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### A Meta-Regression Analysis to Evaluate the Influence of Branched-Chain Amino Acids in Lactation Diets on Sow and Litter **Growth Performance**

Julia P. Holen Kansas State University, jpholen@k-state.edu

Mike D. Tokach Kansas State University, Manhattan, mtokach@k-state.edu

Jason C. Woodworth Kansas State University, jwoodworth@ksu.edu

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## A Meta-Regression Analysis to Evaluate the Influence of Branched-Chain Amino Acids in Lactation Diets on Sow and Litter Growth Performance

#### **Abstract**

A meta-regression analysis was conducted to evaluate the effects of branched-chain amino acids (BCAA) in lactating sow diets on litter growth performance, sow body weight change, and sow feed intake. Thirtyfour publications that represented 43 trials with similar dietary Lys, but varying BCAA were used to develop a database that contained 167 observations. Diets from each trial were reformulated using NRC nutrient loading values in an Excel-based spreadsheet. Significant predictor variables within three optimum equations developed for litter ADG included the count of weaned pigs per litter, NE, SID Lys, CP, sow ADFI, Val:Lys, Ile:Lys, and Leu:Val. The equations suggest that the number of pigs weaned per litter and increasing NE, ADFI, SID Lys, and CP for sows are large, positive drivers for litter growth. Among the BCAA, the models for litter ADG indicate a positive influence of increasing Ile:Lys and Val:Lys and reducing Leu:Val on litter growth. For sow BW change, significant predictor variables within two competing models included litter size at 24 h, sow ADFI, Leu:Lys, and Ile+Val:Leu. The models suggest that litter size after cross-fostering at the start of lactation influences the predicted degree of sow BW change, and increased sow ADFI will improve, or minimize, BW change during lactation. Within the BCAA, the models indicate that increasing dietary Leu:Lys will minimize sow BW change during lactation. Lastly, the optimum equation for sow ADFI included Leu:Trp, SID Lys, NE, CP, and Leu:Lys as significant predictive variables. The model indicates that reducing Leu:Trp and increasing Leu:Lys will positively impact sow feed intake during lactation. Overall, the prediction equations suggest that BCAA play an important role in litter growth, sow BW change, and feed intake during lactation; however, the influence of BCAA on these criteria is much smaller than that of other dietary components such as NE, SID Lys, sow ADFI, and CP. These responses suggest that the three BCAA are essential for lactating sow and litter growth performance, but the predicted influence of Leu, Ile, and Val differ among litter ADG, sow weight loss, and sow daily feed intake.

#### **Keywords**

branched-chain amino acids, lactation, litter performance, sow

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#### **Authors**

Julia P. Holen, Mike D. Tokach, Jason C. Woodworth, Joel M. DeRouchey, Jordan T. Gebhardt, Evan C. Titgemeyer, and Robert D. Goodband



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# A Meta-Regression Analysis to Evaluate the Influence of Branched-Chain Amino Acids in Lactation Diets on Sow and Litter Growth Performance<sup>1</sup>

Julia P. Holen, Mike D. Tokach, Jason C. Woodworth, Joel M. DeRouchey, Jordan T. Gebhardt,<sup>2</sup> Evan C. Titgemeyer, and Robert D. Goodband

#### Summary

A meta-regression analysis was conducted to evaluate the effects of branched-chain amino acids (BCAA) in lactating sow diets on litter growth performance, sow body weight change, and sow feed intake. Thirty-four publications that represented 43 trials with similar dietary Lys, but varying BCAA were used to develop a database that contained 167 observations. Diets from each trial were reformulated using NRC<sup>3</sup> nutrient loading values in an Excel-based spreadsheet. Significant predictor variables within three optimum equations developed for litter ADG included the count of weaned pigs per litter, NE, SID Lys, CP, sow ADFI, Val:Lys, Ile:Lys, and Leu:Val. The equations suggest that the number of pigs weaned per litter and increasing NE, ADFI, SID Lys, and CP for sows are large, positive drivers for litter growth. Among the BCAA, the models for litter ADG indicate a positive influence of increasing Ile:Lys and Val:Lys and reducing Leu:Val on litter growth. For sow BW change, significant predictor variables within two competing models included litter size at 24 h, sow ADFI, Leu:Lys, and Ile+Val:Leu. The models suggest that litter size after cross-fostering at the start of lactation influences the predicted degree of sow BW change, and increased sow ADFI will improve, or minimize, BW change during lactation. Within the BCAA, the models indicate that increasing dietary Leu:Lys will minimize sow BW change during lactation. Lastly, the optimum equation for sow ADFI included Leu: Trp, SID Lys, NE, CP, and Leu:Lys as significant predictive variables. The model indicates that reducing Leu:Trp and increasing Leu:Lys will positively impact sow feed intake during lactation. Overall, the prediction equations suggest that BCAA play an important role in litter growth, sow BW change, and feed intake during lactation; however, the influence of BCAA on these criteria is much smaller than that of other dietary components such as NE, SID Lys, sow ADFI, and CP. These responses suggest that the three BCAA are

<sup>&</sup>lt;sup>1</sup> The authors gratefully acknowledge financial support from the United Soybean Board.

<sup>&</sup>lt;sup>2</sup> Department of Diagnostic Medicine/Pathobiology, College of Veterinary Medicine, Kansas State University.

<sup>&</sup>lt;sup>3</sup> National Research Council. 2012. Nutrient Requirements of Swine: Eleventh Revised Edition. Washington, DC: The National Academies Press. https://doi.org/10.17226/13298.

essential for lactating sow and litter growth performance, but the predicted influence of Leu, Ile, and Val differ among litter ADG, sow weight loss, and sow daily feed intake.

#### Introduction

The branched-chain amino acids (BCAA) Ile, Leu, and Val are three dietary essential amino acids for lactating sows necessary for both skeletal muscle and milk protein synthesis. However, structural similarities among the BCAA can create antagonisms and impaired utilization within their catabolism pathway. Leucine is the primary enzymatic stimulator of branched-chain amino acid aminotransferase (BCTA) and branched-chain  $\alpha$ -ketoacid dehydrogenase (BCKD), where the BCAA are reversibly converted to their analogous  $\alpha$ -keto acids and then irreversibly decarboxylated. Under dietary conditions of high Leu, increased catabolism of the other BCAA (Val and Ile) may occur.

Since the late 1990s, sows are producing larger and heavier litters. Common lactation diets that include corn and corn co-products often contain high levels of Leu, which may decrease the utilization of Ile and Val. We hypothesized that the differences in lactating sow performance in response to BCAA concentrations, especially Val, might be due to interactions with high Leu concentrations. Therefore, the objective of this regression analysis was to summarize studies evaluating the effects of BCAA in lactation diets and develop a statistical model to predict the influence of the interrelationships of BCAA on sow and litter growth performance.

#### Materials and Methods

#### **Database**

A literature search was conducted through the Kansas State University Libraries, utilizing the Academic Search Premier, CAB Direct, and Web of Science search engines to identify research articles that evaluated the impact of BCAA in lactating sow diets on sow and litter growth performance. Key search terms included sow AND lactation AND one of the following terms: branched-chain amino acids, amino acids, isoleucine, leucine, valine, canola meal, corn gluten meal, crude protein, dried distillers grains with solubles, soybean meal, or tryptophan.

In total, 34 publications that represented 43 trials from 1997 to 2020 were used to develop a database that contained 167 observations defined as treatments within study (Table 1). Diets for each trial were reformulated using NRC³ nutrient loading values in an Excel-based spreadsheet. Amino acids were expressed on a standardized ileal digestible (SID) basis. The predictor variables evaluated in the statistical model to predict litter ADG and sow BW change included sow ADFI, parity, lactation length, start litter size, litter size at weaning, crude protein (CP), net energy (NE), Lys, Ile:Lys, Leu:Lys, Met:Lys, Met+Cys:Lys, Thr:Lys, Trp:Lys, Val:Lys, total BCAA:Lys, Ile:Leu, Val:Leu, Leu:Ile, Val:Ile, Leu:Val, Ile:Val, Ile+Val:Leu, Ile:Trp, Leu:Trp, Val:Trp, total BCAA:Trp, and daily AA intakes. The predictor variables evaluated in the statistical model to predict sow ADFI included those previously stated except for daily AA intakes.

<sup>&</sup>lt;sup>4</sup> Harper, A. E., R. H. Miller, and K. P. Block. 1984. Branched-chain amino acid metabolism. Annu. Rev. Nutr. 4:409-454. doi:10.1146/annurev.nu.04.070184.002205.

#### Statistical analysis

Regression model equations were developed with the MIXED procedure of SAS (v. 9.4, SAS Institute, Cary, NC) and utilized the inverse of reported squared SEM with the WEIGHT statement to account for heterogenous errors across studies. Predictor variables were assessed with a step-wise manual forward selection for model inclusion. Additionally, statistically significant (P < 0.05) predictor variables were required to provide an improvement of at least 2 Bayesian information criteria to be included in the final model.

#### **Results and Discussion**

#### Litter average daily gain

The equations suggest that the number of pigs weaned per litter and increasing NE, ADFI, SID Lys, and CP concentration for sows are large, positive drivers for litter growth (Table 2). Among the BCAA, the models for litter ADG indicate a positive influence of increasing Ile:Lys and Val:Lys on litter growth. Additionally, the developed models for litter ADG indicate that the relationship among BCAA is important, such that a high ratio of Leu:Val had a significantly negative influence on litter gain. Multiple studies have attempted to distinguish an appropriate Val requirement for lactating females, however, some studies did not control Leu:Lys across the Val treatments evaluated. The wide range in Leu:Val ratios across studies may explain some of the conflicting responses observed, whereas lowering the Leu:Lys ratio could limit the negative effects of Leu on catabolism of the other BCAA and, subsequently, the negative influence of increasing Leu:Val ratios on litter gain.

#### Sow body weight change

The models for sow BW change suggest that litter size after cross-fostering at the start of lactation influences the predicted degree of sow BW change, and increased sow ADFI will improve, or minimize, BW change during lactation. The models indicate that increasing dietary Leu:Lys will decrease sow BW loss during lactation. Under conditions where Leu is not limiting, the sow may preferentially utilize Leu for maternal body protein deposition resulting in more nutrients being used for body weight gain and fewer for milk production. Similarly, the negative predictive factor for Ile+Val:Leu indicates that increasing concentrations of Ile and Val relative to Leu can increase sow BW loss during lactation.

#### Sow average daily feed intake

When evaluating the impact of BCAA on sow feed intake, the model indicates that reducing Leu:Trp and increasing Leu:Lys positively impact lactation feed intake. The beneficial impact of increasing Leu:Lys contrasts with research that has been conducted in growing-finishing pigs, where diets with excess Leu, imbalanced BCAA, or over-supplementation of BCAA could negatively impact ADFI. However, the model suggests that reducing Leu:Trp in diets with increasing Leu will improve feed intake for lactating sows. However, these responses have yet to be evaluated among lactating sows.

To conclude, the prediction equations for litter ADG suggest that Leu, Ile, and Val impact litter growth, but the effects of BCAA are much smaller than the effects of dietary NE, Lys, and CP. Furthermore, the models suggest that increasing Leu:Lys and reducing Ile+Val:Leu ratios can positively influence and minimize sow BW change

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during lactation. Although interactions among BCAA within the mammary gland occur, the sow may preferentially utilize Leu for whole body protein synthesis and thus, increasing the dietary concentrations of Leu could decrease sow BW loss. Additionally, our model suggests that reduced Leu:Trp and increased Leu:Lys positively influence sow feed intake during lactation. Certainly, the three BCAA are essential for the lactating sow, but the predicted influence of Leu, Ile, and Val differ among the models developed for sow and litter performance.

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Table 1. Summary of publications within the meta-regression analysis to predict influence of branched-chain amino acids on lactating sow performance<sup>1</sup>

Publication	Trials	Sows,	Average pigs weaned/ litter	Average ADFI, kg	SID Lys,	Range of SID Ile:Lys, %	Range of SID Leu:Lys, %	Range of SID Val:Lys, %	Range of SID Trp:Lys, %
Richert et al. (1996)	1	203	10.2	6.2	0.79	73	145	70-119	23
Libal et al. (1997)	1	115	8.4	6.1	0.67	57	151	68	15-22
Richert et al. (1997a)	2	202	9.9	4.5	0.77 or 1.14	74-78	119-124	75-118	24
Richert et al. (1997b)	1	185	10.8	6.1	0.80	49-135	133-134	70-154	23
Touchette et al. (1998a)	1	257	9.8	4.5	0.78-0.80	65-81	151-173	74-89	18-23
Touchette et al. (1998b)	1	116	10.0	4.0	1.03	78	154	85-96	24
Johnston et al. (1999)	2	267	9.7	5.3	0.69-0.70	65 or 83	163 or 187	76 or 92	18 or 23
Carter et al. (2000)	1	231	10.2	5.8	0.76	70	161	79-136	21
Moser et al. (2000)	1	306	10.6	5.9	0.78	70-121	158-209	78-128	22
Southern et al. (2000)	1	79	10.3	5.5	0.92-0.94	78-84	159-169	85-94	23
Gaines et al. (2006)	2	468	10.0	6.4	0.75-0.79	73-77	144-165	70-131	22
Song et al. (2010)	1	307	9.8	6.6	0.84-0.90	63-81	169-210	76-95	15-23
Devi et al. (2015)	1	18	11.7	5.5	0.93	74	152	81-86	21
Greiner et al. (2015)	3	522	10.2	6.2	1.02-1.09	62-77	132-203	68-88	17-21
Huber et al. (2015)	1	38	10.1	5.7	0.72-0.73	73-81	135-175	111-112	24-25
Sotak-Peper et al. (2015)	1	134	11.9	6.0	0.93-0.94	77-84	161-202	84-94	22-23
Craig et al. (2016)	2	109	12.8	7.6	1.14 or 1.30	57-67	107-125	72-119	20-22
Fan et al. (2016)	2	225	10.5	6.1	0.86	69	172	80	18-33
Huber et al. (2016)	1	23	9.7	5.1	0.72-0.73	74 or 81	135 or 175	110 or 112	24
Strathe et al. (2016)	1	558	13.4	6.2	0.99-1.00	54-56	99-102	66-105	18-19
Choi et al. (2017)	1	60	9.9	5.0	0.94-0.99	63-64	132-135	89-90	23
Greiner et al. (2017)	1	284	11.9	5.2	0.95	56	165	69	14-19
Velayudhan et al. (2017)	1	45	10.5	7.4	0.87	57-79	130-166	71-87	20-23
Xu et al. (2017)	1	32	9.8	4.3	0.83	64	142	74-133	17
Greiner et al. (2018)	2	714	10.3	5.5	1.02-1.09	57-78	123-155	63-84	17-23
Liu et al. (2018)	1	180	10.3	4.6	0.83-0.90	60-74	137-158	77-81	16-22
Gao et al. (2019)	1	60	9.8	3.6	1.23	65	130-153	72-102	19
Greiner et al. (2019)	1	422	11.7	5.2	0.97	65	114	55-102	19
Hojgaard et al. (2019)	1	520	13.0	6.7	0.87-0.88	54-80	99-141	65-89	22-26
Shang et al. (2019)	1	45	10.2	5.1	0.81-0.82	76-81	158-173	113-116	23
Zhang et al. (2019)	1	54	9.8	5.2	0.89-0.90	57-79	113-163	85-87	19-23
Gourley et al. (2020)	1	131	12.9	5.5	1.05	60-76	130-152	85	20-23
Ma et al. (2020)	1	48	10.0	5.7	0.71-0.72	68-84	155-216	80-103	18
Zhang et al. (2020)	2	24	10.7	6.2	0.89-0.90	58 or 79	113 or 161	85 or 87	19 or 23

<sup>&</sup>lt;sup>1</sup>Reported standardized ileal digestible (SID) amino acid ranges represent diet composition utilizing NRC (National Research Council. 2012. Nutrient Requirements of Swine: Eleventh Revised Edition. Washington, DC: The National Academies Press. https://doi.org/10.17226/13298.) or CVB (CVB, 2020. Tabellenboek Voeding Varkens 2020. CVB-reeks nr. 63. http://www.cvbdiervoeding.nl/.) nutrient loading values.

<sup>&</sup>lt;sup>2</sup>Standardized ileal digestible Lys ranges varied slightly within some studies during diet reformulation and conversion of total Lys to SID Lys.

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Table 2. Regression equations to predict sow and litter growth performance<sup>1</sup>

Variable <sup>2</sup>	Equation <sup>3</sup>	BIC <sup>4</sup>			
Litter ADG, kg					
Model 1	= -4.8199 + (0.1967 × pigs weaned per litter) + (0.000568 × NE, kcal/kg) + (1.0735 × SID Lys, %) + (0.8119 × ADFI, kg) - (0.06202 × ADFI × ADFI) + (0.0012 × Val:Lys, %) + (0.000963 × Ile:Lys, %)	-230.1			
Model 2	= -5.1198 + (0.2002 × pigs weaned per litter) + (0.000679 × NE, kcal/kg) + (0.805 × SID Lys, %) + (0.8065 × ADFI, kg) - (0.06097 × ADFI × ADFI) + (0.000902 × Val:Lys, %) + (0.01763 × CP, %)	-231.6			
Model 3	= -4.8731 + (0.1988 × pigs weaned per litter) + (0.000676 × NE, kcal/kg) + (0.7224 × SID Lys, %) + (0.7882 × ADFI, kg) - (0.05954 × ADFI × ADFI) + (0.0214 × CP, %) - (0.00048 × Leu:Val, %)	-231.4			
Sow BW change, kg					
Model 1 <sup>5</sup>	= -43.5295 - (0.1748 $\times$ start litter size) + (5.5202 $\times$ ADFI, kg) + (0.03143 $\times$ Leu:Lys, %)	532.3			
Model 2 <sup>5</sup>	= -33.3003 - (0.5108 × start litter size) + (5.6935 × ADFI, kg) - (0.02421 × Ile+Val:Leu, %)	533.2			
Sow ADFI, kg	= $13.7105$ - $(0.00187 \times Leu:Trp)$ + $(2.4641 \times SID Lys, \%)$ - $(0.00315 \times NE, kcal/kg)$ - $(0.1047 \times CP, \%)$ + $(0.006263 \times Leu:Lys, \%)$	189.9			

 $<sup>^1\!\</sup>text{Model}$  adjusted for heterogenous errors using the inverse of squared SEM.

 $<sup>^{2}\</sup>mathrm{ADG}=\mathrm{average}\ \mathrm{daily}\ \mathrm{gain}.\ \mathrm{ADFI}=\mathrm{average}\ \mathrm{daily}\ \mathrm{feed}\ \mathrm{intake}.\ \mathrm{BW}=\mathrm{body}\ \mathrm{weight}.$ 

<sup>&</sup>lt;sup>3</sup>Amino acid ratios expressed on standardized ileal digestible (SID) basis.

<sup>&</sup>lt;sup>4</sup>Bayesian information criterion.

<sup>&</sup>lt;sup>5</sup>Start litter size = count of piglets placed per litter at 24 h postpartum (after cross-foster).