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Immunization against gonadotropin-releasing factor (GnRF) in market gilts: Effect on growth and carcass parameters, and impact of immunization timing.

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ABSTRACT

Reproductive cycling in fattening gilts can be associated with undesirable effects, such as estrus-related aggressive behavior, reduced feed intake and, in production systems where gilts are co-housed with entire males, unwanted pregnancy. Immunization against Gonadotrophin Releasing Factor (IM) can temporarily suppress ovarian activity, including related negative consequences on animal welfare and productivity. Feed intake has been shown to be higher after IM, resulting in both increased growth and increased carcass fat. A series of studies was conducted to confirm these effects on production and look at their dynamics over time. Three trials were performed to a similar design, each involving 240 gilts divided into 4 experimental groups at 12 weeks of age. One group remained untreated while the others had the two dose, IM course completed 8, 6 or 4 weeks before harvest, which was on a single day at 24, 25 or 26 weeks of age depending on the study. Feed intake was measured daily and bodyweight weekly, allowing growth parameters to be calculated on a weekly basis and for specific longer periods. Carcass weight, backfat depth and lean meat percentage were recorded at harvest. No effects were observed before the second application of the immunological product (V2) and completion of the IM course. Starting in the second week after V2 all IM groups showed a marked and consistent increase in Average Daily Feed Intake (ADFI), typically peaking at over 120% of the control group 3 to 4 weeks after V2 and then slowly declining, but still remaining elevated at 8 weeks. Weekly Average Daily Gain (ADG) showed a similar pattern but with a faster decline, resulting in the initially favorable impact on feed efficiency becoming less favorable as the V2 to harvest interval (V2—H) progressed. Carcass weights were higher in IM gilts and backfat depths were greater, with the effects increasing with increasing V2—H. Correspondingly, carcass lean meat percentage tended to decrease, although the higher carcass weights meant that the absolute weight of lean meat remained similar or higher. Carcass yield was generally unaffected by IM, but some between-group differences were statistically significant, and it is possible that different factors predominated at different times after V2, creating a complex relationship with V2—H duration. The optimum IM protocol will depend on local conditions and production objectives but, as a generalization and assuming *ad libitum* feeding, a shorter V2—H will favor efficient growth, while a longer duration will maximize carcass changes, such as increased fat coverage. It is suggested that the growth performance changes seen after IM in gilts might be viewed as a process of adjustment to a heavier and fatter target body type.

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1. Introduction

The principle of using IM to produce a temporary suppression of gonadal activity has been known for many years and a commercial product for use in pigs has been available since 1998 (Mackinnon and Pearce, 2007a). GnRF is produced by the hypothalamus in both males and females and acts on the pituitary gland to stimulate the release of gonadotrophins (Luteinizing Hormone, Follicle Stimulating Hormone), which in turn stimulate the gonads, whether these be testes or ovaries. Although GnRF itself is not immunogenic, conjugation of GnRF, or a structurally similar analogue, to a larger protein can create antigenic molecules that will stimulate the production of antibodies capable of binding to and neutralizing endogenous GnRF. For as long as these persist at an effective concentration, they can block the action of GnRF and, consequently, gonadal function, in either sex.

IM is widely practiced in commercial pig production, particularly in male animals, where it provides an alternative to the traditional practice of physically castrating young piglets: a procedure that is increasingly criticized on animal welfare grounds. Castration of male pigs, either physically or immunologically, is primarily done to prevent the occurrence of boar taint, an unpleasant taste that can occur in the meat of entire male pigs after puberty (EFSA , 2004). It also, however, has considerable implications for the efficiency of pig production. Entire males, with the benefit of their endogenous steroid hormones, are typically leaner and more feed efficient than castrated animals, although their growth may sometimes be limited by undesirable sexual and aggressive behavior in late fattening (Cronin et al., 2003). Replacing physical castration early in life with IM a few weeks before harvest allows animals to spend a significant proportion of their lives as entire males, improving overall production efficiency (Mackinnon and Pearce, 2007b). The transition to IM status is accompanied by increases in appetite, growth rate and fat deposition (Dunshea et al., 2001; Zamaratskaia et al., 2008) making the timing of onset of IM in relation to time of harvest a parameter that producers can manipulate to target specific growth and carcass quality objectives. Numerous production studies in male pigs have been conducted, which are summarized in a recent meta-analysis (Poulsen Nautrup et al., 2018).

Although most attention has been focused on males, the idea that the suppression of ovarian function through IM might have commercial application in females is long-standing (Zeng et al., 2002a). Nearly all female pigs are reared entire (not ovariectomized), and many will commence reproductive cycling before reaching harvest age, particularly with modern genetic lines and the trend to rear pigs to heavier weights. Unwanted pregnancy is a risk whenever cycling gilts are mixed with uncastrated males and is a recognized problem in specialist production systems, such as that for Iberian pigs, where animals spend a part of their lives outdoors, grazing acorns in areas accessible to wild boar. IM in females was first used commercially in such animals. Regarding secondary effects on growth performance, it is known that the period of estrus in a female pig is associated with a reduction in feed intake (Friend, 1973) so an impact from IM might be expected, and this has been confirmed by several authors (McCauley et al., 2003; Oliver et al., 2003; Daza et al., 2014; Bohrer et al., 2014; Van den Broeke et al., 2016; Rodrigues et al., 2018).

It is now well documented, both by the above and in a recent meta-analysis (Poulsen Nautrup et al., 2020), that IM in females results in increases in feed intake, growth, and fat deposition, as it does in males. There has not yet, however, been a detailed investigation of the impact of immunization timing and the duration of V2—H, which is the period when any changes would be expected to occur.

This paper describes results for *ad libitum* fed gilts from a program of three related studies in female pigs, designed to investigate the impact of IM and varying the length of V2—H on growth performance and carcass composition. Although not reported in this paper, the studies also included experimental groups on restricted feeding regimens. These had no impact on the results described here, which stand on their own, but they are mentioned in the context of the experimental design and randomization procedure.

2. Materials and methods

The study program comprised three, consecutive production trials, referred to as S1, S2, and S3, respectively. The protocols used were identical except for ages at harvest, which were 24 weeks (S1), 26 weeks (S2) and 25 weeks (S3). All work was carried out in strict accordance with the recommendations of the Guide for the Care and Use of Laboratory Animals of the National Animal Experimentation Control Council of Brazil (CEUA). The three studies were individually approved by the Ethics Committee of Animal Experiments of Akei Animal Research.

2.1. Animals and animal husbandry

In each study, 480 cross-bred commercial gilts (Camborough X AG 337, PIC Genetics) of 12 weeks of age (84 ± 1 day) were obtained from a pre-screened, 1800-sow, farrow to finish farm in São Paulo state, Brazil. 240 of these gilts were allocated to the *ad libitum* fed experimental groups that are reported here. The source farm was negative for Porcine Reproductive and Respiratory Syndrome virus (PRRSv) and positive for Porcine Circovirus Type 2 (PCV2), Influenza A virus (IAV—S), *Mycoplasma hyopneumoniae* and *Haemophilus parasuis*, but without signs of active infection at the times of animal selection. Gilts were individually examined prior to enrollment to confirm good health.

The studies themselves were conducted at Akei Animal Research Facility (Fartura, São Paulo, Brazil). The same curtain-sided, partially-slatted-floor barn was used for all three studies, with cleaning and resting between them. The barn contained 99 pens distributed in 3 rows of 33, with each pen measuring 2 × 2.9 m and equipped with one nipple drinker and one, two-hole feeder, leaving approximately 4.6 m^2 of useable pig space. Pigs were stocked at 5 per pen and 96 pens were used on each occasion. 48 pens, distributed throughout the barn, contained the *ad libitum* fed animals. A sexually mature boar was walked past the pens once daily from the beginning of each study.

Four corn and soya bean-based diets were used over the course of each study. These were formulated to meet the published Tables for Brazilian Nutritional Requirements (Rostagno et al., 2017) and supplied 15.4% (Growth 1), 13.9% (Growth 2), 12.6% (Finishing 1) and 11.6% (Finishing 2) of protein, respectively. Commencing at 12 weeks of age the diets were fed to all experimental groups for 3, 4, 4 and 2 weeks in S1; 2, 4, 4, and 2 weeks in S2; and 3, 4, 4 and 3 weeks in S3.

To confirm health and welfare, animals were observed daily on an individual basis by a person trained and experienced in swine husbandry. Any animal not considered normal was examined by a veterinarian and appropriate treatment given and recorded. Temperature and humidity conditions within the barn were automatically recorded using a data logger (Hobo® Temperature / RH data logger (accuracy ±0.2 °C): Onset Computer Corp., Bourne, MA, USA).

2.2. Experimental design

Each study included 4 *ad libitum*-fed experimental groups with 60 animals per group, as described in Table 1. One group (T1) remained as an untreated control and three groups (T2, T3 and T4) were immunized against GnRF using Vivax® (Zoetis, São Paulo, SP, Brazil), also known as

Table 1
Experimental groups and timing of treatment relative to time of harvest (weeks).

Group	No. gilts	V1 timing	V2 timing	Feeding regimen
T1	60	NA	NA	*Ad libitum*
T2	60	−8	−4	*Ad libitum*
T3	60	−10	−6	*Ad libitum*
T4	60	−12	−8	*Ad libitum*

Improvac®, Improvest® and InnoSure® in other countries. This immunological product contains 0.4 mg of a GnRF analog-diphtheria toxoid conjugate as antigen and 300 mg of diethylaminoethyl-dextran as adjuvant per 2 ml dose. It is given as a course of two injections, with the first dose priming the immune system, but producing no physiological effect, and the second dose stimulating anti-GnRF antibody production and consequent suppression of gonadal activity a few days after administration. As per the manufacturer's directions, each treated gilt received two doses, given 4 weeks apart by subcutaneous injection to different sides of the neck, with the second dose timed for either 4 weeks (T2), 6 weeks (T3) or 8 weeks (T4) prior to harvest. No placebo injections were given to the control group (T1) as the studies were designed to compare the alternatives as they would be used in commercial practice.

Gilts were allocated to their treatment groups using a split plot design, with feeding regimen as the whole plot and treatment regimen as the split plot. Animals were ranked by the weight at time of enrollment and randomly allocated to *ad libitum* or restricted feeding in blocks of 20. Within the former, and again after blocking by body weight, 5 gilts were randomly allocated to each of the four relevant treatment groups, which occupied four adjacent pens in the barn. Gilts within the same pen received the same treatment, making the pen the experimental unit.

2.3. In vivo growth performance

Daily feed intake was recorded for each pen by deducting the weight of remaining feed from the weight of feed originally provided for that day. Pigs were individually weighed on the day of enrollment and then weekly, with all days of treatment administration coinciding with a day of weighing. The final on-farm weighing was performed the day before harvest.

Based on the above data, Average Daily Feed Intake (ADFI) and Average Daily Gain (ADG) were calculated on a weekly basis to investigate the pattern of response over time. ADFI, ADG and Feed Conversion Ratio (FCR, defined as feed/gain) were also calculated for the following periods of interest: the interval between the first (V1) and second (V2) Vivax injections, V2—H, and the total duration of the study, which corresponded to the typical commercial fattening period.

2.4. Harvest and carcass evaluation

Gilts were shipped to a commercial abattoir either the evening before or the morning of harvest, which was on the same day for all animals in a study. Before shipment pigs were slap tattooed on both shoulders and both hams with the same number as their ear tag. Gilts were fasted for approximately 12 h before harvest.

Transport and harvest followed standard commercial procedures and applicable Brazilian regulations. Measurements of backfat depth and loin width were obtained 30 min after bleeding and evisceration using a Hennessy Grading Probe 7 (HGP7) (Hennessy Grading Systems, New Zealand) between the last thoracic vertebra (T14) and the first lumbar vertebra (L1). The same operator performed all measurements. After evisceration carcasses were weighed (head-on) using an over-head rail scale to provide the hot carcass weights (HCW). Carcass yield for each pig was calculated by dividing the HCW by the final liveweight obtained on farm. Carcass lean content (as %) was calculated from the HCW, backfat and loin width measurements using the formula 54.449 - (0.5623 x backfat) + (0.198 x loin width), as provided by the probe manufacturer.

2.5. Estrus occurrence

Although comparison of estrus occurrence was not a primary study objective, gilts were exposed daily to a mature boar from the beginning of each study and observed for physical signs and behaviors possibly associated with estrus expression: redness, swelling or discharge from the vulva, standing reflex, and mounting activity. No samples were taken for estrus related hormone measurements.

2.6. Statistical analysis

Although similar in design, the three studies were not exact replicates and the data were analyzed separately. Within the *ad libitum* feed program, the ADG, ADFI and FCR results for each period (V1 to V2; V2—H, and total fattening period, respectively) as well as carcass weight data (final live weight, carcass weight and carcass yield) and carcass composition data (backfat depth, loin width, lean meat percentage and lean meat weight) were analyzed with a general linear mixed model, where the fixed effect of treatment is included and the random effects include block and residual. Treatment groups were compared to the relevant, non-immunized control group for each period and Tukey's test was used wherever pair-wise comparisons of treatments were made. Randomization plans and all statistical analyses were performed using SAS (version 9.4, SAS Institute, Cary, NC).

For backfat depth and loin width an additional analysis was made using carcass weight as a covariate.

3. Results

3.1. Growth performance – weekly results

The weekly results for ADFI and ADG give insight into the progression of treatment effects over time. To allow trends to be visualized, the results are presented graphically with descriptive comments. For clarity line graphs are used, but it should be kept in mind that each data point represents the mean value for the previous week.

To give context, and illustrate the difference between the three studies, which were conducted at different times of year, the actual ADFI and ADG results for the three T1 control groups are considered first (Fig. 1A and B). As might be expected for values calculated over such a short period, there was considerable week to week variation, especially for ADG. Beyond this, however, temporary declines in both parameters were noted in S1 pigs starting at around 20 weeks of age, which corresponded to a period of hot weather with high temperature and humidity fluctuations. There were also declines in ADG for the final week before harvest, which may have reflected the start of the pre- harvest fasting period and some loss of gut fill before the final weighing.

To more clearly show possible treatment effects, by reducing the impact of environmental and management factors that affected all pigs, the weekly results for the IM groups are presented as a percentage of their within-study T1 control group. Weekly calculations of ADFI for animals in S1, S2 and S3, respectively (Figs. 2A to 2C) showed no response to IM after V1 or in the week immediately following V2, but all treatment groups, in all three studies, showed a marked increase starting in the second week and rising to a maximum during the third or fourth week after V2, with consumption typically being over 20% higher than that of the control. In those groups maintained as IM for longer (T3, T4) the magnitude of the response then appeared to slowly decline, although it was still substantial in T4 gilts 8 weeks after V2.

Weekly results for ADG (Figs. 3A to C) showed more variability than those for ADFI, even when values were expressed relative to the control, but a general pattern was still observable that seemed initially similar to that for ADFI, with performance relative to control showing a marked rise in the second week after V2 and peaking at 3 to 4 weeks. The subsequent decline, however, appeared to be more rapid, with no on-going superiority in weekly growth by 8 weeks after V2.

3.2. Growth performance – results for specific periods

As might be anticipated from the weekly data, results for ADFI (Table 2) showed no statistically significant differences compared to the relevant, in-study control between V1 and V2, but consistent and highly

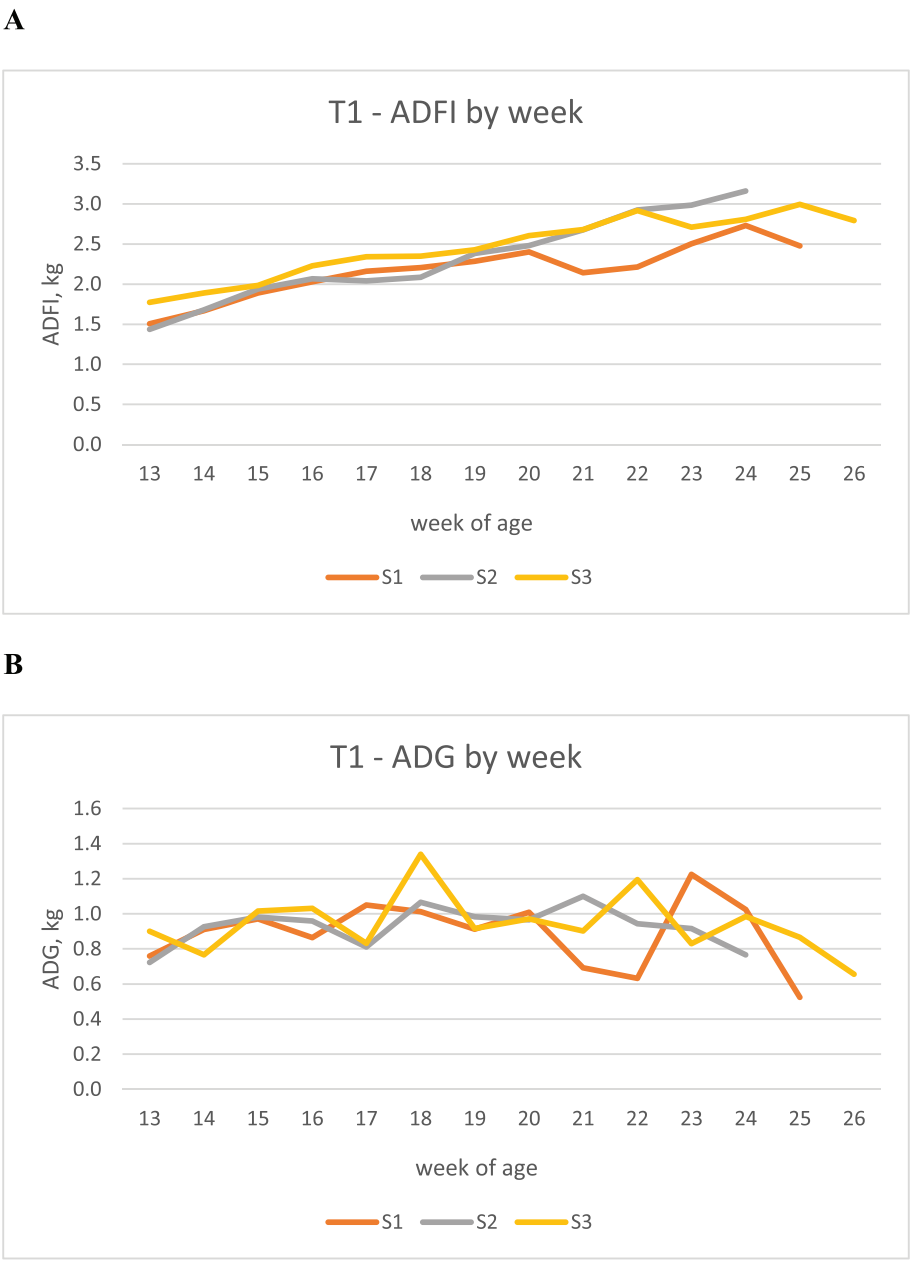


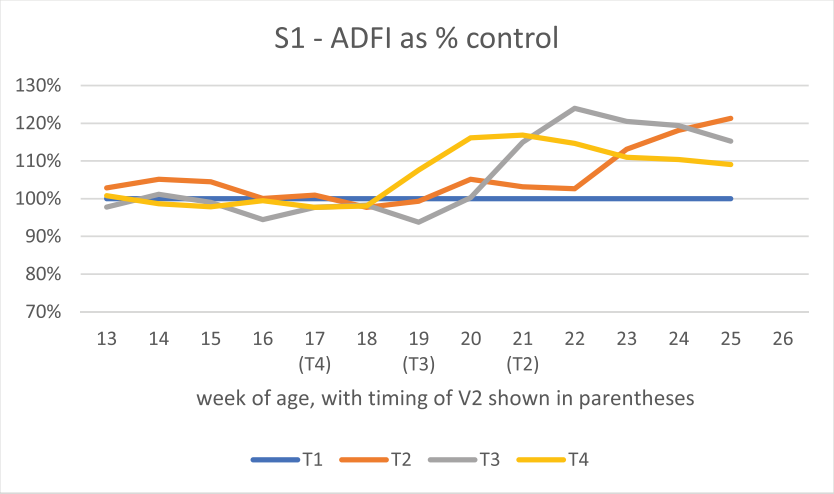
Fig. 1. ADFI (kg) and ADG (kg), calculated on a weekly basis, for non-immunized control groups (T1) in Studies 1, 2 and 3.

significant increases in V2—H ($P < 0.001$ for all IM groups). When diluted over the entire fattening period (12 weeks of age to harvest), the increases in ADFI ranged from 0.08 to 0.23 kg/day and were still individually significant over the relevant T1 control except for group T2 in S3, although the result for this group (0.08 kg/day) also represented a positive numerical trend ($P < 0.1$). In S1 the overall ADFI results for the three IM groups were similar to each other (2.31 (T2), 2.32 (T3), and 2.31 (T4) kg/day v 2.17 for T1), but in S2 and S3 the groups with the longer periods of IM (T3, T4) had significantly higher overall ADFIs than the T2 groups as well as the T1 control (2.52 (T3), 2.55 (T4) v 2.40 (T2) and 2.32 (T1) in S2; 2.71(T3), 2.65 (T4) v 2.54 (T2) and 2.46 (T1) in S3).

ADG results for the same periods (Table 3) showed no differences in the period V1 to V2, except for group T2 in S2, where ADG was significantly less than that of T1 (0.897 v 0.956 kg/day, $P = 0.036$). Reference to the weekly results (Fig. 2B) suggests that this primarily reflected a difference in the final week of V1-V2, immediately before the administration of V2. A possible explanation, related to the weighing procedure on the day of V2, is suggested in the Discussion section. During V2—H, growth rates compared to the relevant T1 control were significantly increased in all IM groups, with the exception of T4 in S1, where the increase over T1 was not statistically significant (0.921 v 0.895 kg/day, $P = 0.227$). ADGs for T2 and T3 in S1 were significantly higher during V2—H (0.958 v 0.883 kg/day, $P = 0.028$ and 0.940 v 0.872 kg/day, $P = 0.009$, respectively), but were less marked than in S2 and S3, where increases were numerically larger and all highly significant ($P < 0.001$). Within each study the magnitude of the ADG increase over the T1 control in V2—H was numerically highest for the T2 groups (0.075, 0.182 and 0.184 kg/day in S1, S2 and S3, respectively) and lowest for the T4 groups (0.026, 0.085 and 0.076 kg/day), which is consistent with the weekly pattern seen in Fig. 2 where the increased growth appeared to be concentrated in the first few weeks after V2. When calculated over the entire fattening period all IM groups were statistically superior to T1 in S2 and S3, but not different to each other. In S1 there was no statistically significant effect of treatment on overall ADG.

The results for FCR (Table 4) are a direct calculation from those for ADFI and ADG (ADFI/ADG). There were no differences in FCR during

A



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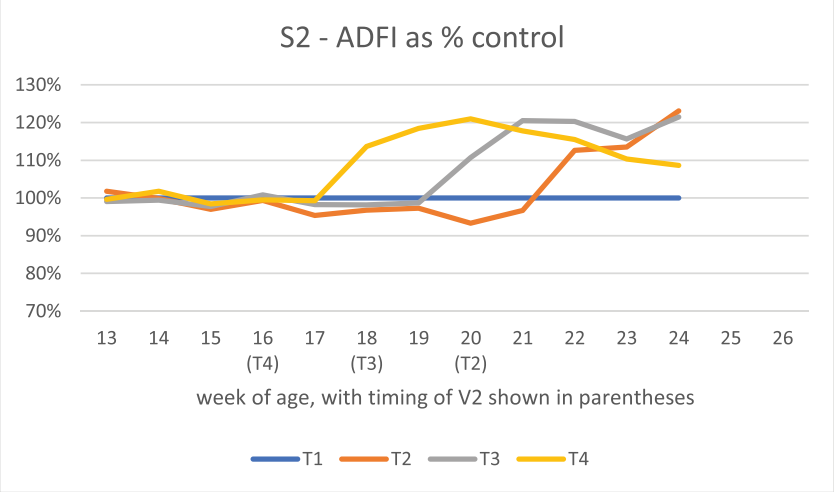

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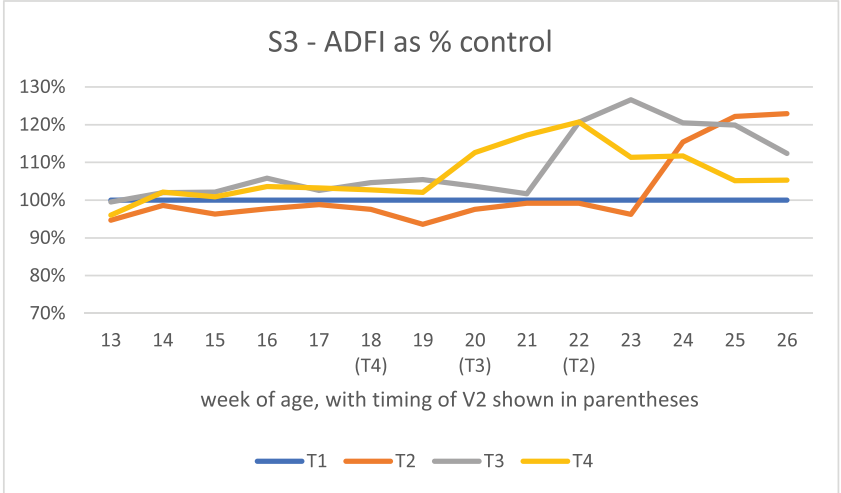
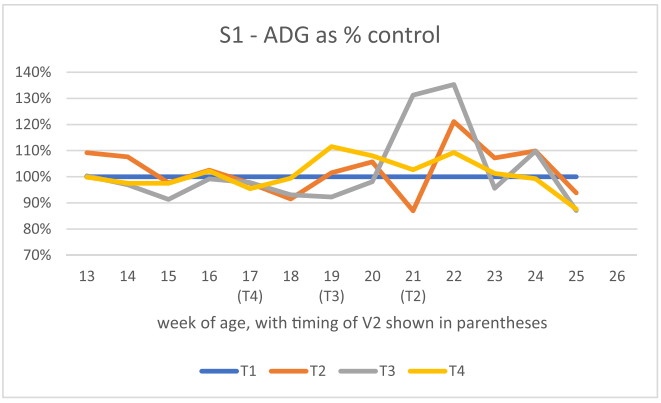


Fig. 2. ADFI, calculated weekly, for IM groups (T2, T3, T4) expressed as a percentage of the within-study control group (T1) for Studies 1, 2 and 3.

A



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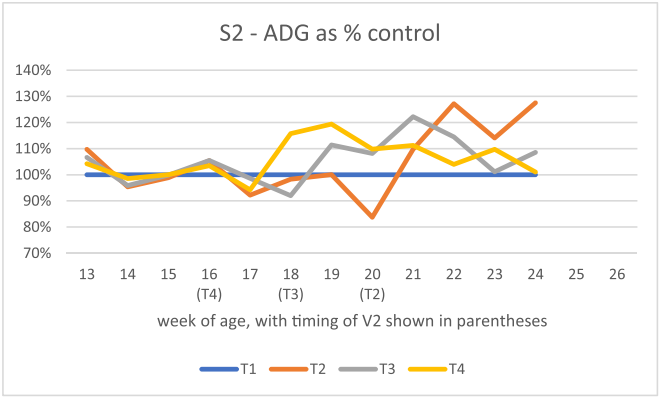

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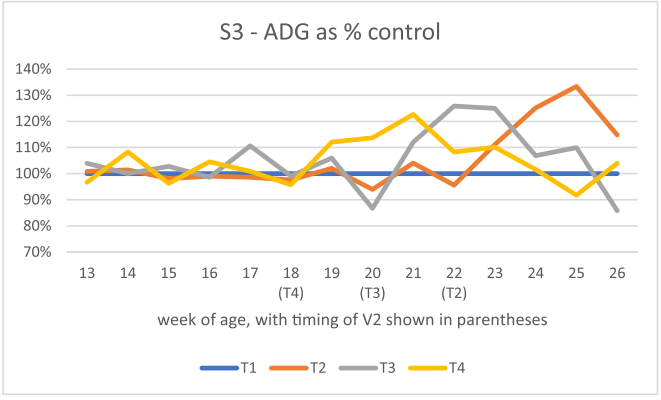

Fig. 3. ADG, calculated weekly, for IM groups (T2, T3, T4) expressed as a percentage of the within-study control group (T1).

the period V1- V2 except for T3 in S3, where FCR was significantly higher than T1 (2.50 v 2.40, $P = 0.002$). This apparently anomalous result will be discussed later. For V2—H, groups T3 (2.98 v 2.77, $P = 0.008$) and T4 (2.85 v 2.65, $P = 0.006$) in S1 and group T4 in S2 (2.81 v 2.71, $P = 0.034$) had a significantly higher FCR than their respective controls. Group T2 in S3, however, had a significantly lower FCR than T1 (3.16 v 3.37, $P = 0.004$) and group T2 in S2 also showed a trend in this direction (2.87 v 3.08, $P = 0.061$). When assessed over the full fattening period, FCR compared to the control was significantly higher for T3 and T4 in S1 (2.54, 2.54 and 2.41 for T3, T4 and T1, respectively) and for group T3 in S3 (2.71 v 2.61). Other differences to the control were not significant, but there were differences between the IM groups

Table 2
ADFI (kg/day) for the periods between V1 and V2, V2 to harvest, and the total duration of the studies.

Treatment group (V2 relative to harvest, weeks)		T1 (NA)	T2 (−4)	T3 (−6)	T4 (−8)	SE	*P*-value
Period	Weeks of age						
Study 1							
V1 to V2							
	13–17	1.94	–	–	1.91	0.054	0.574
	15–19	2.17	–	2.08	–	0.062	0.171
	17–21	2.26	2.29	–	–	0.065	0.633
V2 to harvest							
	17–25	2.37	–	–	2.62	0.052	<0.001
	19–25	2.41	–	2.79	–	0.053	<0.001
	21–25	2.48	2.83	–	–	0.055	<0.001
Total fattening period							
	12–25	2.17a	2.31b	2.32b	2.31b	0.043	<0.001
Study 2							
V1 to V2							
	12–16	1.78	–	–	1.78	0.044	0.927
	14–18	2.03	–	2.01	–	0.045	0.576
	16–20	2.25	2.15	–	–	0.052	0.064
V2 to harvest							
	16–24	2.59	–	–	2.93	0.051	<0.001
	18–24	2.77	–	3.19	–	0.059	<0.001
	20–24	2.94	3.29	–	–	0.069	<0.001
Total fattening period							
	12–24	2.32a	2.40b	2.52c	2.55c	0.037	<0.001
Study 3							
V1 to V2							
	14–18	2.22	–	–	2.28	0.051	0.242
	16–20	2.43	–	2.53	–	0.052	0.060
	18–22	2.66	2.59	–	–	0.058	0.258
V2 to harvest							
	18–26	2.74	–	–	3.04	0.053	<0.001
	20–26	2.82	–	3.30	–	0.058	<0.001
	22–26	2.83	3.23	–	–	0.061	<0.001
Total fattening period							
	12–26	2.46a	2.54a	2.71b	2.65b	0.038	<0.001

a,b,c - groups with different letters within the same row are statistically different at $P \leq 0.05$.

themselves, with the T2 groups having a significantly lower (better) FCR than T3 and T4 in S2 (2.44 v 2.54 and 2.55) and T3 in S3 (2.56 v 2.71).

3.3. Carcass evaluation

Consistent with the growth performance results, final live weights (Table 5) were not different in S1 but there was a highly significant impact of IM in S2 and S3, with T3 and T4 in S2 being significantly higher than the untreated control (115.55 and 116.24 v 111.51 kg) and all IM groups being so in S3 (132.86, 134.13 and 133.21 v 128.12 kg). A similar pattern was observed at carcass level, although pairwise comparisons to the control were only significant for the longer IM groups: T4 in S2 (83.55 v 79.37 kg), and T3 and T4 in S3 (95.14 and 94.75 v 91.46 kg). Overall impact on carcass yield was highly significant for S3 ($P = 0.002$) and approached significance for S2 (0.062) but was not significant in S1. The only significant difference between a treatment group and the control was a lower yield for T2 in S3 (70.43% v 71.37%), although in S2 T2 was significantly lower than T4 (70.76% v 71.89%). A numerical pattern of T2 having the lowest carcass yields (70.76% and 70.43%) and T4 the highest (71.89% and 71.16%) was seen in both S2 and S3.

Backfat depth (Table 6) was significantly increased by IM in all three

Table 3
ADG (kg/day) for the periods between V1 and V2, V2 to harvest, and the total duration of the studies.

Treatment group (V2 relative to harvest, weeks)		T1 (NA)	T2 (−4)	T3 (−6)	T4 (−8)	SE	P-value
Period	Weeks of age						
Study 1							
V1 to V2							
	13–17	0.949	–	–	0.930	0.033	0.567
	15–19	0.960	–	0.917	–	0.033	0.195
	17–21	0.907	0.880	–	–	0.033	0.425
V2 to harvest							
	17–25	0.895	–	–	0.921	0.021	0.227
	19–25	0.872	–	0.940	–	0.026	0.009
	21–25	0.883	0.958	–	–	0.034	0.028
Total fattening period							
	12–25	0.901	0.924	0.910	0.911	0.015	0.798
Study 2							
V1 to V2							
	12–16	0.897	–	–	0.910	0.028	0.650
	14–18	0.954	–	0.943	–	0.029	0.691
	16–20	0.956	0.897	–	–	0.028	0.036
V2 to harvest							
	16–24	0.961	–	–	1.046	0.019	<0.001
	18–24	0.969	–	1.079	–	0.022	<0.001
	20–24	0.966	1.148	–	–	0.029	<0.001
Total fattening period							
	12–24	0.939a	0.984b	0.991b	1.000b	0.014	0.022
Study 3							
V1 to V2							
	14–18	1.054	–	–	1.044	0.030	0.739
	16–20	1.015	–	1.015	–	0.030	0.985
	18–22	0.996	0.982	–	–	0.030	0.684
V2 to harvest							
	18–26	0.920	–	–	0.996	0.020	<0.001
	20–26	0.912	–	1.031	–	0.024	<0.001
	22–26	0.841	1.025	–	–	0.031	<0.001
Total fattening period							
	12–26	0.946a	0.990b	1.000b	0.989b	0.013	0.047

a,b,c - groups with different letters within the same row are statistically different at P ≤ 0.05.

studies ($P \leq 0.001$, 0.014, and 0.005 for S1, S2 and S3, respectively). Except for T2 in S3, where the results were similar (15.84 v 15.86 mm), all IM groups had a numerically higher backfat depth than their T1 control, with the difference being statistically significant for all T4 groups (15.77 v 13.42 mm in S1, 15.96 v 13.89 mm in S2, 18.25 v 15.86 mm in S3) and for T3 in S1 (16.09 v 13.42 mm). Backfat depth generally increased with the duration of IM, with T4 also being significantly higher than T2 in S2 and S3 (15.96 v 14.46 mm and 18.25 v 15.84 mm, respectively). Differences became smaller when carcass weight was used as a covariate in the analysis and in S2 overall significance was lost for this parameter (a P value of 0.014 became 0.120), but it remained significant in S1 (<0.001) and S3 (0.024).

The overall impact of IM on loin width was just significant in S2 ($P = 0.050$), with significance being lost ($P = 0.079$) with carcass weight as a covariate. Equivalent figures were 0.073 and 0.095 in S1, suggesting a possible trend, and 0.193 and 0.178 in S3. Numerical results showed no consistent pattern, with T2 having the highest value in S1 and S3 but the lowest in S2.

Reflecting the influence of backfat depth in the formula used, values for lean meat % were typically lower than T1 for the longer IM groups and the overall impact was either significant or approaching significance in all 3 studies ($P = 0.041$, 0.055 and 0.011 in S1, S2 and S3, respectively), although pairwise comparisons of individual treatment groups to the control were not significant. When calculating the actual quantity of lean meat, however, the higher carcass weights compensated for this resulting in higher numerical values in S2 and S3.

3.4. Signs of possible estrus activity

Although not reported in detail in this paper, the physical observations made at the time of boar exposure confirmed the expected suppression of estrus activity with IM. Using the presence of a standing reflex, which was always associated with some reddening and/or swelling of the vulva in our studies, as the most reliable indicator of estrus, and taking the last 4 weeks pre- harvest, such behavior was observed in 30.6% (27%, 28% and 37% in S1, S2 and S3, respectively) of untreated animals (T1) and 3.5% (5%, 2% and 4%) of IM animals (T2, T3 and T4), with most of the latter being either in the T4 group, or in T2 gilts during the first week after V2.

4. Discussion

This paper includes information on growth performance and carcass composition from three separate studies, each with 4 experimental groups. The studies are not exact replicates and they have not been combined for quantitative analysis. The similarity in design, however, facilitates qualitative comparison and identification of consistencies and differences in the pattern of results obtained, both of which can help in developing an overall picture of the production impact of IM in gilts.

The most striking effect of IM is that on ADFI. There was no change, positive or negative, after V1, but a marked and highly significant increase in all groups after V2. Multiple authors, using the same commercial preparation, have noted the same effect (McCauley et al., 2003; Oliver et al., 2003; Daza et al., 2014; Van den Broeke et al., 2016; Rodrigues et al., 2018). An exception is Bohrer et al. (2014) who

Table 4
FCR for the periods between V1 and V2, V2 to harvest, and the total duration of the studies.

Treatment group (V2 relative to harvest, weeks)		T1 (NA)	T2 (−4)	T3 (−6)	T4 (−8)	SE	P-value
Period	Weeks of age						
Study 1							
V1 to V2							
	13–17	2.04	–	–	2.05	0.024	0.742
	15–19	2.26	–	2.27	–	0.045	0.783
	17–21	2.50	2.61	–	–	0.063	0.073
V2 to harvest							
	17–25	2.65	–	–	2.85	0.059	0.006
	19–25	2.77	–	2.98	–	0.071	0.008
	21–25	2.83	2.96	–	–	0.069	0.067
Total fattening period							
	12–25	2.41a	2.49ab	2.54b	2.54b	0.030	<0.001
Study 2							
V1 to V2							
	12–16	1.98	–	–	1.95	0.023	0.191
	14–18	2.13	–	2.13	–	0.031	0.972
	16–20	2.35	2.40	–	–	0.038	0.184
V2 to harvest							
	16–24	2.71	–	–	2.81	0.041	0.034
	18–24	2.88	–	2.95	–	0.064	0.244
	20–24	3.08	2.87	–	–	0.105	0.061
Total fattening period							
	12–24	2.47ab	2.44a	2.54b	2.55b	0.033	<0.001
Study 3							
V1 to V2							
	14–18	2.11	–	–	2.19	0.038	0.062
	16–20	2.40	–	2.50	–	0.023	0.002
	18–22	2.68	2.65	–	–	0.083	0.739
V2 to harvest							
	18–26	2.99	–	–	3.05	0.062	0.302
	20–26	3.10	–	3.20	–	0.092	0.275
	22–26	3.37	3.16	–	–	0.065	0.004
Total fattening period							
	12–26	2.61a	2.56a	2.71b	2.68ab	0.031	0.034

a,b,c - groups with different letters within the same row are statistically different at $P \leq 0.05$.

reported only "episodical changes in ADFI", with an increase between 4 and 7 weeks after V2, but no significant effect when measured over the full, and relatively long, V2—H period of 10 weeks. The reason is not clear although it can be noted that the feed consumption of the untreated control gilts was already high, certainly compared to our studies.

A novel aspect of this current work is the availability of ADFI results by week. The pattern of response shown by the weekly data is remarkably similar between all 9 of the IM groups, where the timing of V2 varied from 16 to 22 weeks of age. At least within this range, age at time of IM onset does not seem to be important, with a feed intake response consistently occurring in the second week after V2. Van den Broeke et al. (2016), working with individually penned gilts, obtained a similar result. They tracked feed consumption daily for 14 days after V2 and identified 5 to 6 days as the time the increase commenced.

Along with the increase in ADFI, all IM groups also showed an increase in ADG relative to the T1 control for V2—H (not statistically significant for T4 in S1) ranging from 0.026 to 0.184 kg/day. The T2 groups, which had the shortest V2—H of 4 weeks, showed the highest numeric increases compared to T1. The T4 groups, which had an 8-week interval, showed the lowest, although the fact that they were applicable for longer meant that, within each study, the ADG impacts of all treatment groups were similar when averaged over the full fattening period. These results are consistent with previous publications (Oliver et al., 2003; Daza et al., 2014; Van den Broeke et al., 2016; Rodrigues et al., 2018), which also report a rise in ADG following V2, again with the highest values generally associated with shorter post-V2 measurement periods.

The weekly results for ADG give additional perspective on the interaction between growth and IM duration. Although the figures show considerable week to week fluctuation (discussed in the next paragraph), even when expressed relative to the control group, it is still possible to perceive a pattern in the data. There is no obvious effect before V2 but an increase relative to control afterwards, certainly evident in the second week, possibly even in the first, and then peaking after 3 to 4 weeks. Following the peak, however, the advantage over the control appears to diminish quite rapidly, certainly faster than the increase in ADFI, which has implications for FCR that will be discussed later.

As mentioned, the weekly figures for ADG show high variability, which is probably not surprising. The calculation is based on the difference between two measurements of bodyweight and, when the interval between them is short, this will be small relative to the weights being measured and potentially influenced by normal day to day fluctuations as well as growth. Expressing results as a percentage of the control group is intended to minimize variation caused by environmental and non-treatment factors, on the assumption that these should affect all groups and not influence relative performance. In retrospect, however, there is a concern that this may not always have been the case when animals were weighed on a day of treatment, as the control group did not receive a placebo injection with the associated disturbance to routine. It is only speculation, but between-group differences in one or more of feeding, drinking, defecation or urination behavior before weighing is a theoretically possible explanation for the relatively sharp drops in weekly ADG seen in some groups (T2 in S1 and S2, T3 in S3) for the week before administration of V2, which were calculated using the weight measured on the day of V2.

The above may also explain a surprising outlier result for FCR in S3. In general, and as expected given the results for ADFI and ADG, there are

Table 5
Mean final liveweights, hot carcass weights and carcass yields of control and immunized gilts.

Treatment group (V2 relative to harvest, weeks)		T1 (NA)	T2 (−4)	T3 (−6)	T4 (−8)	SE	P-value
Study 1	Final liveweight (kg)	119.32	120.98	119.99	119.81	1.41	0.501
	Hot carcass wt. (kg)	85.12	86.60	86.41	86.07	1.02	0.478
	Carcass yield (%)	71.41	71.58	71.95	71.81	0.36	0.949
Study 2	Final liveweight (kg)	111.51a	114.89ab	115.55b	116.24b	1.39	<0.001
	Hot carcass wt. (kg)	79.37a	81.32ab	82.45ab	83.55b	1.07	<0.001
	Carcass yield (%)	71.24ab	70.76a	71.39ab	71.89b	0.041	0.062
Study 3	Final liveweight (kg)	128.12a	132.86b	134.13b	133.21b	1.45	<0.001
	Hot carcass wt. (kg)	91.46a	93.59ab	95.14b	94.75b	1.09	0.001
	Carcass yield (%)	71.37b	70.43a	70.92ab	71.16ab	0.30	0.002

a,b,c - groups with different letter within a row are statistically different at $P \leq 0.05$.

Table 6
Backfat depth, loin width and lean meat content of control and immunized gilts.

Treatment group (V2 relative to harvest, weeks)		T1 (NA)	T2 (−4)	T3 (−6)	T4 (−8)	SE	P-value
Study 1	Backfat (mm)	13.42a	15.13ab	16.09b	15.77b	0.65	<0.001
	Backfat with cov[1].	13.51a	14.86ab	15.88b	15.67b	0.61	<0.001
	Loin width (mm)	59.01	64.80	62.43	61.20	1.89	0.073
	Loin width with cov[1].	59.13	64.47	62.10	61.00	1.82	0.095
	Lean meat %	58.59	58.81	57.77	57.70	0.53	0.041
	Lean meat kg	49.88	50.88	49.90	49.65	0.74	0.525
Study 2	Backfat (mm)	13.89a	14.46a	14.51a	15.96b	0.56	0.014
	Backfat with cov[1].	14.07	14.38	14.29	15.60	0.54	0.120
	Loin width (mm)	57.75	56.64	58.85	59.86	1.47	0.050
	Loin width with cov[1].	58.06	56.52	58.52	59.26	1.47	0.079
	Lean meat %	58.09	57.55	57.96	57.34	0.41	0.055
	Lean meat kg	46.06	46.77	47.76	47.87	0.70	0.030
Study 3	Backfat (mm)	15.86a	15.84a	17.09ab	18.25b	0.76	0.005
	Backfat with cov[1].	16.30ab	15.86a	16.84ab	18.02b	0.73	0.024
	Loin width (mm)	66.05	68.76	67.13	66.52	1.28	0.193
	Loin width with cov[1].	66.89	68.81	66.66	66.14	1.24	0.178
	Lean meat %	58.62ab	59.17b	58.15ab	57.39a	0.51	0.011
	Lean meat kg	53.61	55.35	55.33	54.33	0.76	0.054

a,b,c - groups with different letter within a row are statistically different at $P \leq 0.05$.
[1] Re-analysis using carcass weight as a covariate.

no differences in FCR between treated and control groups prior to V2. The exception is T3 in S3, where FCR is very significantly worse than T1 in this period ($P = 0.002$). This would not have occurred had the bodyweight measurement on the day of V2 been on-trend.

Considering the period V2—H, IM increases both ADFI and ADG. Any intervention that does this can potentially be positive, neutral, or negative for FCR, depending on the balance between the two effects. In our study FCR was lower (improved) in all T2 groups, being significantly so in S3 and showing a trend ($P \leq 0.1$) in S1 and S2. The groups with a longer IM period, however, tended to have worse FCR values than the control, with highly significant differences in S1, where growth rates were relatively low. This change in direction with duration of IM can explained by the weekly patterns in ADFI and ADG: the increase in ADG tailed off more quickly than that in ADFI, gradually shifting the impact on FCR from favorable to unfavorable. A similar trend can be seen in the published literature when it is examined in detail. Most authors report no impact on FCR from IM in gilts (McCauley et al., 2003; Oliver et al., 2003; Daza et al., 2014; Van den Broeke et al., 2016; Rodrigues et al., 2018) and this is also the finding of the meta-analysis (Poulsen Nautrup et al., 2020). Bohrer et al. (2014) report an improvement (expressed as a higher gain:feed ratio), even with a long V2—H of 10 weeks. Reference to the sub-periods described in the paper, however, reveals that the improvement occurred in the first 4 weeks after V2 and was gradually diluted thereafter. Similarly, Daza et al. (2014) found no overall effect on FCR with a 10-week V2-H, but this was because a significantly better FCR in the first 44 days after V2 was counter-balanced by a significantly worse FCR in the final 25 days.

Although the results after V2 are of high scientific interest as they reflect physiological changes, it is growth performance averaged over the entire fattening period that is economically important. For S2 and S3 the overall results essentially reflect the dilution of the V2—H findings over a longer period. All IM groups had a higher ADG, and hence final liveweight, than the control, but within each study they were similar to each other, with the ADG increases ranging from 0.044 to 0.061 kg/day. Final ADFIs, however, were higher for the longer IM groups T3 and T4, resulting in these groups also having FCRs that were significantly higher (worse) than both the control (by 0.07 to 0.1) and T2 (by 0.1 to 0.15).

The overall results from S1 are different but are explainable from the circumstances of the trial. Fig. 1A shows that between 20 and 23 weeks of age, the feed intake of the S1, T1 control group was depressed. Temperature and humidity records show that this corresponded to a period of hot, variable weather of the type that is recognized to reduce pig performance (Renaudeau et al., 2011). At the same time there was also a marked decline in weekly ADG (Fig. 1B), followed by some wide fluctuations. A similar pattern was observed in a restricted fed control group in S1 (not reported in this paper), which in reality was also an *ad libitum* group as the voluntary feed intake was below the restriction level. It can be assumed that all the gilts in this study were subject to environmental conditions likely to depress appetite and growth at the time when the maximum IM impact on these parameters would be expected, at least for groups T3 and T4.

Looking at the overall fattening period results for the gilts in S1, all IM groups had a higher ADFI than T1, but there was no difference between them. ADG increases over T1 were small and not significant, particularly for T2 and T4, and as a result all IM groups showed a statistically significant increase in FCR. The obvious interpretation of these results is that the performance benefit of IM will be reduced if conditions are sub-optimal at the time it is expected to occur. While this is probably true, it is only one study and more data are needed before firm conclusions can be drawn about the impact of IM in such circumstances. The V2—H results do still show a significant growth response and, interestingly, the effects on carcass composition are not noticeably different to those in the other studies.

Taken over all 3 studies, our results for carcass parameters generally confirm the findings of other authors, but with some additional insights. Higher ending live weights lead to higher carcass weights and Daza et al. (2014),Gamero-Negron et al., (2015), Van den Broeke et al. (2016) and Rodrigues et al. (2018) all found no difference in carcass yield (dressing percentage) between IM and entire gilts, which was also the result of the meta-analysis (Poulsen Nautrup et al., 2020). The same is mostly true in our studies, but there were some statistically significant differences and a pattern, at least in S2 and S3, of the T2 groups having the lowest carcass yields, even compared to the control, and the T4 groups the highest. A more detailed study would be required to confirm the finding, but it is possible that several different factors are influencing carcass yield, operating on different timelines and in different directions, and that their interaction is creating a complex, non-linear relationship with IM duration. Examples are the shrinkage of the female genital tract as described by Rodrigues et al. (2018), that would be expected to increase carcass yield, and the higher feed intake, that might reduce it through increases in gut fill and intestinal mass, as has been shown in male IM pigs (Boler et al., 2014). The impact of the former might be expected to increase with duration of IM and age of gilt, whereas it is logical to think that the latter might eventually moderate, once pigs adapt to the higher feed intake and the relative increase in ADFI over the control anyway starts to decline.

In terms of carcass composition, most authors and the meta-analysis have reported an increase in backfat depth with IM in gilts (McCauley

et al., 2003; Oliver et al., 2003; Daza et al., 2014; Bohrer et al., 2014; Van den Broeke et al., 2016; Poulsen Nautrup et al., 2020). Rodrigues et al. (2018) are an exception in reporting no change, but the numerical results in their paper show a small increase of 1 mm and are consistent with the overall trend. Although not always significant, our results also clearly show an increase in backfat that goes beyond that expected from the increase in carcass weight and appears to increase with duration of IM. The latter observation is consistent with results in Daza et al. (2014) showing that measurements of subcutaneous fat depth *in vivo* continued to increase relative to an untreated control in the final 25 days of a 10-week IM period, although they did not remark on this in the paper.

Some of the papers cited above do not include calculations of lean meat percentage, but Bohrer et al. (2014) and Van den Broeke et al. (2016) both reported significant decreases in this parameter alongside the increase in fat depth. Rodrigues et al. (2018) again reported no change, but there was a non-significant decrease of 0.8 percentage points. Our results also generally show some decrease, which is not surprising as lean meat percentage is a calculated value partly derived from the backfat measurement, with which it is negatively correlated. The other contributing parameter is the loin width, which did not give a consistent pattern of results in our studies. Although lean meat percentage was typically reduced, the higher carcass weights in S2 and S3 resulted in an increase in the actual quantity (kg) of lean meat, based on the same formula.

It seems to be a general assumption in the scientific literature and elsewhere that the IM performance changes in gilts result from suppression of estrus and removal of the known negative effects of estrus on individual feed consumption and, possibly, group feeding behavior. Although logical there appears be no direct proof for this explanation and Van den Broeke et al. (2016) have already raised doubts. In their experiment, with individually housed gilts, all animals showed an increase in ADFI at around the same time, although hormone measurements showed that only some were cycling. The consistency of the ADFI response in our studies, in terms of both timing and magnitude, also suggests that suppression of estrus cannot be the full explanation.

The rise in feed intake in gilts is very similar to that observed in boars following the onset of IM. Although this lacks a full physiological explanation, it is not observed following immunization of physically castrated animals and seems clearly linked to the immunological suppression of gonadal function (Van den Broeke et al., 2016). As mentioned by Dunshea et al. (2013) the onset of IM leads to a fundamental change in the metabolism of IM male pigs, allowing their lives to be divided into two phases, boar and castrate, but with the second, at least initially, reflecting the unique characteristics of animal transitioning from one state to another. Information on physically castrated males is readily available and in general they are fatter and less muscular than uncastrated animals. Depending on nutritional management they may also be heavier (Zeng et al., 2002b). A male pig that is immunologically castrated in adolescence is suddenly converted to an animal with a castrate hormonal status but a boar body composition. The changes in growth performance during the transition phase can be viewed as a physiological response to restore balance between the two.

From a production perspective, a similar conceptual model seems to fit the results observed in gilts. Seeing the increase in appetite as a short-term adjustment to having a heavier and fatter target body type can explain the data and provide a useful tool to make predictions about management practices, such as feed restriction. Information on physically castrated female pigs is limited but castration through ovariectomy was practiced in some traditional rearing systems and the available publications are generally compatible with the hypothesis. Peinado et al. (2008), Serrano et al. (2009) and Peinado et al. (2012) all report physically castrated gilts having fatter carcasses than entire animals. Comparisons of growth performance are complicated by the fact that ovariectomy is a traumatic procedure. Serrano et al. (2009) reported depression of both ADFI and ADG in the period immediately after surgery. In later periods, however, both were significantly increased compared to entire gilts. Peinado et al. (2008) and Gómez-Fernández et al. (2013) also reported significant increases in both over certain time periods, although Peinado et al. (2012) did not. The question whether physical castration would produce the same results as IM, if it could be performed without trauma at the same age, is unfortunately impossible to answer, but the data are compatible with the proposition that physically castrated animals have a fatter target body type.

Different producers have different production objectives. For some, for example those rearing pigs for dry cured ham production, carcass quality is the major driver and increasing fat coverage in gilts can be highly desirable. To achieve this a long duration of IM is likely to work best. In many countries, however, improving production efficiency is usually the priority and FCR is a key metric. In such circumstances a relatively short duration of IM may produce the best return, especially if pigs are fed *ad libitum*. Management practices such as feed restriction may offer further improvement, but more work is required to identify the optimal protocol. Nutrition is also an area for further investigation. The gilts in our studies were all fed to the requirements of the untreated animals and as a result the diet may have been unnecessarily high in protein for IM animals that were eating more and depositing fat. Reducing protein would not only represent a cost saving but could also improve the FCR number, as using dietary protein rather than carbohydrate to synthesize fat is an inefficient process.

5. Conclusion

IM in gilts results in predictable secondary effects on growth performance and carcass composition. Following full immunization both ADFI and ADG increase, but the latter moderates first resulting in an initially favorable impact on FCR becoming less favorable over time. Carcass weights are higher and carcass composition shows a progressive shift to increased fat content. The duration of the IM phase (V2—H) before harvest is therefore a parameter that producers can manipulate to achieve specific production objectives. It is suggested that the changes seen may reflect adaptation to a heavier, fatter target body type.

Declaration of Competing Interest

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