did not notice a significant difference in gestation lengths between the different ART, while Chavatte-Palmer et al. (2002) demonstrated no significant differences between the birth weights of IVEP and AI calves. Another reason for heavier birth weights in calves born after ART, is the induction of the large/abnormal offspring syndrome (LOS/AOS), a syndrome associated with inappropriate control of the epigenome, and characterized by fetal overgrowth and placental abnormalities (Rivera, 2020). The syndrome has important consequences for farmers and their animals, due to the low survival of offspring and high probability of dystocia, often requiring cesarean section (Nava-Trujillo and Rivera, 2023). Since the omission of serum or bovine serum albumin, as well as the co-culture with somatic cells, much less LOS/AOS has been reported by the cattle industry, although increased birth weights after ART are still observed (Rivera, 2020; Chavatte-Palmer and De Schauwer, 2023). Johanson and Berger (2003) described a 13% increase in odds for dystocia per kg increase in birth weight, resulting in 2.7 times more perinatal mortality. As such, applying MOET, IVEP or cloning on dairy farms may warrant increased vigilance at parturition, by the farmer or farming staff.

 In livestock, maternal nutritional status during gestation has been described as a major contributor in developmental programming and offspring outcomes (Reynolds and Caton, 2012; Reynolds et al., 2017). Most developmental programming research has focused on maternal undernutrition during gestation in sheep and beef cattle (Wallace et al., 2006; Wu et al., 2006; Greenwood and Cafe, 2007; Greenwood et al., 2009; Micke et al., 2010; Barcelos et al., 2022). Maternal undernutrition is linked to intrauterine growth retardation and low birth weights through endocrine effects, including decreased fetal insulin and insulin-like growth factor (IGF) 1 and 2 concentrations, increased fetal cortisol and a decreased growth of skeletal muscle (Bell et al., 2005). However, the effects of restricted maternal nutrition on birth weight are variable (Chavatte-Palmer et al., 2015; Sinclair et al., 2016). Birth weight can be low or unaffected, depending on the timing, severity and duration of the dietary insult (Holland and Odde, 1992; Greenwood and Cafe, 2007; Kenyon and Blair, 2014; Chavatte-Palmer et al., 2015). Undernutrition (feeding below the energy requirements for maintenance and lactation) in intensively farmed dairy cows could be considered a rare phenomenon, since both nulliparous and lactating multiparous dams are generally fed according to their requirements. However, undernutrition may still be present in dairy cattle due to the lactating cows’ inability to cope with negative energy balance during the post-partum period (Van Eetvelde et al., 2017), or because of the inability to provide a suitable amount of eating spaces (Oetzel, 2014; Sundrum, 2015) which may cause competition or bullying and lead to limited feed intake in some animals. On large-scale new entry farming systems in harsher climates, the feed supply and the quality of the forage may be seasonally influenced, e.g. forage quality may be poor in summer in the tropics or during severe winters in more temperate regions (Chamberlain, 2023). Furthermore, overstocking cows in pasture-based dairy systems (Chamberlain, 2023), grazing heifer herds on a lower quality pastures away from prime grazing areas reserved from the milking herd (Verdon, 2023), as well as seasonal variation of forage quality and availability may cause nutritional deficiencies as well (Hogan and Phillips, 2016; Verdon, 2023). Regardless of the management system, dairy cattle differ from other species as they combine lactation with the intra-uterine growth of their offspring. Especially in dairy cows selected towards high milk yield, partitioning energy as well as specific nutrients towards the growing fetus and the mammary gland might become challenging. Furthermore, Gao et al. (2012) noted that reducing the energy density of the maternal diet during the last 21 days before parturition had a negative effect on birth weight, body length and height, abdominal, thoracic and umbilical girth, immunity, and antioxidation capability of neonatal calves.

Maternal overnutrition during gestation can also have detrimental effects on the developing fetus (Reynolds et al., 2017). In adolescent overfed ewes, it has been shown repeatedly, that there is an altered hierarchy of nutrient partitioning between maternal body growth and fetal development. Overfeeding adolescent, gestating ewes gave rise to lighter progeny due to impaired growth of both the fetus and the placenta, consequent to a greater nutrient partitioning towards maternal body growth (Wallace et al., 2006). In cattle, maternal overnutrition and fetal programming has not been as extensively studied as undernutrition (Abuelo, 2020), although in a recent meta-analysis by Barcelos et al. (2022) the effects of different levels of energy and protein supply during gestation in beef cows were depicted. Higher protein and energy supply during gestation resulted in higher calf birth weight, however, the magnitude of the response became more discrete when the protein and energy supply were excessive (Barcelos et al., 2022). Fat cow syndrome (metabolic, digestive, infectious and reproductive disorders affecting the obese periparturient dairy cow), first described by Morrow (1976), has many similarities with the human metabolic syndrome (De Koster and Opsomer, 2012), and as such it is likely that there are similar links between overconditioned pregnant dairy cows and increased risk of metabolic disease in their offspring (Opsomer et al., 2017). Also, changes in body composition of dairy cows during late gestation could negatively affect calf development (Abuelo, 2020).

 In recent years, *in utero* heat stress during late gestation has been extensively studied. Dairy cows exposed to late gestation heat stress give birth to offspring with significantly lower birth weights (Tao et al., 2012; Monteiro et al., 2014; Dahl et al., 2019; Almoosavi et al., 2020; Ouellet et al., 2020). Heat stressed dams have a lower dry matter intake, thus impeding fetal nutrient supplies (Ouellet et al., 2020). Additionally, others suggest that the placenta, exchanging all nutrients and oxygen between dam and fetus, responds to this impeding nutrition by expanding the cotyledonary surface (Reynolds et al., 2006). This is in corroboration with the findings of Van Eetvelde et al. (2016), who observed placental adaptations based on calving season, in which an increase of cotyledonary surface was evident in cows calving during the hottest months. As a result of late gestation heat stress, heat stressed cows calve on average 2-4 days earlier than cooled cows (Tao et al., 2012; Dado-Senn et al., 2020; Dado-Senn et al., 2021), which may contribute to the lower birth weights, although other studies found lower birth weights without differences in gestation length (Karimi et al., 2015). As such, reduced birth weights are probably a combined result of a reduced gestation length and an impaired placental development (Cattaneo et al., 2023). Next to reduced birth weights, heat stress also affected fetal heart, liver, kidney, and immune organ (thymus and spleen) weights compared to calves without heat stress (Ahmed et al., 2021). Moreover, the apparent efficiency of IgG-absorption, cellular immune function, plasma total protein, hematocrit (Tao et al., 2012), and insulin levels are reduced, and insulin sensitivity is elevated in newborn heat stressed calves, compared to calves born in colder months (Kamal et al., 2014; Kamal et al., 2015).

In nulliparous dams, dam age influences fetal development as well, associating both very young and older age with lower birth weights (Van Eetvelde and Opsomer, 2017). Kamal et al. (2014) found a curvilinear relationship between dam age and calf birth weight. Neonatal calves born out of very young (<22 months) and older heifers (>25.5 months) were born with lower birth weights (Kamal et al., 2014), suggesting that in the very young dams, continued growth of the dam competes with fetal growth as shown in adolescent ewes (Wallace et al., 2006). Van Eetvelde and Opsomer (2017) suggested that older heifers might have conceived later because of suboptimal growth, related to lower IGF-1 concentrations, which may be responsible for the low birth weight of their calves as well (Wathes et al., 2008; Brickell et al., 2009). Older dams (parity 3-6) with higher milk yields were also found to give birth to smaller calves (Swali and Wathes, 2006), possibly due to lower insulin and IGF-1 concentrations in older dams (Taylor et al., 2004). Similarly, Kamal et al. (2014) found that high maternal milk yield during gestation was associated with reduced calf birth weight. They also established that a longer lactation length (high persistency) in combination with a shorter dry period was associated with the birth of smaller calves (Kamal et al., 2014), indicating a further negative effect on the developing fetus (Van Eetvelde and Opsomer, 2020). In contrast, Harati et al. (2024) found higher birth weights in calves from dams with greater levels of milk production, suggesting that genetics can be influenced by environment and thus cause differences between herds. Additionally, it has been shown that calves born to dams suffering from metabolic and oxidative stress during gestation are smaller at birth and show some metabolic and inflammatory responses that could influence disease susceptibility (Ling et al., 2018).

 Birth weight, however, does not take into account possible changes in body composition such as adiposity and skeletal development, and is therefore not the most adequate indicator of prenatal development (Wathes, 2022). Finally, high birth weight has been shown to increase the risk for dystocia and perinatal mortality (Johanson and Berger, 2003), while low birth weights have been linked to an increased incidence of unexplained stillbirth (Berglund et al., 2003; Windeyer et al., 2014). Birth weight has also been found to be significantly correlated with the predicted weight of dairy heifers up to 400 days of age, as with every 1-kg increase in birth weight, there was a 2.5-kg increase in the predicted weight at 400 days of age (Hurst et al., 2021). The significant positive correlation of calf birth weight with later predicted weights described by Bazeley et al. (2016) and Hurst et al. (2021) suggests that dairy calves cannot totally compensate postnatally for restricted growth *in utero* (Wathes, 2016).

* 1. Postnatal growth and body composition

Whilst postnatal growth in calves is largely dependent on feeding strategies, it is also related to birth weight (Van Eetvelde and Opsomer, 2020). As discussed above (2.1. Birth weight), heat stress during the dry period resulted in calves born with a lower birth weight (Tao et al., 2012). Tao et al. (2012) also found that calves born to heat stressed dams suffered from compromised transfer of passive immunity as well as lower weaning weights, compared to calves born to cooled dams. In contrast, others did not find differences in weaning weights or average daily gain (ADG) in calves born out of heat stressed heifers, although they also found a lower apparent efficiency in IgG absorption and lower serum IgG concentrations throughout the preweaning period, compared to calves born out of cooled heifers (Davidson et al., 2021). Lundborg et al. (2003) found that calves born with a lower birth weight grew more rapidly than their heavier counterparts. Similarly, low birth weight offspring from primiparous dams were no longer smaller at 3 months of age (Swali and Wathes, 2007), which is indicative for catch-up growth (Wathes, 2022). In contrast, low birth weight calves from multiparous dams remained smaller until at least 9 months of age (Swali and Wathes, 2006), which suggests a different underlying cause for *in utero* growth restriction in these low birth weight calves. Interestingly, Dahl et al. (2016) describe that low birth weight calves born to heat stressed dams resulted in mature cows with a smaller frame size, rather than a lower body weight. This might be explained by the fact that maternal heat stress during the dry period enhances the whole-body insulin response of calves after weaning, which suggests the possibility of accelerated lipogenesis and fat deposition in early life (Tao et al., 2014). The number of muscle fibers is set at birth (Albrecht et al., 2013), and an increasing body of evidence shows that the level of maternal nutrition during gestation can alter fetal skeletal muscle development, with long-term effects on offspring growth and performance (Du et al., 2010). Zhu et al. (2006) describe a reduced muscle mass and altered muscle fiber distribution, as well as an increased fat accumulation in offspring from nutrient-restricted ewes. Similarly, Long et al. (2012) found that *in utero* undernutrition in cattle increased the average adipocyte diameter in subcutaneous, mesenteric and omental adipose tissue in their offspring. As such, there is evidence of early postnatal catch-up in body weight, and altered body composition, resulting in adiposity (Louey et al., 2005). This bears remarkable similarities with studies of intrauterine growth retardation in humans, where small size at birth and rapid postnatal catch-up growth have been associated with increased adiposity and negative effects on later health and fertility (Ong, 2007; de Zegher et al., 2017). Moreover, Swali and Wathes (2007) reported that catch-up growth in dairy cattle resulted in a slightly higher body weight at calving, accompanied by a larger weight loss after parturition. This may indicate a greater degree of body tissue mobilization (Van Eetvelde and Opsomer, 2017), with possible increased risks for insulin resistance and metabolic disorders around parturition (De Koster and Opsomer, 2013).

Van Eetvelde and Opsomer (2017) reviewed possible consequences of pre- and postnatal environment on later performance in dairy cattle. They describe that the outcome of intrauterine programming is dependent on whether or not there is a ‘match’ or ‘mismatch’ between the pre- and postnatal environment (Van Eetvelde and Opsomer, 2017). They hypothesize that after intrauterine undernutrition, a restricted diet postnatally creates a ‘match’ between the pre- and postnatal environment, hence the offspring will thrive due to its adapted phenotype (Figure 1). However, when a postnatal abundance of nutrients follows intrauterine undernutrition, a ‘mismatch’ between the pre- and postnatal life might develop, which may be detrimental to the calf’s future growth, health, and performance (Van Eetvelde and Opsomer, 2020).

In human medicine, there is a dilemma whether or not small for gestational age born infants should experience catch-up growth. Ong (2007) states that a ‘healthy catch-up growth’ with close monitoring of weight and adiposity, should be the goal of future research. Further research on small for gestational age or low birth weight calves, postnatal (catch-up) growth, body composition, and the effects of catch-up growth on later performance and longevity in the dairy industry is warranted.

* 1. Fertility

Developmental programming of fertility in cattle has recently been extensively reviewed by Em. Prof. Dr. Claire Wathes (2022), and as others in this Special Issue will address prenatal effects on different aspects of fertility, only a brief overview will be provided here.

 Lafontaine et al. (2023b) compared dairy cattle derived from MOET, IVEP, and AI concerning their fertility traits. They found that animals derived from IVEP took between 3.06 and 4.44 more days to conceive than their AI and MOET counterparts, and that IVEP and MOET derived cows scored 1 point lower than their parents on the daughter fertility index compared to the AI derived cows (Lafontaine et al., 2023b).

Dam parity is described to influence fertility of the offspring, although conflicting results have been found (Wathes, 2022). Swali and Wathes (2007) found that offspring from primiparous dams conceived more rapidly during their first service period than those of multiparous dams, while fertility in the first lactation was similar between both groups. Conversely, Akbarinejad et al. (2018) described that offspring from multiparous cows were significantly more fertile than offspring from nulliparous dams, in terms of days to first service, first service conception rate, number of services per conception and calving to conception interval. They recently confirmed these results, and demonstrated higher anti-Müllarian hormone (AMH) concentrations in offspring born out of old multiparous dams, compared to offspring of nulli- and primiparous dams (Bafandeh et al., 2023). The superior fertility of offspring from multiparous dams may be related to the higher AMH concentrations and larger ovarian reserves of these offspring, probably contributing to their on farm longevity (Bafandeh et al., 2023). Furthermore, a recent study on nulliparous dairy heifers revealed that as the ADG increased from the pre-breeding period to the first pregnancy diagnosis, the AMH concentration in their offspring was reduced, suggesting that excessive growth of the dam prior to conception and in early gestation could negatively impact the ovarian reserve of the offspring (Thomson et al., 2024). Banos et al. (2007) concluded that the optimal first-calving age was between 24 and 29 months, to achieve better fertility profiles in their progeny. They found that early calving dams (18 to 23 months) had daughters with a 7% higher body condition score and a 3 days earlier first service compared to daughters of late calving dams (30 to 36 months), however, the progeny of early calving dams needed 7% more inseminations and had a 7.5% higher return rate (Banos et al., 2007). These results were corroborated by Brickell et al. (2009) who found that heifers growing fast during the first months of life were younger at first breeding, but needed more inseminations to become pregnant.

 Walsh et al. (2014) described a greater antral follicle count (AFC) in offspring from dams lactating during gestation compared to non-lactating dams. Furthermore, daughters of average yielding dams showed better fertility results, with significantly lower ages at first service, conception and first calving, compared to daughters born out of lower or higher yielding dams (Wathes, 2022).

Dietary restriction during early gestation gave rise to female offspring with lower AFC, lower AMH, and greater FSH concentrations at birth, but similar age at puberty compared to calves born to non-restricted dams (Mossa et al., 2013). This study provides evidence for a negative impact of maternal undernutrition on the ovarian reserve of the offspring (Mossa et al., 2015).

Dam heat stress has been widely studied in relation to its prenatal effects on the reproductive performance of dairy cattle offspring. Pinedo and De Vries (2017) described season of conception to influence offspring fertility, with cows that were conceived in winter being reproductively superior to summer conceived cows. An adverse effect of dry period heat stress on offspring fertility was reported by Kipp et al. (2021). Their study revealed that even a very limited environmental stress (temperature-humidity index (THI) ≥ 50) in any of the 8 weeks before parturition can worsen calving to conception intervals and impair conception rates of the offspring (Kipp et al., 2021). Such transgenerational heat stress effects were also observed by Akbarinejad et al. (2017), who described that mainly second and third trimester heat stress could negatively impact offspring fertility by increasing days to first service, calving to conception interval, the amount of repeat breeders, number of services per conception, and by decreasing first service conception rate. Also, they found that AMH concentrations were lower in heat stressed compared to unstressed offspring (Akbarinejad et al., 2017). Similarly, Succu et al. (2020) and Makiabadi et al. (2023) also reported lower AMH concentrations in dairy calves that suffered *in utero* heat stress during the first trimester of gestation.

Lastly, the anogenital distance (AGD), being the distance between the center of the anus and the clitoral base, is considered a marker for prenatal androgen exposure and later fertility in many species, including cattle (Gobikrushanth et al., 2017). The AGD is a novel indicator for reproductive performance in lactating dairy cattle and nulliparous heifers, and is inversely related to fertility measures (Akbarinejad et al., 2019; Carrelli et al., 2021; Carrelli et al., 2022). More recently, other than the AGD to the clitoris (AGDc), the AGD to the vulva (AGDv), and the anogenital ratio (the ratio between the AGDv and AGDc) have also been shown to be associated with dairy heifer fertility, and seem to be pre- rather than postnatally determined (Beci et al., 2023). In this regard, Dewulf et al. (2023) recently demonstrated that some dairy calves are prenatally exposed to isoflavones, originating from isoflavone-rich components (e.g. soybeans, rapeseed, linseed, red clover, alfalfa,…) in the ration fed to their dams. Isoflavones are a subgroup of phytoestrogens, which are natural plant substances structurally similar to 17-β-estradiol, and are capable of binding to estrogen receptors and can interact with the metabolism of steroid hormones (Pilsáková et al., 2010). Although more research is needed, the results of Dewulf et al. (2023) indicate that depending on the maternal diet, some calves are exposed to isoflavones during the developmentally most sensitive period of their lives, and may have effects on developing organ systems like the reproductive system. As stated above, AGDc is considered a marker for prenatal exposure to androgens (Gobikrushanth et al., 2017), so further research about the effects of prenatal exposure to endocrine disruptors, such as isoflavones, on the AGD might be warranted.

* 1. Milk yield

Besides age and weight of a heifer at first parturition, several prenatal factors have been associated with first lactation milk yield (Van Eetvelde and Opsomer, 2020). Maternal age has been described to have an effect on life performance of progeny, with high yielding progeny being born from the youngest mothers, whereas low yielding cows were born from the oldest dams (Astiz et al., 2014). Many other studies confirmed that older dams produce offspring with a lower milk yield in their first, second and third lactations (Banos et al., 2007; Berry et al., 2008; González-Recio et al., 2012; Van Eetvelde et al., 2020). Nevertheless, it should be mentioned that there have been fairly rapid genetic improvements for milk yield and productive life over the past decades, through the use of AI and genomic selection (García-Ruiz et al., 2016), leading to differences in in milk yield due to genotypic superiority of the younger animals in the herd. Thus, to distinguish the effects of genetic improvements from those due to developmental programming is challenging.

Other than maternal age or parity, the level of maternal milk yield during gestation has been found to be negatively correlated with offspring milk yield. The overall effect of maternal milk yield on daughter milk yield during their first 3 lactations was significant, with increasing maternal milk yield being associated with lower daughter milk yield (Banos et al., 2007). Similarly, Berry et al. (2008) found a reduced progeny milk yield during the first and third lactation, with increased maternal milk yield during gestation. González-Recio et al. (2012) argued that the higher the maternal milk yield during gestation, the greater the negative effects of prenatal programming, preventing the offspring of the most productive cows from fully expressing their additive genetic value during their adult lives. However, the interaction between dam parity and dam milk yield and its further influence on progeny performance needs to be further explored (Van Eetvelde et al., 2021).

Furthermore, carry over effects of gestational heat stress on dairy cattle progeny have been described as well. Pinedo and De Vries (2017) found that season of conception had a relevant impact on milk yield (by 70 and at 305 days in milk), with cows that were conceived in winter having greater milk yields than cows that were conceived in summer. Heifers born from heat stressed dams produced less milk across the first 35 weeks in their first lactation, compared to heifers born to cooled dams (Monteiro et al., 2016). As described above (2.1. Birth weight), late gestation heat stress has been associated with changes in the phenotype of dairy calves, such as lower birth weight and high insulin sensitivity (Kamal et al., 2014; Tao et al., 2014; Kamal et al., 2015). Whether these early-life adaptations in insulin traits exert long-term effects on the metabolic function in later life, ultimately negatively impacting the animal’s milk yield, is unknown (Kamal et al., 2015). If these alterations of insulin traits in dairy calves persist in later life, as they do in newborns confronted with intrauterine growth restriction in other species, they may contribute to adverse metabolic outcomes, such as adiposity and related metabolic diseases, both known to decrease milk yield (Mericq et al., 2017; Opsomer et al., 2017).

Interestingly, maternal milk yield itself seems to be programmed by the gender of the calf the dam is gestating. Cows favor daughters, producing significantly more milk when gestating a heifer compared to gestating a bull calf. Moreover, the sex of the calf gestated during the first parity has persistent consequences for the milk yield in the subsequent parity, with female progeny increasing dam milk yields (Hinde et al., 2014).

* 1. Longevity

Longevity is an important trait for the dairy industry from both an economic and a social point of view (Van Eetvelde et al., 2021). A greater longevity and productive lifespan of cows can improve the profitability of a herd by resulting in lower culling rates, and a lower need for replacement heifers (Horn et al., 2012), thus improving the environmental footprint (Grandl et al., 2019), while it is also encouraged by the public’s opinion, in terms of animal welfare (Stefani et al., 2018). Farmers are criticized for the short productive lifespan of their dairy cows, with only a minority of animals surviving to a fourth lactation (Bell et al., 2010), implying that most cows are culled before reaching their full potential (Van Eetvelde et al., 2021).

An extensive study by Van Eetvelde et al. (2021) researched cows that reached a lifetime milk yield of ≥100,000 kg (hundred tonne cows). Hundred tonne cows have the ability to delay involuntary culling due to fertility or health problems, and are not voluntarily culled because of inadequate production. Therefore, they can be considered exceptional ‘athletes’, as they combine longevity with very high functionality (Van Eetvelde et al., 2021). Van Eetvelde et al. (2021) established that breeding values for milk yield, fertility, udder and claw health, as well as high scores for conformation traits like udder, feet and legs, were positively associated with the likelihood to become a hundred tonne cow, and that cows born in September and born out of heifers had higher odds of reaching a lifetime milk yield of ≥100,000 kg.

Others also found unfavorable effects of late gestation heat stress on longevity traits. Monteiro et al. (2016) described that a greater percentage of *in utero* cooled heifers reached their first lactation compared with *in utero* heat stressed heifers. Similarly, Laporta et al. (2020) found that *in utero* heat stressed heifers (as a daughter and granddaughter) had increased culling risks before their first calving and a reduced productive life and lifespan. Season of conception also had a relevant impact on dairy cow survival, with winter conceived cows having higher odds to survive to a second calving than summer conceived cows (Pinedo and De Vries, 2017).

Lastly, we recently described that telomere length in newborn dairy heifers is influenced by prenatal factors (Meesters et al., 2023). Interestingly, telomere length is a heritable trait in cattle, which is associated with the productive lifespan of dairy cattle (Seeker et al., 2018). We found that telomere length at birth was negatively associated with dam age at parturition, mainly in dams calving for the first time. We also demonstrated that the median THI during the third trimester of gestation was negatively associated with the calves’ telomere length. These results also suggest that selecting heifers born in winter, out of young dams might contribute to increased longevity in dairy cattle (Meesters et al., 2023).

1. **Conclusions**

There is clear evidence that maternal and environmental modulations during the prenatal period have long-lasting consequences for the offspring’s future health, performance and longevity. Intrauterine and post-natal growth, body composition, fertility, milk yield, survival and lifespan have all been described to be prenatally programmed. Addressing adverse effects of developmental programming will require management strategies to be adapted. Heat stress abatement during late gestation might reduce negative effects of *in utero* heat stress on the offspring’s later performance. Furthermore, minimizing undernutrition in different management systems may reduce adverse effects of nutritional and metabolic programming of the progeny. For example, by taking preventive measures to cope with negative energy balance during the postpartum period in intensive dairy farming systems, or by improving grazing management and supplementing the grazed diet to address seasonal variability in pasture-based systems. Modulating postnatal catch-up growth in calves, e.g. by managing postnatal nutrition to prevent excessive postnatal growth but promote prolonged moderate growth, may prevent the development of metabolic diseases later in life. Lastly, selecting replacement heifers born out of nulliparous dams and born during the colder months may help increase the longevity of a dairy cow.

**Author contributions**

M.M. wrote the main manuscript text. All authors critically reviewed the manuscript. All authors read and approved the final version of the manuscript.

**Declaration of Competing Interest**

The authors declare no competing interest.

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Figure 1: Offspring adaptations following a match or mismatch between the pre- and postnatal environment. Created with [BioRender.com](https://www.biorender.com/). **IN** **COLOUR**