Physiological and Genetic Aspects of some Fitness Traits Performance in Pigs

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Summary

Inbreeding has negative effects on various pig traits, of which litter size, survival and weight traits are of considerable interest to researchers because they have high economic importance and affect the survival of the related pig population. These traits are complexly influenced by many interacting biological, nutritional, management and environmental factors. Studying the physiological mechanism of the effects of these factors including inbreeding depression on these traits may help prevent or reduce the caused economic loss. This review briefly summarises the physiological mechanisms affecting litter size, piglets born alive/dead and birth weight with an emphasis on genetic and biological factors. In addition, studies detecting genes, or quantitative trait loci that affect the traits mentioned, are also discussed.

Key words

pigs, inbreeding depression, physiology, litter size, stillborn piglets, birth weight

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Received: July 6, 2023 | Accepted: September 18, 2023 | Online first version published: February 14, 2024

Introduction

Inbreeding depression, which is the reduction in performance due to inbreeding, has been documented in pig populations (Doekes et al., 2021; Mei et al., 2022; Wang et al., 2022; Zhang et al., 2022). Studies have shown that inbreeding may lead to a decrease in the reproductive performance, such as a negative effect on litter size (the total of number piglets born and the number of piglets born alive), as well as a decrease in growth traits (Köck et al., 2009; Mei et al., 2022; Zhang et al., 2022). The impact of inbreeding coefficients, determined through pedigree-based and Single Nucleotid Polymorhism (SNP) based methods, was found to be significant on the total number of piglets at birth (TNB) and the number of piglets born alive (NBA) in a study conducted on a Large White pig population. In terms of inbreeding depression on litter weight at birth, the study found that only SNP-based inbreeding coefficients exhibited a substantial correlation (Zhang et al., 2022). According to Doekes et al. (2021), the detrimental impact of inbreeding was observed in various characteristics, and there was no indication that primary fitness traits such as reproductive or survival traits were more affected than other traits, such as production or morphological traits.

However, traits such as litter size, number of piglets born alive/dead and birth weight are not only important for commercial farms (Lee et al., 2020; Li et al., 2020; Threadgold et al., 2021) but also for conservation. Pig breeds have been selected and various strategies have been implemented with the aim of increasing litter size, increasing birth weight and reducing stillborn rates (Riddersholm et al., 2021; Threadgold et al., 2021). This is also a concern for conservation farms, alongside their primary focus on preserving genetic diversity. Therefore, the inbreeding depression that occurs in these traits, together with other influencing factors, is likely to have an impact on animal breeding programmes.

Inbreeding depression, which may arise from higher maintenance metabolism (Ketola and Kotiaho, 2009), can be associated with a decrease in immune response (Charpentier et al., 2008; Reid et al., 2003). However, it is challenging to determine and measure the physiological processes that contribute to the negative impact on an organism's fitness resulting from inbreeding, regardless of the genetic factors involved (Fox and Reed, 2011; Kristensen et al., 2010; Losdat et al., 2016). Although there have been numerous studies identifying genes influencing litter size (Distl, 2007; Ernst and Steibel, 2013; Vaishnav et al., 2023; Mo et al., 2022; Sell-Kubiak et al., 2022), birth weight (Te Pas et al., 1999; Jiang et al., 2002; Tomás et al., 2006; Zhang et al., 2014; Wang et al., 2016; Li et al., 2020; Lee et al., 2020) and piglet born alive/dead (Cassady et al., 2001; Chen et al., 2019; Wu et al., 2019), the investigation of the genetic changes induced by inbreeding remains unpublished and is a challenge due to the incomplete understanding and discovery of the overall genetic factors influencing these traits.

This review aims to study physiological and genetic aspects of some fitness traits performance in pigs which are common in studies of inbreeding depression effects.

Physiological and Genetic Aspects of Some Fitness Traits Performance in Pigs

Litter Size

Throughout the research conducted, a consistent trend of increasing litter size has been observed. According to Lanferdini et al. (2018) the litter size ranged from 9 to 16 piglets through the examined database. One year later, Feldpausch et al. (2019) reported the average litter size was 13.18 piglets when analysing two datasets from EU and US studies with emphasize that the EU studies averaged 2.12 more pigs per litter comparing to the U.S. studies. Danish pig production witnessed a significant increase from 11.8 total born piglets per litter in 1992 to 19.6 total born piglets per litter in 2020 (Riddersholm et al., 2021). The average TNB was 17.1 ± 3.4 (mean ± SD), with 16.1 ± 3.1 live born and 1.0 ± 1.4 stillborn (5.8%) piglets (Van den Bosch et al., 2022).

Litter size, as a complex and sex-limited trait, is influenced by a range of biological, nutritional, management, and environmental factors (Luković and Škorput, 2015; Vaishnav et al., 2023). The determination of physiological litter size in pigs involves several components that contribute to its complexity, such as ovulation rate, fertilization, embryonic development, uterus capacity and fetal survival (Argente, 2016; Distl, 2007). Argente (2016) found out that the selection for ovulation rate or/and prenatal survival had been proposed to improve litter size indirectly. In pigs, it is common to observe high rates of fertilization, typically exceeding 90 to 95% that can provide the number of potential embryos needed to increase litter size (Geisert and Schmitt, 2001). Therefore, embryonic loss, especially during the 2nd to 3rd week of gestation is a significant hurdle to increasing litter size in pigs (Geisert and Schmitt, 2001). According to Langendijk (2021), the majority of prenatal losses in pigs occur during the embryonic phase (before day 35), with 20 to 30% of embryos lost by day 21, and an additional 10 to 15% lost by day 35. Variations in embryonic growth and elongation rates during the peri-attachment period (day 12-30 of pregnancy) can potentially modify the uterine environment, resulting in decreased survival rates for less-developed conceptuses (Tan et al., 2022). The success or failure of pregnancy in pigs is likely to be decided within the first 30 days of gestation (Almeida and Dias, 2022). In the period of mid-gestation (day 50-70 of pregnancy), accelerated fetal growth has the potential to surpass the uterine capacity, thereby causing the arrest of neighboring littermates due to overcrowding of conceptus attachment sites (Tan et al., 2022).

In addition, the maternal uterine condition during gestation is crucial for achieving good reproductive performance in pigs, which includes factors such as litter size, number of live or stillborn piglets and growth (Argente, 2016). If the interaction between the embryos and the uterus is insufficient, the pregnancy may be lost, or there may be a compromise in embryo survival (Langendijk, 2021). Moreover, a litter with many mummified fetuses found at farrowing can be caused by various stressors experienced by the sow or developing offspring during the earlier stages of gestation, such as rough handling, poor nutrition, environmental stressors, or disease stress (Hines, 2021). Maternal nutrition during pregnancy, whether it is undernutrition or overnutrition, can alter organ structure, impair prenatal and neonatal growth and development and reduce feed efficiency for lean tissue gains in pigs (Ji et al., 2017).

Studies have consistently found a reduction in litter size with increasing levels of inbreeding (Köck et al., 2009; Saura et al., 2015; Zhang et al., 2022). The estimation suggests that, on average, there is a reduction of 0.137 percent in the mean of a trait in domestic animals including pigs for every 1 percent increase in inbreeding, indicating the presence of inbreeding depression (Leroy, 2014). In a separate study conducted on Austrian Large White and Landrace pigs, it was observed that both litter and dam inbreeding negatively impacted all reproductive traits, specifically by 10% increase of litter and dam inbreeding coefficient, the weaned litter size decrease 0.16 – 0.29 piglets (Köck et al., 2009). However, in the case of Large White pigs, sire inbreeding did not have a significant effect, while in Landrace pigs, it surprisingly showed a significant increase of total number of piglets born (0.45) and born alive (0.43) with 10% of sire inbreeding coefficient (Köck et al., 2009). In addition, this research also figured out the effects of both old and new inbreeding on reproductive traits in general. A study on Iberian pigs also found out that an increase of 10% in FHOM (frequency of homozygosity) on chromosome 13 was associated with a decrease of approximately 0.121 in TNB and 0.117 in NBA (Saura et al., 2015). According to Zhang et al. (2022) an increase of 10% in inbreeding coefficient contributed to a decrease of approximately 0.5 piglets both for TNB and NBA. Silió et al. (2016) reported that there were significant negative impacts of new and fast inbreeding on litter size of Torbiscal pigs. Specifically, a 10% increase in new inbreeding resulted in a decrease of 0.20 born piglets per litter, while 1% increases in total and new inbreeding rates led to reductions of 0.03 and 0.02 piglets, respectively. For Gamito pigs, the reduction of 0.91 piglets due to a 10% increase in old inbreeding and a decrease of 0.17 piglets associated with X-linked genes inbreeding were found.

Traits such as ovulation rate, embryonic survival, uterine capacity and litter size (total number of piglets born and total number of piglets born alive) were affected by genetic factor (Chen et al., 2022; Yu et al., 2022; Zak et al., 2017; Zhang et al., 2020). However, the heritability of the embryonic survival rate and ovulation rate was quite high, ranging from 0.14 – 0.42 (Zak et al., 2017) while the heritability of litter size was in lower range of 0.06 – 0.09 (Chen et al., 2022; Yu et al., 2022; Zhang et al., 2020). This can be inferred that the negative effects of inbreeding on litter size in pigs are likely mediated indirectly through the regulation of ovulation and embryonic survival. There is a complex genetic regulation of pigs' litter size, with the mapping of more than 50 quantitative trait loci (QTL) associated with litter size traits in pigs (Distl, 2007; Ernst and Steibel, 2013). Recent relevant research has indicated that in pigs there are multiple genes that have a significant impact on litter size and its component traits, both at allelic and genome-wide levels (Vaishnav et al., 2023). Litter size traits in pigs have been linked to over 12 candidate genes (Mo et al., 2022; Sell-Kubiak et al., 2022)

While there have been numerous studies documenting the increasing trend of litter size in commercial pigs, limited data exists regarding litter size in conservation pigs. Litter size, a multifaceted trait that is influenced by various biological, nutritional, management, and environmental factors, exhibits complexity and sexual dimorphism. This trait has also been studied in terms of estimating the influence of inbreeding depression on it. Despite some studies identifying genes that affect litter size, this trait still exhibits low heritability, so the underlying physiological mechanisms of inbreeding depression on this trait remain unclear. Further research is needed to fully understand the genetic and physiological aspects of inbreeding depression and its impact on litter size.

Piglets Born Alive/Dead.

The proportion of stillborn piglets can vary from 5.0% to 14.3% (Langendijk and Plush, 2019; Lanh and Nam, 2022). The number of piglets born alive is determined by subtracting any stillborn piglets from the total litter size (Threadgold et al., 2021). Modern breeding sows have undergone selection processes to enhance their litter sizes, resulting in increasing the number of piglets weaned and ultimately sold. However, a correlation exists between increased litter sizes and reduced viability of piglets (Rutherford et al., 2013). To enhance the number of piglets born alive and subsequently improve the weaning count, achieving production targets might be more effectively accomplished by prioritizing the reduction of stillbirths rather than solely focusing on increasing the overall litter size (Threadgold et al., 2021).

Leenhouwers et al. (2003) classified stillbirth into four categories: non-fresh (characterized by partial brown skin colour resulting from tissue degradation and autolysis), prepartum (occurring before delivery), intrapartum (taking place during the farrowing), and postpartum (occurring shortly after birth). Non-fresh and prepartum stillbirths are primarily attributed to infectious agents, while intrapartum and postpartum piglet deaths are predominantly caused by non-infectious factors (Leenhouwers et al., 2003; Vanderhaeghe et al., 2013). Among all stillborn piglets, 10% experienced mortality shortly prior to farrowing, 75% died during the actual farrowing process, and the remaining 15% of death occurred immediately after farrowing (Leenhouwers et al., 1999). Therefore, studying physiological mechanism of stillborn piglets would focus on non-infectious factors.

Physiological mechanisms that affect piglets born alive or dead can be influenced by various factors including genetic factors, maternal factors (body condition, litter size, parity, gestation length, farrowing duration), piglet factors (birth interval, birth order, birth weight) and environmental factors (Vanderhaeghe et al., 2013). According to Jatfa et al. (2018) approximately 70% of the risk factors associated with stillbirth can be attributed to non-infectious factors, in which genotype, dystocia and hypoxia were emphasized. Therefore, in this review the component factors namely the genotype, litter size and birth weight were considered to clarify.

The heritability of stillborn piglets and NBA are relatively low ranging around 0.05 – 0.08 and 0.015 – 0.12, respectively (Hollema et al., 2020; Ogawa et al., 2019; Paixão et al., 2019), and they are influenced by a large number of genetic loci with effects that are low to moderate in magnitude (Bergfelder-Drüing et al., 2015). In addition, heritability based on the sire and dam components for stillborn piglets ranged between 0.08 to 0.24, respectively (Strange et al., 2013). This means that genetic factors have a limited influence on total number of piglets born dead.

According to Vanderhaeghe et al. (2013) the incidence of stillborn piglets was genetically affected by both sows and piglets themselves. Leenhouwers et al. (2003) clarified that the sow's genetic factors were found to affect the probability of mortality during the farrowing process while the piglets' genetic factors were found to influence mortality rates before and right after farrowing. Variations in the occurrence of stillbirth among different lines or breeds of pigs can be attributed to a complex interplay of genetic factors (Leenhouwers et al., 1999; Vanderhaeghe et al., 2010). Although Imaeda et al. (2021) found out that the incidence of stillborn piglets was higher in Microminipigs compared to other pig breeds, this could be because of the too small body size of Microminipig. Canario et al. (2006) found out that the weight of stillborn piglets from Meishan sows was significantly lower than piglets born from Large White, Laconie male line and F1 Duroc x Large White sows. This difference was speculated by the ability to limit conceptus growth and crowing uterine based on the vascularity of the placenta and the homogeneity of placenta weight in a litter of Meishan pigs (Canario et al., 2006). Leenhouwers et al. (1999) similarly reported that purebred lines tend to have a higher number of stillborn piglets (+0.5 to 1 piglet) per litter compared to crossbred lines. However, the authors also noted that the differences in the number of stillborn piglets among different lines might vary depending on the litter size or parity under consideration (Leenhouwers et al., 1999). It seems that the incidence of stillborn piglets and total number of piglets born alive are at some extent affected by the genetic factor, but the majority effects are indirect through the interaction of litter size, birth weight, parities and other components.

The latest version of quantitative trait loci (QTL) mapping in the pig genome encompasses a total of 28,720 identified QTLs (Chen et al., 2019). Among these QTLs, a subset of 2,129 QTLs has been specifically identified for reproduction traits, including 163 QTLs associated with "Total number born alive", 97 QTLs associated with "Number of stillborn", and 95 QTLs associated with "Mummified pigs" (Chen et al., 2019). A study has identified specific regions on the pig genome (QTL SSC5, SSC13) that are linked to early lethality, contributing significantly to the occurrence of stillborn piglets (Cassady et al., 2001). Wu et al. (2019) reported some specific regions on the pig genome affecting the number of mummified and stillborn piglets, specifically being SSC3 (for Landrace at parity 3) and SSC9 (for Large White at parity 2), in which the effect genes ASTN1/BRINP2 on SSC9 was also identified.

The research findings indicated that the relationship between litter size and stillbirth was not linear (Vanderhaeghe et al., 2013). Both large and small litters showed an increased likelihood of stillbirth, suggesting that the probability of stillbirth was higher in both extremes of litter size (Vanderhaeghe et al., 2013). However, a recent research found that each additional piglet added to the litter resulted in a linear increase of 0.5% in the percentage of stillbirths (Van den Bosch et al., 2022). Andersson et al. (2016) reported that larger litters could lead to a rise in the number of piglets born dead, a decline in the proportion of piglets successfully weaned, and greater variability in the overall quality of the piglets. In the presence of larger litter sizes, low-birth weight piglets face increased disadvantages when competing with their littermates, and this disadvantage is further intensified when the litters come from older sows (Cabrera et al., 2012). There was a high positive correlation (r = + 0.98) between increase number of newborn in the litter and stillborn piglets since the proportion of stillborn piglets increased significantly from 5.9% to 14.6% when the number of piglets in the litter increased from 7-11 to 17-21 piglets (Siraziev and Gruzdova, 2020).

An increase in litter size is connected with fetal crowding and the extended durations of farrowing (Rutherford et al., 2013; Van Rens and van der Lende, 2004), which subsequently increases the risk of hypoxia for the piglets (Herpin et al., 2001). Van den Bosch et al. (2023) have also confirmed that prolonged farrowing can reduce piglet survival during birth or in the first day of life as successive uterine contractions may hinder oxygen supply from the mother to the fetus through the placenta and umbilical cord. According to Roongsitthichai and Olanratmanee (2021); Threadgold et al. (2021) asphyxia and dystocia during birth are significant factors leading to stillbirths and early mortality in live-born piglets. However, Van den Bosch et al. (2022) found no interaction between litter size and prolonged farrowing duration although both of these two factors had independently detrimental effect on stillborn piglets. In addition, Van den Bosch et al. (2022) suggested that litter size had a greater influence on stillbirth percentages compared to the duration of farrowing.

In another aspect, a small litter size has a negative impact on the proportion of stillborn piglets (Canario et al., 2006; Knol et al., 2002a), as it is potentially associated with the presence of oversized piglets, resulting in difficulties during the farrowing process (Vanderhaeghe et al., 2013). Furthermore, small litters (less than 6 piglets) frequently indicate reproductive abnormalities, which in turn lead to diminished chances of piglet survival when compared to intermediate litters (6-11 piglets) (Cecchinato et al., 2008).

In relation to stillbirth rate, a low birth weight of the litter (< 0.8 kg) was frequently cited as a commonly reported risk factor (Gourley et al., 2020; Le Cozler et al., 2002; Leenhouwers et al., 2003; Nam and Sukon, 2021; Udomchanya et al., 2019; Vanderhaeghe et al., 2013; Zaleski and Hacker, 1993). Gourley et al. (2020) reported that there was a significant association (P < 0.01) between an increased stillborn rate and larger litters with heavier litter weights and lighter piglet weight at birth. There was a significant difference in piglets birth weight of piglets born alive and piglets born dead (1175 vs. 1002 g, P < 0.001), respectively (Udomchanya et al., 2019). In the same research, the occurrence of stillborn piglets was higher among piglets with a birth body weight of ≤ 1000 g compared to those with a birth body weight of 1001-1300 g or > 1300 g. According to the findings, piglets weighing between 0.1-0.6 kg more than the average birth weight of their litter exhibited the lowest risk of intrapartum stillbirth (Nam and Sukon, 2021). Conversely, piglets smaller than the average birth weight of their litter and those excessively heavy had a higher probability of being stillborn (Nam and Sukon, 2021). The presence of a low birth weight could indicate a diminished quality of uterine support, such as under or malnutrition of the sow, which in turn can lead to reduced overall vitality of the litter during the onset of parturition (Vanderhaeghe et al., 2013). In addition, lower body weight piglets may have relatively smaller umbilical cords that are more susceptible to umbilical rupture (Vanderhaeghe et al., 2013). According to Mota-Rojas et al. (2006), Zaleski and Hacker (1993) piglets with lower body weight may exhibit reduced efficiency in utilizing oxygen due to their lower blood haemoglobin concentration that make them more susceptible to hypoxia during farrowing. In contrast, piglets with heavy birth weight (> 2.1 kg) may experience dystocia, leading to prolong farrowing duration, resulting in hypoxia (Canario et al., 2006; Nam and Sukon, 2021; Vanderhaeghe et al., 2013). Several studies reported a higher incidence of stillbirths and lower individual birth weights in male piglets compared to their female counterparts, speculating that male piglets were more risky to be born dead (Canario et al., 2006; Knol et al., 2002b; Vanderhaeghe et al., 2013). Knol et al. (2002b) documented that selecting for a higher average birth weight had the potential to reduce postnatal mortality but concurrently could lead to an increase in the proportion of stillborn piglets.

Both litter size and birth weight have effects on piglets born alive or dead in a way of optimum threshold, meaning that the detrimental effects happen to the two extreme values of those factors. In addition, these two factors exhibit a causal relationship that influences the piglets born alive or dead, and their interplay is also influenced by various other factors such as environmental conditions and dam-piglet interactions. It is important to note that their effects are not independent but rather interconnected within a complex system.

Saura et al. (2015) detected inbreeding depression on total number of piglets born alive in Iberian pigs, identifying one region on chromosome 13 associated with inbreeding depression. When analysing the pedigree data using all available information, the estimates of inbreeding depression for NBA indicated a value of -0.197 ± 0.092, representing the negative impact on NBA per 10% increase in the inbreeding coefficient (Fped). Significant reductions were observed in the number of piglets per 10% increase in the inbreeding coefficients Fsnp (-0.121 ± 0.047), Froh (-0.230 ± 0.087), and Froh_long (-0.181 ± 0.074) for SSC13.

The proportion of stillborn piglets can range from 5.0% to 14.3%, and reducing stillbirths is important for improving production targets. Genetic factors have a limited influence on the number of stillborn piglets, with heritability estimates ranging from 0.05 to 0.08. The occurrence of stillbirths is affected by genetic factors in both sows and piglets. Litter size and birth weight also play significant roles in stillbirth rates. Both large and small litter sizes increase the probability of stillbirth, and low birth weight is associated with higher stillbirth rates. Inbreeding depression has been observed in some pig populations, negatively impacting the number of piglets born alive.

2.3. Birth Weight

It can be seen from Table 1 that the average birth weight of piglets is around 1.5 kg, ranging from 0.3 – 3.3 kg. Most of the published research is related to prolific pig breeds (Landrace, Yorkshire, Duroc or mixed), so they shared similar average birth weights, except for Piau pig breed which is Brazilian pure pig breed having lower average birth weight (0.997 kg). This could be because different genotype made the birth weight variations. According to Moreira et al. (2020) litters of high prolific sows comparing to low prolificacy had 43% higher average birth weight of total piglets born and total piglets born alive. This can be explained by the fact that high prolific sows, after many years of selection targeting for bigger litter size, have bigger litter birth weight.

Within commercial practice, birth weight is widely utilized as the predominant indicator to assess a piglet's vigour of survival until the weaning stage (Tucker et al., 2021). The threshold for defining low birth weight piglets was determined based on a raw value derived from analysing the relationship between birth weight and the statistical increase in the risk of mortality (Mugnier et al., 2023).

Table 1. Studies reporting average birth weight of piglets

Study	Journal	Genetics	Parity	Obs. (piglets)	Average Birth weight (kg)	Average litter weight (kg)
Lanferdini et al. (2018)	Livestock science	NA	All	3,294	1.45 (0.8 – 2.1)	NA
Feldpausch et al. (2019)	Translational Animal Science	Large White x Landrace; Triumph TR4 x PIC 1050	1-9	4,068	1.51 ± 0.38 (0.5 – 2.3)	NA
Moreira et al. (2020)	Animal Physiology and Animal Nutrition	Yorkshire, Landrace, Large White	All	7,148	1.53 (1.23 – 1.89)	NA
Baxter et al. (2011)	Applied Animal Behaviour Science	Landrace x (Large White x Duroc)	All	757	1.46 ± 0.02	19.98±1.04
Hellbrügge et al. (2008)	Animal	German Landrace	NA	13,971	1.5 ± 0.4 (0.3 – 3.3)	11.2 ± 3.6
De Oliveira et al. (2022)	Tropical Animal Health and Production	Piau breed	NA	3,548	0.997 ± 0.271 (0.3 – 1.766)	NA
Nam and Sukon, (2021)	Veterinary World	(Landrace xYorkshire) x Duroc	All	1,257	1.4 ± 0.4	NA
Riddersholm et al. (2021)	Animals	Danish Landrace x Danish Yorkshire (DanBred Duroc)	1-10	8,677	1.235±0.335 (0.29 – 2.91)	NA

Note: NA: not available information; Obs: Observations

Feldpausch et al. (2019) suggested that piglets with birth weight around 1.11 kg had more chance to survive until weaning than the others.

Research indicates that increased parity and larger litter sizes have detrimental effects on piglet birth weight, resulting in a decline in the average birth weight along with an increased level of variability (Kitkha et al., 2017). Birth weight of the piglets is affected by large litter size as there is an association between larger litter sizes and reduced birth weights (Heuß et al., 2019). Peltoniemi et al. (2021) also agreed that increasing litter sizes concomitantly resulted in decreased piglet birth weight and increased within-litter birth weight variations. Each additional piglet born to a litter linearly decreased average piglet birth weight (17.6 g, $P < 0.01$), increased farrowing duration (11min, $P < 0.01$), and increased stillbirth (0.5%, $P = 0.04$) (Van den Bosch et al., 2022). In addition, according to Riddersholm et al. (2021) the impact of litter size on piglet birth weight (PBW) was found to be statistically significant; for each additional piglet within a litter, the average PBW decreased by 19.5 g for first-parity sows and 21.7 g for sows with 2nd to 9th parities. PBW of sows from parity 2-9 decreased by 25.8 g with increasing weaning to insemination interval ($P < 0.001$). Furthermore, birth weight of piglets and within-litter birth weight variations were also affected by the parity of the sows, with unfavourable affections coming from older sows (Riddersholm et al., 2021).

The development of the litter is influenced by the quality of follicles, which is determined in the period prior to insemination (Riddersholm et al., 2021). It was reported that the length of the previous lactation had an influence on litter size (Hoshino and Vanketsu, 2009) and a weaning-to-insemination interval of less than eight days had a negative impact on the high within-litter variation in piglet birth weight compared to intervals above 21 days (Wientjes et al., 2013). After the insemination, intrauterine environment with nutritional status of the sow become important factors for placenta and litter development (Riddersholm et al., 2021). Inadequate placenta function poses a hindrance to the growth and development of foetus (Town et al., 2004) as well as the size and effectiveness of the placenta can impact PBW and its variation (Che et al., 2017). In sows, the crowded uterine affects the sex ratio of litter, the development of placenta and the expression of embryonic myogenin in early gestation (Tse et al., 2008) so that increased litter size has negative effects on piglet birth weight and birth weight variations.

Previous research has indicated that the heritability of birth weight was low, ranging from 0.02 to 0.21 (Kaufmann et al., 2000). According to Zaalberg et al. (2023), heritability estimates were high for mean litter weight at birth (0.33) but low for litter size traits (0.04-0.08) and individual piglet weight (0.06-0.07), with maternal heritability being significantly higher for individual piglet weight than direct heritability. However, applying a Bayesian multivariate threshold-linear model to a dataset of 22,483 piglets revealed significant estimates indicating maternal and direct heritability for birth weight ranging from 0.29 to 0.36, respectively (Nguyen et al., 2021). Another research using the similar model for data of 21,835 individual piglets reported similar results with maternal and direct heritability for birth weight range from 0.28 to 0.36, respectively (Roehe et al., 2010). In relation to piglet birth weight, the heritability of birth weight variability was documented in previous studies, with estimates ranging from 0.08 to 0.12 (Damgaard et al., 2003; Wittenburg et al., 2008). These studies indicated that the heritability of birth weight was in the wide range from 0.02 to 0.36 and the variation in birth weight was influenced significantly by both foetal genetic factors and maternal genetic effects, making it valuable to identify the specific genes or variants responsible for this variability.

The examination of candidate genes such as MyoD (Te Pas et al., 1999) , MSTN (Jiang et al., 2002), and DBH (Tomás et al., 2006) has led to the identification of several markers associated with birth weight. A total of 17 genomic regions associated with birth weight were identified, with 12 of them overlapping with previously reported QTL regions for piglet birth weight, average birth weight and litter birth weight (Zhang et al., 2014). A genome-wide association study (GWAS) on 82 sows with extreme birth weight variability identified 266 genome-wide significant SNPs ($P < 0.01$), enriched on chromosomes 7, 1, 13, 14, 15, and 18, and further analysis revealed genes related to plasma glucose homeostasis (GLP1R), lipid metabolism and maternal-fetal lipid transport (AACS, APOB, OSBPL10, and LRP1B), suggesting their potential role in birth weight variability (Wang et al., 2016). Recently, some more genes associated with birth weight were reported based on genome-wide association study (GWAS), being SKOR2, SMAD2, VAV3, NTNG1 (Li et al., 2020), and ARAP2 and TSN (Lee et al., 2020).

The biological mechanism underlying piglet birth weight involves a combination of genetic, maternal and uterine environmental factors. In this combination, the heritability of birth weight ranges from 0.02 to 0.36, indicating a significant contribution of both foetal and maternal genetic effects. Several candidate genes have been associated with birth weight, providing insights into the genetic basis of birth weight variability in pigs. Larger litter sizes have a negative effect on piglet birth weight, resulting in decreased average birth weight and increased variability. Factors such as the quality of follicles, weaning-to-insemination interval, and placenta function also influence piglet birth weight and birth weight variation within litters.

Conclusions

In conclusion, there is consistent increase in piglet litter size, which is determined by factors like ovulation rate, embryonic survival, uterine capacity, and genetic factors. The occurrence of stillborn piglets is influenced by a combination of genetic factors, litter size and birth weight, but their relationships are holistic. Regarding piglet birth weight, various factors are involved, including genotype, litter size, parity of the sow, follicle quality, nutritional status of the sow and placenta function. Both foetal and maternal genetic factors contribute to the overall variation in birth weight, which highlights the potential for further research in identifying specific genes or variants associated with birth weight variability. The negative impact of inbreeding on litter size, piglets born alive/dead, birth weight (or litter weight) is limited to detecting an inverse correlation between inbreeding coefficient and the traits. Further studies are needed to understand the physiological mechanism effects.

CRediT authorship contribution statement

István Nagy: Conceptualization, Supervision, Validation, Writing – Reviewing, Editing. **Nguyen Anh Thi:** Conceptualization, Investigation, Methodology, Writing – Original draft preparation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

Almeida F.R.C.L., Dias A.L.N.A. (2022). Pregnancy in Pigs: The Journey of an Early Life. Domest Anim Endocrinol 78: 106656. doi: 10.1016/j.domaniend.2021.106656

Andersson E., Frössling J., Engblom L., Algers B., Gunnarsson S. (2016). Impact of Litter Size on Sow Stayability in Swedish Commercial Piglet Producing Herds. Acta Vet Scand 58: 31. doi: 10.1186/s13028-016-0213-8

Argente M.J. (2016). Major Components in Limiting Litter Size. Insights from Animal Reproduction; Payan Carreira, R., Ed.; InTech: London, UK 87–114.

Baxter E.M., Jarvis S., Sherwood L., Farish M., Roehe R., Lawrence A.B., Edwards S.A. (2011). Genetic and Environmental Effects on Piglet Survival and Maternal Behaviour of the Farrowing Sow. Appl Anim Behav Sci. 130: 28–41.

Bergfelder-Drüing S., Grosse-Brinkhaus C., Lind B., Erbe M., Schellander K., Simianer H., Tholen, E. (2015). A Genome-Wide Association Study in Large White and Landrace Pig Populations for Number Piglets Born Alive. PLoS One 10: e0117468. doi:10.1371/journal.pone.0117468

Cabrera R.A., Lin, X., Campbell J.M., Moeser A.J., Odle J. (2012). Influence of Birth Order, Birth Weight, Colostrum and Serum Immunoglobulin G on Neonatal Piglet Survival. J Anim Sci Biotechnol. 3: 42. doi: 10.1186/2049-1891-3-42

Canario L., Cantoni E., Le Bihan E., Caritez J.C., Billon Y., Bidanel J.P., Foulley J.L. (2006). Between-Breed Variability of Stillbirth and Its Relationship with Sow and Piglet Characteristics. J Anim Sci 84 (12): 3185–3196. doi: 10.2527/jas.2005-775

Cassady J.P., Johnson R.K., Pomp D., Rohrer G.A., Van Vleck L.D., Spiegel E.K., Gilson K.M. (2001). Identification of Quantitative Trait Loci Affecting Reproduction in Pigs. J Anim Sci 79 (3): 623-633. doi: 10.2527/2001.793623x

Cecchinato A., Bonfatti V., Gallo L., Carnier P. (2008). Survival Analysis of Preweaning Piglet Survival in a Dry-Cured Ham-Producing Crossbred Line. J Anim Sci 86 (10): 2486–2495. doi: 10.2527/jas.2007-0825

Charpentier M.J., Williams C.V., Drea C.M. (2008). Inbreeding Depression in Ring-Tailed Lemurs (*Lemur catta*): Genetic Diversity Predicts Parasitism, Immunocompetence and Survivorship. Conserv Genet. 9 (6): 1605–1615. doi: 10.1007/s10592-007-9499-4

Che L., Yang Z., Xu M., Xu S., Che L., Lin Y., Fang Z., Feng B., Li J., Chen D., Wu D. (2017). Maternal Nutrition Modulates Fetal Development by Inducing Placental Efficiency Changes in Gilts. BMC genomics 18 (1): 1–14. doi: 10.1186/s12864-017-3601-1

Chen Z., Zhang Z., Wang Z., Zhang Z., Wang Q., Pan Y. (2022). Heterozygosity and Homozygosity Regions Affect Reproductive Success and the Loss of Reproduction: A Case Study with Litter Traits in Pigs. Comput Biol Chem. 20: 4060–4071. doi: 10.1016/j.csbj.2022.07.039

Chen Z., Ye S., Teng J., Diao S., Yuan X., Chen Z., Zhang H., Li J., Zhang Z. (2019). Genome-Wide Association Studies for the Number of Animals Born Alive and Dead in Duroc Pigs. Theriogenology 139: 36–42. doi: 10.1016/j.theriogenology.2019.07.013

Damgaard L.H., Rydhmer L., Løvendahl P., Grandinson K. (2003). Genetic Parameters for Within-Litter Variation in Piglet Birth Weight and Change in Within-Litter Variation during Suckling. J Anim Sci 81 (3): 604–610. doi: 10.2527/2003.813604x

De Oliveira L.F., Lopes P.S., Dias L.C.D.C.M., Silva L.M.D.E., Silva H.T., Guimarães S.E.F., Marques D.B.D., Silva D.A.D., Veroneze R. (2022). Estimation of Genetic Parameters and Inbreeding Depression in Piau Breed Pigs. (preprint) doi: 10.21203/rs.3.rs-1619371/v1

Distl O. (2007). Mechanisms of Regulation of Litter Size in Pigs on the Genome Level. Reprod Domest Anim 42 (Suppl. 2): 10–16. doi: 10.1111/j.1439-0531.2007.00887.x

Doekes H.P., Bijma P., Windig J.J. (2021). How Depressing Is Inbreeding? A Meta-Analysis of 30 Years of Research on the Effects of Inbreeding in Livestock. Genes 12 (6): 926. doi: 10.3390/genes12060926

Ernst C.W., Steibel J.P. (2013). Molecular Advances in QTL Discovery and Application in Pig Breeding. Trends Genet. 29: 215–224. doi: 10.1016/j.tig.2013.02.002

Feldpausch J.A., Jourquin J., Bergstrom J.R., Bargen J.L., Bokenkroger C.D., Davis D.L., Gonzalez J.M., Nelssen J.L., Puls C.L., Trout W.E. Ritter, M.J. (2019). Birth Weight Threshold for Identifying Piglets at Risk for Preweaning Mortality. Transl Anim Sci. 3 (2): 633–640. doi: 10.1093/tas/txz076

Fox C.W., Reed, D.H. (2011). Inbreeding Depression Increases with Environmental Stress: An Experimental Study and Meta-Analysis. Evolution 65 (1): 246–258. doi: 10.1111/j.1558-5646.2010.01108.x

Geisert R.D., Schmitt R.A.M. (2001). Early Embryonic Survival in the Pig: Can It Be Improved? J Anim Sci. 80 (E Suppl. 1): E54-E65. doi: 10.2527/animalsci2002.0021881200800ES10009x

Gourley K.M., Calderon H.I., Woodworth J.C., DeRouchey J.M., Tokach M.D., Dritz S.S., Goodband R.D. (2020). Sow and Piglet Traits Associated with Piglet Survival at Birth and to Weaning. J Anim Sci. 98 (6): skaa187. doi: 10.1093/jas/skaa187

Hellbrügge B., Tölle K.H., Bennewitz J., Henze C., Presuhn U., Krieter J. (2008). Genetic Aspects Regarding Piglet Losses and the Maternal behaviour of Sows. Part 1. Genetic Analysis of piglet Mortality and Fertility Traits in Pigs. Animal 2 (9): 1273–1280. doi: 10.1017/S1751731108002504

Herpin P., Hulin J.C., Le Dividich J., Fillaut M. (2001). Effect of Oxygen Inhalation at birth on the Reduction of Early Postnatal Mortality in Pigs. J Anim Sci 79 (1): 5–10. doi: 10.2527/2001.7915

Heuß E.M., Pröll-Cornelissen M.J., Neuhoff C., Tholen E., Große-Brinkhaus C. (2019). Invited review: Piglet Survival: Benefits of the Immunocompetence. Animal 13 (10): 2114–2124. doi: 10.1017/S1751731119000430

Hines E. (2021). Developmental Milestones during Pig Gestation. Available at: https://extension.psu.edu/developmental-milestones-during-pig-gestation [Accessed 23 June 2023].

Hollema B.L., Zwiers S., Hermesch S. (2020). Genetic Parameters for Haemoglobin Levels in Sows and Piglets as well as Sow Reproductive Performance and Piglet Survival. Animal 14 (4): 688–696. doi: 10.1017/S1751731119002532

Hoshino Y., Koketsu Y. (2009). An Evaluation of the Impact of Increased Lactation Length on the Reproductive Efficiency of Sows in commercial Herds. J Vet Med Sci 71 (3): 299–303. doi: 10.1292/jvms.71.299

Imaeda N., Ando A., Matsubara T., Takasu M., Nishii N., Miyamoto A., Ohshima S., Kametani Y., Suzuki S., Shiina T., Ono T., Kulski J.K., Kitagawa H. (2021). Stillbirth Rates and Their Association with Swine Leucocyte Antigen Class II Haplotypes in Microminipigs. Anim Biosci 34 (11): 1749–1756. doi: 10.5713/ab.20.0763

Jatfa J.W., Wachida N.M., Ijabo H.M., Adamu S.S. (2018). Aflatoxicosis Associated with Swine Stillbirth in the Piggery Farm University of Agriculture Makurdi. Curr Trends Biomedical Eng Biosci- 13(5):, 555873. doi: 10.19080/CTBEB.2018.13.555873

Ji Y., Wu Z., Dai Z., Wang X., Li J., Wang B., Wu G. (2017). Fetal and Neonatal Programming of Postnatal Growth and Feed Efficiency in Swine. J Anim Sci Biotechnol 8: 42. doi: 10.1186/s40104-017-0173-5

Jiang Y.L., Li N., Fan X.Z., Xiao L.R., Xiang R.L., Hu X.X., Du L.X., Wu, C.X. (2002). Associations of T→A Mutation in the Promoter Region of Myostatin Gene with Birth Weight in Yorkshire Pigs. Asian Austral J Anim 15, 1543–1545.

Kaufmann D., Hofer A., P. Bidanel J., Künzi N. (2000). Genetic Parameters for Individual Birth and Weaning Weight and for Litter Size of Large White Pigs. J Anim Breed Genet. 117: 121–128. doi: 10.1111/j.1439-0388.2000x.00238.x

Ketola T., Kotiaho J.S. (2009). Inbreeding, Energy Use and Condition. J Evolution Biol. 22 (4): 770–781. doi: 10.1111/j.1420-9101.2009.01689.x

Kitkha S., Boonsoongnern A., Ratanavanichrojn N., Jirawattanapong P., Pinyopummin A. (2017). Effects of the Higher Parity and Litter Size on Piglet Birth Weight and Survival Rate of Later Born Piglets. Thai J Vet Med. 47 (1): 79-86.

Knol E.F., Ducro B.J., van Arendonk J.A.M., van der Lende T. (2002a). Direct, Maternal and Nurse Sow Genetic Effects on Farrowing-, Pre-Weaning- and Total Piglet Survival. Livest Prod Sci 73 (2-3): 153–164. doi: 10.1016/S0301-6226(01)00248-2

Knol E.F, Leenhouwers J.I., Van der Lende T. (2002b). Genetic Aspects of Piglet Survival. Livest Prod Sci 78 (1): 47–55. doi: 10.1016/S0301-6226(02)00184-7

Köck A., Fuerst-Waltl B., Baumung R., 2009. Effects of Inbreeding on Number of Piglets Born Total, Born Alive and Weaned in Austrian Large White and Landrace Pigs. Arch Anim Breed 52 (1): 51–64. doi: 10.5194/aab-52-51-2009

Kristensen T.N., Pedersen K.S., Vermeulen C.J., Loeschcke V. (2010). Research on Inbreeding in the 'Omic' Era. Trends Ecol Evol 25: 44–52. doi: 10.1016/j.tree.2009.06.014

Lanferdini E., Andretta I., Fonseca L.S., Moreira R.H.R., Cantarelli V.S., Ferreira R.A., Saraiva A., Abreu M.L.T. (2018). Piglet Birth Weight, Subsequent Performance, Carcass Traits and Pork Quality: A Meta-Analytical Study. Livest Sci. 214: 175–179. doi: 10.1016/j.livsci.2018.05.019

Langendijk, P. (2021). Latest Advances in Sow Nutrition during Early Gestation. Animals (Basel) 11 (6): 1720. doi: 10.3390/ani11061720

Langendijk P., Plush K. (2019). Parturition and Its Relationship with Stillbirths and Asphyxiated Piglets. Animals 9 (11): 885. doi: 10.3390/ani9110885

Lanh D.T.K., Nam N.H. (2022). High Stillbirth Rate in a Swine Farm in Vietnam and Associated Risk Factors. J Adv Vet Anim Res. 9 (11): 13–18. doi: 10.5455/javar.2022.i564

Le Cozler Y., Guyomarc'h C., Pichodo X., Quinio P.Y., Pellois H. (2002). Factors Associated with Stillborn and Mummified Piglets in High-Prolific Sows. Anim Res. 51 (3): 261–268. doi: 10.1051/animres:2002017

Lee J., Lee S.M., Lim B., Park J., Song K.L., Jeon J.H., Na C.S., Kim J.M. (2020). Estimation of Variance Components and Genomic Prediction for Individual Birth Weight Using Three Different Genome-Wide SNP Platforms in Yorkshire Pigs. Animals 10 (12): 2219. doi: 10.3390/ani10122219

Leenhouwers J.I., Van Der Lende T., Knol E.F. (1999). Analysis of Stillbirth in Different Lines of Pig. Livest Prod Sci. 57 (3): 243–253. doi: 10.1016/S0301-6226(98)00171-7

Leenhouwers J.I., Wissink P., van der Lende T., Paridaans H., Knol E.F. (2003). Stillbirth in the Pig in Relation to Genetic Merit for Farrowing Survival1. J Anim Sci. 81 (10): 2419–2424. doi: 10.2527/2003.81102419x

Leroy G. (2014). Inbreeding Depression in Livestock Species: A Review and Meta-Analysis. Anim Genet. 45 (5): 618–628. doi: 10.1111/age.12178

Li Y., Li B., Yang M., Han H., Chen T., Wei Q., Miao Z., Yin L., Wang R., Shen J., Li X., Xu X., Fang M., Zhao S. (2020). Genome-Wide Association Study and Fine Mapping Reveals Candidate Genes for Birth Weight of Yorkshire and Landrace Pigs. Front Genet. 11:183. doi: 10.3389/fgene.2020.00183

Losdat S., Arcese P., Sampson L., Villar N., Reid J.M. (2016). Additive Genetic Variance and Effects of Inbreeding, Sex and Age on Heterophil to Lymphocyte Ratio in Song Sparrows. Funct Ecol. 30 (7): 1185–1195. doi: 10.1111/1365-2435.12586

Luković Z., Škorput D. (2015). Factors Influencing Litter Size in Pigs. Cabi Reviews 2015: 1-9. doi: 10.1079/PAVSNNR201510006

Mei Q., Vitezica, Z.G., Li J., Zhao S., Legarra A., Xiang T. (2022). Impacts of Additive, Dominance and Inbreeding Depression Effects on Genomic Evaluation by Combining Two SNP Chips in Canadian Yorkshire Pigs Bred in China. Genet Sel Evol. 54: 69. doi: 10.1186/s12711-022-00760-4

Mo J., Lu Y., Zhu S., Feng L., Qi W., Chen X., Xie B., Chen B., Lan G., Liang J. (2022). Genome-Wide Association Studies, Runs of Homozygosity Analysis and Copy Number Variation Detection to Identify Reproduction-Related Genes in Bama Xiang Pigs. Front Vet Sci. 9: 892815. doi: 10.3389/fvets.2022.892815

Moreira R.H.R., Pérez Palencia J.Y., Moita V.H.C., Caputo L.S.S., Saraiva A., Andretta I., Ferreira R.A., de Abreu M.L.T. (2020). Variability of Piglet Birth Weights: A Systematic Review and Meta-Analysis. J Anim Physiol Anim Nutr. 104 (2): 657–666. doi:10.1111/jpn.13264

Mota-Rojas D., Trujillo M.E., Martínez J., Rosales A.M., Orozco H., Ramírez R., Sumano H., Alonso-Spilsbury M. (2006). Comparative Routes of Oxytocin Administration in Crated Farrowing Sows and Its Effects on Fetal and Postnatal Asphyxia. Anim Reprod Sci. 92 (1-2):123-43. doi: 10.1016/j.anireprosci.2005.04.012

Mugnier A., Chastant S., Lyazrhi F., Saegerman C., Grellet A. (2023). Definition of Low Birth Weight in Domestic Mammals: A Scoping Review. Anim Health Res Rev. 23 (2):157-164. doi: 10.1017/S146625232200007X

Nam N.H., Sukon P. (2021). Non-Infectious Risk Factors for Intrapartum sSillbirth in a Swine Farm in the North of Vietnam. Vet World 14 (7): 1829–1834. doi: 10.14202/vetworld.2021.1829-1834

Nguyen T.Q., Knap P.W., Simm G., Edwards S.A., Roehe R. (2021). Evaluation of Direct and Maternal Responses in Reproduction Traits Based on Different Selection Strategies for Postnatal piglet Survival in a Selection Experiment. Genet Sel Evol. 53: 28. doi: 10.1186/s12711-021-00612-7

Ogawa S., Konta A., Kimata M., Ishii K., Uemoto Y., Satoh M. (2019). Estimation of Genetic Parameters for Farrowing Traits in Purebred Landrace and Large White Pigs. J Anim Sci. 90 (1): 23–28. doi: 10.1111/asj.13120

Paixão G., Martins Â., Esteves A., Payan-Carreira R., Carolino N. (2019). Genetic Parameters for Reproductive, Longevity and Lifetime Production Traits in Bísaro Pigs. Livest Sci. 225: 129–134. doi: 10.1016/j.livsci.2019.05.010

Peltoniemi O., Yun J., Björkman S., Han T. (2021). Coping with Large Litters: The Management of Neonatal Piglets and Sow Reproduction. J Anim Sci Technol. 63 (1): 1–15. doi: 10.5187/jast.2021.e3

Reid J.M., Arcese P., Keller L.F. (2003). Inbreeding Depresses immune Response in Song Sparrows (*Melospiza melodia*): Direct and Inter–Generational Effects. Proc Biol Sci. 270 (1529):2151-2157. doi: 10.1098/rspb.2003.2480

Riddersholm K.V., Bahnsen I., Bruun T.S., de Knegt L.V., Amdi C. (2021). Identifying Risk Factors for Low Piglet Birth Weight, High Within-Litter Variation and Occurrence of Intrauterine Growth-Restricted Piglets in Hyperprolific Sows. Animals 11 (9): 2731. doi: 10.3390/ani11092731

Roehe R., Shrestha N.P., Mekkawy W., Baxter E.M., Knap P.W., Smurthwaite K.M., Jarvis S., Lawrence A.B., Edwards S.A. (2010). Genetic Parameters of Piglet Survival and birth Weight from a Two-Generation Crossbreeding Experiment under Outdoor Conditions Designed to Disentangle Direct and Maternal Effects1. J Anim Sci. 88 (4): 1276–1285. doi: 10.2527/jas.2009-2287

Roongsitthichai A., Olanratmanee E. (2021). Fetal Mortality Associated with Backfat Thickness at First Mating and First Farrowing of the Primiparous Sows Raised in a Commercial Herd in Thailand. Trop Anim Health Prod. 53: 175. doi: 10.1007/s11250-021-02624-3

Rutherford K.M.D., Baxter E.M., D'Eath R.B., Turner S.P., Arnott G., Roehe R., Ask B., SandØe P., Moustsen, V.A., Thorup F., Edwards S.A., Berg P., Lawrence A.B. (2013). The welfare implications of large litter size in the domestic pig I: biological factors. Anim Welf. 22 (2):199–218. doi: 10.7120/09627286.22.2.199

Saura M., Fernández A., Varona L., Fernández A.I., de Cara M.Á.R., Barragán C., Villanueva B. (2015). Detecting Inbreeding Depression for Reproductive Traits in Iberian Pigs Using Genome-Wide Data. Genet Sel Evol. 47 (1): 1. doi: 10.1186/s12711-014-0081-5

Sell-Kubiak E., Dobrzanski J., Derks M.F.L., Lopes M.S., Szwaczkowski T. (2022). Meta-Analysis of SNPs Determining Litter Traits in Pigs. Genes (Basel) 13 (10) 1730. doi: 10.3390/genes13101730

Silió L., Barragán C., Fernández A.I., García-Casco J., Rodríguez M.C. (2016). Assessing Effective Population Size, Coancestry and Inbreeding Effects on Litter Size Using the Pedigree and SNP Data in Closed Lines of the Iberian Pig Breed. J Anim Breed Genet. 133 (2): 145–154. doi: 10.1111/jbg.12168

Siraziev R., Gruzdova O. (2020). The State of Litter of Pigs in the Conditions of the Complex, In: E3S Web of Conferences 203, EDP Sciences, 01008. doi: 10.1051/e3sconf/202020301008

Strange T., Ask B., Nielsen B. (2013). Genetic Parameters of the Piglet Mortality Traits Stillborn, Weak at Birth, Starvation, Crushing and Miscellaneous in Crossbred Pigs1. J Anim Sci. 91 (4): 1562–1569. doi: 10.2527/jas.2012-5584

Tan C., Huang Z., Xiong W., Ye H., Deng J., Yin Y. (2022). A Review of the Amino Acid Metabolism in Placental Function Response to Fetal Loss and Low Birth Weight in Pigs. J Anim Sci Biotechnol. 13 (1):28. doi: 10.1186/s40104-022-00676-5

Te Pas M.F.W., Soumillion A., Harders F.L., Verburg F.J., van den Bosch T.J., Galesloot P., Meuwissen T.H.E. (1999). Influences of Myogenin Genotypes on Birth Weight, Growth Rate, Carcass Weight, Backfat Thickness and Lean Weight of Pigs. J Anim Sci. 77 (9): 2352–2356. doi: 10.2527/1999.7792352x

Threadgold T., Greenwood E.C., Van Wettere W. (2021). Identifying Suitable Supplements to Improve Piglet Survival during Farrowing and Lactation. Animals 11 (10): 2912. doi: 10.3390/ani11102912

Tomás A., Casellas J., Ramírez O., Pérez-Enciso M., Rodríguez C., Noguera J.L., Sánchez A. (2006). Polymorphisms of the Porcine Dopamineβ-Hydroxylase Gene and Their Relation to Reproduction and Piglet Survivability in an Iberian × Meishan F2 Intercross. Anim Genet. 37 (3): 279–282. doi: 10.1111/j.1365-2052.2006.01457.x

Town S.C., Putman C.T., Turchinsky N.J., Dixon W.T., Foxcroft G.R. (2004). Number of Conceptuses *in utero* Affects Porcine Fetal Muscle Development. Reproduction 128 (4): 443–454. doi: 10.1530/rep.1.00069

Tse W.Y., Town S.C., Murdoch G.K., Novak S., Dyck M.K., Putman C.T., Foxcroft G.R., Dixon W.T. (2008). Uterine Crowding in the Sow Affects Litter Sex Ratio, Placental Development and Embryonic Myogenin Expression in Early Gestation. Reprod Fertil Dev. 20 (4): 497–504. doi: 10.1071/rd07200

Tucker B.S., Craig J.R., Morrison R.S., Smits R.J., Kirkwood R.N. (2021). Piglet Viability: A Review of Identification and Pre-Weaning Management Strategies. Animals 11 (10): 2902. doi: 10.3390/ani11102902

Udomchanya J., Suwannutsiri A., Sripantabut K., Pruchayakul P., Juthamanee P., Nuntapaitoon M., Tummaruk P. (2019). Association between the Incidence of Stillbirths and Expulsion Interval, Piglet Birth Weight, Litter Size and Carbetocin Administration in Hyper-Prolific Sows. Livest Sci. 227: 128–134. doi: 10.1016/j.livsci.2019.07.013

Vaishnav S., Chauhan A., Ajay A., Saini B.L., Kumar S., Kumar A., Bhushan B., Gaur G.K. (2023). Allelic to Genome Wide Perspectives of Swine Genetic Variation to Litter Size and Its Component Traits. Mol Biol Rep 50: 3705–3721. doi: 10.1007/s11033-022-08168-5

Van den Bosch M., Soede N., Kemp B., van den Brand H. (2023). Sow Nutrition, Uterine Contractions and Placental Blood Flow during the Peri-Partum Period and Short-Term Effects on Offspring: A Review. Animals (Basel) 13 (5): 910. doi: 10.3390/ani13050910

Van den Bosch M., van de Linde I.B., Kemp B., van den Brand H. (2022). Disentangling Litter Size and Farrowing Duration Effects on Piglet Stillbirth, Acid–Base Blood Parameters and Pre-Weaning Mortality. Front Vet Sci. 9: 836202. doi: 10.3389/fvets.2022.836202

Van Rens B.T., van der Lende T. (2004). Parturition in Gilts: Duration of Farrowing, Birth Intervals and Placenta Expulsion in Relation to Maternal, Piglet and Placental Traits. Theriogenology 62 (1-2):331-52. doi: 10.1016/j.theriogenology.2003.10.008

Vanderhaeghe C., Dewulf J., de Kruif A., Maes D. (2013). Non-Infectious Factors Associated with Stillbirth in Pigs: A Review. Anim Reprod Sci. 139 (1-4):76-88. doi: 10.1016/j.anireprosci.2013.03.007

Vanderhaeghe C., Dewulf J., De Vliegher S., Papadopoulos G.A., de Kruif A., Maes D. (2010). Longitudinal Field Study to Assess Sow Level Risk Factors Associated with Stillborn Piglets. Anim Reprod Sci. 120 (1-4):78-83. doi: 10.1016/j.anireprosci.2010.02.010

Wang S., Yang J., Li G., Ding R., Zhuang Z., Ruan D., Wu J., Yang H., Zheng E., Cai G., Wang X., Wu Z. (2022). Identification of Homozygous Regions With Adverse Effects on the Five Economic Traits of Duroc Pigs. Front Vet Sci 9: 855933. doi: 10.3389/fvets.2022.855933

Wang, X., Liu, X., Deng, D., Yu, M., Li, X. (2016). Genetic Determinants of Pig Birth Weight Variability. BMC Genet 17, 15. https://doi.org/10.1186/s12863-015-0309-6

Wientjes, J.G.M., Soede, N.M., Knol, E.F., Van den Brand, H., Kemp, B. (2013). Piglet Birth Weight and Litter Uniformity: Effects of Weaning-to-Pregnancy Interval and Body Condition Changes in Sows of Different Parities and Crossbred Lines. J Anim Sci 91, 2099–2107.

Wittenburg, D., Guiard, V., Teuscher, F., Reinsch, N. (2008). Comparison of Statistical Models to Analyse the Genetic Effect on Within-Litter Variance in Pigs. Animal 2, 1559–1568. https://doi.org/10.1017/S1751731108002851

Wu, P., Wang, K., Zhou, J., Yang, Q., Yang, X., Jiang, A., Jiang, Y., Li, M., Zhu, L., Bai, L. (2019). A Genome Wide Association Study for the Number of Animals Born Dead in Domestic Pigs. BMC genetics 20, 1–10.

Yu, G., Wang, C., Wang, Y. (2022). Genetic Parameter Analysis of Reproductive Traits in Large White Pigs. Anim Biosci 35, 1649–1655. https://doi.org/10.5713/ab.22.0119

Zaalberg, R.M., Chu, T.T., Bovbjerg, H., Jensen, J., Villumsen, T.M. (2023). Genetic Parameters for Early Piglet Weight, Litter Traits and Number of Functional Teats in Organic Pigs. Animal 17, 100717.

Zak, L.J., Gaustad, A.H., Bolarin, A., Broekhuijse, M.L.W.J., Walling, G.A., Knol, E.F. (2017). Genetic Control of Complex Traits, with a Focus on Reproduction in Pigs. Mol Reprod Dev 84, 1004–1011. https://doi.org/10.1002/mrd.22875

Zaleski, H.M., Hacker, R.R. (1993). Variables Related to the Progress of Parturition and Probability of Stillbirth in Swine. Can Vet J 34, 109.

Zhang, L., Zhou, X., Michal, J.J., Ding, B., Li, R., Jiang, Z. (2014). Genome Wide Screening of Candidate Genes for Improving Piglet Birth Weight Using High and Low Estimated Breeding Value Populations. Int J Biol Sci 10, 236–244. https://doi.org/10.7150/ijbs.7744

Zhang, S., Zhang, J., Olasege, B.S., Ma, P., Qiu, X., Gao, H., Wang, C., Wang, Y., Zhang, Q., Yang, H., Wang, Z., Ding, X., Pan, Y. (2020). Estimation of Genetic Parameters for Reproductive Traits in Connectedness Groups of Duroc, Landrace and Yorkshire Pigs in China. J Anim Breed Genet 137, 211–222. https://doi.org/10.1111/jbg.12431

Zhang, Y., Zhuo, Y., Ning, C., Zhou, L., Liu, J.F. (2022). Estimate of Inbreeding Depression on Growth and Reproductive Traits in a Large White Pig Population. G3 12, jkac118.

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