

PERFORMANCE CHARACTERISTICS OF WEANED PIGS ON ZINC SUPPLEMENTATION: A META-ANALYSIS

OGBUEWU, I. P.^{1,2*} – MBAJIORGU, C. A.²

¹*Department of Animal Science and Technology, Federal University of Technology, P.M.B. 1526 Owerri, Imo State, Nigeria*

²*Department of Agriculture and Animal Health, University of South Africa, Florida Science Campus, Private Bag X6, Florida 1710, South Africa*

**Corresponding author*

e-mail: dr.ogbuewu@gmail.com; ifeanyi.ogbuewu@futo.edu.ng

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Abstract. The profitability of a swine enterprise depends heavily on high productivity, which to some extent can be achieved using trace elements. However, there are discordant results on the impact of zinc (Zn) supplementation, one of such trace elements on performance indices of weaned pigs. This study aimed to use the meta-analytic method to assess the impact of Zn supplementation on growth performance [i.e., average daily feed intake (ADFI), feed to gain ratio (F/G), average daily gain (ADG) and blood Zn levels] of weaned pigs. 1200 studies on the impact of Zn supplementation on growth performance were identified in a systematic search performed in Google Scholar, PubMed and Scopus databases and screened based on set inclusion criteria. Thirty studies met the inclusion criteria. Pooled results showed that Zn supplementation had a small effect on ADFI [standardised mean difference (SMD) = 0.33; 95% confidence interval (CI): 0.23 to 0.44] and F/G (SMD = 0.18; 95% CI: 0.05 to 0.30), but had a moderate effect on ADG (SMD = 0.63; 95% CI: 0.49 to 0.77) in weaned pigs. Additionally, Zn supplementation had a large effect on blood Zn (SMD = 2.83; 95% CI: 2.13 to 3.52). Subgroup analyses revealed that moderator variables [duration of supplementation (DOS), supplementation level (SL), Zn form and number of pigs included in each group] influenced the results of the meta-analysis, taking cognizance of heterogeneity. Meta-regression analyses found that moderators accounted for most of the sources of heterogeneity. It is concluded that Zn supplementation increased ADG and blood Zn in weaned pigs.

Keywords: *weaned pigs, zinc, growth performance, blood zinc, meta-analysis*

Introduction

Zn is one of the trace elements that influences growth and productivity of weaned pigs (Zhang et al., 2018a). It is an activator or a component of several enzymes involved in reproduction, immune function, antioxidant defense and cell proliferation. Some studies have shown that Zn improves gut health and intestinal barrier functions by increasing the expression of the tight-junction genes as well as small intestinal insulin-like growth factor -1 (IGF-1) and IGF-1 receptor genes (Li et al., 2006). Haung et al. (2009) found that natural feedstuffs are low in Zn, but do contain several factors limiting Zn absorption in the small intestine which call for adequate Zn supplementation in the diets of weaned pigs. NRC (1998) has set the Zn requirements for weaned pigs at 100 mg/kg feed. Several studies have evaluated the effect of Zn dose levels below or above the NRC (1998) recommended level on performance of weaned pigs (Hill et al., 2000; Fernandez et al., 2014; Cemin et al., 2019; Diao et al., 2021). Some investigators found no difference in the effect of Zn supplementation on the performance of weaned pigs (Carlson et al., 2004; Cho et al., 2015), while others found differences (Schell and Kornegay, 1996; Martínez

et al., 2005; Cemin et al., 2019). These variable reports may be ascribed to differences in breeds, sex, and rearing conditions (Pierozan et al., 2016; Ogbuewu et al., 2022).

The use of meta-analytic method to increase statistical power, identify research gaps and resolve conflicting findings among investigations that addressed the same research question has been highlighted (Hedges and Pigott, 2004; Koricheva et al., 2013). Meta-analysis is an advanced statistical method that aggregates the effect of intervention across studies that addressed the same research objective to provide a more robust estimate of the effects by increasing statistical power (Lean et al., 2014). Presently, no meta-analysis has been performed to evaluate the effect of Zn supplementation in weaned pig performance. Therefore, the objective this study was to assess the effect of dietary Zn supplementation on growth performance and blood Zn levels of weaned pigs using meta-analysis.

Materials and methods

Article selection guidelines

Google Scholar, PubMed and Scopus databases were searched for studies that evaluated the impact of Zn supplementation on the performance of weaned pigs using the following keywords: zinc, weaned pigs, ADFI, ADG, F/G and blood Zn. References of identified articles were manually reviewed for other relevant publications. Eligibility criteria for the meta-analysis were based on PICO method. PICO stands for Population (i.e., weaned pigs), Intervention (i.e., Zn supplementation), Comparison [i.e., diets with Zn (treatment group) and diets without Zn (control group)] and Outcomes (i.e., ADFI, F/G, ADG and blood Zn). Studies included in the meta-analysis were selected based on following inclusion criteria: (i) Controlled studies that examined the effect of diets with Zn (treatment group) and without Zn (control group) supplementation on the performance of clinically healthy weaned pigs. (ii) Studies were selected if they reported ADFI, ADG, F/G or blood Zn and their measure of variance [i.e., standard error (SE), standard deviation (SD), or 95% CI] for effect size computation. Studies that used animals other than weaned pigs were excluded. Studies that examined the effect of Zn in combination with other feed additives were also excluded. Also excluded were reviews and studies performed in diseased pigs. Identified studies were evaluated for eligibility, and disagreements were resolved through consensus. 1200 studies were identified and 30 studies were considered suitable for inclusion in the meta-analysis following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (*Figure 1*).

Data extraction and analysis

Data on the surname of the first author, year of publication, study location, study design and modifier variables (i.e., number of pigs in each treatment group, duration of supplementation, supplementation level and Zn form) were extracted in each of the article that met the inclusion criteria (*Tables 1a and b*). Data generated from the 30 studies that met eligibility were analysed in OpenMEE software by Brown University (Wallace et al., 2016). Results were presented as SMD at 95% CI using random-effects model. SMD was considered significant when the lower and upper CIs did not include zero (Koricheva et al., 2013). SMD was designated as small (0.2), moderate (0.5) and large effect (≥ 0.8) using the method of Cohen (1992). To explore sources of heterogeneity, data were partitioned using the following modifiers: number of pigs in each treatment group

(< 40 vs > 40), duration of supplementation (≤ 21 d vs > 21 d), supplementation level (1 - 100, 101 - 250, 251 - 500, 501 - 1000, 1001 - 1500, 1501 - 2000, 2001 - 2500, 2501 - 3000 and > 3000 mg/kg) and Zn form (inorganic, organic and nano). Heterogeneity was calculated using Q-statistic and I^2 - index (Higgins and Thompson, 2002), and considered significant at $p < 0.05$. Results of subgroup and meta-regression analyses were also considered significant at $p < 0.05$. Sensitivity analysis was performed using the method of Lean et al. (2009) to determine the robustness of the results of the meta-analysis. Publication bias was examined through funnel plot asymmetry and fail-safe number, Nfs (Sterne and Harbord, 2004). According to Jennions et al. (2013), the results of the meta-analysis can be considered robust, despite the presence of publication bias when the Nfs is higher than $5 * [(n = \text{number of comparison}) + 10]$.

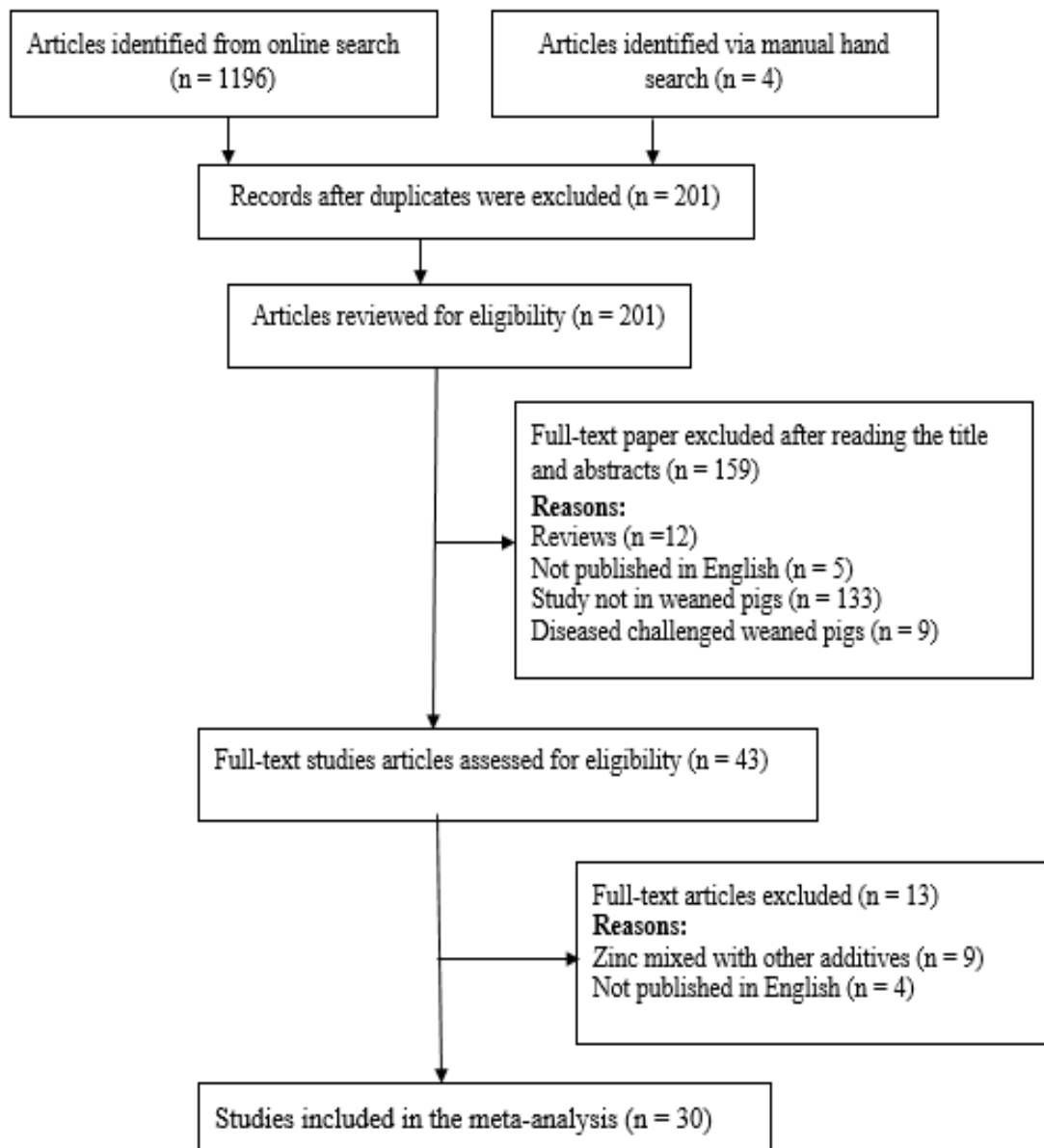


Figure 1. Flow chart of the articles selection process for the meta-analysis

Table 1a. Characteristics of studies included in the meta-analysis

References	Country	Continent	Studied moderators				Outcomes
			Zn form	SL (mg/kg)	NPT	DOS (d)	
Diao et al. (2021)	China	Asia	OZn/IZn	100	24	1-28	FI, FCE, BWG
Hill et al. (2014)	USA	North America	OZn/IZn	0 -100	50	1-38	FI, FCE, BWG
Schell and Kornegay (1996)	USA	North America	OZn/IZn	0 - 3000	20	1-14	FI, FCE, BWG
van Heugten et al. (2013)	USA	North America	OZn/IZn	0 -160	16	1-35	FI, FCE, BWG
Zhang et al. (2020)	China	Asia	IZn	0-3000	36	1-28	FI, FCE, BWG
Broom et al. (2006)	UK	Europe	IZn	0-3100	52	1-20	FI, FCE, BWG
Buff et al. (2005)	USA	North America	OZn/IZn	0-2000	10	1-35	FI, FCE, BWG
Hollis et al. (2005)	USA	North America	OZn/IZn	0-2500	123	1-28	FI, FCE, BWG
Hu et al. (2012)	China	Asia	IZn	0-2000	36	1-14	FI, FCE, BWG
Hu et al. (2013)	China	Asia	IZn	0- 2250	42	1-14	FI, FCE, BWG
Li et al. (2016)	Taiwan	Asia	OZn/IZn/NZn	0- 120	24	1-45	FI, FCE, BWG
Pei et al. (2019)	China	Asia	NZn	0-3000	30	1-21	FI, FCE, BWG, Blood Zn
Pérez et al. (2011)	USA	North America	IZn	0-3000	20/44	1-28/1-42	FI, FCE, BWG
Zhang et al. (2018b)	China	Asia	OZn/IZn	0-800	36	1-28/1-42	FI, FCE, BWG
Wang et al. (2010)	China	Asia	OZn	0-3000	30	1-35	FI, FCE, BWG, Blood Zn
Carlson et al. (2004)	USA	North America	OZn/IZn	0-2000	51	1-42	FI, FCE, BWG, Blood Zn
Cho et al. (2015)	Korea	Asia	IZn/NZn	0-3000	35	1-42	FI, FCE, BWG, Blood Zn
Hahn and Baker (1993)	USA	North America	OZn/IZn	0-5000	30	1-21	FI, FCE, BWG, Blood Zn
Han and Thacker (2010)	Korea	Asia	IZn	0-2500	30	1-14/1-28	FI, FCE, BWG, Blood Zn
Lei and Kim (2018)	South Korea	Asia	IZn	0-2500	32	1-42	FI, FCE, BWG, Blood Zn
Mavromichalis et al. (2001)	USA	North America	IZn	0-3000	30	1-21	FI, FCE, BWG
Milani et al. (2017)	Brazil	South America	IZn/NZn	0-3000	32	1-35	FI, FCE, BWG, Blood Zn
Molist et al. (2011)	Spain	Europe	IZn	0-3000	16	1-12	FI, BWG
Namkung et al. (2006)	Canada	North America	IZn	0-3000	36	1-14	FI, FCE, BWG
Poulsen (1995)	Denmark	Europe	IZn	0-4000	36	1-42	FI, FCE, BWG
Walk et al. (2015)	UK	Europe	IZn	0-3500	80	1-20	FI, FCE, BWG, Blood Zn
Walk et al. (2013)	UK	Europe	IZn	0-3500	48	1-21/1-42	FI, FCE, BWG, Blood Zn
Wang et al. (2011)	China	Asia	OZn	0-1200	48	1-28	FI, FCE, BWG
Williams et al. (2005)	USA	North America	IZn	0-2000	35	1-19	FI, FCE, BWG, Blood Zn
Wedekind et al. (1994)	USA	North America	IZn	0-80	32	1-42	FI, FCE, BWG, Blood Zn

DOS - Duration of supplementation; d - day; NZn - Nano zinc; ADFI - Average daily feed intake; F/G feed – to - gain ratio,; ADG – Average daily gain

Table 1b. Breed and experimental design of studies in the thirty articles included in the meta-analysis

Reference	Breed	APBE	IBW (kg)	Number of treatment	Replication	Pigs/replicate	Number of pigs	
							Expt groups	Ctl group
Diao et al. (2021)	Duroc x landrace x Yorkshire	-	8.81	4	6	4	72	24
Hill et al. (2014)	[Yorkshire × Landrace] × PIC	18	-	10	10	5	450	50
Schell and Kornegay (1996)	Yorkshire, Duroc × Hampshire	26	6.63	4	4	5	60	20
van Heugten et al. (2013)	[Landrace × Yorkshire] × [Hampshire × Duroc]	21	6.45	6	4	4	80	16
Zhang et al. (2020)	Duroc × Landrace × Yorkshire	28	8.92	5	6	6	144	36
Broom et al. (2006)	Duroc × Landrace × Large White	23	6.80	4	8	7 or 8	156	52
Buff et al. (2005)	-	21	6.20	5	10	1	40	10
Hollis et al. (2005)	-	20.6	6.30	8	26	4 or 5	492	123
Hu et al. (2012)	Duroc × Landrace × Yorkshire	27	7.20	5	6	6	144	36
Hu et al. (2013)	Duroc × Landrace × Yorkshire	21	6.12	5	6	7	168	42
Li et al. (2016)	Duroc × Landrace × Yorkshire	28	8.04	4	4	6	72	24
Pei et al. (2019)	Duroc × Landrace × Large White	-	9.37	5	3	10	120	30
Pérez et al. (2011)	Duroc × Landrace × Yorkshire	19	5.80	4	7	6 or 7	132	44
Zhang et al. (2018b)	Duroc × Landrace × Large White	-	8.47	6	6	6	180	36
Wang et al. (2010)	Duroc × Landrace × Yorkshire	-	7.68	4	3	10	90	30
Carlson et al. (2004)	PIC: C22 × TF4	17	5.14	6	17	3	255	51
Cho et al. (2015)	Duroc × Landrace × Yorkshire	21	6.50	4	7	5	105	35
Hahn and Baker (1993)	Yorkshire, Duroc × Hampshire	28	6.20	5	3	6	72	18
Han and Thacker (2010)	Duroc × Landrace × Yorkshire	24	6.28	5	3	10	120	30
Lei and Kim (2018)	Duroc × Landrace × Yorkshire	28	7.42	6	8	4	160	32
Mavromichalis et al. (2001)	-	15	5.20	5	5	6	120	30
Milani et al. (2017)	-	21	5.89	5	8	4	128	32
Molist et al. (2011)	(Large White × Landrace) × Pietrain	21	6.70	4	8	2	48	16
Namkung et al. (2006)	Yorkshire	16-19	5.90	3	6	10	120	60
Poulsen (1995)	-	28	-	6	6	6	180	36
Walk et al. (2015)	PIC337	28	9.50	9	4	20	640	80
Walk et al. (2013)	Duroc × Landrace × Large White	21	7.10	6	8	6	240	48
Wang et al. (2011)	Rongchang	28	8.40	4	6	8	144	48
Williams et al. (2005)	Yorkshire, Duroc × Landrace × Yorkshire	18	5.70	6	5	7	175	35
Wedekind et al. (1994)	Yorkshire x Landrace x Hampshire x Duroc	28	-	6	4	8	160	32

IBW - Initial body weight; APBE - Age of pigs at the beginning of the experiment; PIC - Pig Improvement Company

Results

Characteristics of included studies

1200 studies that evaluated the impacts of Zn supplementation on performance of weaned pigs were identified, of which 30 articles were considered suitable for the meta-analysis (*Tables 1a and b and Fig. 1*). The articles utilised for the analysis span for 28 years (1993-2021). 43% of the articles published between 1993 and 2010 and 57% were published after 2010 (*Table 2*). The most commonly used Zn additives were ZnO, ZnSO₄, Zn-met, ZnONP, and the least used Zn additives were ZnOMMT, ZnAAch, and ZnLact. Majority of the studies utilised for the analysis were performed in China, USA, Korea, and UK. Inorganic Zn source (64.29%) was the most used, followed with organic Zn sources (28.57%), and the least used was ZnONP (7.14%). Most of the studies included in the meta-analysis fed Zn for more than 21 days.

Growth performance and blood Zn concentrations

Tables 3 and 4 show that Zn had a small effect on ADFI (SMD = 0.33; 0.23 to 0.44) and F/G (SMD = 0.18; 0.05 to 0.30) in weaned pigs. Dietary Zn supplementation for ≤ 21 days had a moderate effect on ADFI, while Zn supplementation for > 21 days had a small effect on ADFI. Zn form and NPT had small impacts on ADFI in weaned pigs. SL at 1001 – 1500 and 2501 – 3000 mg/kg feed had moderate effects on ADFI while SL at 2001 – 2500 mg/kg feed had a large effect on ADFI. However, SL between 1 and 1000 mg/kg feed had small effects on ADFI in weaned pigs. DOS, NPT and SL had small effects on F/G. The magnitude of effect sizes for F/G was large in pigs fed nano Zn (SMD = 0.62; 0.17 to 1.06) and small in those fed organic Zn (SMD = 0.14; -0.11 to 0.39) and inorganic Zn (SMD = 0.15; 0.01 to 0.29). Pooled results as presented in *Table 5* show that Zn supplementation had a moderate magnitude of effect on ADG (SMD = 0.63; 0.49 to 0.77). In terms of ADG, studies that used > 40 pigs in each treatment group and fed Zn for ≤ 21 days had large effect estimates, while those studies that used < 40 pigs in each treatment group and fed Zn for >21 days had moderate effect estimates. The magnitude of effect sizes was large in pigs fed nano Zn (SMD = 1.04; 0.17 to 1.92) and inorganic Zn (SMD = 0.84; 0.66 to 1.02), and small in pigs offered organic Zn (SMD = 0.21; -0.03 to 0.44). SL at levels > 1000 mg/kg feed had a large effect on ADG. However, SL at ≤ 1000 mg/kg feed had small effects on ADG, except for SL at 251-500 mg/kg feed that had a moderate effect on ADG. *Table 6* shows that Zn had a large effect on blood Zn levels (SMD = 2.83; 2.13 to 3.52). DOS, NPT, SL and Zn form had large effects on blood Zn.

Heterogeneity and publication bias

Tables 2 to 5 show evidence of significant heterogeneity (I^2) among the articles included in the meta-analysis, and I^2 ranged from 85 to 98%. Subgroup analysis results as shown in *Tables 2-5* could not resolve the problem of significant heterogeneity. *Table 7* found significant linear relationships between studied moderators (DOS, LS, and Zn form) and ADFI in pigs. There is significant treatment-predictor interaction effect between DOS and Zn form ($Q = 16.91$, $P < 0.001$; $R^2 = 27\%$) and SL and Zn form ($Q = 25.62$, $P < 0.001$; $R^2 = 23\%$) for ADFI. There was no significant linear relationship between NPT and ADFI. NPT and its interactions with SL, DOS, and Zn form were predictors of Zn effect on F/G in weaned pigs. There were also significant linear relationships existed between ADG and moderators (DOS and Zn form). Significant

treatment-predictors interaction effect was found between BWG and modifiers (DOS*Zn form, SL*NPT, and SL*Zn form). Our results suggest that modifiers and their interactions were significant predictors of the effect of Zn on blood Zn levels in weaned pigs. Publication bias was evaluated and presented as funnel graphs (*Fig. 2a-d*). The funnel plots were asymmetry, indicating the presence of publication bias among the selected articles. The Rosenberg's Nfs for the database were 456 (ADFI), 5194 (F/G), 39680 (ADG), and 14579 (blood Zn), and were higher than the calculated values of 685, 655, 705 and 275, respectively.

Table 2. Definition of variables and their % distribution in the matrix

Variables	levels	Definition	% distribution in the matrix
Study country	China		26.67
	USA	United State of America	36.67
	UK	United Kingdom	10
	Taiwan		3.33
	Korea		10
	Brazil		3.33
	Spain		3.33
	Canada		3.33
	Denmark		3.33
Continent	Asia		40.00
	North America		40.00
	Europe		16.67
	South America		3.33
Zinc sources	ZnSO4	Zinc sulphate	13.57
	ZnO	Zinc oxide	38.08
	mZnO	Modified zinc oxide	
	ZnONP	Zinc oxide nanoparticle	8.49
	ZnOMMT	Montmorillonite zinc oxide	1.99
	Zn-Prot	Zinc protein	5.08
	ZnAAco	Zinc amino acid complex	3.39
	ZnAAch	Zinc amino acid chelate	1.99
	ZnLact	Zinc lactate	1.99
	ZnGly	Zinc glycine	3.39
	ZnMet	Zinc methionine	10.17
	ZnLys	Zinc lysine	3.39
	TBZC	Tetrabasic zinc chloride	3.39
	ZnPS	Zinc polysaccharide	5.08
Zn form	IZn	Inorganic zinc	64.29
	OZn	Organic zinc	28.57
	NZn	Nano zinc	7.14
DOS (day)	≤ 21		40
	>21		60
SL (mg/kg)	1 - 100		13.24
	101 - 250		11.76
	251 - 500		10.29
	501 - 1000		13.24
	1001 - 1500		5.88
	1501 - 2000		16.18
	2001 - 2500		8.82
	2501 - 3000		16.18
	>3000		4.41
Publication year	≤ 2010 (1993-2010)		43.33
	>2010 (2011-2021)		56.67

Table 3. Average daily feed intake of weaned pigs on dietary Zn supplementation

Pooled/ Sub analysis	SMD	95% CI	SE	p-Val	Heterogeneity (%)			
					Q	df	p-Val	I ²
Pooled	0.33	0.23, 0.44	0.05	< 0.001	915.15	134	< 0.001	85
DOS (days)								
≤ 21	0.62	0.37, 0.86	0.13	< 0.001				
> 21	0.20	0.10, 0.30	0.05	< 0.001				
SL (mg/kg)								
1 - 100	0.12	-0.07, 0.30	0.09	0.224				
101 - 250	0.10	-0.24, 0.43	0.17	0.568				
251 - 500	0.24	0.03, 0.44	0.10	0.023				
501 - 1000	0.17	-0.24, 0.57	0.21	0.424				
1001 - 1500	0.58	0.38, 0.78	0.10	< 0.001				
1501 - 2000	0.42	0.06, 0.78	0.19	0.024				
2001 - 2500	0.93	0.54, 1.32	0.20	< 0.001				
2501 - 3000	0.64	0.29, 0.99	0.18	< 0.001				
> 3000	0.40	-0.13, 0.93	0.27	0.137				
Zn form								
Inorganic	0.49	0.36, 0.62	0.07	< 0.001				
Organic	0.06	-0.09, 0.20	0.08	0.466				
Nano	0.34	-0.37, 1.05	0.36	0.352				
NPT								
< 40	0.30	0.15, 0.45	0.08	< 0.001				
> 40	0.38	0.24, 0.52	0.07	< 0.001				

SL - Supplementation level; DOS - Duration of supplementation; NPT - Number of pigs in each treatment group; SMD - Standardised mean difference; SE - Standard error; Q - Cochran statistic; I - Confidence interval; DF - Degree of freedom; I² - Inconsistency index

Table 4. Feed to gain ratio of weaned pigs on dietary Zn supplementations

Pooled/ Subanalysis	SMD	95% CI	SE	p-Val	Heterogeneity (%)			
					Q	df	p-Val	I ²
Pooled	0.18	0.05, 0.30	0.06	0.005	1140.44	128	< 0.001	89
DOS (day)								
≤ 21	0.21	-0.01, 0.43	0.11	0.060				
> 21	0.16	0.01, 0.30	0.07	0.032				
SL (mg/kg)								
1 - 100	0.40	0.02, 0.78	0.19	0.041				
101 - 250	0.03	-0.13, 0.20	0.08	0.698				
501 - 1000	0.05	-0.23, 0.33	0.14	0.733				
1001 - 1500	0.08	-0.18, 0.35	0.13	0.542				
1501 - 2000	0.20	-0.18, 0.58	0.19	0.309				
2001 - 2500	0.15	-0.07, 0.37	0.11	0.188				
2501 - 3000	0.01	-0.24, 0.27	0.13	0.919				
> 3000	-0.07	-0.56, 0.41	0.25	0.762				
Zn form								
Inorganic	0.15	0.01, 0.29	0.07	0.043				
Organic	0.14	-0.11, 0.39	0.13	0.273				
Nano	0.62	0.17, 1.06	0.23	0.006				
NPT								
< 40	0.08	-0.04, 0.19	0.06	0.191				
> 40	0.38	0.14, 0.62	0.062	0.005				

SL - Supplementation level; DOS - Duration of supplementation; NPT - Number of pigs in each treatment group; SMD - Standardised mean difference; SE - Standard error; Q - Cochran statistic; CI - Confidence interval; DF - Degree of freedom; I² - Inconsistency index

Table 5. Average daily gain of weaned pigs on dietary Zn supplementations

Pooled/ Subanalysis	SMD	95% CI	SE	p-Val	Heterogeneity (%)			
					Q	df	p-Val	I ²
Pooled	0.63	0.49, 0.77	0.07	< 0.001	1737.87	138	< 0.001	92
DOS (days)								
≤ 21	0.92	0.57, 1.26	0.18	< 0.001				
> 21	0.52	0.36, 0.67	0.08	< 0.001				
SL (mg/kg)								
1 - 100	0.48	0.14, 0.81	0.17	0.006				
101 - 250	0.26	-0.10, 0.61	0.18	0.161				
251 - 500	0.51	0.26, 0.76	0.13	< 0.001				
501 - 1000	0.20	-0.29, 0.68	0.25	0.424				
1001 - 1500	0.91	0.62, 1.19	0.15	< 0.001				
1501 - 2000	0.84	0.29, 1.38	0.28	0.003				
2001 - 2500	1.11	0.85, 1.36	0.13	< 0.001				
2501 - 3000	0.98	0.53, 1.43	0.23	< 0.001				
> 3000	0.82	-0.05, 1.70	0.45	0.066				
Zn form								
Inorganic	0.84	0.66, 1.02	0.09	< 0.001				
Organic	0.21	-0.03, 0.44	0.12	0.081				
Nano	1.04	0.17, 1.92	0.45	0.019				
NPT								
< 40	0.53	0.34, 0.72	0.10	< 0.001				
> 40	0.86	0.63, 1.10	0.12	< 0.001				

SL - Supplementation level; DOS - Duration of supplementation; NPT - Number of pigs in each treatment group; SMD - Standardised mean difference; SE - Standard error; Q - Cochran statistic; CI - Confidence interval; DF - Degree of freedom; I² - Inconsistency index

Table 6. Blood Zn concentrations of weaned pigs on dietary Zn supplementations

Pooled/ Subanalysis	SMD	95% CI	SE	p-Val	Heterogeneity (%)			
					Q	df	p-Val	I ²
Pooled	2.83	2.13, 3.52	0.35	< 0.001	2609.80	52	< 0.001	98
DOS (days)								
≤ 21	6.64	5.15, 8.12	0.76	< 0.001				
> 21	0.96	0.31, 1.60	0.33	0.004				
SL (mg/kg)								
1 - 100	-0.91	-2.59, 0.78	0.86	0.291				
251 - 500	1.73	0.85, 2.61	0.45	< 0.001				
501 - 1000	1.20	0.28, 3.71	0.877	0.023				
1501 - 2000	3.75	1.88, 5.63	10.96	< 0.001				
2501 - 3000	3.76	1.88, 5.64	0.96	< 0.001				
> 3000	8.03	2.71, 13.34	2.71	0.003				
Zn form								
Inorganic	3.57	2.52, 4.62	0.54	< 0.001				
Organic	1.36	0.86, 1.87	0.26	< 0.001				
NPT								
< 40	2.44	1.62, 3.26	0.42	< 0.001				
> 40	4.27	2.87, 5.66	0.71	< 0.001				

SL - Supplementation level; DOS - Duration of supplementation; NPT - Number of pigs in each treatment group; SMD - Standardised mean difference; SE - Standard error; Q - Cochran statistic; CI - Confidence interval; DF - Degree of freedom; I² - Inconsistency index

Table 7. Meta-regression comparing the associations between moderators and measured outcomes

Outcomes	Moderators	Q _M	df	R ² (%)	p-Val
ADFI	DOS	11.60	1	11	0.0007
	SL	16.30	8	7	0.0378
	Zn form	12.50	2	9	0.0020
	NPT	0.386	1	0	0.535
	DOS * Zn form	16.91	2	27	0.0002
	SL * Zn form	25.62	8	23	0.0012
F/G	DOS	0.15	1	0	0.700
	SL	8.46	8	2	0.390
	Zn form	3.76	2	1	0.152
	NPT	6.32	1	4	0.012
	NPT * SL	71.65	8	46	2.30E-12
	NPT * DOS	24.09	1	22	9.21E-07
ADG	NPT * Zn form	5.99	1	13	0.014
	DOS	5.11	1	3	0.0238
	SL	12.50	8	3	0.1320
	Zn form	16.00	2	10	0.0003
	NPT	3.46	1	2	0.0628
	DOS * Zn form	15.63	2	20	0.00040
Blood Zn	SL * NPT	21.45	8	19	0.00604
	SL * Zn form	8.95	2	8	0.0114
	DOS	37.60	1	42	8.81E-10
	SL	36.30	8	36	1.56E-05
	Zn form	3.49	1	6	0.062
	NPT	1.80	1	2	0.179
	DOS * SL	9.14	5	56	1.04E-01
	DOS * NPT	0.89	1	44	3.46E-01
	DOS * Zn form	0.54	1	42	4.63E-01
	SL * NPT	0.89	3	31	8.29E-01
SL * Zn form	1.27	4	31	8.66E-01	

* - Interaction; ADFI - Average daily feed intake; F/G - Feed to gain ratio; ADG - Average daily gain; DOS - Duration of supplementation; SL - Supplementation level; NPT - Number of pigs per treatment group; P - probability value; Q_M - Coefficient of moderators, DF - Degree of freedom, R² - Amount of heterogeneity explained by the moderators

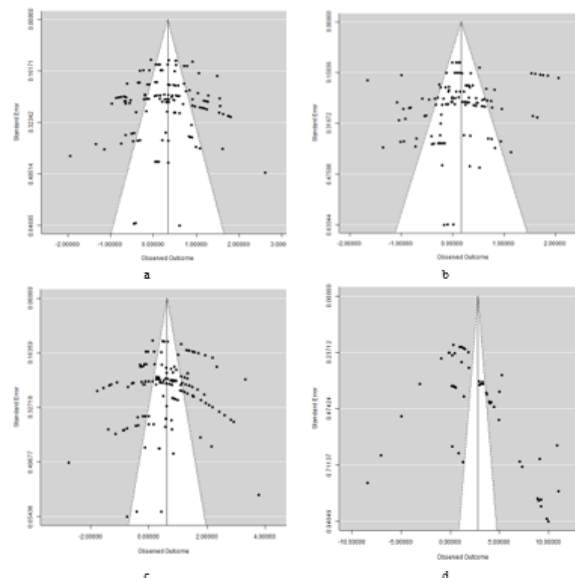


Figure 2. Funnel graphs of the effect of zinc supplementation on (a) ADFI, (b) F/G, (c) ADG, and (d) blood Zn concentration in weaned pigs

Discussion

The increased use of Zn supplementation in the diets of weaned pig could be attributed to the campaign to reduce the use of antibiotics in animal production industry. The fact that more than 60% of the studies included in the meta-analysis are from China and USA is consistent with the recent report that China and USA are the leading countries in global pig production (Hu and Cowling, 2020). Most of the papers included in this study used ZnO followed by ZnSO₄ and Zn-met, and this agrees with Abd El-Hack et al. (2017) that ZnO and ZnSO₄ were the two inorganic feed-grade Zn source used in the animal production industry. The observed increase in the number of studies that used Zn-met in comparison with other organic sources in the current study support the results of Rahman et al. (2002) that Zn-met was better than inorganic Zn sources (ZnO and ZnSO₄) in terms of bioavailability, and has become part of recent feed additives utilised in the pig industry (Jahanian et al., 2008).

The results of this meta-analysis indicate that zinc supplementation had a moderate effect on ADG in weaned pigs. The enhanced ADG in weaned pigs fed Zn-enriched diets could be attributed to the ability of Zn enhance cellular immunity (Liu et al., 2014) as well as promotes muscle cell proliferation and differentiation (Fernandez et al., 2014). This is similar to others (Broom et al., 2006; Diao et al., 2021), who reported 5 - 12% increase in ADG in weaned pigs fed diets supplemented with Zn in comparison with controls. This meta-analysis shows that zinc supplementation has a large effect on blood Zn concentrations in weaned pigs, implying that dietary Zn may have reached a point in the body where excretion cannot keep pace with absorption, resulting in progressive increases in blood Zn (Hill et al., 2000).

The results of this meta-analysis showed moderate to large effect on ADFI in weaned pigs fed high dose of Zn (2001-3000 mg/kg feed) for ≤ 21 days. Furthermore, inclusion of high doses of Zn in the diets of weaned for ≤ 21 days had large impact on ADG. This agrees with Daio et al. (2021), who reported the positive effect of Zn in pigs during weaning when the pigs are vulnerable to nutritional, environmental and psychological stress leading to alterations in intestinal integrity and immune response, causing scouring and poor growth (Campbell et al., 2013). There is evidence that nano and organic Zn sources are more bioavailable than Zn from inorganic sources (Hill et al., 2014; Daio et al., 2021). In this meta-analysis, the impact of Zn on growth traits was evident in weaned pigs fed nanosized ZnO; supporting the concept that nano Zn has higher bioavailability, and can meet the requirements of weaned pigs at lower dietary concentrations.

There is evidence of high heterogeneity and meta-regression analysis found that tested moderators and their interactions accounted most of the sources of heterogeneity. Results showed that Zn form is a predictor of Zn effect on BWG (Pierozan et al., 2016; Cemin et al., 2019; Daio et al., 2021). Our model revealed that NPT and SL were not significant predictors of Zn intervention on ADFI, blood Zn and ADG in weaned pigs. In addition, there were no relationships between F/G and aspects of moderators. The effect of factors such as diet composition, sex, breed, stocking density, and others (Pierozan et al., 2016), not examined in this study could have accounted for the residual heterogeneity not explained by the model. There is evidence of publication bias in this meta-analysis and this is of no consequence as the Nfs number was higher than the thresholds needed to declare the mean effect size significant, despite the presence of publication bias (Jennions et al., 2013).

Conclusion

Results demonstrated the addition of zinc in weaned pig diets had large effect on blood Zn, moderate effect on average daily gain and small effect on average daily feed intake and feed – to – gain ratio in weaned pigs despite the inconsistent results in the literature. Incorporation of high doses of zinc in weaned pig diets increased ADG and blood Zn. However, the use high doses of zinc in the diets of weaned pigs should be discouraged because of environmental pollution resulting from zinc excretion. The current study demonstrated the presence of significant heterogeneity among studies included in the meta-analysis and meta-regression analysis showed that tested moderator variables accounted for most of the sources of variations. The present study showed that Zn source influenced the outcomes of the meta-analysis.

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