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First Round

Reviewer comments

We appreciate your help. The following is our detailed response to expert opinions. We have also modified the full text, with the main changes highlighted in red font. Thank you for your continuous help and guidance.

Reviewer A

Thank you for addressing this interesting topic. As the last systematic review has been updated in 2011, it seems reasonable to conduct a new systematic review with latest studies.
However, I have some doubts about the methods and concluded to reject for the publication. I have not reviewed the results and discussions.
My concerns are as below.

Comment 1:Search strategy needs to be better mentioned. Repeatable keywords and search methods for each database are recommended to be mentioned.
Reply 1:Thanks to the expert for this suggestion. We have added detailed search methods in the text. And because five months had passed since the last database search, we researched each database until October 2023 using the modified search method.
Changes in the text: Please see Page 5, line 123 to133. The modifications in the text are as follows:
Search strategy
We searched PubMed, Medline, Embase, Web of Science, Cochrane Central Register of Controlled Trials databases, Wanfang, and CNKI databases from establishing the database to October 2023. The search strategy was performed using the medical subject headings (MeSH)
and keywords, which included four groups:(1) “Neonate” or “Newborn*” or “Infant” or “Low-birth-weight Infant” or “Low birth weight” or “Premature ” or “Very low birth weight” or “Preemie*” or “Premie*” ; (2)“Incubator*” or “Incubators, infant”; (3)“Infant equipment” or “baby equipment” or “cot” or “cot-nurs*” or “crib*” or “equipment, infant” or “Isolette” or “Heated water-filled mattress”; (4)“Weaning” or “transfer*” or “discontinue” .We used the
Boolean operator "AND" combination with four group terms in every database to search.
Manual search was also conducted as a complementary method by reviewing the reference lists and prospective citation search for all retrieved studies.

Comment 2:Protocol registry (e.g. Prospero) was not mentioned. It is recommended to register systematic review protocol before conducting the study which ensure that the authors followed the predefined protocol (i.e. not made up as the study goes).
Reply 2: Thanks to the experts for the reminder. Our study was not registered, but our meta-analysis was produced strictly following the systematic review process. We also wrote a limitation in the Limitation section: the current study was not registered, and there may be a small bias, but we still strictly followed the steps of the systematic review.
Changes in the text: Please see Page 12, line 303 to 304.

Comment 3: The authors needs to explain why they included non-randomised trials for this systematic review. This may affect the study quality.
Reply 3: We understand the experts' questions. Due to the small number of relevant randomized controlled trials, non-randomized controlled trials were added to increase the pooled sample size. After

the final screening, only one non-randomized controlled trial study that met the inclusion criteria was included in this meta analysis. However, in this revision, we used the Minors (Methodological Index For Non-randomized Studies) scale to evaluate literature quality, which resulted in a lower grade. After discussion and comprehensive consideration by the research team, this non-randomized controlled trial study was deleted, and the study results were reorganized. The entire text has been significantly revised.
Changes in the text: Please see main Page 6-10, line 160 to 242.

Comment 4: I wondered why the authors did not include temperature instability (hypothermia episode) as an outcome considering the main feature of the incubator is temperature control.
Reply 4: Thank you for the expert's question. We have considered this issue in the early stage, but there are few reports on the indicator of temperature stability in the included RCTs, and only one RCT report details temperature stability indicators. The included RCTs all have documented incubator weaning steps. Once hypothermia occurs in premature infants after being out of the incubator within 72 hours, an additional wrap was added to the infant, and the temperature was checked afterward. If the infant's temperature cannot be maintained≥36.5℃, they will be returned to the incubator. Therefore, we chose the number of infants returned to the infant to measure temperature stability. Based on expert advice, we have added two research reports on the indicator for the proportion of low temperature during 72 hours post-transfer as one of the primary outcomes. The study reports no statistically significant difference in the proportion of infants having low temperature during 72 hours post-transfer[risk ratio 0.6 (95% CI 0.36 to 1.01) in the two groups.
Changes in the text:Please see main Page 9, line 205 to 212.The modifications in the text are as follows:

Proportion of low temperature during 72 hours post-transfer

Two studies reported that proportion of infants having at least one episode of low temperature during 72 hours post-transfer, and there was no heterogeneity between studies: Chi^2=0.68, df=1(P=0.41), I^2=0%) ;therefore, we used fixed-effect model.The result showed no significant difference (P=0.05) in an effect value of risk ratio=0.60, 95% CI[0.36,1.01].

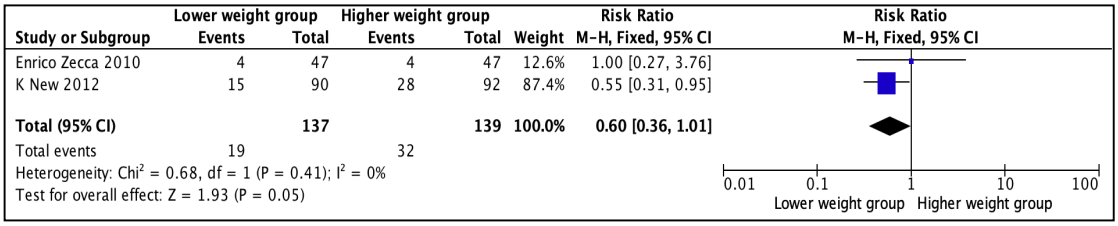

Figure 5. Forest plot for proportion of low temperature during 72 hours post-transfer

Reviewer B

The review discusses our current knowledge of optimal weight for transfer of premature infants in an incubator to an open crib. The authors found that transferring premature to an open crib around 1600 to 1700 grams is safe and beneficial.

Although the topic is not novel, more than 10 years have passed since the similar review, it would be worthwhile to revise the evidence of the advancing neonatal care. The manuscript is well written and I have only minor comments.

Comment 1:As the authors have commented, the number of papers is small and there seems to be little interest in this area of research. In this sense, were there any issues that have been identified by this study? What future research are needed?
Reply 1: Thanks to the experts for recognition and reminder of this study. We have added relevant content to the text.
Changes in the text:Please see Page 12-13, line 305 to 316.The modifications in the text are as follows:
In conclusion, our results indicate that it is feasible and safe for preterm infants in stable condition to be transferred to open cribs when their weight is 1600g without adverse clinical outcomes, which can increase weight gain velocity during hospitalization.Future research hopes to conduct more randomized controlled trials and expand the sample size; secondly, detailed records of skin-to-skin contact, breastfeeding, or nutritional intake of premature infants in cribs, e.g., in addition, the outcome indicators included in the study should be comprehensive, the definition of indicators should be clear; increase discharge indicator monitoring, and extend the follow-up time as long as possible to track and register various long-term indicators of premature infants, this includes not only increases in weight, length and head circumference but also measures such as duration of breastfeeding and neurodevelopmental outcomes.

Comment 2: Page 13, first paragraph, line 8: If the authors aim were "To validate whether 1700g can serve as a suitable weaning weight standard", this should also be written in the abstract and the introduction.
Reply 2:Thanks to the experts for the reminder. After careful consideration, based on the definition of the weight range of the two groups in the RCTs included, this study is to validate whether 1600g can serve as a suitable weaning weight standard rather than 1700g. We have added our aims in the abstract and introduction and made changes elsewhere in the text.
Changes in the text:Please see main Page 1, line 19 to 20;Page 4, line 100 to 103.

Comment 3: Were there any difference in the treatment level of the recruited patients?
Reply 3:Thanks to the experts for the questions. The premature infants included in the study were all in medically stable condition (normal temperature, no apnea, no oxygen requirement, no sepsis, and no phototherapy requirement, etc.).And the research sites are all in the neonatal unit, which has the conditions to treat newborns. Therefore,we think there is little difference in the level of treatment.

Reviewer C
Editorial note: Reviewer C has made some amendments in the manuscript, please see attached.
Reply :Thank you for your reminder. We have revised the full text according to the revised draft provided by experts.

Comment 1: Overall an interesting review of a topic of debate. Translation needs a significant amount of work and there are several sentences/figures missing.
Reply 1:Thanks to the experts for recognition of this study. Thank you very much for your detailed review of the article. We have revised the full text according to your revision comments.

Second Round

Editorial Comments (Please do not delete this section. Editorial comments should also be replied point by point)

Reply:We appreciate your help. The following is our detailed response. We have also modified the full text, highlighting the main changes in blue font. Thank you for your continuous help and guidance.

Comment 1: In the title, it is recommended to explicitly state the specific lower weight limit, "1600g," for infants to enhance clarity for readers.
Reply 1:Thanks to the expert for this suggestion.We changed the title to "Clinical effectiveness and safety of 1600g as a standard weaning weight for transferring premature infants to an open crib: systematic review and meta-analysis"
Changes in the text: Please see Page 1, line 1 to 3.

Comment 2: In the abstract-background section, elucidate the rationale behind the authors' emphasis on the 1600g threshold as an appropriate weaning weight standard.
Reply 2:Thanks to the experts for the reminder.We have added relevant content.
Changes in the text: Please see Page 1, line18 to 23.The modifications in the text are as follows:

Most randomized controlled trial studies use 1600g as the initial weaning weight, and there were differences in outcome indicators and results between studies. Therefore, this meta-analysis validated whether 1600g can be a suitable weaning weight standard and evaluated its clinical effectiveness in providing healthcare professionals with a reference value for relevant decision-making.

Comment 3: The phrase "Intervention measures: the premature infants who were transferred from incubators to cribs" is inappropriate, considering that both intervention and control groups were transitioned to an open cot. The authors may consider specifying "infants weighing approximately 1600g."
Reply 3:Thanks to the experts for the reminder.We have modified the relevant content.
Changes in the text: Please see Page 4, line110 to 113.The modifications in the text are as follows:

Intervention measures: transferring of preterm infants from an incubator to an open cot at a lower body weight compared with higher body weight. “Lower” is defined as transfer reaching 1600-1700g, and “higher” is defined as transfer reaching 1700g or more.

Comment 4: The authors did not specify the effect measure employed in the synthesis or presentation of results (e.g., risk ratio, odds ratio).
Reply 4:Thanks to the experts for the reminder.We have added relevant content in the Methods section.
Changes in the text: Please see Page 6, line153 to 157.The modifications in the text are as follows:

Weighted mean difference (WMD) and 95% confidence interval (CI) were used to combine the effect values of the continuous indicators using the inverse variance analysis method. We presented results as a summary risk ratio with 95% confidence intervals for dichotomous data using the Mantel-Haenszel analysis method.

Comment 5: Clearly articulate the criteria for choosing between random-effect and fixed-effects models, along with appropriate references. Additionally, specify whether weighted mean difference or standardized mean difference was utilized.
Reply 5:Thanks to the experts for the reminder.We have added relevant content in the methods section.
Changes in the text: Please see Page 6, line153 to 160.The modifications in the text are as follows:

Weighted mean difference (WMD) and 95% confidence interval (CI) were used to combine the effect values of the continuous indicators using the inverse variance analysis method. We presented results as a summary risk ratio with 95% confidence intervals for dichotomous data using the Mantel-Haenszel analysis method. The I^2 and Chi^2 statistics were used to test for heterogeneities. If $P \leq 0.1$, $I^2 > 50\%$, indicating significant heterogeneity, we used the random-effects model; if $P > 0.1$, $I^2 \leq 50\%$, we used the fixed-effect model for analysis.

Comment 6: Regarding the statement "This study used median, range, and sample size to estimate the mean and standard deviation (18)," consider providing the formula or specific calculation method in the text if available.

Reply 6:Thanks to the expert for this suggestion.We have added formula in the Methods section.

Changes in the text: Please see Page 6, line164 to 165.The modifications in the text are as follows:

This study used median, range, and sample size to estimate the mean and standard deviation (18). For example, if $n>25$, median$\approx$MD and $15<n\leq 70$, $SD\approx\frac{R}{4}$; $n>70$, $SD\approx\frac{R}{6}$, R refer to range.

Comment 7: The sentence "The X2 test was used to test for heterogeneities. If P≤50%, the heterogeneity between the studies was small, and the fixed-effect model was used for analysis. A random effects model was used if P≥50%, indicating significant inter-study heterogeneity" should possibly be "P>0.10" instead of "P≤50%" to accurately reflect the threshold for significance.

Reply 7:Sorry, we expressed it incorrectly. Modifications have been made in the text.

Changes in the text: Please see Page 6, line158 to 161.The modifications in the text are as follows:

The I^2 and Chi^2 statistics were used to test for heterogeneities. If $P \leq 0.1$, $I^2 > 50\%$, indicating significant heterogeneity, we used the random-effects model; if $P > 0.1$, $I^2 \leq 50\%$, we used the fixed-effect model for analysis.

Comment 8: In the methods section, describe any techniques employed to tabulate or visually present results of individual studies and syntheses, such as the forest plot.

Reply 8:Thanks to the experts for the reminder.We have added relevant content in the Statistical analysis.

Changes in the text:Please see Page 6, line153 to 161.The modifications in the text are as follows:

A meta-analysis was performed using RevMan 5.4 software. Weighted mean difference (WMD) and 95% confidence interval (CI) were used to combine the effect values of the continuous indicators using the inverse variance analysis method. We presented results as a summary risk ratio with 95% confidence intervals for dichotomous data using the Mantel-Haenszel analysis method. The I^2 and Chi^2 statistics were used to test for heterogeneities. If $P \leq 0.1$, $I^2 > 50\%$, indicating significant heterogeneity, we used the random-effects model; if $P > 0.1$, $I^2 \leq 50\%$, we used the fixed-effect model for analysis.Forest plot showing the results of pooled effect value and heterogeneity.

Comment 9: When stating "4 literatures were finally included," it would be advantageous to include the reference numbers of the studies for better readability and verification, both in the text and tables.

Reply 9:Thanks to the experts for the reminder.We have indexed reference numbers for included studies appearing in the full text.

Changes in the text:Please see the full text.

Comment 10:The authors should associate each article with its specific reference in each result section so that the reader can at any time double-check and easily navigate through the results. For example, “Length of stay (LOS) was reported in three studies”.

Reply 10:Thanks to the experts for the reminder.We have marked the literature related to each indicator in result section.

Changes in the text:Please see Page 9-11, line184 to 222.

Comment 11:In Table 1, include the last names of the authors of the included studies. Provide more comprehensive details in the table, such as gender, the weaning protocol (including the procedure for transferring infants), and measures taken after transitioning to an open crib.
Reply 11:Thanks to the expert for this suggestion.We supplemented the characteristics of the included literature, including author, year, setting, study group and sample size, inclusion and exclusion criteria, weaning procedure, meta-analysis outcome indicators.
Changes in the text: Please see Page 8, Table 1.

Comment 12: In Figure 1, if a "study" comprises multiple reports, ensure that the number in the box labelled "studies included in review" is not zero.
Reply 12: Thanks to the experts for the reminder.In the flow chart, we modified it to “Studies included in Meta-analysis (n=4)”
Changes in the text:Please see Page 7, Figure 1.