ARTICLE

Effectiveness of Premature Infant Oral Motor Intervention (PIOMI) as pre-feeding oral motor stimulation among preterm infants at the neonatal intensive care unit: a meta-analysis

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OBJECTIVE: The increasing survival rate of preterm infants has led to long-term complications associated with prematurity, such as oral feeding difficulties. The review aims to determine the effectiveness of early and easily administered premature infant oral motor intervention (PIOMI) among preterm infants 32 weeks and less admitted to the Neonatal Intensive Care Unit, through a meta-analysis.

MATERIALS AND METHODS: Eligible studies were retrieved from six databases (PubMed, MEDLINE, Cochrane Library, Google Scholar, Physiotherapy Evidence Database, and International Clinical Registry Platform) and PIOMI website. These were screened based on established selection criteria. The statistical analysis was conducted using the STATA

RESULTS: A total of eight randomized-clinical trials, with 290 participants between 26 to 32 weeks gestational age, were included in the meta-analysis. The study suggested that PIOMI may reduce the transition from gavage to independent oral feeding by 2 days (SMD = –1.97, z = 4.33, p = 0.001, 95% CI = –2.86 to –1.08), increase weight gain by 810 g (SMD=0.81, z=3.45, p=0.001, 95% CI = 0.35 to 1.27), and shorten hospital stay, compared to the control group.

CONCLUSION: Preterm infant oral motor intervention (PIOMI) can be considered in NICUs to improve clinical outcomes of preterm infants 32 weeks gestational age or less.

KEYWORDS: *premature infant oral motor intervention, prematurity, infant, oral motor stimulation*

INTRODUCTION

Prematurity is one of the global healthcare burdens to date. The estimated preterm birth is 15 million infants annually, with rates ranging from 5% to 18% across countries. (1) The Philippines ranked 8th with the most significant number of preterm births, with a rate of 13.3 per 100 live births. (2) The increasing survival rate of preterm infants has led to long-term complications associated with prematurity, compelling the need for supportive healthcare services. One of the crucial concerns is establishing safe and independent oral feeding, as it is one of the three physiologic competencies of preterm newborns for hospital discharge. (3) Oral feeding is a complex skill that involves an interplay between the central nervous, respiratory, and neuromuscular systems. A delay or disruption in any of these leads to oral feeding difficulties (4). The suck-swallow-breath coordination is developed at 32 to 34 weeks, predisposing preterm infants to oral feeding difficulties. Studies on earlier initiation of oral feeding among extremely and very preterm infants found it beneficial in achieving earlier postmenstrual age at full independent oral feeding and discharge.(5,6) A retrospective study by Jadcherla et al. showed that preterm infants on tube feedings had significantly lower cognitive, communication, and motor composite scores than those discharged on partial or full oral feeding at 18-24 months. (7) Preterm infants, therefore, have short and long-term benefits when oral feeding difficulties are addressed earlier. Studies on oral motor stimulation vary on the age of initiation of intervention, ranging from 29 to 36 weeks post menstrual age (PMA), and the time at which it was initiated. Despite these variations, oral motor therapy significantly shortened hospital days, duration of parenteral nutrition and transition from gavage to oral feeding, and increased feeding efficiency and milk intake. (8-10)

One of the oral motor interventions being studied is the Premature Infant Oral Motor Intervention (PIOMI). It is a standardized 5-minute oral motor therapy explicitly developed for preterm infants. It is adapted from the 15-minute Beckman Oral Motor Intervention (BOMI) designed for infants and children with developmental delays and feeding difficulties. Studies on PIOMI administered between 29 to 36 weeks postmenstrual age (PMA) significantly reduced the transition time to full oral feeding and hospital stay, increased breastfeeding rates at 1 and 3 months after discharge at the NICU, and improved Neonatal Oro Motor Assessment Scale (NOMAS). (11-14) While many studies support the benefits of administering oral motor stimulation, its implementation in the Philippines remains challenging due to the need for more trained therapists. A study by Majoli et al. comparing parent and professional-administered PIOMI did not establish a significant difference in the transition time to full oral feeding, weight gain, or the length of hospital stay. (11) This suggests that PIOMI, as an oral motor

intervention, can be administered even by non-professionals following appropriate training.

Studies on oral motor interventions have shown benefits, such as decreasing the transition time to full oral feeding and hospital stay among preterm infants. However, they are not commonly practiced in the NICU due to a lack of well-designed research and trained therapists. This study aims to determine the effectiveness of early and easily administered oral motor stimulation in oral feeding among extremely and very preterm infants. Findings in this study may help the NICU implement an oral feeding protocol among preterm infants at risk for oral feeding difficulties.

The World Health Organization defines preterm as babies born alive before 37 weeks of pregnancy. It is categorized based on the gestational age at birth, extremely preterm (less than 28 weeks), very preterm (between 28 to 32 weeks), and moderate to late preterm (32 to 37 weeks). It can also be categorized based on birthweight, low birth weight (< 2500g), very low birth weight (< 1500g), and extremely low birth weight (<1000g). An estimated 15 million infants, equivalent to 1 in 10, are born preterm annually. The rates range between 5% and 18% across 184 countries. (1) The Philippines ranked 8th with the most significant number of preterm births with a rate of 13.3 per 100 live births [1, 2].

Prematurity is a significant healthcare burden and is among the leading cause of infant mortality and long-term morbidity. UNICEF reported that prematurity is the leading cause and accounts for 32.7% of neonatal mortality in the Philippines. (12) Fortunately, the improvements in perinatal care and advancing technology have increased the survival of preterm infants. However, these also led to an increasing population of infants with morbidities associated with prematurity, particularly growth and development. In this regard, studies on preventing morbidities should also be a central health priority.

Oral feeding is one of the common concerns in the latter days of hospitalization. It is a complex skill that involves an interplay between the central nervous, respiratory, and neuromuscular systems. A delay or disruption in any of these functions leads to prolonged oral feeding maturation (4). The development of oral feeding skills begins in utero, evidenced by swallowing amniotic fluid at 11 to 12 weeks, oral gag-reflex at 12 to 16 weeks, sucking and swallowing reflex by 28 weeks.(17,18) Prematurity and medical conditions such as respiratory diseases, brain injury, and necrotizing enterocolitis, deprive preterm infants of sensory and motor experiences during critical brain development when oral feeding skills are established. These factors increase the risk of preterm infants for substantial delays in achieving full independent feedings. Consequently, delayed

delayed oral feeding results in prolonged hospitalization, increased hospital cost, growth and developmental delays, and a high rehospitalization rate. The retrospective cohort study of Jadcherla et al. demonstrated that among 194 preterm infants, 40% were discharged on tube feedings due to feeding difficulties. Neurodevelopment follow-up at 18 to 24 revealed that those on full tube feedings had significantly lower cognitive ($p<0.01$), communication ($p=0.03$), and motor composite scores ($p<0.01$). It further concluded that full oral feeding achieved at first NICU discharge was associated with superior feeding milestones and less long-term neurodevelopment impairment (NDI) compared with full or partial tube feeding.(7) Rinat and colleagues observed that early feeding difficulties among extremely preterm infants are at risk for poor motor outcomes at 4 to 5 years corrected age. Thus, early diagnosis and intervention are warranted.(15)

Literature on oral feeding difficulties and their impact and complications are relatively lacking and new compared to the other morbidities associated with prematurity. Studies on the timing of initiation of oral feeding showed beneficial results when started earlier. Gentle et al. compared oral feeding initiation at < 33 weeks postmenstrual age (PMA), cue-based feeding, and practitioner-driven feeding in infants unable to achieve independent oral feedings by 36 weeks on PMA at independent oral feeding and discharge. They found that earlier oral feeding initiation among very preterm infants was associated with decreased PMA at independent oral feeding and discharge as opposed to cue-based feeding with insignificant reduction of the outcomes.(5) Similarly, Simpson et al. reported that earlier initiation of oral feeding 48 hours after achieving full gavage feeding of 120ml/kg/day accelerated the transition time to independent oral feeding compared to practitioner-driven feeding.(6)

The Preterm Infant Oral Motor Intervention (PIOMI) is a standardized oral stimulation program developed by Brenda Knoll. It was based on the principles of Beckman Oral Motor Intervention (BOMI), an oral motor intervention designed for term infants, children, and adults with developmental delays with feeding difficulties. It consists of 11 oral motor steps and is usually performed in 15 minutes. The PIOMI, on the other hand, is a 5-minute oral motor stimulation designed explicitly for preterm infants. It comprises 8 steps to activate muscle contraction and movement against resistance to build strength as shown in Appendix 1. The techniques were modified to accommodate the oral cavity's small size and ensure the preterm infant's correct positioning. It can be started before oral feeding hemodynamically stable preterm infants. (11)

Like other methods of oral motor intervention, studies on PIOMI differ in the

timing of initiation of intervention (29 to 34 weeks gestational age), frequency, and duration (7 to 10 days). Regardless of these differences, studies showed a significant reduction in the number of days from gavage to oral feeding and a decrease in the number of hospital days (11-14, 24). Contrary to other studies, Thakkar et al. found that it improved weight gain. (20) Arora et al. showed that it improved the Neonatal Oro Motor Assessment Scale, a reliable tool for the evaluation of neonatal sucking patterns in both preterm and term infants.(10)

Regarding the easiness of administration, Majoli et al. found no significant difference between parent-administered versus professional-administered premature infant oral motor intervention in terms of transition time to full oral feeding, weight gain, or the length of hospital stay among infants between 31 to 32 weeks PMA. It also increased the parents' satisfaction and enhanced their perception of their capability to care for their infant in the parent-administered group.(11)

Despite substantial evidence of the benefits of early oral motor intervention, it is not commonly practiced in most NICUs because of a lack of trained professionals. Also, not all preterm infants follow the expected normal oral feeding development. Initiation of oral feeding often leaves clinicians with the question of how long to wait before initiating alternative means to facilitate sustained oral feeding before discharge. In this regard, studies on oral feeding intervention for infants in the NICU are essential to facilitate an earlier transition to full oral feeding and hospital discharge.

Objectives of the study

General Objective:

To determine the effectiveness of Preterm Oral Motor Intervention as a pre-feeding oral motor stimulation among preterm infants less than or equal to 32 weeks gestational age.

Specific Objectives:

To determine if Preterm Infant Oral Motor Intervention among preterm infants less than or equal to 32 weeks gestational age

Reduces the transition from tube to oral feeding.

Increases weight gain.

Decreases the duration of hospital stay.

METHODOLOGY

This meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guidelines and was conducted between July and September 2023.

We conducted a thorough electronic search through PubMed, MEDLINE, the Cochrane Library, Google Scholar, Physiotherapy Evidence Database (PEDro), non-English databases, and unpublished clinical trials through the International

Clinical Registry Platform (iCRTP) from 2011 to August 2023. The developer of PIOMI was also asked for possible references and unpublished articles. The citation or reference lists of eligible studies were also reviewed for relevant articles. The MeSH terms and free text words used were Preterm Infant, OR Premature Infant OR Prematurity OR Neonatal Prematurity, AND Pre-feeding OR before feeding, AND Premature Infant Oral Stimulation OR PIOMI, AND Randomized-controlled trials OR controlled clinical trial OR clinical trial. The studies were excluded based on the inclusion and exclusion criteria, and the full-text articles of the remaining studies were retrieved and screened.

The included studies were prospective randomized clinical trials evaluating the effects of the Preterm Infant Oral Motor Intervention (PIOMI) in transition to independent oral feeding, weight gain, and length of hospital stay.

The inclusion criteria were: (a) Population: Preterm infants born on or before 32 weeks age of gestation and admitted to NICU, (b) Design: Randomized clinical trials, (c) Language: English, (d) Intervention: Premature Infant Oral Motor Intervention administered on or before 32 weeks age of gestation.

The exclusion criteria were: (a) Population: Preterm infants more than 32 weeks age of gestation and not admitted to the NICU, (b) Intervention: Other oral motor intervention/stimulation, (c) Design: Non-randomized clinical trials, (d) Language: Studies not written in English and also unavailable full-text articles. Preterm infants over 32 weeks were excluded from this study to minimize bias from the expected oral feeding development skills. The primary investigator and co-investigator performed an independent and thorough screening of abstracts generated by the search strategy and reviewed the full-text articles of eligible studies. There were no discrepancies between the two reviewers.

The risk of bias of the included studies were appraised and classified as low, moderate or unclear, and high risk using the Cochrane Collaboration's GRADE (2011). This critical appraisal tool evaluates a trial in the following areas: 1. sequence generation, 2. blinding, 3. allocation concealment, 4. incomplete outcome data, 5. selective outcome reporting, and 6. other sources of bias. The answers to all domains of bias based on an algorithm generates a proposed judgement on the risk of bias. A low risk of bias indicates low risk assessment in all domains; unclear risk means unclear risk assessment for all domains; and, high risk denotes a high-risk assessment in one or more key domains.

The primary outcome in this analysis is the transition to full independent oral feeding for the control and intervention groups. The secondary outcomes are length of hospital stay and weight gain.

The co-investigator and a research assistant conducted the data extraction, including the study design, facility location, patient population, control/comparator, intervention, and all outcomes, and were tabulated in Table 1. For the missing data, the authors were contacted to provide the data or were computed based on appropriate statistics.

The statistical analyses were conducted using STATA MP Parallel Edition Statistical Software, Version 18, College Station, TX: StataCorp LP. The outcomes were continuous variables and are presented as standardized mean difference, alongside their corresponding 95% confidence intervals. A p-value ≤ 0.05 was considered statistically significant. Heterogeneity or between-study variations in the included studies was evaluated using Q statistics test, I^2 statistics, and tau squared (τ^2) statistics. I^2 values more than 50% denote substantial heterogeneity, while a significant Q-statistic implies a statistically significant heterogeneity. For an outcome with substantial heterogeneity ($I^2 \geq 50\%$) random-effects model was used to calculate the mean effect size and the source of heterogeneity was examined using a subgroup analysis. In contrast, a fix-effects model was used in studies with homogenous outcomes ($I^2 < 50\%$) .

RESULT

Study Selection

Figure 1 shows the summarized flowchart of the study selection process. Ninety-seven (97) articles were retrieved based on the search strategy. Articles were excluded at each stage for the reasons. Twenty-seven studies were excluded from the initial screening because of ongoing studies and other study designs. Eight articles were reviewed and included in the meta-analyses.

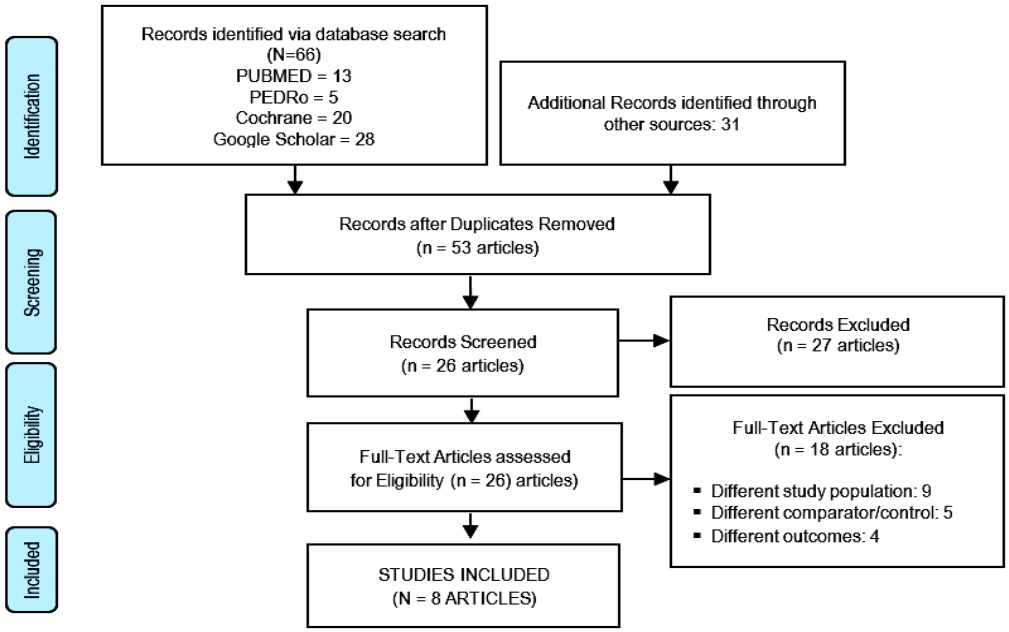


Figure 1. PRISMA Flow Diagram of Study Selection

Study Characteristics of Individual Studies

All eight included studies were prospective randomized controlled trials comparing the effect of PIOMI with standard care or sham intervention among preterm infants born less than or equal to 32 weeks gestational age. The cumulative sample was 290 participants: 147 in the PIOMI group and 143 in the control group.

One study was done in 2 NICU centers in Turkey, while the rest were single-centered studies from India (4), Iran (1), Egypt (1), and the USA (1). Six studies were included for the transition from gavage to full oral feeding, two studies for weight gain, and all studies for the length of hospital stay. The duration and frequency of the PIOMI in the intervention group varied from 7 to 14 days and once a day to three times a day.

Randomization, either by block or computer generation, was mentioned in all studies. Blinding of the participants and assessors was also reported in all studies. Table 1 presents a summary of the characteristics of the clinical trials included in the study.

Table 1. Characteristics of Included Research Studies (N=8)

Study (Year) And Country	Population Sample (N) Groups (n)	Method/ Design	Comparator	Intervention	Outcomes
Arora et al. (2014), India[10]	N: 30 Control: 14 PIOMI: 16 Inclusion: Born 28 – 32 weeks GA, no respiratory support for 48 hours, on full gavage feeding (150ml/kg/day), Exclusion: Preterm infants with RDS, and chronic medical complications (BPD, IVH, PVL, NEC, Chromosomal anomalies, or craniofacial malformation)	Randomized clinical trial	Sham Intervention (Unstructured oral intervention)	PIOMI TID for 7 days	1. Neonatal Oro Motor Assessment Scale (NOMAS) 2. Transition time to reach full independent wait spoon feeds 3. Duration of hospital stay, 4. Weight gain after the intervention

Bandyo-padhyay et al. (2023,) India[21]	N: 32 Control: 16 PIOMI: 16 Inclusion: Born 28 – 32 weeks GA, physiologically stable at the time of intervention, on full gavage feedings (150ml/kg) and in transition from gavage to spoon feeds, receiving Non-nutritive sucking (NNS) and Kangaroo Mother Care (KMC) as part of routine care. Exclusion: Preterm infants with IVH ≥ grade 2, NEC stage ≥ 2, PVL, BPD, and chromosomal anomalies or congenital malformations, history of perinatal asphyxia, and neonatal jaundice for exchange transfusion	Randomized clinical trial	Standard care including non-nutritive sucking and Kangaroo mother care	PIOMI BID until full feeding (lasted for 9 days)	1. Transition to full spoon feeding 2. Episodes of bradycardia, or desaturation during or immediately after spoon feeding, blood culture positive sepsis 3. Duration of hospital stay
Ghomi et al. (2019) Iran [22]	N: 30 Control: 15 PIOMI: 15 Inclusion: Born 26- 29 weeks GA, physiologically stable at the time of intervention, AS of ≥ 6 at 5 mins of birth, parental consent Exclusion: Congenital disorders or chromosomal abnormalities, chronic medical conditions (BPD< IVH gr 3 & 4, NEC, asphyxia, seizures, neonatal jaundice for exchange transfusion	Randomized clinical trial	Standard care	PIOMI OD x 10 days	1. Transition to full oral feeding 2. Weight gain 3. Length of hospital stay
Guler et al. (2018) India [23]	N: 60 Control: 30 PIOMI: 30 Inclusion: Born 26 to 29 weeks GA, Stable vital signs for at least 24 hours, Respiratory support of oxygen cannula, oxygen hood, and CPAP, APGAR score ≥ 4 at 1 and 5 minutes of life, IVH limited to grade 1 and 2	Randomized controlled design	Sham intervention	PIOMI OD for 14 days	1. Sucking capacity: sucking power, sucking time, and sucking amount 2. Feeding transition - Tube feeding to first bottle feeding - Tube feeding to initiation of breast feeding 3. Anthropometrics 4. Length of hospital stay (Enrollment to day of discharge)

Lessen (2011) USA [9]	N: 19 Control: 9 PIOMI: 10 Inclusion: Born between 26-29 weeks GA, AGA, clinically stable but could be receiving oxygen per high flow cannula Exclusion: Congenital anomalies, NEC, brain injury including IVH > grade 1, history of prenatal illicit drug exposure, on assistive ventilation more than high flow nasal cannula,	Randomized clinical trial	Standard of care	PIOMI OD X 7 days	1. Feeding progression (first to full oral feeding) 2. Length of hospital stay (Enrollment to discharge)
Mahmoodi et al (2019) Turkey [24]	N: 40 Control: 20 PIOMI: 20 Inclusion: Born 28 to 32 weeks GA, Fed at least 10 cc/kg gavage feeding, lack of any disorders such as cleft lip and palate, and congenital disorder Exclusion: Preterm infants with sepsis, congenital heart disease, NEC, severe	Randomized clinical trial	Routine care	PIOMI OD for 7 days	1. Premature Oral Feeding Readiness Scale (POFRAS) 2. Tube feeding to initiation of first oral feeding 3. Length of hospital stay
Osman et al. (2016) Egypt [25]	N: 75 Control: 25 Group 1: PIOMI low dose Group 2: PIOMI high dose Inclusion: Born 30 to 32 weeks GA, AGA Exclusion: Preterm infants with congenital anomalies, NEC, brain injury including IVH, receiving assisted ventilation or high flow nasal cannula ≥ 4L/min, clinically unstable	Randomized clinical trial	Sham intervention (no unstructured oral motor intervention)	Group 1: OD for 7 days Group 2: OD until full feeding	1. Transition to full oral feeding (first to full oral feeding) 2. Length of hospital stay (Admission to discharge) 3. Weight gain
Sasmal et al. (2023) India [26]	N: 29 Control: 14 PIOMI: 15 Inclusion: Born 26 to 32 weeks GA, birthweight < 1500, APGAR score ≥ 6 at 5th min after birth, without - or with respiratory support via nasal cannula ≤ 2 L/min or nasal prong 0.1 – 0.2 L/min Exclusion: history of prenatal illicit drug exposure, congenital and chromosomal anomalies, medical conditions such as BPD, severe asphyxia, NEC, neonatal jaundice for exchange transfusion, seizures, IVH grade 3 & 4, PVL, on assistive ventilation other than high flow nasal cannula, sepsis, on NPO, and SGA, and transferred to other hospital	Randomized controlled trial	Routine care	PIOMI BID x 7 days	1. Premature Oral Feeding Readiness Scale (POFRAS) 2. Early Feeding Skill (EFS) 3. Preterm Infant Breastfeeding Behavior Scale (PIBBS) 4. Transition to full oral feeding (First to full oral feeding) 5. Duration of hospital stay (from admission to discharge) 6. Weight gain 7. Feeding mode at discharge

Risk of Bias (ROB) and Quality of Evidence Assessment using the Cochrane GRADE Tool

The Cochrane GRADE Tool, illustrated in Figures 2a and 2b, was used for the risk of bias and the quality of evidence assessment. Figure 2a shows a low risk of selection bias due to random sequence generation and allocation concealment, detection bias due to blinding of outcome assessors, attrition bias due to incomplete outcome data, and other biases. However, there is approximately 40% high risk for performance bias due to the lack of blinding of participants and personnel. There is about 60% unclear risk of bias for reporting bias due to selective reporting of results and data.

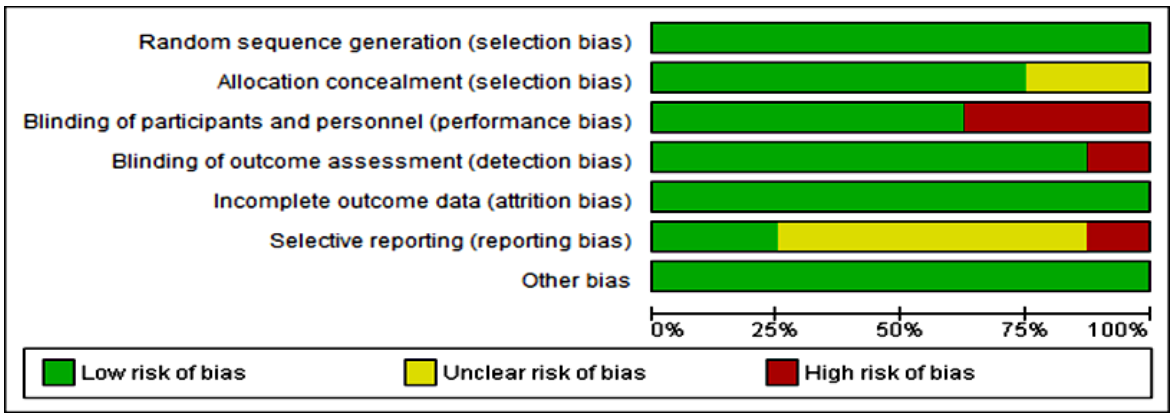


Figure 2a. Risk of Bias Assessment Graph of the Included Studies using the Cochrane GRADE Tool

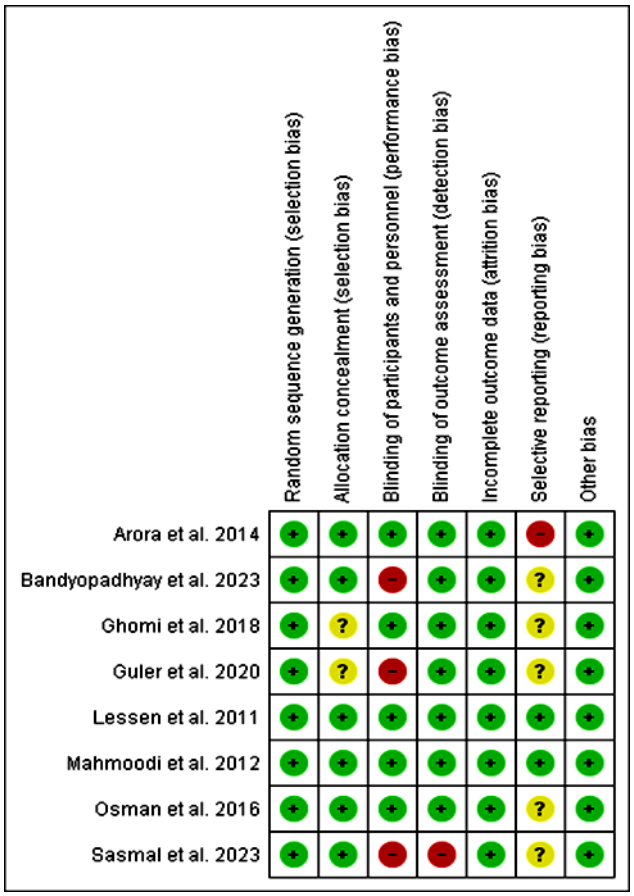
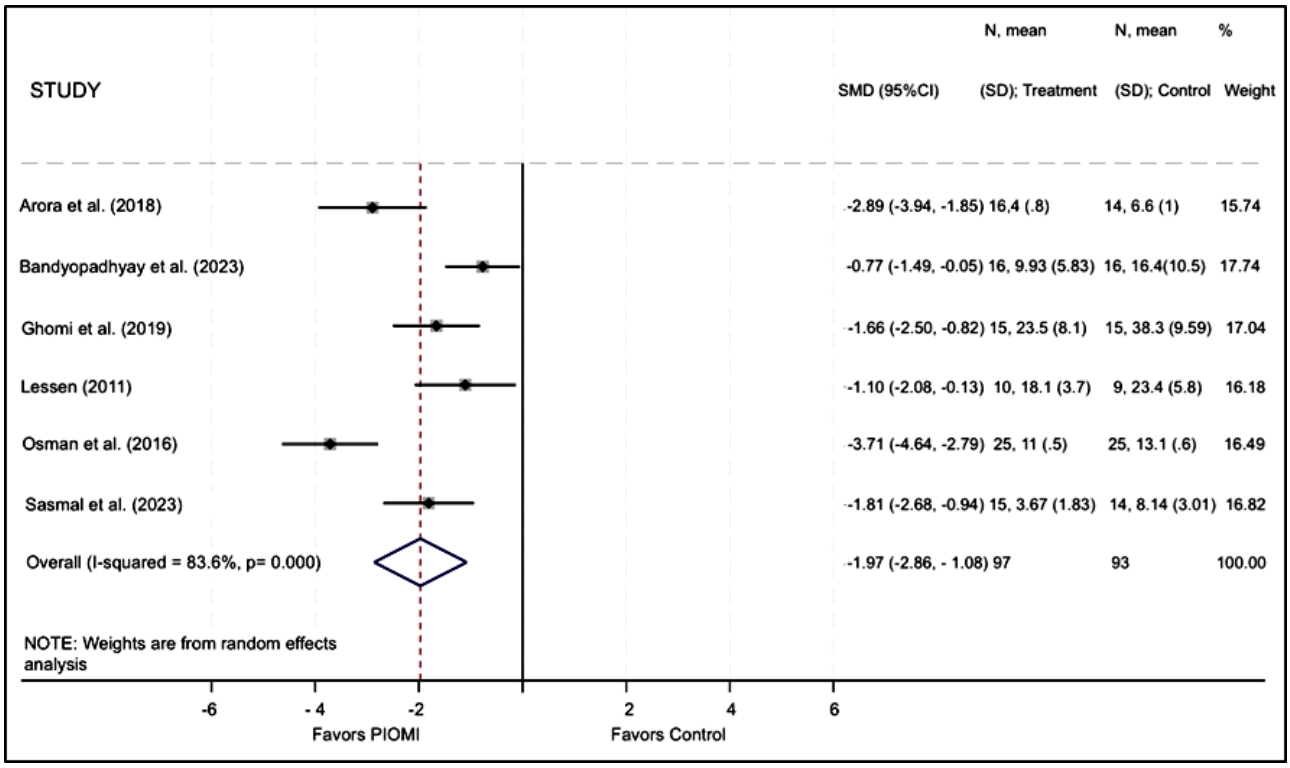


Figure 2b. Risk of Bias Assessment Summary of the Included Studies

Six studies were included in the transition from tube to full oral independent feeding. Figure III shows the pooled standardized mean difference in the transition time to full oral feeding between the PIOMI and the control groups. The random-effects model analysis included 190 participants, 97 in the PIOMI group and 93 in the control group. The forest plot shows that the transition time was 1.97 days shorter in the PIOMI group (SMD=–1.97, z=4.33, p=0.001, 95% CI = –2.86 to –1.08) than in the control group.

Figure 3. Pooled Standardized Mean Difference in the Transition Time to Full Oral Feeding between the PIOMI Group and the Control Group



However, there was a significant high between-study variation among the included studies
(χ^2=30.50, p=0.001; I^2=83.60%; τ^2=1.03).

To identify the possible source of heterogeneity in the feeding transition, subgroup analyses were conducted according to four groupings: 1. start of measurement of the transition time to full oral feeding, full gavage feeding vs. first oral feeding, 2. duration of PIOMI (7 Days vs. >7 Days), 3. Frequency of PIOMI (7 Times vs. >7 Times), and 4. age of gestation. Figures IV to VI demonstrate the forest plot of the subgroup analyses.

The subgroup analysis, according to the start of measurement of transition shown in Figure 4, indicated that the heterogeneity

between the included studies was not significantly different (χ^2=3.68, p=0.005). Among those which measured the transition at the start of full gavage feeding, the random-effects model results showed that those in the PIOMI group reached full independent oral feeding 1.72 days shorter than the control group (SMD=–1.72, z=2.91, p=0.004, 95% CI = –2.89 to –0.56). The heterogeneity, however, remained significantly substantial (χ^2=10.97, p=0.004; I^2=81.80%; τ^2=0.86). Similarly, studies that measured transition at the start of the first oral feeding resulted 2.21-day shorter in achieving full independent oral feeding in the PIOMI group compared to control group (SMD=–2.21, z=2.89, p=0.004, 95% CI = –3.71 to –0.71) but still with significant high heterogeneity (χ^2=15.85, p=0.001; I^2=87.40%; τ^2=1.54).

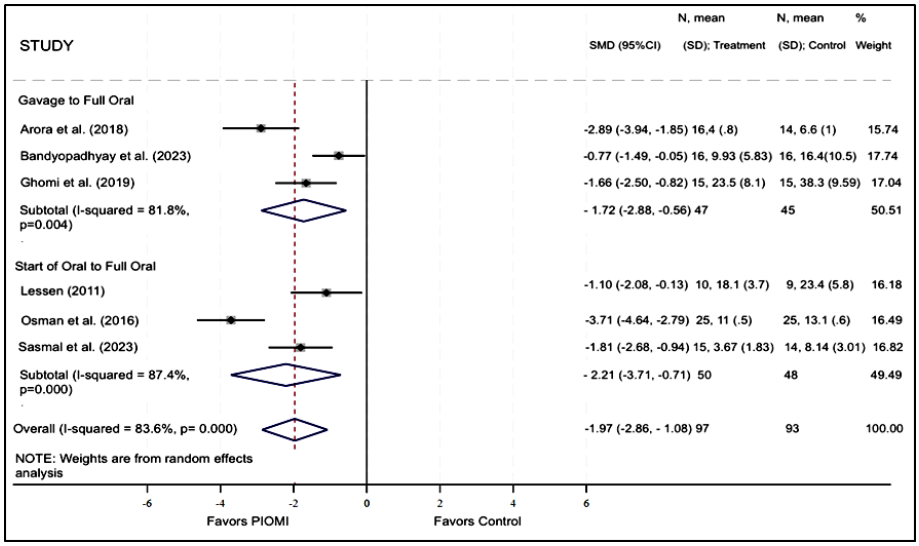


Figure 4. Pooled Standardized Mean Difference in the Transition Time to Full Oral Feeding between the PIOMI Group and the Control Group according to the Start of Measurement of the Transition Time

Figure 5A shows the subgroup analyses according to the duration of PIOMI and indicated that the heterogeneity in the two subgroups were significantly different (χ^2=10.89, p=0.001), with most heterogeneity coming from the 7 days duration subgroup. Studies which had PIOMI for 7 days, showed that the transition was 2.38-day shorter in the PIOMI group (SMD=–2.38, z=4.10, p=0.001, 95% CI = –3.53 to –1.24), and the estimated heterogeneity was significantly high (χ^2=17.10, p=0.001; I^2=82.50%; τ^2=1.11). Similarly, results for the articles which had PIOMI for >7 days indicated that the transition was 1.19-day shorter in the PIOMI group (SMD=–1.19, z=2.66, p=0.008, 95% CI = –2.06 to –0.31). This subgroup did not have a significant substantial heterogeneity (χ^2=2.51, p=0.113; I^2=60.20%; τ^2=0.24).

The subgroup analysis according to the frequency of PIOMI (Figure 5B) showed that

that the estimated heterogeneity was statistically significant between the two subgroups (χ^2=4.75, p=0.029), and most of the heterogeneity was detected in PIOMI administered for the seven times subgroup. The results of the studies with PIOMI performed seven times indicated that the transition time between the PIOMI and control groups was not significantly different (SMD=–2.41, z=1.85, p=0.064, 95% CI = –4.97 to 0.14), and with high heterogeneity (χ^2=14.47, p=0.001; I^2=93.10%; τ^2=3.17). On the other hand, the subgroup analysis with PIOMI administered >7 times showed that the transition time in the PIOMI group was significantly 1.73 days shorter (SMD=–1.73, z=4.07, p=0.001, 95% CI = –2.56 to –0.90) than the control group. The subgroup analysis, however, still had a significantly substantial heterogeneity (χ^2=11.29, p=0.010; I^2=73.40%; τ^2=0.53).

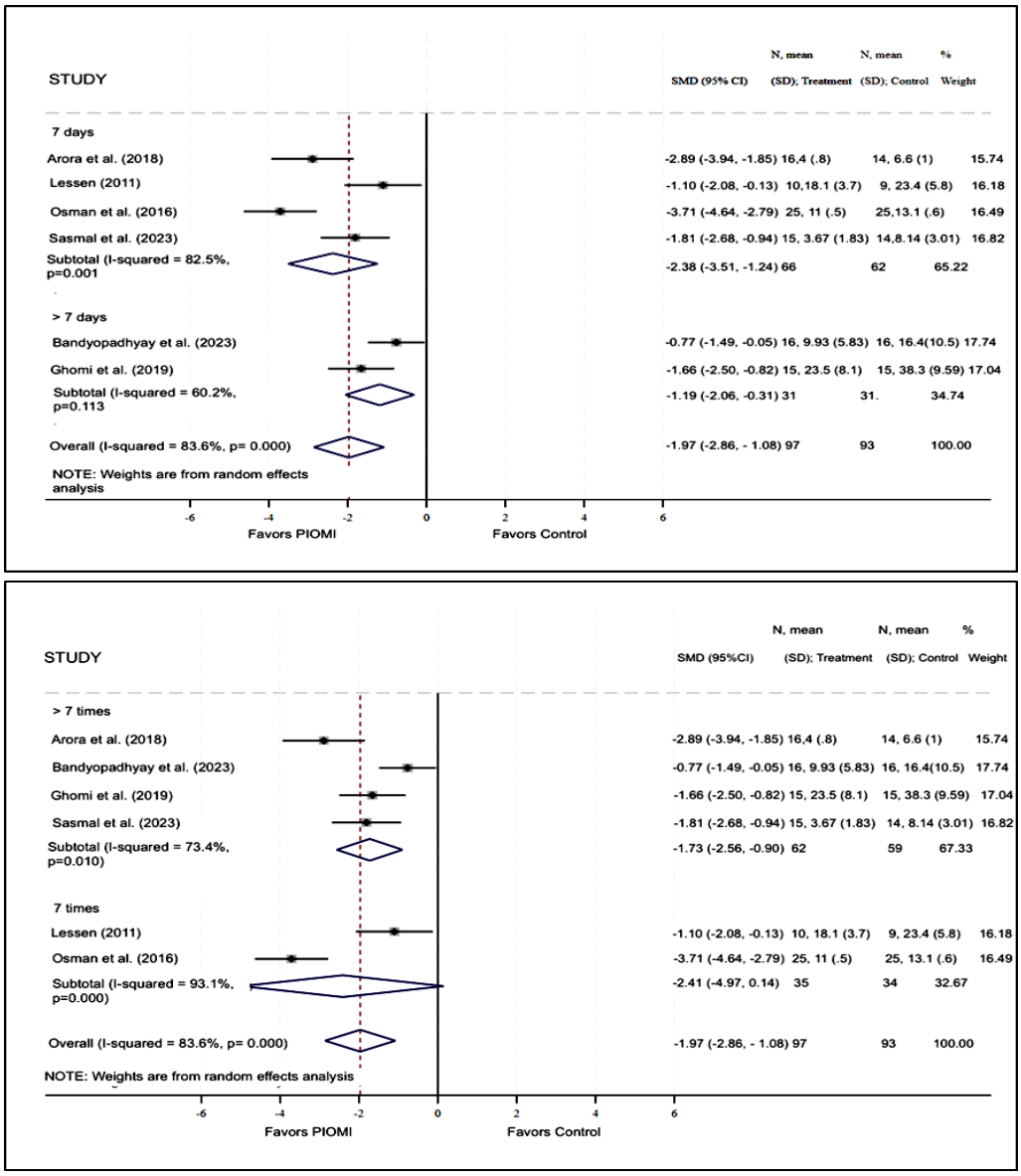


Figure 5. Pooled Standardized Mean Difference in the Transition Time to Full Oral Feeding between the PIOMI Group and the Control Group according to (A) the Duration and (B) the Frequency of PIOMI

The subgroup analysis according to age of

The subgroup analysis according to age of gestation (Figure 6) shows that the heterogeneity between the two groups were significant (χ^2=19.33, p=0.001), and most of the between-study variance was detected in the 30 to 32 weeks of gestation group (76.90%). In the 28 to 29 week of gestation group, the transition time was 1.15-day shorter in the PIOMI group (SMD=–1.15, z=4.17, p=0.001, 95% CI = –1.69 to –0.61) than in the control group, and the heterogeneity in this subgroup was not substantial (χ^2=2.52, p=0.284; I^2=20.60%; τ^2=0.05). The transition time in the subgroup of 30 to 32 weeks of gestation was 2.80-days shorter (SMD=–2.80, z=4.82, p=0.001, 95% CI = –3.93 to –1.66) in the PIOMI group than in the control group, but with substantial heterogeneity (χ^2=8.66, p=0.013; I^2=76.90%; τ^2=0.77).

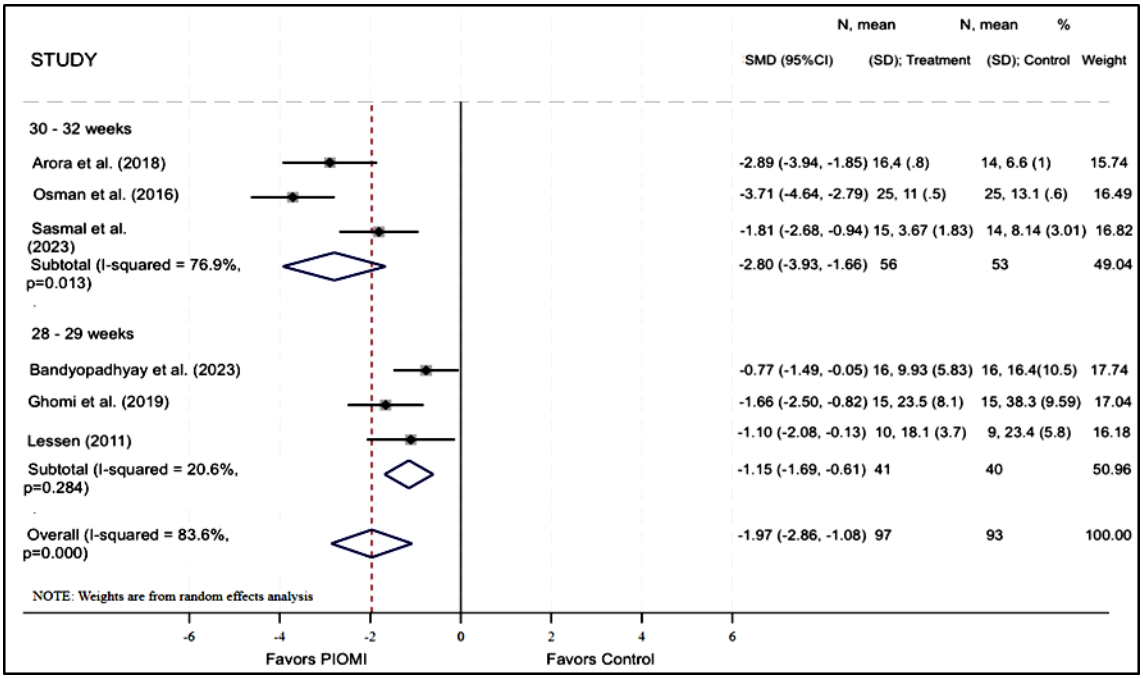


Figure 6. Pooled Standardized Mean Difference in the Age of Gestation between the PIOMI Group and the Control

Pooled Estimate for the Standardized Mean Difference in Weight Gain

The pooled standardized mean difference in weight gain between the PIOMI and the control groups is presented in Figure 7. Fixed-effects model analysis of two studies with 79 participants, 40 in the PIOMI group and 39 in the control group, showed that the weight gain in the PIOMI group was 810 grams significantly higher (SMD=0.81, z=3.45, p=0.001, 95% CI = 0.35 to 1.27) than in the control group. Analyses also indicated that there was no heterogeneity among the included studies (χ^2=0.03, p=0.871; I^2=0.00%, τ^2=0.00).

Pooled Estimate for the Standardized Mean Difference in the Duration of Hospital Stay

Figure 8 depicts the pooled standardized mean difference in the duration of hospital stay between the two groups. There was good homogeneity in the 8 studies that included 290 participants, 147 in the PIOMI group and 143 in the control group (χ^2=5.77, p=0.567; I^2=0.00%; τ^2=0.00); Fixed-effects model analysis showed that the duration of hospital stay was 0.47-day significantly shorter in the PIOMI group (SMD=–0.47, z=3.93, p=0.001, 95% CI = –0.71 to –0.24) compared to the control group.

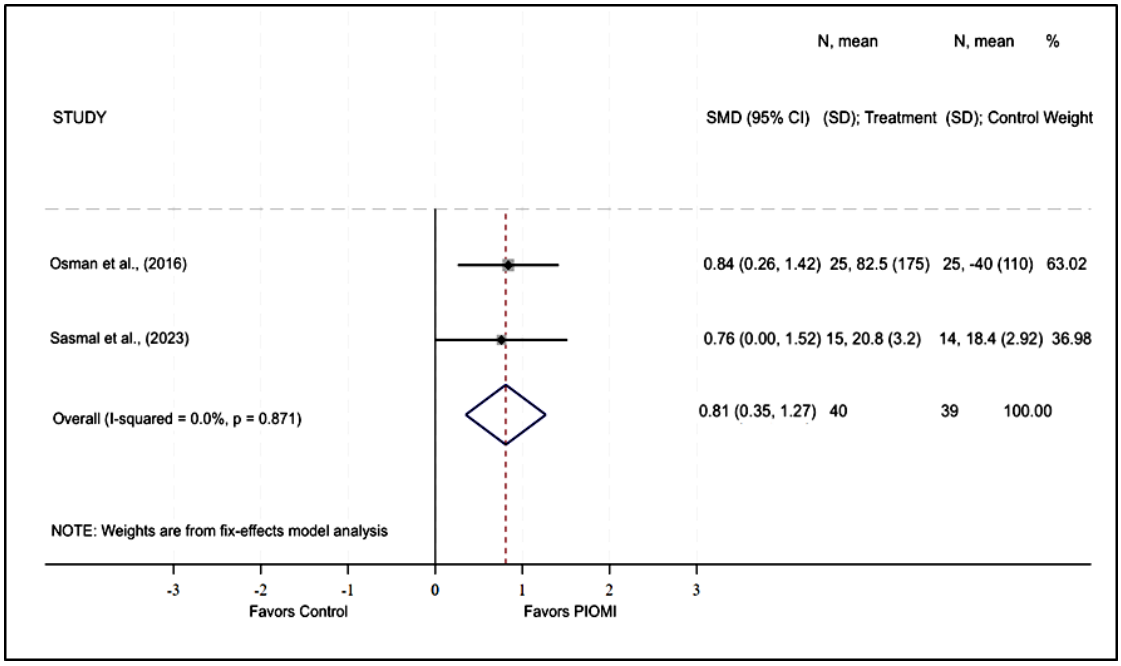


Figure 7. Pooled Standardized Mean Difference in the Weight Gain between the PIOMI Group and the Control Group

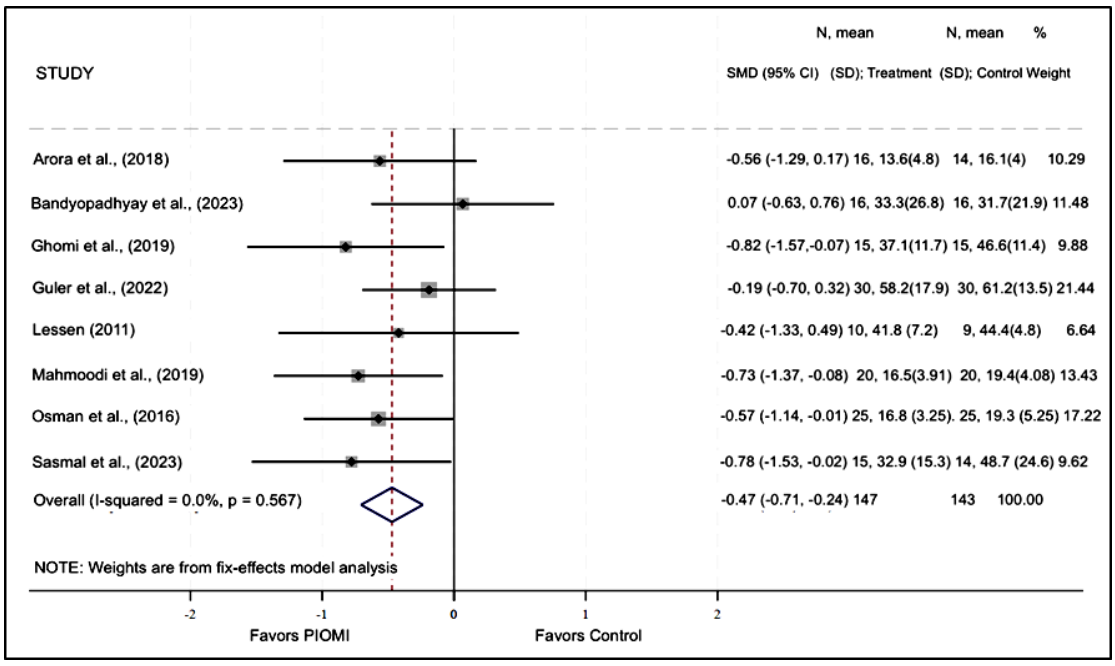


Figure 8. Pooled Standardized Mean Difference in the Duration of Hospital Stay between the PIOMI Group and the Control

Publication Bias

The graphical analyses of publication bias using contour-enhanced funnel plots are shown in Figure 9. These plots show funnel asymmetry for the transition time to full oral feeding and weight gain. The formal statistical tests for publication bias using Begg's adjusted rank correlation test and Egger's regression asymmetry test showed that the likelihood of publication bias for the outcomes of transition to oral feeding and weight gain (p>0.05) were unlikely.

Table 3. Statistical Assessment of Publication Bias of the Different Study Outcomes

Outcomes	Number of Studies	Begg's Test		Egger's Test	
		Estimate	p-value (Two-Tailed)	Bias Estimate	p-value (Two-Tailed)
Transition Time to Full Oral Feeding (Days)	6 Studies	1.13	0.26	–11.82	0.176
Weight Gain (Grams)	2 Studies	0.00	1.00	–0.87	1.000
Duration of Hospital Stay (Days)	8 Studies	0.37	0.71	–1.59	0.436
*Significant at 0.05 †Significant at 0.01					

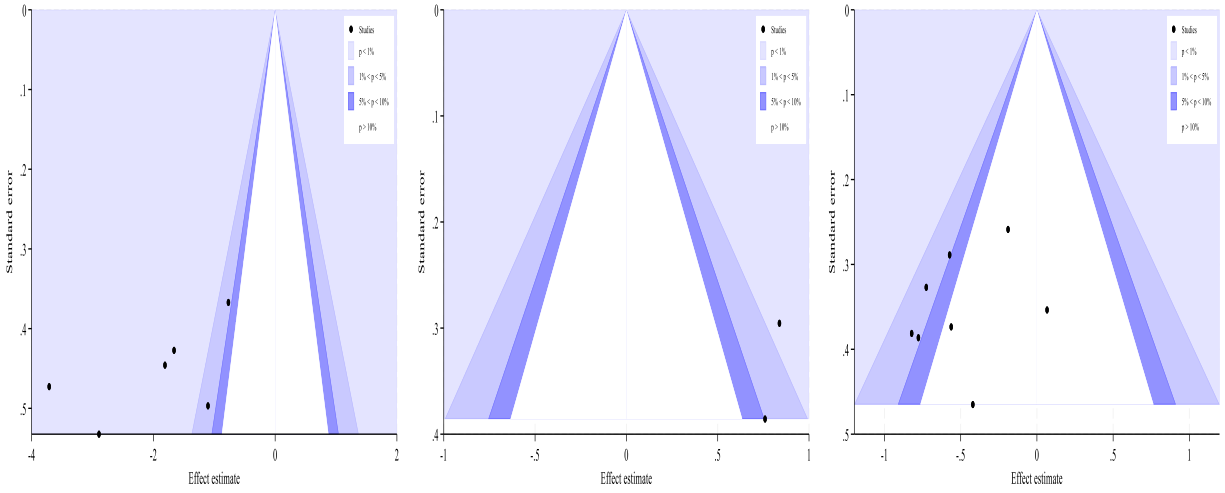


Figure 9. Contour-Enhanced Funnel Plots for the Analysis of Publication Bias for the Pooled Estimates of the Transition Time to Full Oral Feeding (Left Plot), Weight Gain (Middle Plot), and Duration of Hospital Stay (Right Plot) between the PIOMI Group and the Control Group

DISCUSSION

The survival of preterm infants has dramatically improved with medical innovation. In line with this, NICU's best practices should also parallel these developments to minimize long-term complications associated with prematurity.

Independent feeding is the most common barrier to discharge and is a significant factor for prolonged hospitalization.(5) Randomized controlled trials and meta-analysis studies on various oral motor interventions among preterm infants have shown benefits in transitioning to full oral feeding and length of hospital stay. (9,8)

The study was conducted to determine if PIOMI as an oral motor intervention among preterm infants born 32 weeks gestational age or less improves transition to full oral feeding, length of hospital stay, and weight gain. We excluded articles that involved preterm infants more than 32 weeks of gestational age and employed other multiple oral motor techniques. PIOMI was chosen over the other OMS because it requires less time to administer and is tolerated by preterm infants as early as 29 weeks without an unfavorable response.(9) It also has a standardized training method, published intervention fidelity (27), and can be administered by non-professionals comparably to professionals (11). The meta-analysis by Gonzalez et al. specified that PIOMI may be the best intervention for improving oral motor function in preterm infants among the oral motor interventions. (28) In contrast to the meta-analysis done by Jyoti et al. on PIOMI (29), preterm infants over 32 weeks of gestation were excluded to minimize the bias associated with the maturation of the suck-swallow-breathing reflex with increasing gestational age. No reviews on the effect of PIOMI among preterm infants 32 weeks gestational age or less have been found to date.

The Cochrane risk of bias was used to assess the methodological quality of the eight studies. Performance bias is about 40% due to the lack of blinding of participants and personnel. The lack of blinding of the participants cannot affect the results because the target population was preterm infants. Most of the studies involved the primary investigator administering the PIOMI. Since the outcomes are objective measures and assessors were blinded by the allocation, the non-blinding of the primary investigator may not have significantly affected the results. There is almost a 60% unclear risk of reporting bias, specifically for the outcome of weight gain, where only two studies reported the numerical values. The rest of the parameters have a low-risk bias.

Six studies included for the feeding transition showed that the PIOMI group significantly decreased transitioning to full feeding. However, there was high heterogeneity among the studies; thus, four subgroup analyses were performed based on the start of transition (full gavage vs. first oral), duration and frequency of PIOMI administration, and age of gestation at birth. Figures 3-5 show that the timing of the start of the transition and the duration and frequency of PIOMI have high heterogeneity. Figure 6 showed non-substantial heterogeneity among those 28 to 29 weeks of gestation. The results suggest that neither the duration nor frequency of PIOMI administration affected the transition to full oral feeding. The same findings were reported by Chen et al. in which there was a significant reduction in the transition to oral feeding but with high heterogeneity even in the subgroup analyses based on age, country, and duration of intervention.(8) The different practices in oral feeding among preterm infants in the neonatal intensive care units may have contributed to the high heterogeneity in the feeding transition. However, this factor cannot be examined since only one study described the feeding progression protocol (9), and the others stated that no standard feeding protocol was used and oral feeding initiation and progression were based on the discretion of the attending neonatologist. Future studies are needed to investigate the effect of PIOMI among preterm infants using a standard oral feeding protocol for a more objective assessment of feeding initiation and progression.

Five studies reported weight gain as one of the outcomes, but only 2 reported the numerical values (27,28) and the other studies only stated a significant weight gain in the PIOMI group . The pooled analysis showed a significant weight gain in the PIOMI group. The same findings in weight gain were observed by Chen et al. and Greene et al. (8,20), while other studies did not show significant results (9,29).

The length of hospital stay showed a significant decrease in the PIOMI group and homogeneity among the eight studies. Other meta-analyses reported similar results with homogeneity among the included studies. (8,-10, 20)

Three studies showed that PIOMI significantly improved the feeding readiness scale. (14,28,30) Only one study reported adverse events such as sepsis, apnea, and desaturation, but no differences were found between the control and PIOMI groups. (21)

Our findings can guide in implementing an oral feeding protocol in preterm infants, especially in extremely and very preterm infants, in the neonatal intensive care units. The study only included research written in English and with small sample sizes; thus, may affect the credibility of the pooled analysis.

Conclusion

The study suggests that PIOMI can reduce the transition to independent feeding and hospital stay and increase weight gain among preterm infants 32 weeks of gestation or less. However, careful consideration of its clinical use in neonatal intensive care units is warranted due to study variations.

Recommendation

Future well-designed randomized clinical trials on PIOMI may include standard oral feeding protocol in the initiation and progression of feeding to minimize methodological limitations or variations in the results. Studies on the impact of PIOMI on breastfeeding at discharge and at six months of life and long-term neuro-developmental outcomes, as well as the adverse events of PIOMI administration in the extremely and very preterm infants, are also recommended.

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