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Comparative Efficacy of Nutritional Supplements for the Prevention of Respiratory Tract Infections in Children: A Systematic Review and Network Meta-Analysis

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Abstract
Background: This study employs a network meta-analysis to compare the effectiveness of multiple nutritional supplements in preventing childhood respiratory infections.
Methods: Systematically searched PubMed, Embase, Cochrane Library, Web of Science from their inception to 1 September 2025. Included studies were randomized controlled trials evaluating nutritional supplements for preventing respiratory infections in children under 18 years old. The primary outcome was the incidence of respiratory infections. Traditional meta-analysis and Bayesian network meta-analysis were conducted using random-effects models to calculate odds ratios (OR) and their 95% credible intervals (CrI). The cumulative sorted rank curve area (SUCRA) was used to rank the efficacy of each intervention. The Cochrane risk of bias tool was applied to assess the quality of included studies.
Results: A total of 19 articles involving 11,576 children were included. Direct comparison meta-analysis showed no statistically significant differences between low-dose vitamin D, vitamin A, vitamin A combined with zinc, zinc, and placebo. Network meta-analysis formed a closed-loop network, and local inconsistency tests revealed no significant differences in either direct or indirect comparisons. The league table indicated a trend toward reduced risk of childhood respiratory infections with high-dose vitamin D (HVD) compared to placebo [OR=0.76, 95% CrI (0.61, 0.94)]. The cumulative ordered probability (SUCRA) for each intervention was: HVD (82.44%) > LVD (64.81%) > Iron (57.2%) > VA_Zinc (54.56%) > Probiotics (52.49%) > Zinc (42.5%) > VA (23.31%).
Conclusion: This study indicates that among the various nutritional interventions included, HVD demonstrated the greatest potential effect in preventing respiratory infections in children. Direct comparison meta-analyses revealed no statistically significant differences between LVD, VA, VA_Zinc, zinc, and placebo. A network meta-analysis further supported these findings, with league table and SUCRA rankings indicating HVD may offer the optimal efficacy among all interventions.
Keywords: Children; Respiratory tract infections; Nutritional supplements; Prevention; Network meta-analysis

Background

Respiratory tract infections rank among the most common infectious diseases affecting children globally and constitute a primary cause of outpatient visits,

hospitalizations, and antibiotic use(1). Children, particularly those under five years of age, are more susceptible to both upper and lower respiratory tract infections due to their immature immune systems, relatively narrow airway anatomy, and frequent exposure in group settings such as childcare facilities(2, 3). Epidemiological studies indicate that preschool-aged children may experience multiple respiratory infection episodes annually. Recurrent infections not only disrupt sleep, appetite, and daily activities but may also have long-term effects on growth, development, and lung function(4). Furthermore, severe lower respiratory infections remain a significant cause of childhood mortality in some low- and middle-income countries(5). The combination of high incidence and recurrent nature makes respiratory infections a critical public health issue requiring urgent attention globally.

Current prevention and control measures for pediatric respiratory infections primarily involve comprehensive interventions such as vaccination, improving living environments, reducing tobacco exposure, enhancing hand hygiene, and promoting balanced diets(6). However, specific vaccines remain widely unavailable for common respiratory viruses like rhinovirus and respiratory syncytial virus. Antibiotics are only effective against bacterial infections and can easily lead to drug resistance, making reliance on treatment alone insufficient to fundamentally reduce the disease burden(7, 8). Against this backdrop, enhancing the body's innate immune defenses and improving resistance to pathogens has emerged as a critical research direction for preventing childhood respiratory infections. Nutritional status is closely linked to immune function, and nutritional intervention—as a relatively safe, cost-effective, and sustainable strategy—is gaining increasing attention in the field of childhood infection prevention(9, 10).

Multiple nutrients have been demonstrated to play pivotal roles in immune regulation. Vitamin D not only participates in calcium and phosphorus metabolism but also holds a significant position in respiratory mucosal immune defense by modulating monocyte and macrophage function, inducing antimicrobial peptide production, and regulating inflammatory responses(11). Low serum vitamin D levels have been observed to correlate with increased susceptibility to respiratory infections. Zinc, an essential trace element for immune cell development and function, impairs T-cell function and antioxidant capacity when deficient, thereby heightening infection susceptibility(12, 13). Vitamin A helps maintain respiratory epithelial integrity and modulates mucosal immune responses; vitamin C, as an antioxidant, participates in regulating multiple immune cell functions(14). Beyond individual vitamins or trace elements, probiotics have emerged as a research focus in recent years. Probiotics exert indirect protective effects against respiratory infections by modulating gut microbiota composition, enhancing intestinal barrier function, and regulating the “gut-lung axis” immune response(15). Other nutrients such as omega-3 fatty acids, selenium, iron, and various multivitamin supplements have also been proposed to offer potential benefits in infection prevention through anti-inflammatory or immunomodulatory mechanisms (16). Some studies(17) demonstrate that

certain supplements significantly reduce infection incidence or shorten illness duration, while others fail to observe clear benefits. Furthermore, most trials compared only a single supplement against placebo or standard care, lacking direct comparative studies between different nutritional supplements(18). This fragmented evidence structure makes it challenging for clinicians and public health policymakers to determine which specific nutritional interventions among the many available options may offer superior advantages.

Therefore, it is necessary to comprehensively synthesize existing randomized controlled trial evidence through systematic reviews and network meta-analyses to compare the relative efficacy and safety of different nutritional supplements in preventing childhood respiratory infections. This study aims to address the following key questions: Among common nutritional supplements, which interventions may be more effective in reducing the incidence of childhood respiratory infections? What is the relative ranking among different supplements? What is the quality and consistency of the existing evidence? A systematic analysis of these questions will provide clearer evidence-based guidance for nutritional prevention strategies against childhood respiratory infections and direct the design of future high-quality clinical trials.

Methods

The systemic review was supported by the online PROSPERO international prospective register of systemic reviews(19) of the National Institute for Health Research (CRD420251176282).

Literature retrieval

Search PubMed, Embase, Cochrane Library, and Web of Science from the inception of each database to 1 September 2025. The search employed a combination of subject headings and free-text terms: “children,” “pediatric,” “respiratory tract infection,” “upper respiratory infection,” “lower respiratory infection,” “common cold,” “influenza,” “pneumonia,” “nutritional supplement,” “vitamin,” “probiotics,” and “omega-3 fatty acids.” Search strategies were tailored to each database's characteristics. Additionally, reference lists of included studies were manually searched to identify potentially overlooked research.

Criteria for inclusion and exclusion

Inclusion Criteria

(1) Study Population: Children or adolescents aged <18 years.
(2) Study Type: Randomized controlled trials.
(3) Intervention: Any single or combined nutritional supplement for preventing respiratory tract infections.
(4) Control: Placebo, sham control, or usual care.
(5) Outcomes: respiratory tract infections.

Exclusion Criteria

(1) Non-randomized controlled studies, observational studies, reviews, conference abstracts, or animal studies.
(2) Studies involving adults or including children but lacking separately

extractable pediatric data.
(3) Interventions comprising drugs, vaccines, or non-nutritional immune enhancers.
(4) Studies lacking data sufficient for effect size calculation.

Data Extraction

Two researchers independently screened the literature. Initial screening was based on titles and abstracts, followed by full-text review for final inclusion decisions. Disagreements were resolved through discussion or adjudication by a third researcher. A pre-designed data extraction form was used to collect information including: first author, publication year, country, sample size, male-to-female ratio, age range of children, type and dose of intervention, and outcome measures. Missing data were attempted to be obtained by contacting the original authors.

Risk of bias

This study employed the Cochrane-recommended Risk of Bias 2.0 (RoB 2.0) (20) tool to assess the risk of bias in the included randomized controlled trials. This tool systematically evaluates study quality across five domains: risk of bias in the randomization process, risk of bias due to deviation from the intended intervention, risk of bias due to missing outcome data, risk of bias in outcome measurement, and risk of bias due to selective reporting of results. Each domain is rated as “low risk,” “some concern,” or “high risk” based on standardized judgment questions. The overall risk of bias is determined as follows: if any domain is rated high risk, the overall rating is high risk; if no domain is high risk but at least one is rated some concern, the overall rating is some concern; only when all domains are low risk is the overall risk of bias rated low risk. Bias risk assessments were conducted independently by two researchers. Disagreements were resolved through discussion, with a third researcher providing final adjudication when necessary.

Grade assessment

To systematically assess the quality of the evidence included in the study, this research used the GRADING (Grading of Recommendations Assessment, Development, and Evaluation)(21) system to rate the final evidence. The GRADING system is a tool widely used in clinical research that comprehensively evaluates the quality of evidence by assessing factors such as study design, risk of bias, consistency, directness, and precision. According to the GRADING system, evidence quality is divided into four levels: high, moderate, low, and very low.

Data analysis

Statistical analysis first employed traditional pairwise meta-analysis for interventions with direct comparisons, followed by a Bayesian network meta-analysis to simultaneously integrate direct and indirect evidence, comparing the relative efficacy of different nutritional supplements in preventing childhood respiratory infections. Treatment effects were assigned non-informative normal priors, and between-study variance parameters were modeled using weakly informative prior distributions to ensure computational stability and avoid overfitting. All network meta-analyses in

this study were performed using R software (version 4.5.2)(22), with model construction and estimation implemented via the gemtc package (version 1.1-0) and Markov chain Monte Carlo sampling executed using JAGS (Just Another Gibbs Sampler, version 4.3.2). A random-effects model was adopted to account for clinical and methodological heterogeneity across studies. Between-study variance (τ^2) was estimated within the Bayesian framework. Model fit was assessed using the Deviance Information Criterion (DIC), with lower values indicating better fit. For dichotomous outcomes, relative risk was used as the effect measure. All estimates were reported with their 95% credible intervals (CrI). The Bayesian model was run with 4 chains, each completing 50,000 iterations. The first 20,000 iterations served as burn-in to eliminate initialization effects, with the remainder used for posterior estimation. Model convergence was assessed using trace plots and Gelman–Rubin diagnostics(23). Network consistency was assessed using node split analysis; a P value > 0.05 indicated no significant inconsistency between direct and indirect evidence. The relative efficacy ranking of each intervention was estimated using the area under the cumulative ranking curve, with higher values indicating greater potential effectiveness. Heterogeneity between studies was described using variance parameters and the I^2 statistic. Stata software (version 15.0, Stata Corp, College Station, TX, USA) was used to construct traditional funnel plots for assessing publication bias. When ≥10 studies were included, funnel plot symmetry was observed. Additionally, the network command in Stata 15 was employed to construct intervention networks, visually illustrating direct comparative relationships among interventions within included studies. Node size in the network diagram represented the sample size of each intervention study, while line thickness indicated the number of studies comparing two interventions. This clearly presented the network structure and strength of evidence, providing a visual reference for the network meta-analysis. Furthermore, sensitivity analyses based on the rigor of outcome definitions were not feasible due to limited and inconsistently reported data across studies.

Result

Literature search results

As shown in Figure 1, a total of 2,596 articles were retrieved from PubMed (n=741), Embase (n=316), Cochrane Library (n=388), and Web of Science (n=1,151). After removing 449 duplicate records, 2,124 articles were excluded based on title and abstract screening, and 4 articles were excluded after full-text review. Ultimately, 19 randomized controlled trials(24-42) were included.

Key characteristics included in the study

This study included a total of 19 articles involving 11,576 children. The interventions examined were: High doses of vitamin D (HVD) (>5600 IU/week); Low doses of vitamin D (LVD) (≤5600 IU/week); Vitamin A (VA); Zinc; Iron; Probiotics; and VA_Zinc. The specific baseline characteristics are summarized in Table 1. This classification was intended as a pragmatic analytical approach rather than a strict biological threshold.

Risk of bias result

This study employed ROB 2.0 for quality assessment. Results (Figures 2-3) indicate that 2 studies were rated as unclear for their methods of randomization allocation, while 17 studies were rated as low risk. Regarding missing outcome data, 3 studies were rated as unclear for their reporting, while the remaining studies were rated as low risk. Overall, all included studies were of high quality. The certainty of evidence for the primary outcome was assessed using the GRADE framework (Supplementary Material Figure S1). Overall, the certainty ranged from moderate to very low across comparisons. High-dose vitamin D versus placebo was rated as moderate-certainty evidence. Low-dose vitamin D, zinc, and vitamin A versus placebo were rated as low-certainty evidence. The evidence for iron versus placebo was rated as very low certainty.

Effective sample size

Following the framework proposed by Thorlund et al(43). and Lin(44), we quantified the contribution of indirect evidence using the effective sample size (ESS). The results (Supplementary Material Table S1) showed that the gain in information from indirect evidence varied across comparisons. For example, the overall ESS was 2290.7 for HVD versus placebo, 885.9 for LVD versus HVD, and 428.0 for placebo versus iron. After heterogeneity correction, the ESS for placebo versus zinc decreased from 6386.4 to 2008.0, suggesting that the apparent evidence strength for some network estimates was substantially reduced after accounting for between-study heterogeneity.

Consistency test results

Model fit statistics (Supplementary Material Table S2) showed comparable values between the consistency model (DIC = 105.06) and the inconsistency model (DIC = 105.21), indicating no meaningful improvement with the inconsistency model and supporting the assumption of network consistency.

Direct Comparison Meta-analysis

This study employed a direct comparison meta-analysis. The results (Table 2) indicate no statistically significant differences between the following comparisons: LVD vs HVD, VA vs Placebo, VA_Zinc vs Placebo, and Zinc vs Placebo(I^2=76%), the observed heterogeneity may reflect differences in participant age, baseline zinc status, intervention dose and duration, as well as geographic and clinical settings across studies.

Network Meta-analysis

As shown in Figure 4, the study formed a closed network among HVD, LVD, VA; VA_Zinc, Zinc, and placebo. Therefore, a local inconsistency test was applied. Results (Supplementary Material Figure S2) showed that node-splitting analyses did not detect statistically significant inconsistency between direct and indirect comparisons among Placebo vs LVD, VA_Zinc vs Placebo, Zinc vs VA, and Zinc vs VA_Zinc (all P > 0.05), suggesting acceptable local consistency within the network. The league table (Table 3) indicates that compared with placebo, HVD [OR=0.76, 95% CrI (0.61, 0.94)] showed a trend toward reduced risk, with no statistically significant differences among the different interventions. Cumulative probability plots (Figure 5 and

Supplementary Material Table S3) indicate HVD (82.44%) > LVD (64.81%) > Iron (57.2%) > VA_Zinc (54.56%) > Probiotics (52.49%) > Zinc (42.5%) > VA (23.31%).

Convergence of the Bayesian network meta-analysis was satisfactory (Supplementary Material Figures S3–S4). All potential scale reduction factor (PSRF) values approached 1.00, indicating adequate convergence. Trace plots showed good mixing and stationarity of the chains, while density plots were smooth and unimodal, supporting the stability and reliability of the model estimates.

Meta regression

Meta-regression analyses were conducted to explore potential sources of heterogeneity, including age, baseline zinc status, country, and geographic region (Supplementary Table S4). None of these covariates showed a statistically significant association with respiratory tract infections (all $P > 0.05$), suggesting that the observed heterogeneity could not be explained by these study-level factors.

Absolute effect estimates results

Absolute effect estimates are presented in (Supplementary Table S5). Using an assumed baseline risk of 300 per 1000 in the placebo group, high-dose vitamin D was associated with a reduction of 54 cases per 1000 individuals (300 to 246 per 1000). Zinc and probiotics were associated with smaller absolute reductions of 45 and 22 cases per 1000, respectively. In contrast, vitamin A and iron were associated with increases of 68 and 34 cases per 1000, respectively. Low-dose vitamin D and the combination of vitamin A and zinc showed large absolute differences; however, these estimates were accompanied by substantial uncertainty.

Publication bias

This study employed funnel plots to assess publication bias. The results (Supplementary Material Figure S5) indicate that the funnel plots are relatively symmetrical, suggesting a low likelihood of publication bias.

Discussion

This study systematically evaluated the relative efficacy of various nutritional interventions in preventing respiratory infections in children through direct comparisons and network meta-analysis. Results from the direct comparison meta-analysis showed no statistically significant differences between LVD and HVD, VA and placebo, VA_Zinc and placebo, or zinc and placebo. This suggests that the use of low-dose vitamin D, vitamin A, or zinc alone, or the combined intervention of vitamin A and zinc, may have limited efficacy in preventing respiratory infections in children and is unlikely to significantly outperform placebo or standard care. This finding aligns with observations from some previous studies, indicating that the effectiveness of single low-dose interventions in clinical practice may be influenced by multiple factors, including children's baseline nutritional status, dosage, intervention duration, and infection type.

A further network meta-analysis constructed a closed-loop network of interventions including high-dose vitamin D, low-dose vitamin D, vitamin A,

vitamin A plus zinc, zinc, and placebo. Local inconsistency tests confirmed no significant inconsistency between direct and indirect evidence within the network, indicating reliable network analysis results. League table results indicated a trend toward reduced respiratory infection risk with HVD compared to placebo [OR=0.76, 95% CrI (0.61, 0.94)]. Although differences between interventions did not reach statistical significance, this trend suggests HVD may hold potential advantages over LVD or other interventions in preventing childhood respiratory infections. Cumulative probability analysis further supported this conclusion, showing HVD had the highest ranked probability (82.44%), followed by LVD (64.81%), iron (57.2%), VA_Zinc (54.56%), probiotics (52.49%), zinc (42.5%), and VA (23.31%). These findings suggest that high-dose vitamin D may be associated with a relatively higher probability of benefit compared with other interventions; however, these rankings should be interpreted cautiously, as they are based on probabilistic estimates and do not necessarily reflect statistically significant differences between treatments, while the effects of VA or zinc alone are relatively weaker. From a biological mechanism perspective, vitamin D enhances respiratory mucosal defense functions by regulating innate and adaptive immune responses, promoting antimicrobial peptide production, and modulating inflammatory reactions(45, 46). High-dose interventions may more effectively elevate serum vitamin D levels, thereby strengthening immune defenses, which explains the potential advantage demonstrated by HVD in preventing infections(47). The relative ineffectiveness of VA or zinc in this study may be attributed to insufficient dosing, low baseline deficiency rates, or limited intervention duration. Furthermore, while combined VA and zinc supplementation theoretically holds potential for synergistic immune enhancement, current evidence indicates no significant superiority over monotherapy(48, 49). This suggests that practical application requires individualized nutritional status assessment and dose adjustment for each child. Importantly, SUCRA rankings provide a relative probability of effectiveness rather than definitive evidence of superiority. Given that most comparisons showed overlapping credible intervals, the observed ranking differences may not represent clinically meaningful distinctions. Moreover, treatment rankings derived from probabilistic measures are inherently uncertain, and the absence of rank intervals may limit the precision with which these rankings can be interpreted.

Clinical Significance

The findings of this study hold significant clinical relevance. First, they provide a relatively systematic evidence base for nutritional intervention strategies in pediatric respiratory infections. Particularly in the absence of vaccines or specific drug prophylaxis, the judicious use of HVD emerges as a safe, cost-effective, and feasible preventive measure. Second, the network meta-analysis integrates direct and indirect evidence from multiple intervention strategies. This approach not only evaluates the efficacy of individual interventions but also provides a reference for prioritizing different measures, thereby supporting clinical decision-making and public health

guideline development. Furthermore, funnel plot analysis was employed to assess publication bias. The results showed a relatively symmetrical funnel plot, indicating a low likelihood of publication bias and enhancing the credibility of the study conclusions.

Strengths and Limitations

The primary strength of this study lies in its systematic and comprehensive integration of current randomized controlled trial evidence in the field of childhood respiratory infection prevention. It incorporates both direct comparisons and indirect evidence, employing a network meta-analysis approach to rank the relative efficacy of multiple nutritional interventions, thereby providing more comprehensive evidence-based guidance. Heterogeneity was addressed through a Bayesian framework and random-effects model, supplemented by local consistency tests, ensuring the reliability of the network analysis. The SUCRA analysis visually illustrates the relative potential effects of each intervention, offering clear guidance for clinical decision-making and public health intervention strategies. The study also systematically assessed risk of bias using the RoB 2.0 tool, combined funnel plots with Egger's test to analyze publication bias, thereby enhancing the credibility of the findings. Furthermore, this research evaluated not only single interventions like vitamin D, vitamin A, and zinc, but also considered combined interventions (VA_Zinc), which may inform future studies on combined nutritional interventions.

This study has several limitations. First, substantial clinical heterogeneity was observed across the included trials, particularly with respect to intervention dose, duration, participant age, and baseline nutritional status. Although random-effects models were applied, such variability may still limit the generalizability of the findings. Second, the classification of vitamin D dose represents an additional source of uncertainty. Although dosing regimens were standardized into weekly equivalent values to improve comparability, the thresholds used to distinguish between lower- and higher-dose categories were necessarily pragmatic. Moreover, the higher-dose category encompassed a wide range of absolute doses and dosing schedules, which may have obscured potential dose–response relationships. Third, the number of studies available for certain interventions—particularly combined regimens, probiotic-based approaches, and iron—was limited, resulting in imprecise estimates that should be interpreted with caution. Fourth, outcome definitions for respiratory infections varied across studies, including differences in infection type (upper vs. lower respiratory infections), diagnostic methods (physician-diagnosed vs. parent-reported), and confirmation approaches. Such variability may have contributed to heterogeneity and affected the comparability and consistency of pooled estimates. Fifth, although no clear evidence of publication bias was detected, the analysis was restricted to published randomized controlled trials, and the potential influence of unpublished or grey literature cannot be excluded. Sixth, further stratified analyses according to factors such as geographic location, seasonality, vaccination status, or underlying health conditions were

not feasible due to incomplete reporting, which may limit the applicability of the findings to specific populations. Finally, the current evidence primarily reflects short-term preventive effects, and data on long-term efficacy and safety remain limited. In addition, although no significant inconsistency was detected, the relatively small number of studies in some comparisons may have limited the statistical power to identify potential inconsistency within the network. Additionally, the interpretation of SUCRA rankings is subject to uncertainty, particularly when effect estimates are imprecise or differences between interventions are small.

Future Research Directions

Based on the findings of this study, future research should be further deepened in the following areas. First, high-quality, multicenter, large sample randomized controlled trials are needed to clarify the preventive effects of different doses and combinations of nutritional interventions on respiratory infections in children, thereby providing more robust evidence for formulating optimal clinical intervention strategies. Second, stratified analyses should evaluate intervention outcomes considering factors such as children's age groups, gender, baseline nutritional status, regional variations, seasonal changes, and vaccination status. This will help identify potential influencing factors and suitable target populations, enabling personalized and precision interventions. Third, future studies should focus on the long-term efficacy and safety of interventions, particularly the tolerability and potential risks associated with high-dose vitamin D or multi-nutrient combination therapies, thereby ensuring clinical safety. Fourth, integrating immunological and molecular biological markers can help elucidate the mechanisms by which nutritional interventions influence respiratory infections, revealing specific pathways through which different nutrients affect children's immune function. Finally, research on combined intervention strategies (vitamin-mineral combinations, probiotic formulations) should be strengthened to evaluate synergistic effects and optimal dosage combinations, providing scientific evidence for public health interventions and pediatric health management.

Conclusion

This study indicates that among the various nutritional interventions included, High-dose vitamin D showed a relatively higher probability of benefit among the included interventions; however, given the uncertainty in effect estimates and overlapping credible intervals across comparisons, these findings should be interpreted with caution. Direct comparison meta-analyses revealed no statistically significant differences between LVD, VA, VA_Zinc, zinc, and placebo. A network meta-analysis further supported these findings, with league table and SUCRA rankings indicating HVD may offer the optimal efficacy among all interventions.

Declarations

Abbreviations

Odds ratios (OR)

Credible intervals (CrI)

Sorted rank curve area (SUCRA)
high-dose vitamin D (HVD)
Low doses of vitamin D (LVD)
Vitamin A (VA)

Ethics approval and consent to participate not applicable.

Consent for publication: not applicable.

Availability of data and materials: All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Competing Interests: The authors disclose no relevant interest.

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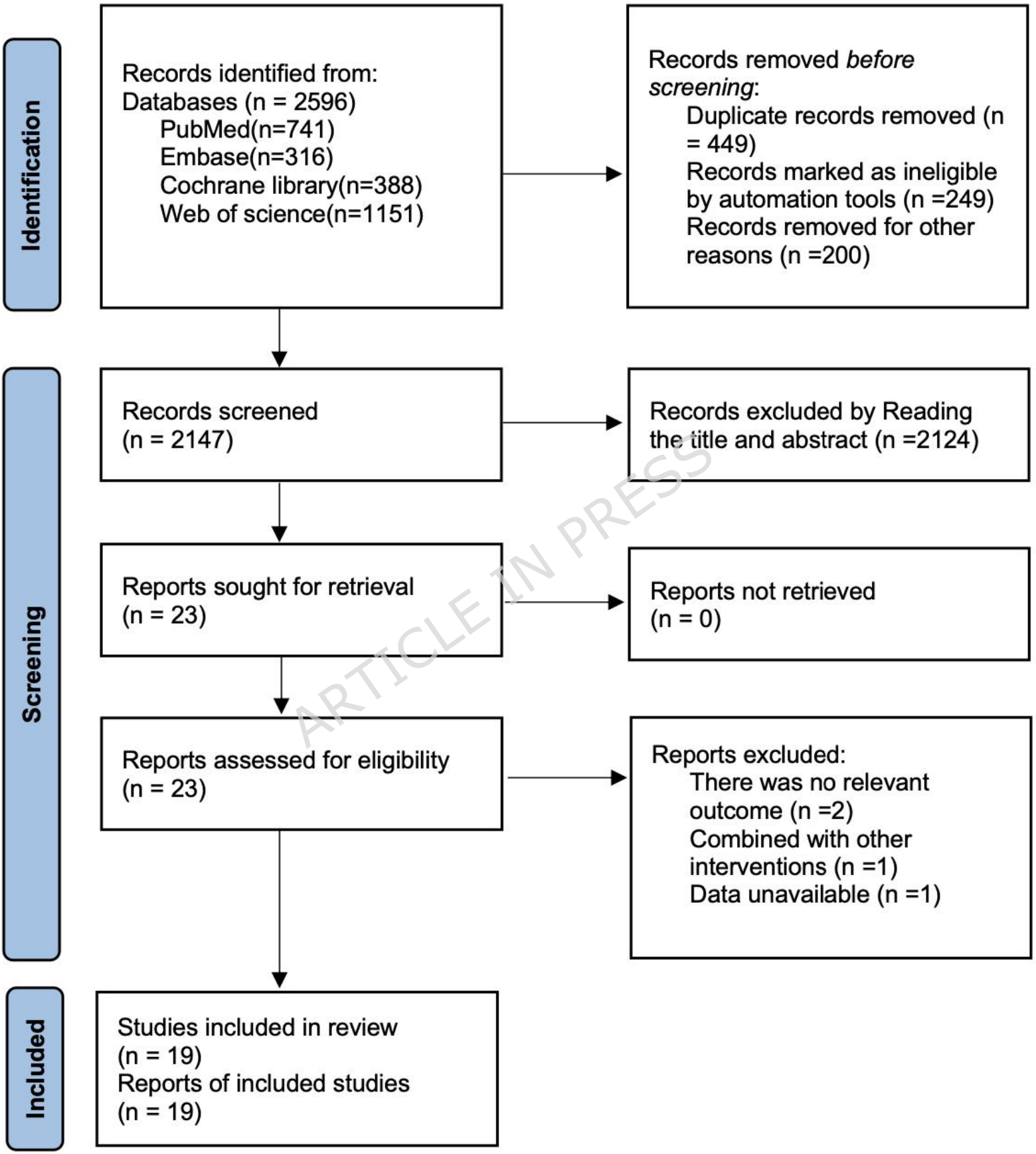

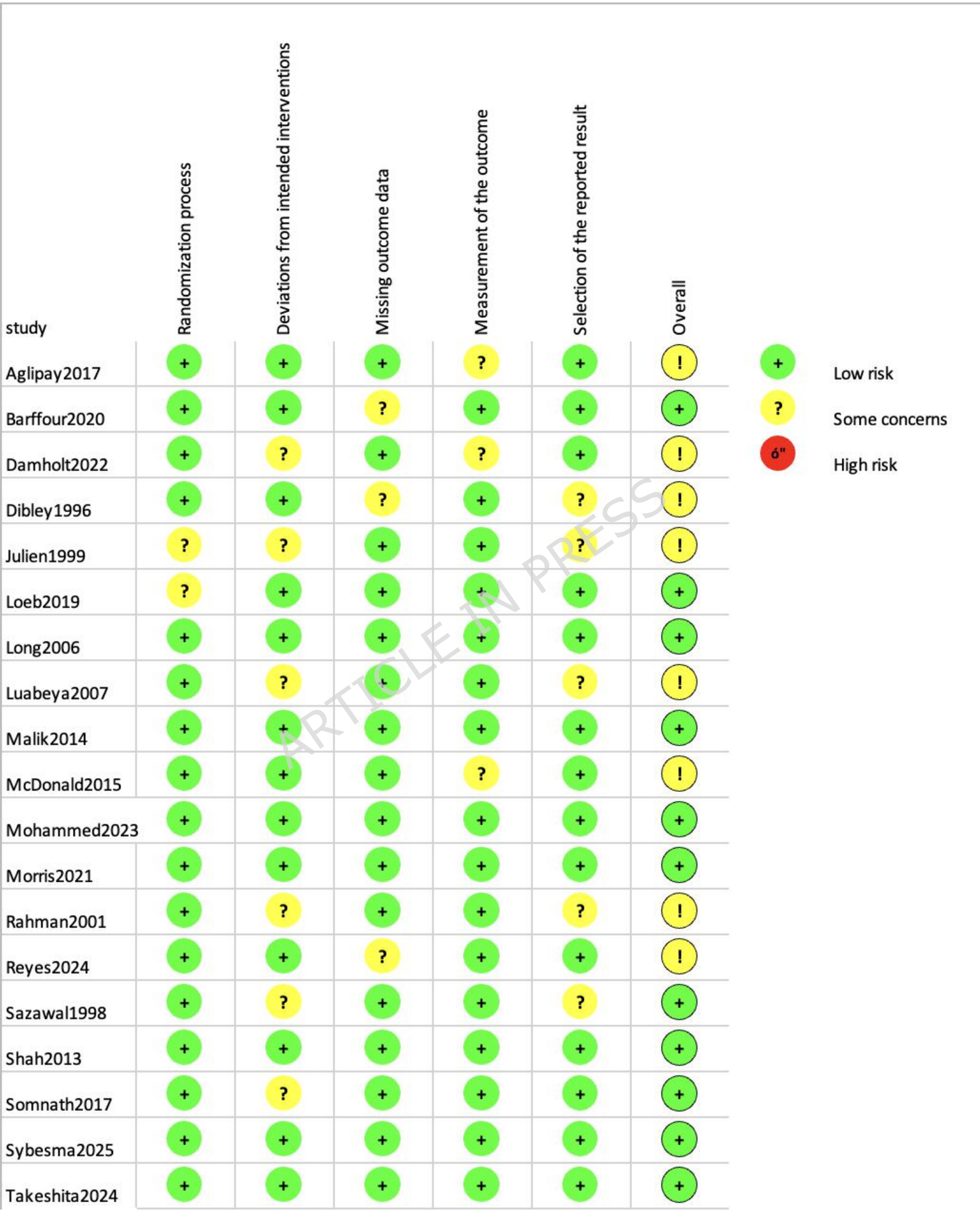

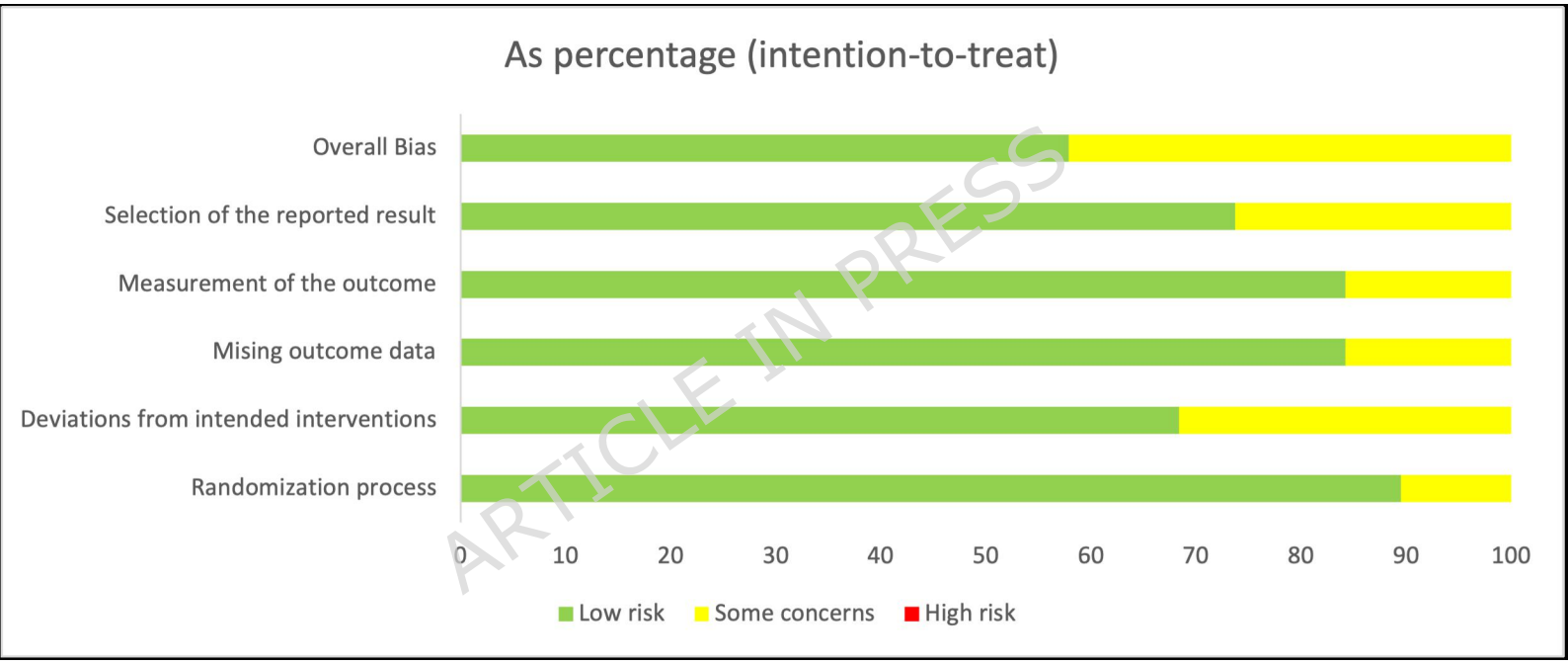

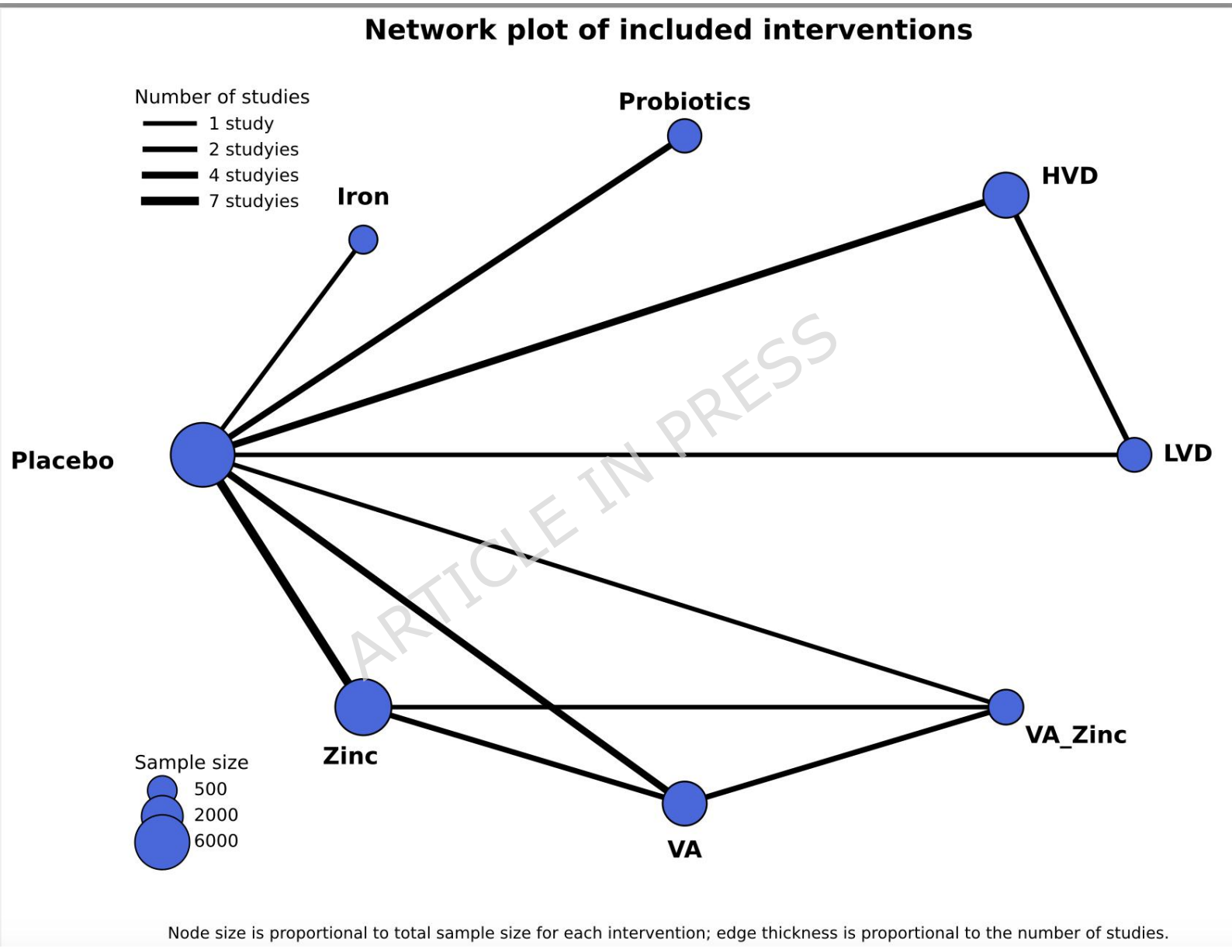

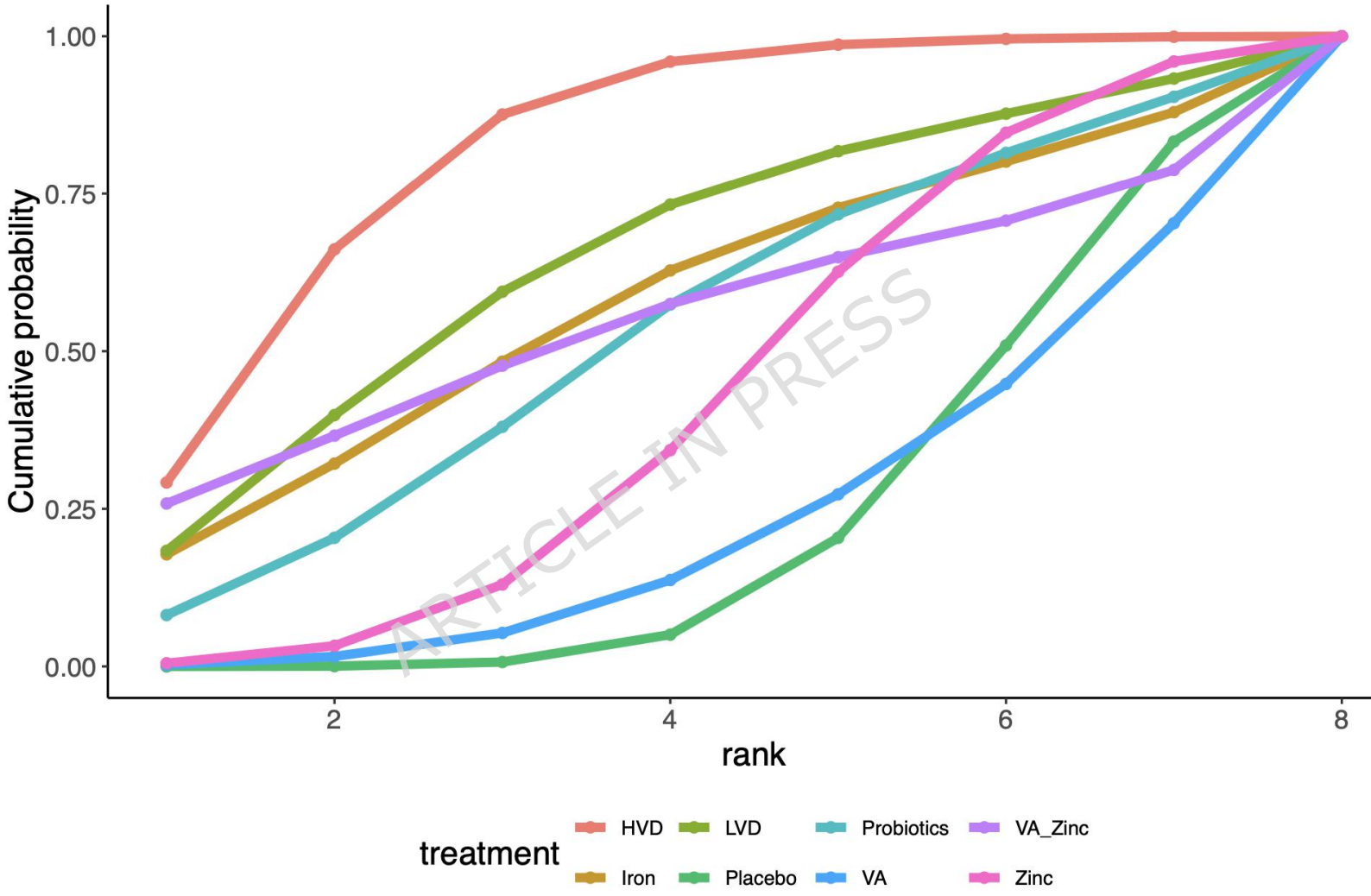

Author	Year	Country	Sample size	Gender (M/F)	Mean age(years)	Intervention	outcomes
Aglipay	2017	Canada	HVD:349 LVD:354	296/404	HVD:2.76 LVD:2.70	HVD:14000IU Vitamin D/week LVD:2800IU Vitamin D/week	F1
Barffour	2020	USA	Zinc:848 Placebo: 847	777/918	Zinc:1.2 Placebo: 1.4	Zinc: 7mg/day	F1
Damholt	2022	Denmark	Probiotics:309 Placebo: 308	304/314	Probiotics:4 Placebo: 4	Probiotics: 10^9 cfu of *L. rhamnosus* GG DSM 33156	F1
Dibley	1996	Indonesia	VA:357 Placebo: 350	360/347	VA:4.2 Placebo: 4.5`	VA:10300IU Vitamin A/week	F1
Julien	1999	Mozambique	VA:71 Placebo: 93	86/78	VA:1.3 Placebo: 1.1	VA:200000 IU Vitamin A/week	F1
Loeb	2019	Canada	HVD:650 Placebo: 650	621/679	HVD:8.6 Placebo: 8.4	HVD:14000IU Vitamin D/week	F1
Long	2006	Mexico	VA:180 VA_Zinc:192 Zinc:181 Placebo: 183	363/373	VA:0.9 VA_Zinc:0.8 Zinc:1.2 Placebo: 0.91	Zinc: 7mg/day VA:10300IU Vitamin A/week	F1
Luabeya	2007	South Africa	VA:113 VA_Zinc:113	100/126	VA:5.2 VA_Zinc:5.1	Zinc: 7mg/day VA:1250IU Vitamin A/week	F1
Malik	2014	India	Zinc:141 Placebo: 131	135/137	Zinc:8.7 Placebo: 8.5	Zinc: 20mg/5ml	F1

McDonald	2015	USA	Zinc:596 Placebo: 604	589/611	Zinc:2.3 Placebo: 3.1	Zinc: 20mg/5ml	F1
Mohammed	2023	UK	Iron:214 Placebo: 214	212/216	Iron:1.8 Placebo: 1.9	Iron: 20 mg	F1
Morris	2021	Canada	HVD:235 Placebo: 234	269/200	HVD:8 Placebo: 9	HVD:28000IU Vitamin D/week	F1
Rahman	2001	USA	Zinc:170 VA:159 Placebo: 161	354/315	Zinc:1.8 VA:1.6 Placebo: 1.9	Zinc: 20mg/day VA:20000IU Vitamin A	F1
Reyes	2024	Chile	HVD:101 LVD:103 Placebo: 99	153/150	HVD:2.3 Placebo: 2.2	HVD:11200IU Vitamin D/week LVD:5600IU Vitamin D/week	F1
Sazawal	1998	India	Zinc:298 Placebo: 311	300/309	Zinc:1.6 Placebo: 1.7	Zinc: 20mg/day	F1
Shah	2013	Australia	Zinc:48 Placebo: 48	50/46	Zinc:48 Placebo: 48	Zinc: 20mg/day	F1
Somnath	2017	India	HVD:78 Placebo: 76	104/50	HVD:1.1 Placebo: 1.1	HVD:10000IU Vitamin D/week	F1
Sybesma	2025	Uganda	Probiotics:98 Placebo: 98	100/96	Probiotics:4.91 Placebo: 4.8	Probiotics: Lacticaseibacillus rhamnosus yoba 2012	F1

Takeshita	2024	Japan	Probiotics:21 Placebo: 20	24/17	Probiotics:2.5 Placebo: 1.9	Probiotics: lactic acid bacterium Pediococcus acidilactici K15	F1

M/F: male/female; HVD: High doses of vitamin D; LVD: Low doses of vitamin D; VA: vitamin A; F1: respiratory tract infections

Outcomes	Pairwise meta-analysis	No of study	Sample size	Heterogeneity (%)	OR 95%CrI
Respiratory Tract Infections	LVD vs HVD	2	703	0	1.10 (0.43,2.68)
	Placebo vs HVD	4	2135	0	1.42 (0.82,2.77)
	Placebo vs Iron	1	428	NA	1.17 (0.45,3.00)
	Placebo vs LVD	1	200	NA	10.59 (0.51,222.25)
	Probiotics vs Placebo	3	851	0	0.90 (0.47,1.74)
	VA vs Placebo	4	1478	0	1.36 (0.74,2.34)
	VA_Zinc vs Placebo	1	375	NA	0.34 (0.05,2.49)
	Zinc vs Placebo	7	5761	76	0.80 (0.51,1.18)
	VA_Zinc vs VA	2	372	0	1.12 (0.40,3.08)
	Zinc vs VA	2	690	0	1.50 (0.68,3.49)
	Zinc vs VA_Zinc	1	254	NA	2.57 (0.35,18.89)

Table 3 League table for Respiratory Tract Infections

OR 95%Crl							
HVD							
0.89 (0.57, 1.39)	Iron						
0.93 (0.69, 1.24)	1.05 (0.61, 1.78)	LVD					
0.76 (0.61, 0.94)*	0.86 (0.58, 1.26)	0.82 (0.57, 1.17)	Placebo				
0.86 (0.6, 1.22)	0.97 (0.6, 1.56)	0.92 (0.58, 1.45)	1.13 (0.85, 1.49)	Probiotics			
0.75 (0.55, 1.01)	0.85 (0.54, 1.31)	0.81 (0.53, 1.23)	0.99 (0.8, 1.22)	0.87 (0.61, 1.25)	VA		
0.88 (0.48, 1.65)	0.99 (0.5, 2)	0.95 (0.48, 1.9)	1.16 (0.66, 2.09)	1.03 (0.55, 1.97)	1.17 (0.68, 2.07)	VA_Zinc	
0.81 (0.63, 1.04)	0.91 (0.61, 1.37)	0.87 (0.59, 1.28)	1.06 (0.93, 1.22)	0.94 (0.69, 1.29)	1.08 (0.87, 1.35)	0.92 (0.51, 1.63)	Zinc